Tetrahedron Vol 47, No 25, pp 4441-4456, 1991
Printed in Great Britain

0040-4020/91 $3 00+ 00

BIOMIMETIC SYNTHESIS OF 12-OXY-PIMARANES FROM 12,13-EPOXY-LABDADIENES

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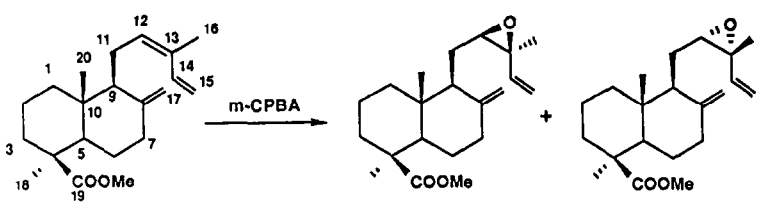
(*Received in UK* 13 *February* 1991)

Abstract: Reactions of methyl 12,13-epoxy-*cis*-communates (3, 4) and methyl 12,13-epoxy-*trans*-communates (5, 6) with BF_3 etherate at 0°C are reported They occur in a stereoselective and stereospecific way yielding mainly C-12 oxygenated pimaranes When the reaction was carried out from 5 and 6 two tetracyclic ketones (17, 18) were also isolated Reaction mechanisms and stereochemical implications are discussed

Monoepoxides of polyenes are appropriate substrata in biomimetic syntheses of terpenoids and steroids [1] The oxirane ring basically plays two roles in these reactions (a) functionalization in a specific position of the molecule, and (b) provision of the required cation for achieving cyclization with a high stereochemical control,[2] by electrophilic opening In this paper we report the results of the opening reactions of methyl 12,13-epoxy-*cis*-communate (3, 4) and methyl 12,13-epoxy-*trans*-communate (5, 6) with BF_3 etherate Most products obtained in these processes are C-12 oxygenated pimaranes in addition to two tetracyclic ketones (17, 18), when epoxides 5 and 6 were used

METHODS AND RESULTS

Epoxidation of methyl *cis*-communate (1) was performed with *m*-CPBA in the selective conditions described by Pascual Teresa *et al* [3] yielding, after chromatographic separation, a mixture of methyl (12*R*,13*S*)-12,13-epoxy-labda-8(17),14-dien-19-oate (3) and methyl (12*S*,13*R*)-12,13-epoxy-labda-8(17),14-dien-19-oate (4) (45% of the reaction products) ^{1}H-NMR of the mixture



1 3 (12*R*, 13*S*) 4 (12*S*, 13*R*)

(3 / 4 ratio 55 / 45)

shows the same signals for H-C_{12} (δ 2 90, br t, J=6 Hz) and Me-C_{13} (δ 1 36, s) in both isomers in accordance with a 12,13-oxirane The δ values of the exocyclic methylene (3 δ 4 48, 4 86, 4 δ 4 75, 4 90) allowed to establish the stereochemistry of the lateral chain since conformational analysis around the C_{11}-C_{12} bond justifies those differences observed in the chemical shifts (figure 1), the less hindranced 3A and 4A conformers should be preferred in a similar way as occurs for C-12 oxygenated labdanes[4] and as deduced from the 11,12 coupling constants In this sense the proximity between H_{endo}-17 and oxygen in compound 4 justifies its deshielded δ value (4 75 ppm) in opposition to that in compound 3 (δ 4 48)

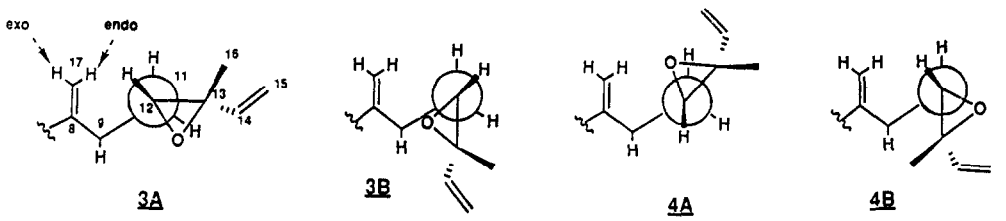
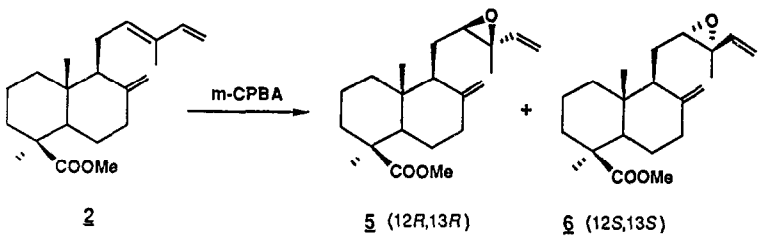


Figure 1

Epoxidation of methyl *trans*-communate (2) yielded a mixture of methyl (12*R*,13*R*)- 12,13-epoxy-labda-8(17),14-dien-19-oate (5) and methyl (12*S*,13*S*)-12,13-epoxy-labda-8(17), 14- dien-19-oate (6) The stereochemistry of the lateral chain in 5 and 6 was



(5 / 6 ratio 60 / 40)

determined in a similar fashion as for 3 and 4, taking into account the multiplicity and coupling constant for H-12 (2d, J = 6 7 Hz for 5 and J = 6 9 Hz for 6) as well as δ values for H-17 (5 δ 4 44, 4 84, 6 δ 4 72, 4 89) in ^{1}H-NMR In accordance with these data, conformational analysis shows A conformers as those more probable for compound 5 and 6 (figure 2)

In both epoxidation reactions a certain stereoselectivity through the formation of 12*R*-isomers is observed It should be related with the fact that the lateral chain of the starting products (1, 2) adopts a preferred conformation around the C_9-C_{11}[5] and C_{11}-C_{12}[6] bonds in order to minimize the interaction exerted by the bicyclic system (figure 3), allowing more easily the attack on the less hindered α side that leads to 12*R*-epoxides This stereoselectivity is consistent with that described for photooxygenation[7] and oxymercuration-demercuration[8] reactions on 1 and 2

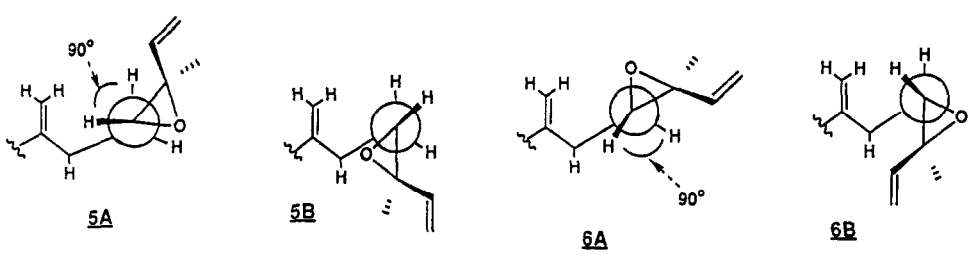
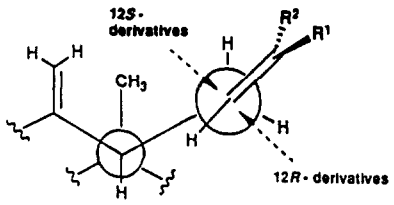


Figure 2



1: R^1 CH_3, R^2 -CH=CH_2
2: R^1 -CH=CH_2, R^2 -CH_3

Figure 3

The oxirane ring opening reactions of methyl 12,13-epoxy-communates were carried out by treatments of mixtures of 3 and 4 with BF_3 etherate in benzene at 0°C Results of these reactions are collected in table 1

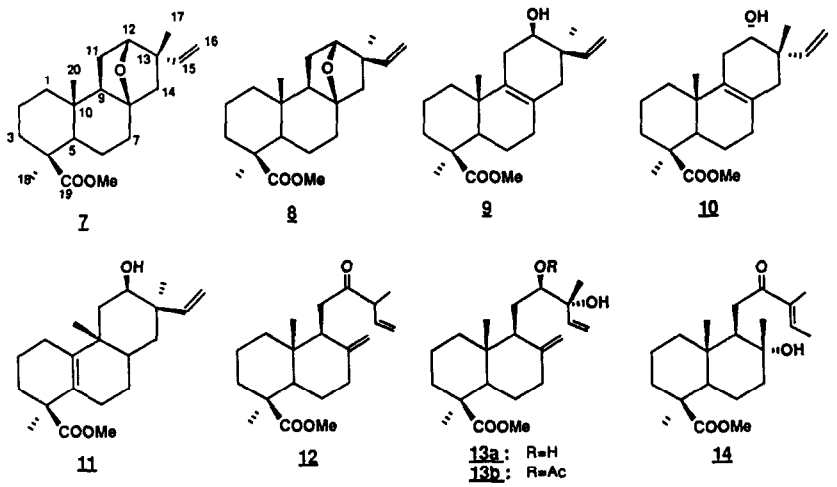


Table 1. Reaction of 3, 4 mixtures with BF_3 etherate

		7	8	9	10	11	12	13	14
R-1	3 (60%) 4 (40%)	2.3%	4 3%	14 7%	11.7%	4 3%	27 9%	1 9%	1 0%
R-2	3 (70%) 4 (30%)	+	+	*	+				
R-3	3 (30%) 4 (70%)	1.0%	1 7%	5 8%	30 7%		20 9%	1 5%	0 8%
R-4	3 (5%) 4 (95%)				*		+		

* main reaction product, + minor reaction product

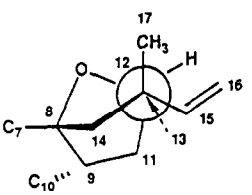
The opening of the oxirane ring followed by a $H_{1,2}$ rearrangement leads to compound 12, and further Δ^{14} isomerization

and stereoselective $\Delta^{8(17)}$ hydration by the less hindered α side leads to **14** Compounds **13** (formed by ring opening and direct hydration) and **14** are minor products originated by the presence of traces of water in the reaction mixture The rest of the products are the result of the cyclization process of the 8(17) double bond through C-13 position of the allyl cation originated in the oxirane opening **7** has been described as a radicallary cyclization product in the oxymercuration-demercuration of methyl *trans*-communate (**2**)[8,9] Its isomer (**8**), detected in a mixture together to **7** (65/35 ratio), shows similar ^{1}H-NMR spectrum to **7**, having the same stereochemistry on C_8 and C_{12} as **7** since H-12 for both compounds has analogous splitting pattern (table 2) On the opposite, **8** possesses *R*-C_{13} configuration deduced from the δ values in ^{13}C-NMR for C_{15} (deshielded) and C_{17} (shielded) respect to those of **7**, as a consequence of different γ-effects exerted by C_{11} and the bridge oxygen (table 3)

Table 2 ^{1}H-NMR data of compounds **7** and **8**

	7[a]	**8**	$\delta_8-\delta_7$
Me-10	δ 0.67 (s)	δ 0 68 (s)	+0 01
Me-13	δ 1 08 (s)	δ 1 09 (s)	+0 01
Me-4	δ 1 17 (s)	δ 1 17 (s)	0
MeO-19	δ 3 59 (s)	δ 3 59 (s)	0
H-12	δ 3 83 (d, 5 5 Hz)	δ 3 92 (d, 5 8 Hz)	+0 09
H-15	δ 5 86 (dd, 18 7, 10 1 Hz)	δ 5 99 (dd, 17 8, 10 5 Hz)	+0 13
H-16	δ 5 00 (dd, 18 7, 1 2 Hz)	δ 4 88 (d, 10 5 Hz)	-0 12
H'-16	δ 5 01 (dd, 10 1, 1 2 Hz)	δ 4 89 (d, 17 8 Hz)	-0 12

[a]See reference 9



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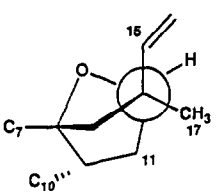

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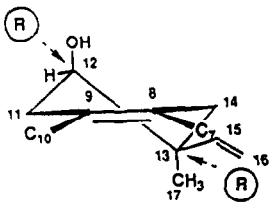
Table 3 ^{13}C-NMR data of C_{15} and C_{17} for compounds **7** and **8**

	7	**8**	**7** (γ-effects)	**8** (γ-effects)
C_{15}	δ 144 05	δ 147 97	gauche (C_{11}) trans (0)	gauche (0) trans (C_{11})
C_{17}	δ 27 38	δ 21 08	gauche (0) trans (C_{11})	gauche (C_{11}) trans (0)

Structural elucidation of alcohols **9** and **10** posed the problem of the stereochemistry on C-12 and C-13 together to the ring C conformation The ^{1}H-NMR spectrum of **9** shows an H-12 signal at δ 3 57 (m, $w_{1/2h}$=10.5 Hz, pseudoequatorial proton) whereas that of **10** is at δ 3 47 (dd, J_1=9 3 Hz, J_2=5 4 Hz, pseudoaxial proton) Furthermore, absolute configuration in C-12 for **9** and **10** was determined by the Horeau method[19] as *R* and *S*, which indicates that both compounds present $^{12}H_{13}$ half-chair conformations (figure 4) The C_{13} configurations for **9** and **10** were established by ^{1}H-NMR induced chemical shift studies with



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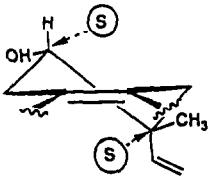

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Figure 4

pyridine-d_5 (table 4) and Eu(dpm)$_3$ (table 5) In both experiments for compound **9** H-15 is approximately two times more deshielded than H-17 indicating that hydroxyl and vinyl groups are in *cis* relative position (*R*-C_{13}) The same *cis* relative position is deduced for compound **10** since the pyridine induced chemical shift on H-15 is also two times greater than that of H-17 (*S*-C_{13}) On the contrary, the P values of H-15 and H-17 for **10** (table 5) are similar, in agreement with an α-pseudoequatorial position of HO-C_{12} equidistant respect to both H-15 and H-17

Table 4 ^{1}H-NMR data in $CDCl_3$ and pyridine-d_5 for compounds **9** and **10**

H	**9** (δ_1, $CDCl_3$)	**9** (δ_2, Py-d_5)	**9** (δ_2-δ_1)	**10** (δ_1, $CDCl_3$)	**10** (δ_2, Py-d_5)	**10** (δ_2-δ_1)
12	3 57	3 87	+0 30	3 47	3 78	+0 30
15	5 88	6 38	+0 50	5 85	6 33	+0 48
16	5 08	5 13-5 24	+0 10	5 01	5 13	+0 12
16	5 10	5 13-5 24	+0 08	5 09	5 18	+0 09
17	0 93	1 15	+0 22	1 05	1 28	+0 23

Table 5. ^{1}H-NMR Eu(dpm)$_3$ induced chemical shifts for compounds **9** and **10**

	M[a] (**9**)						P[b] (**9**)	M[a] (**10**)					P[b] (**10**)
H	0	0 023	0 046	0 078	0 120	0 205		0	0 189	0 337	0 566	0 727	
12	3 57	3 60	3 94	4 00	4 44	5 69	10 34	3 47	3 95	4 20	5 08	5 90	3 34
15	5 88	5 93	5 99	6 13	6 39	7 10	5 95	5 85	6 09	6 22	6 58	6 99	1 57
16	5 08	5 08	5 10	5 18	5 35	5 72	3 12	5 01	5 16	5 22	5 50	5 80	1 09
16	5 10	5 10	5 12	5 15	5 25	5 45	1 70	5 09	5 20	5 27	5 48	5 60	0 70
17	0 93	0 95	0 98	1 06	1 21	1 62	3 37	1 05	1 25	1 38	1 73	2 11	1 46
18	1 20	1 20	1 20	1 20	1 25	1 33	0 63	1 16	1 19	1 20	1 25	1 31	0 21
20	0 80	0 80	0 80	0 80	0 89	1 00	0 98	0 75	0 77	0 80	0 83	0 88	0 18
MeO	3 62	3 63	3 63	3 63	3 66	3 70	0 39	3 59	3 63	3 63	3 68	3 73	0 19

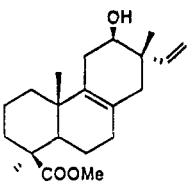
[a]Eu(dpm)$_3$ compound molar ratio, [b]Europium shift parameter (ref 17)

Compounds **11** shows important differences for angular methyles in ^{1}H-NMR and carbons of A and B rings in ^{13}C-NMR spectra respect to **9** and **10** (table 6) **11** should have a rosadiene structure according to the molecular formula deduced from the mass spectrum and δ in ^{1}H-NMR and ^{13}C-NMR spectra Since ring C adopts a chair conformation and H-12 an equatorial position (deduced from ^{1}H-NMR data), the configuration on C_{12} must be *R* On the other hand, the δ value of C_{17} (24 16 ppm) (characteristic of axial methyles on cyclohexane[11]) allows to assign *R* configuration for C_{13}

Table 6. ^{13}C-NMR data for compounds **9**, **10** and **11**

C	9	10	11
5	53 36	53.43	127 00
8	124.91	125 00	37 42
9	132.08	134 13	37.28
10	37 86	37 81	140.51
12	72.51	74.51	74.21
13	39 64	40.30	42.15
15	144.86	140.75	146.46
17	22.95	23 64	24.16

In order to complete the stereochemical study of the 12,13-oxirane ring opening of methyl 12,13-epoxy-communates, a reaction of a mixture of **5** (60%) and **6** (40%) with BF_3 etherate was carried out in the same conditions as for **3** and **4** This reaction yielded the following products **7** (4%), **9** (minor product), **15** (2 5%), **16** (6 3%), **12** (24%), **13a** (1 4%), **14** (0 8%), **17** (7 1%) and **18** (3 5%)



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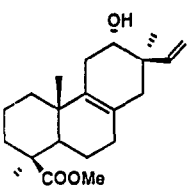

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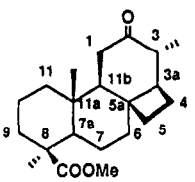

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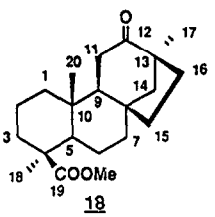

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15 and **16** have been stereochemically characterized making reference to their stereoisomers **9** and **10** in basis to δ values for C_{17} in ^{1}H-NMR (table 7) and ^{13}C-NMR (table 9), located in pseudoequatorial and pseudoaxial positions, respectively

Table 7. ^{1}H-NMR data of H_{12} and H_{15}-H_{17} for compounds **9**, **10**, **15** and **16**

H	9	10	15	16
12	3 57 (m $W_{1/2h}$=10 5 Hz)	3 47 (dd 9 3, 5 4 Hz)	3 55 (m, $W_{1/2h}$=11 Hz)	3 40-3 67 (m)
15	5 88 (dd, 18 0, 11 0 Hz)	5 85 (dd 17 6 10 9 Hz)	5 75 (dd, 18 10 Hz)	5 77 (dd 18 10 Hz)
16	5 08 (dd 18 0 1 2 Hz)	5 01 (dd 17 6, 1 6 Hz)	5 00 (dd 18, 2 Hz)	5 09 (dd 18, 1 8 Hz)
16	5 10 (dd 11 0, 1 2 Hz)	5 09 (dd 10 9 1 6 Hz)	5 03 (dd 10, 2 Hz)	5 12 (dd 10 1 8 Hz)
17	0 93 (s)	1 05 (s)	1 00 (s)	0 93 (s)

Compound **17** shows molecular peak at m/z 332 ($C_{21}H_{32}O_3$) in MS and just two unsaturated carbons in the ^{13}C-NMR spectrum corresponding to cyclohexanone (δ 216 67) and methylic ester (δ 177 68) The rest of spectroscopic data is consistent with the proposed structure, having performed 2D-NMR (^{1}H-^{1}H and one-bond ^{1}H-^{13}C correlations) experiments to complete the ^{1}H-NMR (table 8) and ^{13}C-NMR (table 9) assignments Some signals in the ^{1}H-NMR spectrum strongly support this structure In particular, the δ values and multiplicities of H-1, H-3 and H-11b (table 8) may be only justified through the proposed tetracyclic ketone (figure 5) The mass spectrum also supports the existence of the cyclobutane ring since the base

Table 8 ^{1}H-NMR data for compound **17** and correlations between protons deduced from 2D-NMR experiments

H	δ (multiplicity, Hz)	correlated hydrogens
1	2 37 (d, 8 8)	11b
3	2 36 (q, 7 2)	Me-C$_3$ (not 3a)
3a	1 04-1 12 (m)	4, 5$_1$
4	1 79-1 87 (m)	5$_1$, 5$_2$, 3a
5$_1$	1 18-1 27 (m)	3a, 4, 5$_2$
5$_2$	2 10-2 24 (m)	4, 5$_1$
6ax[a]	1 29-1 43 (m)	6eq, 7, 7a
6eq=7eq	2 19-2 30 (m)	6ax, 7ax, 7a
7ax[a]	1 58-1 70 (m)	6, 7eq, 7a
7a	1 80-1 86 (m)	6, 7
9ax	0 89-1 04 (m)	9eq, 3
9eq	2 10-2 19 (m)	9ax, 10, 11eq
10ax	1 33-1 49 (m)	10eq, 9, 11
10eq	1 68-1 82 (m)	9, 10ax, 11eq
11ax	0 80-0 92 (m)	10ax, 11eq
11eq	1 45-1 60 (m)	9eq, 10, 11ax
11b	1 52 (t, 8 8)	1
Me-C$_3$	1 05 (d, 7 2)	3

a These values may be reserved

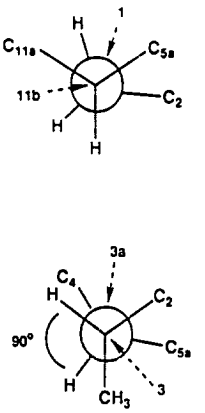


Figure 5 C_{11b}-C_1 and C_3 C_{3a} bond angles for compound **17**

peak at m/z 121, typical of labdanes with alkoxy carbonyl group on C_4 and 8(17) double bond[12] as well as of alkoxycarbonyl pimaranes with $\Delta^{8(14)}$ unsaturation,[13] indicates that the fragmentation pattern is directed by a double bond in those positions which can be only originated from the cyclobutane breakage in both directions (scheme 1) Furthermore the main fragmentations are justified through the radical-ion **I** being the same as for **12**

Compound **18** could not be resolved from **17** However, the studies of ^{1}H and ^{13}C-NMR spectra and 2D-NMR experiments (table 10) allowed to identify **18** as methyl 12-oxo-beveran-19-oate

DISCUSSION

A different behaviour in the electrophilic oxirane opening reactions is observed depending on the stereochemistry of the 12,13-epoxides used, according to the skeleton types originated in these reactions Although the product of $H_{1,2}$ rearrangement (**12**) represents about a 25% in reactions from either 12,13-epoxy-*cis*-communates or 12,13-epoxy-*trans*-communates, the relative ratio of cyclization products versus **12** is 25% higher in reaction from *cis*-isomers In addition, 12,13-epoxy-*trans*-communates show a different cyclization pattern to tetracyclic ketones **17** and **18**, which represents a 10%

Scheme 1 Main fragmentations observed in the MS of compound 17

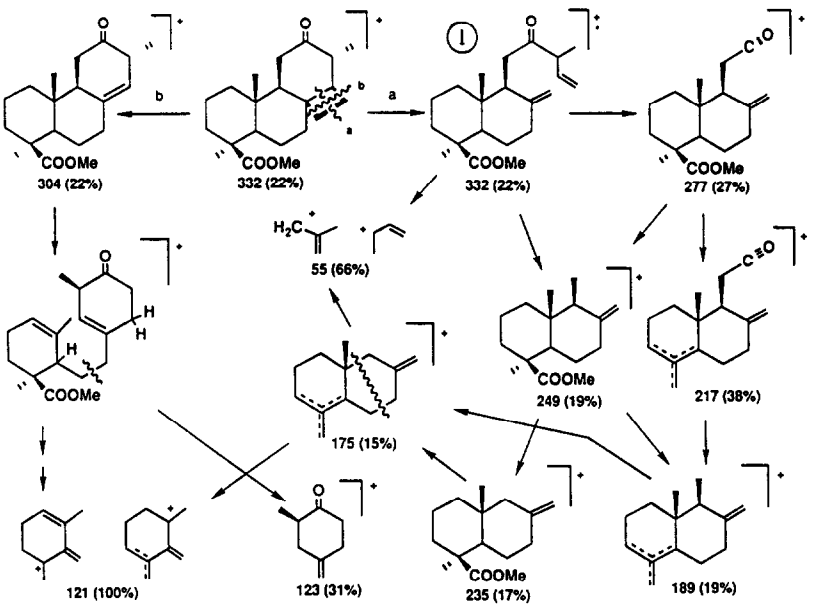


Table 9 ^{13}C-NMR data[a] for compounds 3-12 and 14-18

C	3	4	5	6	7	8	9	10
1	39 26	38 98	39 01	39 28	41 49	41 68	39 96	36 62
2	19 90	19 87	19 82	19 87	18 73	18 75	19 50	19 39
3	38 14	38 13	38 09	38 09	38 28	38 27	37 74	37 62
4	44 26	44 25	44 21	44 21	43 86	43 86	43 86	43 71
5	56 15	56 08	56 03	56 12	54 61	54 60	53 36	53 43
6	26 01	26 04	25 98	25 98	20 79	20 78	20 61	20 49
7	38 51	38 41	38 35	38 44	32 20	32 08	33 03	32 36
8	147 80	148 33	148 25	147 53	85 58	85 44	124 91	125 00
9	53 86	53 78	53 69	54 09	55 47	56 04	132 08	134 13
10	40 07	40 01	39 89	40 08	36 61	36 70	37 86	37 81
11	23 34	22 80	23.22	23 72	26 91	26 16	28 96	30 89
12	65 44	65 43	64 59	64 68	84 22	84 22	72 51	74 51
13	60 46	61 20	60 04	59 43	48 31	46 31	39 64	40 30
14	136 31	136 54	140 88	140 98	50 08	52 33	37 39	42 53
15	117 81	117 68	115 53	115.53	144 05	147 97	144 86	140 75
16	21 40	21 36	15 37	15 00	113 03	109 86	113 26	114 42
17	107 53	106 83	106 80	107 73	27 38	21 08	22 95	23 64
18	28 77	28 76	28 73	28 73	28 80	28 81	28 36	28 29
19	177 58	177 63	177 58	177 50	177 92	177 91	177 97	177 89
20	12 38	12 62	12 59	12 40	14 75	14 93	17 13	17 05
MeO	51 13	51 09	51 08	51 08	51 09	51 09	51 09	51 02

Table 9 (continuation)

C	11	12	14	15	16	17	18
1	25 26	39 14	39 43	36 82	36 64	38 58 (C-11)	38 35
2	19 98	19 78	18 95	19 48	19 43	18 80 (C-10)	19 49[f]
3	36 48	37 92	37 79	37 67	37 66	37 91 (C-9)	37 91
4	46 88	44 19	43 84	43 84	43 75	43 77 (C-8)	44 32
5	127 00	55 92	55 19[c]	53 27	53 20	49 62 (C-7a)	53 67
6	27 15	25 72	22 22	20 52	20 57	26 05 (C-7)[d]	19 98[f]
7	24 59	38 07	44 70	32 85	32 48	24 61 (C-6)[d]	20 57
8	37 42	148 47	72 79	125 22	124 73	40 97 (C-5a)[e]	45 52
		148 83					
9	37 28	50 01	56 47[c]	132 71	133 88	52 79 (C-11b)	48 88
		50 19					
10	140 51	39 37	38 99	37 85	37 92	38 58 (C-11a)[e]	40 09
11	36 89	37 08	32 79	29 39	28 62	36 54 (C-1)	33 03
		37 26					
12	74 21	210 28	202 73	72 50	72 16	216 67 (C-2)	222 50
13	42 15	50 97	138 29	40.20	40 86	49 37 (C-3)	49 02
		51 76					
14	32 96	137 83	136 61	39 31	43 28	56 61 (C-3a)	43 34
		137 97					
15	146 46	116.54	11 53	144 88	146 30	20 64 (C-4)	27 56
		116 67					
16	114 20	15 88	14 76	112 90	114 54	41 13 (C-5)	24 08
		16 00					
17	24 16[b]	105.88	22 75	20 52	14 04	16 95 (Me-C$_3$)	21 11
		106 29					
18	24 40[b]	28 64	28 66	28 36	28 35	28 67 (Me-C$_8$)	29 30
19	178 29	177 43	177 63	177 99	177 95	177 68 (MeOO<u>C</u>-C$_8$)	178 02
20	20 64	12 81	13 31	17 25	17 08	12 45 (Me-C$_{11a}$)	13 46
MeO	51 75	51 11	51 18	51 12	51 10	51 15 (H$_3$<u>C</u>-OOC-C$_8$)	51 15

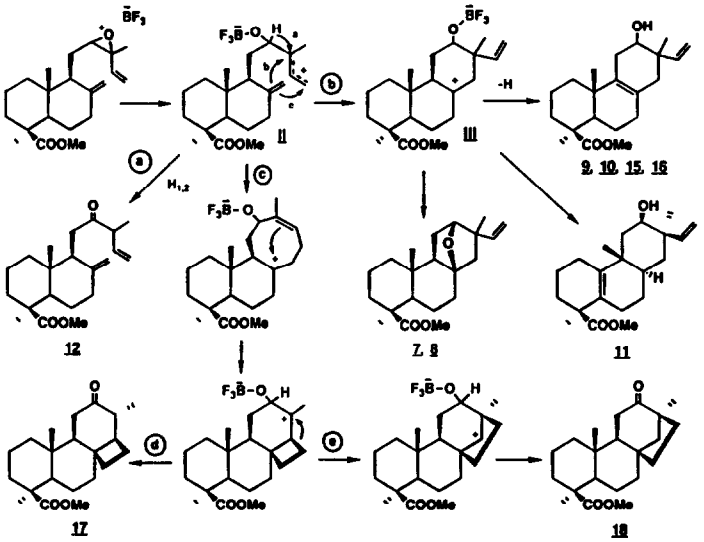
[a] The spectra were run at 75 MHz (except 12, at 20 MHz) in $CDCl_3$
δ values are given in ppm downfield from TMS
[b-f] Values bearing the same superscript may be interchanged

Table 10. ^{1}H-NMR data for compound 18 and correlations between protons deduced from 2D-NMR experiments

H	δ (multiplicity; Hz)	correlated hydrogens
1ax	0 95-1 06 (m)	1eq 2 3eq 20
1eq	1 65-1 77 (m)	1ax 2 3
2ax	1 40-1 51 (m)	2eq 1 3
2eq	1 72-1 81 (m)	2ax 1ax 3
3ax	0 92-1 02 (m)	3eq 2 1eq
3eq	2 11-2 22 (m)	3ax 2 1
5	1 29 (br d 18)	6
6β	1 65-1 79 (m)	6α 5 7
6α	1 88-1 99 (m)	6β, 5 7
7	1 81-1 92 (m)	6
11α	1 72-1 82 (m)	11β
11β	2 11-2 22 (m)	11α
14α β	1 83-1 97 (m)	*

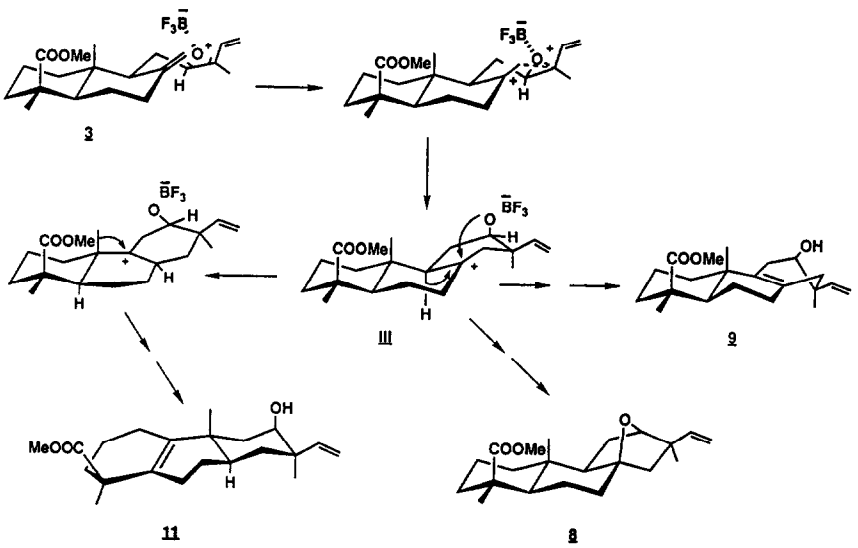
The proposed formation mechanisms for the products of these reactions are summarized in scheme 2 Compounds 3 and 4 originate cyclizations through route b only, whereas their isomers 5 and 6 do it through route c as well Since the opening of the oxirane ring is accomplished by breaking of the C_{13}-O bond, the tricyclic compounds formed ought to retain the C_{12} configuration of the oxiranes of which they come from (7 and 8 are necessarily originated from 3) In this sense,

Scheme 2



the stereochemical aspects of these processes have been clarified by the reactions performed with 4 (95% of purity), which yielded compound 10 (12-*S*) almost exclusively, and by that performed on a mixture of 3 (70%) and 4 (30%), which basically led to 9 (12-*R*) The chirality on C_{13} for compounds 9 and 10 evidences that the original orientation of the sustituents on C_{13} (in compounds 3 and 4, respectively) is quite kept This has also noted in a large-scale reactions from a mixture of 3 (60%) and 4 (40%) (R-1 in experimental section) where compound 8 was predominantly formed as opposed to 7 (65% of 8 versus 35%

Scheme 3



of 7) This means that it is a stereoselective and stereospecific process in which the ring opening and cyclization of $\Delta^{8(17)}$ to the allyl cation II (scheme 2) must be quite synchronic, giving the tertiary cation III that evolves in three different ways (scheme 3), being well-known that leads to 11.[14]

The reaction of 5 and 6 with BF_3 etherate shows similar cyclization to pimaranes, although a higher stereoselectivity is observed as deduced from the sole isolation of epoxide 7 (originated in this case from 5) This fact may be justified by the larger stability of allyl cation IVa (intermediate from 5 that leads to 7) than that of IVb, which yields its C_{13} epimer 8 (figure 6), because of the interaction between the π-8(17) orbitals and the empty orbital of the allyl cation (in IVa) Thus, the transition

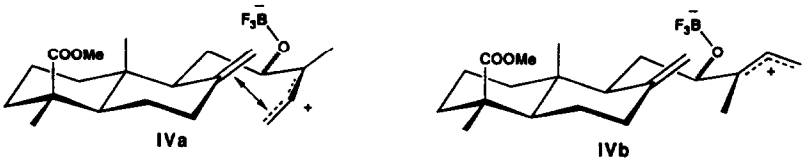


Figure 6

state geometry remains unchanged after the opening of the oxirane ring from 5 On the other hand, from the opening of epoxide 3, the geometry of the resulting allyl cation is the less stable that may lead to a partial epimerization on C_{13}

In relation to the formation of the tetracyclic ketones 17 and 18 the mechanism leading to the eight-member ring is what establishes the difference of the reaction from 5 and 6 respect to that from 3 and 4 Assuming that the oxirane ring opening and the cyclization are synchronic processes, the generation of the eight-members ring from 3 and 4 is not possible as a consequence of the lateral chain inflexibility that keeps C_{15} away from the 8(17) double bond On the opposite, the

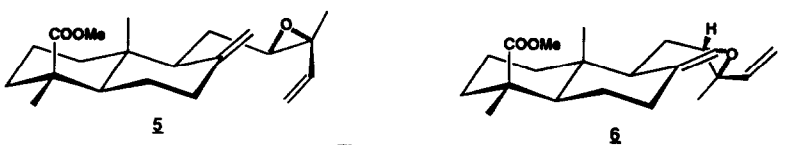
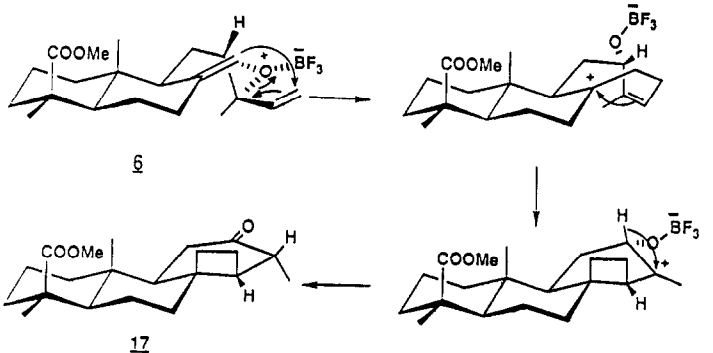


Figure 7

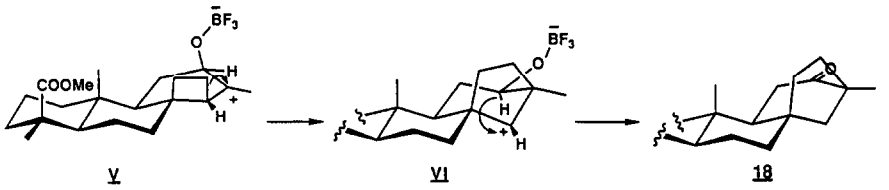
stereochemistry of the oxiranes from methyl *trans*-communate does allow this cyclization pattern (figure 7) Furthermore the evolution of cationic intermediates is different and it depends on the stereochemistry of starting epoxide, from 6 the formation of the cyclobutane takes place stereospecifically through the side α because of steric hindrances of Me-C_{10} (scheme 4) Finally, the 1,2-hydride rearrangement of H-12β leads to 17

Scheme 4



When the starting epoxide is 5 the tetracyclic carbenium V suffers a four-member ring expansion to hybanil cation VI which is stabilized by a $H_{1,3}$ rearrangement of H-12α, the only hydrogen with appropriate stereochemistry to migrate (scheme 5) [15] From these considerations it can be finally deduced that ketones 17 and 18 are stereospecifically generated from each methyl 12,13-epoxy-*trans*-communate

Scheme 5



V VI 18

EXPERIMENTAL

Melting points were determined using a Reichert type Kofler microscope and are uncorrected Optical rotations have been determined on a Perkin-Elmer Model 141 polarimeter, using $CHCl_3$ as solvent (the concentration was of 10 mg/mL) UV spectra were recorded in MeOH on a UV-Vis Bausch-lamb model spectronic 2000 spectrometer and IR spectra on a Perkin-Elmer Model 983G spectrometer with samples between sodium chloride plates or as potassium bromide pellets ^{1}H-NMR spectra were recorded on Bruker WP 80 SY (80 MHz) and Bruker AM 300 (300 MHz) spectrometers using TMS or $CHCl_3$ as standard and $CDCl_3$ as solvent ^{13}C-NMR spectra were run at 75 MHz and 20 MHz on Bruker AM 300 and Bruker WP 80 SY instruments 2D-NMR (^{1}H-^{1}H and one-bond ^{1}H-^{13}C correlations) experiments were performed on a Bruker AM 300 spectrometer MS spectra were obtained on a Hewlett-Packard 5988A mass spectrometer using an ionizing voltage of 70 eV Chromatographic separations were carried out by conventional column on Merck silica gel 60 (70-230 mesh) and by flash column on Merck silica gel 60 (230-400 mesh) using eluents of increasing polarity from hexane to diethyl ether Analytical TLC was performed on 0 25 mm thick layers of Merck silica gel 60G using a 7% phosphomolybdic acid solution (in ethanol) to develop the spots Preparative TLC was carried out on 1 00 mm thick layers of Merck silica gel 60 PF_{254} gipshalting visualizing the bands with a 254 nm ultraviolet light Mixtures of compounds with a similar Rf in TLC were column chromatographed on 20% $AgNO_3$/silica gel

Isolation of methyl *cis*-(1) and *trans*-communate (2)

1 and 2 were obtained from the acidic fraction (previously sterefied with diazomethane in Et_2O) of the hexane extract of berries of *Juniperus communis* L [16]

Epoxidation of methyl *cis*-communate (1)

To a stirred solution of 1 (1 00 g, 3 16 mmol) in CH_2Cl_2 (100 mL), a solution of *m*-CPBA (0 59 g, 3 41 mmol) in CH_2Cl_2 (120 mL) was added dropwise in 2h at room temperature An aqueous solution of 10% Na_2SO_3 (12 5 mL) was added After adding 35 5 mL of saturated $NaHCO_3$ solution, the reaction mixture was extracted with $CHCl_3$, washed with water and dried over Na_2SO_4 After removal of the solvent, the residue (1 02 g) was column chromatographed on silica gel yielding the following fractions (a) 20 mg (eluted with hexane-Et_2O 99 1) of a mixture of 4 (30%) and **methyl (12*R*,13*S*)-12,13-epoxy-labda-8(17),14-dien-19-oate (3)** (70%), $[\alpha]_D$ +61 0°, ^{1}H-NMR (80 MHz) δ 0 50 (s, Me-10), 1 18 (s, Me-4), 1 36 (s, Me-13), 2 90 (br t, J=6

Hz, H-12), 3 60 (s, MeO-19), 4 48 (br s, H-17), 4 86 (br s, H'-17), 5 13-5 46 (m, H-15), 5 82 (dd, J_1 = 18 Hz, J_2 = 10 Hz, H-14), ^{13}C-NMR in table 9, EIMS m/z (rel int)· 332 (M^+, 1), 317 (M^+-CH_3, 1), 273 (M^+-COOMe, 2), 249 (M^+-C_5H_7O, 1), 189 (249$^+$-HCOOMe, 14), 161 (16), 133 (20), 121 (100), 93 (48), 83 ($C_5H_7O^+$, 21), 79 (60), 55 (76) (b) 250 mg (eluted with hexane-Et_2O 98 2) of a mixture of **3** (60%) and **4** (40%) (c) 160 mg (eluted with hexane-Et_2O 97 3) of a mixture of **3** (30%) and **4** (70%) (d) 43 mg (eluted with hexane-Et_2O 96 4) of **methyl (12*S*,13*R*)-12,13-epoxy-labda-8(17),14-dien-19-oate (4)** $[\alpha]_D$ +36 0°, IR (KBr) ν 3085, 1646, 990, 927 (CH=CH_2), 3085, 1646, 890 (C=CH_2), 1728, 1230, 1155 (COOMe), ^{1}H-NMR (80 MHz) δ 0 50 (s, Me-10), 1 18 (s, Me-4), 1.36 (s, Me-13), 2 90 (br t, J=6 Hz-12), 3 60 (s, MeO-19), 4 75 (br s, H-17), 4 90 (br s, H'-17), 5 13-5 46 (m, H-15), 5 80 (dd, J_1 = 18 Hz, J_2 = 10 Hz, H-14), ^{13}C-NMR in table 9

Reaction of a mixture of 3 (60%) and 4 (40%) with BF_3:etherate. (R-1)

To a solution of a mixture of **3** and **4** (3 15 g, 9 47 mmol) in dry benzene (260 mL) under N_2 atmosphere, 2.60 mL (21 mmol) of BF_3 etherate was added at 0ºC After stirring for 12 min the reaction mixture was poured onto a 5% $NaHCO_3$ solution (1300 mL) and extracted with Et_2O (3x100 mL) The organic layer was washed with water and dried over Na_2SO_4 After removal of the solvent the residue (2 77 g) was flash column chromatographed on silica gel (120 mg) yielding the following compounds

Methyl 12-oxo-labda-8(17),14-dien-19-oate (12) 613 mg eluted with hexane-Et_2O 96 4, oil $[\alpha]_D$ +31 6°, IR (neat) ν 3079, 1642, 990, 920 (CH=CH_2), 3079, 1642, 884 (C=CH_2), 1721 (C=O), 1721, 1228, 1154 (COOMe), ^{1}H-NMR (80 MHz) δ 0 53 (s, Me-10), 1 16 (d, J=7 Hz, Me-13), 1 20 (s, Me-4), 3 05-3 47 (m, H-13), 3 62 (s, MeO-19), 4 31 (br s, H-17), 4 74 (br s, H'-17), 5 14 (br d, J=10 Hz, H-15), 5 17 (br d, J=17 Hz, H'-15), 5 58-6 08 (m, H-14), ^{1}H-NMR (80 MHz, double resonance) irradiated hydrogen [affected hydrogens] H-13 [Me-13 and H-14 (dd, J_1 = 17 Hz, J_2 = 10 Hz)], ^{13}C-NMR in table 9, EIMS m/z (rel int) 332 (M^+, 25), 277 (M^+-C_4H_7, 59), 272 (13), 249 (M^+-C_5H_7O, 34), 235 (249$^+$-CH_2, 27), 234 (36), 217 (M^+-C_4H_7-HCOOMe, 100), 189 (43), 175 (28), 121 (82), 109 (51), 91 (30), 81 (32)

Methyl (8*R*,12*R*)-8,12-epoxy-pimar-15-en-19-oate (8) and **methyl (8*R*,12*R*)-8,12-epoxy-isopimar-15-en-19-oate (7).** 144 mg of a mixture of **8** (65%) and **7** (35%) eluted with hexane-Et_2O 92 8, oil $[\alpha]_D$ +60 3°, IR (neat) ν 3083, 1636, 996, 911 (CH=CH_2), 1729, 1232, 1191, 1156 (COOMe), 1094, 1041 (C-0-C), ^{1}H-NMR (300 MHz) for both compounds in table 2, ^{13}C-NMR for both compounds in table 9, EIMS m/z (rel int) 332 (M^+, 37), 317 (M^+-CH_3, 100), 273 (M^+-COOMe, 7), 263 (10), 257 (M^+-CH_3-HCOOMe, 4), 223 (11), 163 (13), 121 (26), 109 (31), 81 (27), 79 (26), 55 (26)

Methyl (12*R*,13*S*)-12-hydroxy-rosa-5(10),15-dien-19-oate (11). 50 mg eluted with hexane-Et_2O 85 15, oil $[\alpha]_D$ +73 5°, IR (neat) ν 3526, 1037 (OH), 3080, 1636, 911 (CH=CH_2), 1730, 1238, 1192, 1162 (COOMe), ^{1}H-NMR (300 MHz) δ 1 05 (s, Me-13), 1 14 (s, Me-4), 1 24 (s, Me-9), 3 60 (m, $w_{1/2h}$=9 Hz, H-12), 3 62 (s, MeO-19), 5 15 (dd, J_1 = 17 6 Hz, J_2 = 1.3 Hz, H-16), 5 18 (dd, J_1 = 10 9 Hz, J_2 = 1 3 Hz, H'-16), 5 85 (dd, J_1 = 17 6 Hz, J_2 = 10 9 Hz, H-15), ^{13}C-NMR in table 9, EIMS m/z (rel int) 332 (M^+, 8), 273 (M^+-COOMe, 29), 255 (M^+-COOMe-H_2O, 18), 245 (M^+-COOMe-C_2H_4, 15), 161 (M^+-COOMe-$C_7H_{12}O$, 39), 131 (31), 121 (32), 105 (58), 85 (20), 91 (69), 79 (60), 67 (69), 59 (76), 55 (100), 41 (95)

Methyl (12*R*)-12-hydroxy-pimara-8,15-dien-19-oate (9). 229 mg eluted with hexane-Et_2O 75 25, oil $[\alpha]_D$ +84 2°, IR (neat) ν 3472, 1058 (OH), 3082, 1640, 910 (CH=CH_2), 1730, 1231, 1195, 1163 (COOMe), ^{1}H-NMR (300 MHz) δ 0 80 (s, Me-10), 0 93 (s, Me-13), 1 20 (s, Me-4), 3 57 (m, $w_{1/2h}$=10 5 Hz, H-12), 3 62 (s, MeO-19), 5 08 (dd, J_1 = 18 0 Hz, J_2 = 1 2 Hz, H-16), 5 10 (dd, J_1 = 11 0 Hz, J_2 = 1 2 Hz, H'-16), 5 88 (dd, J_1 = 18 0 Hz, J_2 = 11 0 Hz, H-15), ^{1}H-NMR (300 MHz, pyridine-d_5) δ 0.89 (s, Me-10), 1 15 (s, Me-13), 1 20 (s, Me-4), 3 58 (s, MeO-19), 3 87 (br d, J=6 0 Hz, H-12), 5 13-5 24 (m, H-16), 5 76 (d, J=6 Hz, HO-12),

6 38 (dd, J_1 = 18 0 Hz, J_2 = 11 0 Hz, H-15), ^{1}H-NMR (300 MHz, pyridine-d_5, double resonance) irradiated hydrogens [affected hydrogens] HO-12 [H-12 (t, J = 4 7 Hz)] H-12 [HO-12 (s) and H-11 (located around 2 25 ppm)], H-11 [H-12 (d, J = 6 Hz)], ^{1}H-NMR (80 MHz, $CDCl_3$, Eu(dpm)$_3$) in table 5, ^{13}C-NMR in table 9, EIMS m/z (rel int) 332 (M^+, 38), 317 (M^+-CH_3, 31), 314 (M^+-H_2O, 19), 299 (M^+-H_2O-CH_3, 77), 287 (M^+-H_2O-C_2H_3, 3), 273 (M^+-COOMe, 19), 272 (M^+-HCOOMe, 15), 255 (M^+-COOMe-H_2O, 21), 254 (M^+-HCOOMe-H_2O, 10), 240 (255^+-CH_3, 24), 239 (254^+-CH_3, 100), 213 (240^+-C_2H_3, 8), 212 (239^+-C_2H_3, 5), 199 (13), 183 (24), 173 (27), 167 (22), 164 ($C_{11}H_{16}O^+$, 3), 149 (164^+-CH_3, 70), 146 (164^+-H_2O, 12), 131 (149^+-H_2O, 38), 117 (30), 109 (12), 105 (45), 93 (25), 91 (61), 84 (50), 59 (64), 55 (75), *R* configuration in C-12 was established by the "Horeau method"[10] with an optical rotation of +0 143° and an optical yield of 12.3%

Methyl (12*R*)-12-acetoxy-13-hydroxy-labda-8(17),14-dien-19-oate (13b). 145 mg of a mixture of **13a** (50%) and **14** (50%), eluted with hexane-Et_2O 1 1, were acetylated with Ac_2O/pyridine and chromatographed on silica gel obtaining 42 mg of **13b** (hexane-Et_2O 7 3), oil $[\alpha]_D$ +23 4°, IR (neat) ν 3498, 1034 (OH), 3080, 1660, 892 (C=CH_2), 3080, 1647, 926 (CH=CH_2), 1727, 1242, (AcO), 1727, 1242, 1154 (COOMe), ^{1}H-NMR (80 MHz) δ 0 47 (s, Me-10), 1 15 (s, Me-4), 1.23 (s, Me-13), 2 08 (s, AcO-12), 3.58 (s, MeO-19), 4 48 (br s, H-17), 4 86 (br s, H'-17), 4 93 (t, J = 5 Hz, H-12), 5 18 (dd, J_1 = 10 Hz, J_2 = 2 Hz, H-15), 5 31 (dd, J_1 = 16 Hz, J_2 = 2 Hz, H'-15), 5 92 (dd, J_1 = 16 Hz, J_2 = 10 Hz, H-14), EIMS m/z (rel int) 332 (M^+-AcOH, 3), 314 (M^+-AcOH-H_2O, 3), 272 (M^+-AcOH-HCOOMe, 2), 255 (314^+-COOMe, 4), 254 (314^+-HCOOMe, 2), 201 (11), 161 (11), 121 (56), 93 (24), 81 (23), 71 (39), 55 (31), 43 (100)

Methyl 8α-hydroxy-12-oxo-labd-13-*E*-en-19-oate (14). 23 mg of **14** were column purified (hexane-Et_2O 65 35) from a mixture of **13b** and **14**, oil. $[\alpha]_D$ +40 1°, UV (MeOH) λ max. 222 nm (ε 1500), IR (neat) ν 3480 (OH), 3020, 1640 (C=CH), 1664 (α,β-unsaturated carbonyl), 1728, 1235, 1191, 1153 (COOMe), ^{1}H-NMR (80 MHz) δ 0 64 (s, Me-10), 1 10 (s, Me-8), 1 16 (s, Me-4), 1 78 (br s, Me-13), 1 84 (br d, J = 7 Hz, Me-14), 2.56 (dd, J_1 = 19 Hz, J_2 = 4 Hz, H-11), 2 85 (dd, J_1 = 19 Hz, J_2 = 4 Hz, H'-11), 3 60 (s, MeO-19), 6 79 (br q, J = 5 Hz, H-14), ^{13}C-NMR in table 9, EIMS m/z (rel int) 350 (M^+, 3), 335 (M^+-CH_3, 1), 332 (M^+-H_2O, 3), 317 (M^+-H_2O-CH_3, 2), 289 (8), 373 (2), 235 (5), 205 (11), 179 (17), 175 (9), 121 (15), 83 ($C_5H_7O^+$, 79), 78 (81), 63 (100), 55 (55)

Reaction of a mixture of 3 (70%) and 4 (30%) with BF_3;etherate (R-2)

146 mg (0 44 mmol) of an oxirane mixture enriched in compound **3** (70%) were treated in identical conditions to those of R-1 reaction yielding 180 mg of a reaction crude which ^{1}H-NMR spectrum basically showed signals of compound **9** being also able to detect compounds **7**, **8** and **10**

Reaction of a mixture of 3 (30%) and 4 (70%) with BF_3;etherate. (R-3)

In identical conditions to those of R-1 reaction 2 g (6 33 mmol) of an oxirane mixture enriched in compound **4** were treated obtaining 1 94 g of reaction crude that by flash column chromatography over silica gel yielded **12** (398 mg, hexane-Et_2O 96 4), 51 mg of a mixture of **7** (40%) and **8** (60%) eluted with hexane-Et_2O 94 6, **10** (509 mg, hexane-Et_2O 91 9), **9** (69 mg, hexane-Et_2O 88 12), 73 mg of a mixture of **14** (40%) and the C-12 epimer of compound **13** (60%) eluted with hexane-Et_2O 4 1

Methyl (12*S*)-12-hydroxy-isopimar-8,15-dien-19-oate (10). Oil $[\alpha]_D$ +62.7°, IR (neat) ν 3500, 1057 (OH), 3086, 1644, 922 (CH=CH_2), 1729, 1232, 1199, 1165 (COOMe); ^{1}H-NMR (300 MHz) δ 0 75 (s, Me-10), 1 05 (s, Me-13), 1 16 (s, Me-4), 3 47 (dd, J_1 = 9.3 Hz, J_2 = 5 4 Hz, H-12), 3 59 (s, MeO-19), 5 01 (dd, J_1 = 17 6 Hz, J_2 = 1 6 Hz, H-16), 5 09 (dd, J_1 = 10 9 Hz, J_2 = 1 6

Hz, H'-16), 5 85 (dd, J_1 = 17 6 Hz, J_2 = 10 9 Hz, H-15), ^{1}H-NMR (80 MHz, pyridine-d_5) δ 0 85 (s, Me-10), 1 16 (s, Me-4), 1 28 (s, Me-13), 3.59 (s, MeO-19), 3 78 (br dd, J_1 = 9 Hz, J_2 = 5 Hz, H-12), 5 13 (dd, J_1 = 18 Hz, J_2 = 2 Hz, H-16), 5 18 (dd, J_1 = 11 Hz, J_2 = 2 Hz, H'-16), 6 33 (dd, J_1 = 18 Hz, J_2 = 11 Hz, H-15), ^{1}H-NMR (80 MHz, $CDCl_3$, Eu(dpm)$_3$) in table 5, ^{13}C-NMR in table 9, 2D-NMR experiments in table 10, EIMS m/z (rel int) 332 (M^+, 3), 317 (2), 314 (1), 299 (5), 273 (3), 272 (3), 255 (3), 240 (2), 239 (9), 213 (2), 199 (4), 183 (5), 173 (5), 159 (6), 149 (50), 86 (61), 84 (100), 47 (19), *S* configuration in C-12 was established by the " Horeau method"[10] with an optical rotation of -0 093° and an optical yield of 24 7%

Reaction of 4 with BF_3·etherate. (R-4)

The reaction of 4 (87 mg, 0 26 mmol) with BF_3 etherate was carried out in the same conditions that above in R-1 reaction yielding 119 mg of crude which ^{1}H-NMR spectrum showed signals from compounds 10 (major) and 12 (minor)

Epoxidation of methyl *trans*-communate (2).

2 54 g (8 05 mmol) of 2 were epoxidized in identical conditions as for compound 1 (see above) obtaining 3 g of reaction crude that by column chromatography yielded (hexane-Et_2O 98 2) 1 08 g of a mixture of **methyl (12*R*,13*R*)-12,13-epoxy-labda-8(17),14-dien-19-oate (5)** (60%) and **methyl (12*S*,13*S*)-12,13-epoxy-labda-8(17),14-dien-19-oate (6)** (40%) $[\alpha]_D$ +40 3°, IR (neat) ν 3085, 1647, 990, 915 (CH=CH_2), 3085, 1647, 890 (C=CH_2), 1725, 1233, 1150 (COOMe), ^{1}H-NMR (300 MHz) (a) for compound 5 δ 0 48 (s, Me-10), 1 16 (s, Me-4), 1 37 (s, Me-13), 2 78 (d, J=6 7 Hz, H-12), 3 58 (s, MeO-19), 4 44 (br s, H-17), 4 84 (br s, H'-17), 5 11 (br d, J=10 7 Hz, H-15), 5 25 (br d, J=17 4 Hz, H'-15), 5 59 (dd, J_1=10 7 Hz, J_2=17 4 Hz, H-14), (b) for compound 6 δ 0 49 (s, Me-10), 1 16 (s, Me-4), 1 37 (s, Me-13), 2 77 (d, J=6 9 Hz, H-12), 3 58 (s, MeO-19), 4 72 (br s, H-17), 4 89 (br s, H'-17), 5 11 (br d, J=10 7 Hz, H-15), 5 25 (br d, J=17 4 Hz, H'-15), 5 58 (dd, J_1=10 7 Hz, J_2=17 4 Hz, H-14), ^{13}C-NMR for compounds 5 and 6 in table 9, EIMS m/z (rel int) 332 (M^+, 1), 273 (2), 189 (6), 181 (4), 133 (12), 121 (84), 79 (100), 55 (87)

Reaction of a mixture of 5 (60%) and 6 (40%) with BF_3.etherate. (R-5)

The reaction of 5 and 6 (1 g, 3 01 mmol) with BF_3 etherate was performed as above (reaction final time 30 min) obtaining 935 mg of crude that by flash column chromatography on silica gel yielded 12 (224 mg, hexane-Et_2O 97 3), 7 (37 mg, hexane-Et_2O 95 5), 100 mg of a mixture of 17 (70%) and 18 (30%) eluted with hexane-Et_2O 93 7, 16 (59 mg, hexane-Et_2O 85 15), 32 mg of a mixture of 9 (25%) and 15 (75%) eluted with hexane-Et_2O 7 3, 35 mg of a mixture of 13a (60%) and 14 (40%) eluted with Et_2O

(3*R*,3a*R*,5a*S*,7a*R*,8*S*,11a*R*,11b*R*)-3,8,11a-trimethyl-8-methoxycarbonyl-2-oxo-perhydrocyclobutan[J]phenanthrene(17) and **methyl 12-oxo-beyeran-19-oate (18).** Mp 95-100°C (MeOH), $[\alpha]_D$ +50 2°, IR (KBr) ν 1717 (CO), 1717, 1232, 1193, 1150 (COOMe), ^{1}H-NMR (300 MHz) (a) for compound 17 δ 0 55 (s, Me-11a), 1 05 (d, J=7 2 Hz, Me-3), 1 15 (s, Me-8), 3 62 (s, MeO-), (b) for compound 18 δ 0 78 (s, Me-10), 0 99 (s, Me-13), 1 15 (s, Me-4), 3 62 (s, MeO-19), ^{13}C-NMR for compound 17 and 18 in table 9, 2D-NMR experiments in table 8, EIMS m/z (rel int) 332 (M^+, 22), 304 (22), 289 (9), 278 (6), 277 (27), 273 (21), 272 (16), 249 (19), 245 (8), 235 (17), 234 (22), 217 (38), 189 (19), 181 (17), 175 (15), 123 (31), 121 (100), 109 (48), 81 (41), 55 (66)

Methyl (12*S*)-12-hydroxy-pimara-8,15-dien-19-oate (16). Oil $[\alpha]_D$ +52 3°, IR (neat) ν 3434, 1057 (OH), 3078, 1638, 1005, 913 (CH=CH_2), 1665 (C=C), 1721, 1232, 1194, 1160 (COOMe), ^{1}H-NMR (80 MHz) δ 0 81 (s, Me-10), 0 93 (s, Me-13), 1 20 (s, Me-4), 3 40-3 67 (m, H-12), 3 62 (s, MeO-19), 5 09 (dd, J_1=18 Hz, J_2=1 8 Hz, H-16), 5 12 (dd, J_1=10 Hz, J_2=1 8 Hz, H'-16),

5 77 (dd, J_1 = 18 Hz, J_2 = 10 Hz, H-15), ^{13}C-NMR in table 9

Methyl (12*R*)-12-hydroxy-isopimara-8,15-dien-19-oate (15). Oil $[\alpha]_D$ +97 5°, IR (neat) ν 3463, 1056 (OH), 3084, 1641, 911 (CH=CH_2), 1729, 1231, 1195, 1163 (COOMe), ^{1}H-NMR (80 MHz) δ 0 80 (s, Me-10), 1 00 (s, Me-13), 1 20 (s, Me-4), 3 55 (m, $w_{1/2h}$ = 11 Hz, H-12), 3 63 (s, Me-19), 5 00 (dd, J_1 = 18 Hz, J_2 = 2 Hz, H-16), 5 03 (dd, J_1 = 10 Hz, J_2 = 2 Hz, H'-16), 5 75 (dd, J_1 = 18 Hz, J_2 = 10 Hz, H-15), ^{1}H-NMR (80 MHz, pyridine-d_5) δ 0 92 (s, Me-10), 1 22 (s, Me-4), 1 30 (s, Me-13), 3 57 (s, MeO-19), 3 90 (m, $w_{1/2h}$ = 11 Hz, H-12), 5 00-5 32 (m, H-16), 6 05 (dd, J_1 = 18 Hz, J_2 = 10 Hz, H-15), ^{13}C-NMR in table 9, EIMS m/z (rel int) 332 (M^+, 21), 317 (10), 314 (14), 299 (52), 273 (19), 272 (17), 255 (14), 254 (6), 240 (19), 239 (95), 213 (5), 199 (11), 185 (17), 183 (27), 173 (24), 164 (3), 159 (25), 157 (24), 147 (33), 131 (45), 121 (35), 105 (64), 93 (40), 91 (84), 79 (58), 55 (100)

ACKNOWLEDGEMENTS

We wish to thank the receipt of financial assistance from the Junta de Andalucía

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