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# SELECTIVE AND STEREOCONTROLLED HYDROBORATION OF 13-*EPI*-PIMARADIENE DITERPENOIDS

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Abstract : By introduction of bulky substituents at $C_{16}$ it has been possible to achieve the stereoselective ß-hydroboration-oxidation of the $\Delta^{8(14)}$ double bond in 13-*epi*-pimarane diterpenoids.

Sandaracopimaric acid (**1**) has been used as the starting material in some syntheses of steroids [1,2,3] because of its structure, with $\Delta^{8(14)}$ and $\Delta^{15}$ unsaturations, it permits construction of the D ring. [4,5,6]

At our laboratory we have been following a research line directed towards the synthesis of cardenolide diterpenoid analogues from **1**; for our purposes functionalization at $C_{16}$ and the introduction of a hydroxylated function at position 14ß are necessary.

Previous studies carried out on pimarane diterpenoids have shown that simultaneous functionalization at $C_{14}$ and $C_{16}$ can be achieved by simultaneous hydroboration-oxidation of $\Delta^{8(14)}$ and $\Delta^{15}$ double bonds with diborane-$H_2O_2$ [1,2,7], although this reaction results in the formation of derivatives with both 14α and 14ß-hydroxyl stereochemistries, together with oxidation products at position 15. [8]

An alternative for achieving greater predominance of 14ß hydroboration, is sequential hydroboration-oxidation, first performing a chemo and regioselective hydroboration on the $\Delta^{15}$ unsaturation which, as described, is carried out with the use of bulky organoboranes [7,9], then performing a second hydroboration-oxidation on the $\Delta^{8(14)}$ double bond.

Induction of 14ß-stereoselectivity should be performed by introducing bulky substituents at $C_{16}$ that would exert steric hindrance on the α-face and using small hydroboration reagents to achieve better yields owing to steric hindrance induced by the $C_{10}$ and $C_{13}$ methyl groups.

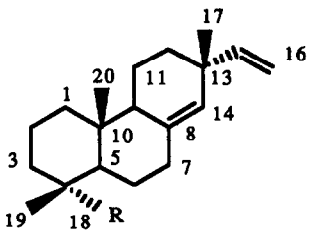
In the present work we studied the influences of different groups at $C_{16}$ on the orientation of the second hydroboration step, attaining stereospecificity to 14ß. Different derivatives of sandaracopimaric acid (**1**) were used as the starting materials.

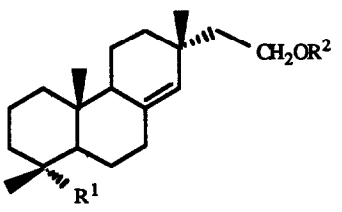
## RESULTS AND DISCUSSION

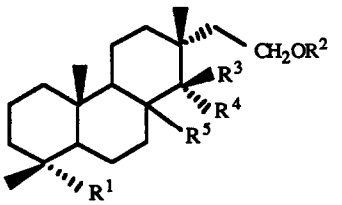
By reaction of **2** with 1M $BH_3$/THF followed by oxidation with $H_2O_2/OH^-$ a complex mixture of

products similar to those described in the literature [1] was obtained; a 3:7 (ß/α) ratio in the oxidation product at $C_{14}$ was observed.

To carry out the chemo and regioselective hydroboration-oxidation on $\Delta^{15}$, BBN [10] was employed. Reaction of **2** with BBN in THF, followed by oxidation with $H_2O_2/OH^-$ yielded only **4**, and in the case of **3** the same treatment followed by acetylation of the reaction product led exclusively to compound **7**. By selective saponification of **7**, using sat. aq. $NaHCO_3$/MeOH, the hydroxyacetate **8** was obtained; subsequently, **8** was protected by reaction with DHP, TBDMSCl or *t*-BDPSiCl, yielding **9**, **10** and **11** respectively, and **4** was transformed into the *tert*-butyldiphenylsilyl derivative **6**.




| | R | | $R^1$ | $R^2$ | | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **1** | COOH | **4** | COOMe | H | **14** | COOMe | H | OH | H | ß-H |
| **2** | COOMe | **5** | COOMe | THP | **15** | COOMe | H | H | OH | α-H |
| **3** | $CH_2OAc$ | **6** | COOMe | *t*-BDPSi | **16** | COOMe | Ac | OAc | H | ß-H |
| | | **7** | $CH_2OAc$ | Ac | **17** | COOMe | Ac | H | OAc | α-H |
| | | **8** | $CH_2OAc$ | H | **18** | $CH_2OAc$ | H | OAc | H | ß-H |
| | | **9** | $CH_2OAc$ | THP | **19** | $CH_2OAc$ | H | H | OAc | α-H |
| | | **10** | $CH_2OAc$ | TBDMS | **20** | $CH_2OAc$ | Ac | OAc | H | ß-H |
| | | **11** | $CH_2OAc$ | *t*-BDPSi | **21** | $CH_2OAc$ | Ac | H | OAc | α-H |
| | | **12** | $CH_2OH$ | Ac | **22** | $CH_2OH$ | H | OH | H | ß-H |
| | | **13** | $CH_2OH$ | H | | | | | | |

Methyl esters **2**, **5**, and **6** and acetoxymethyl derivatives **7**, **9**, **10** and **11**, were used as substrates for hydroboration with $BH_3$ followed by oxidation with $H_2O_2/OH^-$; the results of these experiments are shown in table 1. Substances **14-22**, were identified by comparison with authentic samples previously obtained in our laboratories [2].

The stereochemistries at $C_{14}$ and $C_8$ were deduced from the well established *syn*-addition of borane to olefins and from some nuclear Overhauser experiments performed on substances **17** and **18**. Thus, the nOes observed on H-14 upon irradiation of $Me_{17}$ or $Me_{20}$ unequivocally assigns the14ßH, 8αH stereochemistry for the diacetate **17**. As expected, saturation of both methyl signals in the 14αH, 8ßH diepimeric compound **18**, showed no Overhauser effect on H-14. As a result, $C_{14}$-oxigenated derivatives whose H-14 resonates at high field have 14ßH stereochemistry and those with H-14 at low field would have 14αH stereochemistry. This conclusion agrees with the expected deshielding observed in $Me_{17}$ changing from an axial disposition in the normal series 8ßH (**18**) to an equatorial one in the 8-*epi*-series (**17**) [11].

TABLE 1*

| | COMPOUND | REAGENT | GROUP AT $C_{16}$ | PRODUCTS | 14ß/14α RATIO |
|---|---|---|---|---|---|
| I | **2** | $BH_3$/THF 1M | | **14, 15** | 3 : 7 |
| II | **5** | $BH_3$/THF 1M | -OTHP | **14, 15** | 6 : 4 |
| III | **7** | $BH_3$/THF 1M | -OAc | **20, 21** | 4 : 6 |
| IV | **7** | $BF_3/NaBH_4$ (THF) | -OAc | **20, 21** | 4 : 6 |
| V | **9** | $BH_3$/THF 1M | -OTHP | **18, 19** | 6 : 4 |
| VI | **10** | $BH_3$/THF 1M | -OTBDMS | **20, 21** | 6 : 4 |
| VII | **11** | $BF_3/NaBH_4$ (Diglyme) | -O-*t*-BDPSi | **20** | 14ß only |
| VIII | **6** | $BF_3/NaBH_4$ (Diglyme) | -O-*t*-BDPSi | **14, 22** | 14ß only |

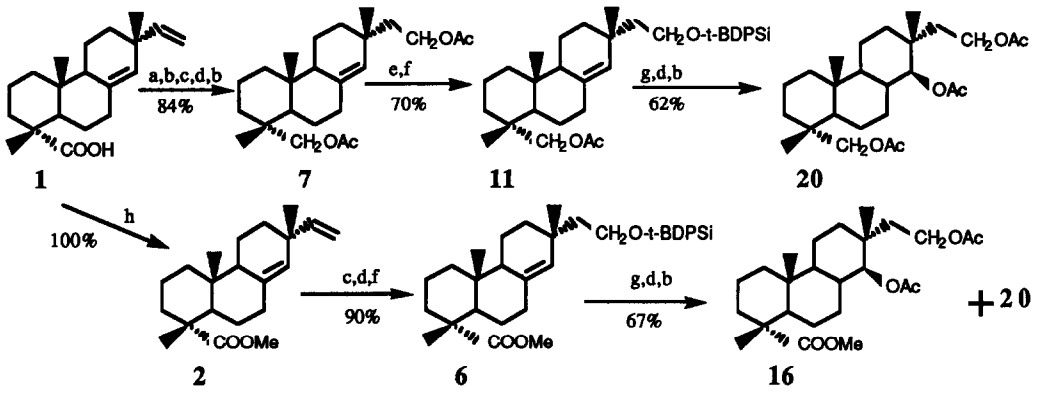
(*) Row II: **14** and **15** were obtained after deprotection of the hydroboration-oxidation product. Rows III-VII: the final substances were obtained by acetylation and deprotection of the hydroboration-oxidation product.

The presence of an acetate group at $C_{16}$ (rows III and IV) leads to an increase in the ß-orientation in hydroboration, although a predominance of products with 14αH-stereochemistry persists. The presence of larger groups at $C_{16}$, such as -OTHP in **5** and **9** (rows II and V) or -OTBDMS (row VI) leads to an inversion in preference of hydroboration attack at $\Delta^{8(14)}$, in which the ß orientation predominates with a ratio of 6:4. The method employed in the hydroboration reaction (Method A : $BH_3$/THF 1M; Method B : $BF_3/NaBH_4$) does not influence the 14ß/14α ratio, as can be observed in the hydroboration-oxidation of diacetate **7** (rows III and IV).

Such findings suggest the possibility of being able to achieve a highly stereoselective hydroboration by introducing a bulkier group at $C_{16}$. The choice of O-*t*-BDPSi as the protecting group of the hydroxyl at $C_{16}$ proved to be very satisfactory since the products obtained in the hydroboration of **10** (row VII) only have the 14ß stereochemistry. The stereospecifity induced by the presence of the O-*t*-BDPSi in $C_{16}$ was confirmed in the hydroboration-oxidation of **6** (row VIII), which yielded the deprotected compound **14** and the reduced one **21**, both exhibiting 14ßOH stereochemistry.

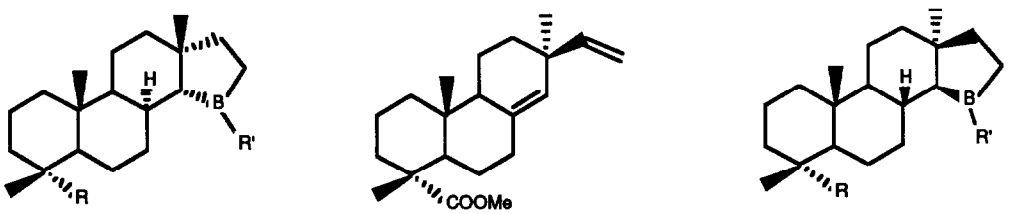
Accordingly, the preparation of 13-*epi*-pimarane compounds, functionalized at 14ß and 16 was performed through derivatives **6** and **11**, following the sequence in scheme I :

SCHEME I




a) $LiAlH_4$/THF b) $Ac_2O$/pyr c) BBN/THF d) $H_2O_2/OH^-$ e) sat. aq. $NaHCO_3$/MeOH f) *t*-BDPSiCl/imidazole g) $BF_3{\cdot}Et_2O/NaBH_4$/diglyme h) $CH_2N_2$/ether

The higher degree of attack through the less hindered α-face during the hydroboration of methyl sandaracopimarate can be acounted for in terms of the formation of a cyclic intermediate **23** that affects the double bond $\Delta^{8(14)}$ and $\Delta^{15}$, similar to the hydroboration product described for other 1,4-diolefins [12,13]. In the absence of $\Delta^{15}$, the degree of α-attack decreases even though the acetate protector group at $C_{16}$ is not very bulky and is an electron donor (table 1, rows III and IV).




**23** **24** **25**

According to our results, the stereochemistry proposed by Herz *et al* [7] for the hydroboration-oxidation products of methyl pimarate **24** should be corrected. These authors propose a preferential attack through the less hindered α-face and stereochemistry of the products through the shielding of 14ßH in the major product compared with the 14αH in the minor product. This stereochemical assignation is contrary to that performed by us on the basis of nOe experiments, such that the hydroboration of methyl pimarate must essentially take place through the ß-face. This finding is not surprising in view of the formation of the intermediate cyclic borane **25** as the hydroboration product.

## EXPERIMENTAL.

General: The solvents and reagents were purified and dried by standard techniques. Mps are uncorrected. The IR spectra were taken on film and $^1$H-NMR spectra were obtained in $CDCl_3$ solution on a 200

MHz spectrometer, unless otherwise stated. Chemical shifts are reported in ppm (δ) downfield from internal TMS. Optical rotations were measured at 20°C on a digital polarimeter.

*Methyl sandaracopimarate (2) and sandaracopimar-18-yl acetate (3) :*

**2** was obtained from sandaracopimaric acid (**1**), by esterification with ethereal diazomethane at room temperature. **3** was prepared from **1** by reduction with $LiAlH_4$ in THF followed by overnight acetylation with $Ac_2O$/pyr.

*Methyl 16-hydroxy-13-epi-pimar-8(14)-en-18-oate (4) :*

3.00 g of **2** (9.48 mmol) in 330 ml of dry THF were added dropwise under $N_2$ to a stirred solution of borabiciclononane (BBN) (1.67 g, 13.7 mmol) in 28 ml of dry THF, . The resulting solution was stirred at room temperature for 3 hours after completing the addition. 36 ml of ethanol, 4.5 ml of 6N NaOH and 9 ml of 33% $H_2O_2$ were carefully added with stirring and ice-cooling. The mixture was heated at 50° C for 1 hour to ensure complete oxidation, then cooled to room temperature. The aqueous layer was saturated with $K_2CO_3$, and thoroughly extracted with ether. The extract was washed with brine, dried ($Na_2SO_4$), filtered and evaporated. Chromatography of the crude product (3.6 g) over silica gel and elution with 7:3 hexane/EtOAc yielded 3.02 g (95%) of **4**.

Mp = 76°C. $[\alpha]^{20}(\lambda)$: +18.9° (589), +19.9° (578), +23.2° (546),+44.3° (436), +79.6° (365), c = 1.47% ($CHCl_3$)

IR : 3380, 1730, 1245, 1060, 870, 835 $cm^{-1}$.

$^1$H-NMR : 0.80 (s, 3H, $Me_{20}$), 0.95 (s, 3H, $Me_{17}$), 1.19 (s, 3H, $Me_{19}$), 3.65 (s, 3H, -OMe), 3.65 (t, 2H, J = 7.4 Hz, H-16), 5.22 (brs, 1H, H-14), ppm.

*Methyl 16-(tetrahydropyran-2-yl)oxy-13-epi-pimar-8(14)-en-18-oate (5) :*

A solution of **4** (2.31 g, 6.90 mmol) and dihydropyran (1.18 g, 14.0 mmol) in dry $CH_2Cl_2$ (70 ml) containing PPTS (Pyridinium *p*-toluenesulfonate) (346 mg, 1.38 mmol), was stirred overnight at room temperature. It was then diluted with ether and washed once with half-saturated brine to remove the catalyst. After the usual work up, 2.88 g (99%) of **5** were obtained.

IR : 3080, 1730, 1250, 1080, 1030, 980, 870 $cm^{-1}$.

$^1$H-NMR (60 MHz) : 0.80 (s, 3H, $Me_{20}$), 0.95 (s, 3H, $Me_{17}$), 1.17 (s, 3H, $Me_{19}$), 3.2-3.9 (m, 10H, H-16, -OTHP), 3.63 (s, 3H, -OMe), 4.51 (m, 1H, -OTHP), 5.23 (brs, 1H, H-14), ppm.

*Methyl 16-tert-Butyldiphenylsilyloxy-13-epi-pimar-8(14)-en-18-oate (6) :*

Imidazole (1.34 g, 11.2 mmol) and *t*--butylchlorodiphenylsilane (2.72 g, 6.12 mmol) were added to a solution containing **4** (2.9 g, 5.10 mmol) in dry DMF (25 ml) under $N_2$. The mixture was kept overnight with stirring. The solution was extracted with EtOAc and successively washed with aqueous $NH_4Cl$ and brine, dried over $Na_2SO_4$ and evaporated to give 5.80 g. After column chromatography on silica gel (eluted with hexane/EtOAc 9:1) **6** (4.90 g, 95%) was isolated.

$[\alpha]^{20}(\lambda)$ : +4.0° (589), +4.2° (578), +5.1° (546), +10.5° (436), +19.8° (365), c = 0.85% ($CHCl_3$).

IR : 3060, 1735, 1600, 1250, 1200, 1180, 1010, 940, 830 $cm^{-1}$.

$^1$H-NMR : 0.77 (s, 3H, $Me_{17}$), 0.88 (s, 3H, $Me_{20}$), 1.03 (s, 9H, -Si-*t*-Bu), 1.18 (s, 3H, $Me_{19}$), 3.64 (s, 3H, -OMe), 3.67 (m, 2H, H-16), 5.14 (brs, 1H, H-14), 7.37 and 7.65 (m, 10H, -Si-$Ph_2$), ppm.

*13-epi-Pimar-8(14)-en-16,18-diol, diacetate (7) :*

Following the procedure described for **4**, hydroboration-oxidation of **3** (2.20 g, 6.64 mmol) with BBN followed by acetylation of the reaction product and flash chromatography gave 2.23 g (86%) of **7**.

$[\alpha]^{20}(\lambda)$ : +12.5° (589), +13.1° (578),+15.1 ° (546), +27.5° (436), +49.6° (365), c = 2.10% ($CHCl_3$).

IR : 3020, 1740, 1650, 860 $cm^{-1}$.

$^1$H-NMR : 0.81 (s, 3H, $Me_{20}$), 0.87 (s, 3H, $Me_{19}$), 0.97 (s, 3H, $Me_{17}$), 2.01 (s, 3H, -OAc), 2.06 (s, 3H, -OAc), 3.65 (d, 1H, J = 10.8 Hz, H-18), 3.86 (d, 1H, J = 18 Hz, H-18'), 4.08 (t, 2H, J = 7.5 Hz, H-16), ppm.

Saponification of **7** :

50 ml of saturated aqueous $NaHCO_3$ were added to a stirred solution of **7** (10.8 g, 27.7 mmol) in 260 ml of methanol and manteined with vigorous stirring for 72 hours at room temperature. The mixture was then diluted with water, extracted with EtOAc and washed with brine. After the usual work up, the crude product (8.70 g) was chromatographied over silica gel (eluents, hexane/EtOAc 9:1, 8:2, 7:3 and 1:1) yielding unreacted **7** (830 mg), **12** (185 mg), **8** (5.90 mg) and **13** (1.21 g).

*16-Acetoxy-13-epi-pimar-8(14)-en-18-ol* (**12**) :

$[\alpha]^{20}(\lambda)$ : +17.6° (589), +18.6° (578),+21.3 ° (546), +38.9° (436), +66.7° (365), c = 1.71% ($CHCl_3$).

IR : 3450, 1730, 1655, 1200, 865 $cm^{-1}$.

$^1$H-NMR : 0.80 (s, 3H, $Me_{19}$), 0.81 (s, 3H, $Me_{20}$), 0.97 (s, 3H, $Me_{17}$), 2.02 (s, 3H, -OAc), 3.10 (d, 1H, J = 10.9 Hz, H-18), 3.38 (d, 1H, J =10.9 Hz, H-18'), 4.08 (t, 2H, J = 7.5 Hz, H-16), 5.19 (brs, 1H, H-14), ppm.

*18-Acetoxy-13-epi-pimar-8(14)-en-16-ol* (**8**) :

Mp = 101°C. $[\alpha]^{20}(\lambda)$: +27.2°(589), +28.6° (578),+32.7°(546), +60.1°(436),+104.5° (365), c =1.23% ($CHCl_3$).

IR : 3400, 1730, 1660, 1250, 1040, 990, 870 $cm^{-1}$.

$^1$H-NMR : 0.81 (s, 3H, $Me_{20}$), 0.87 (s, 3H, $Me_{19}$), 0.95 (s, 3H, $Me_{17}$), 2.06 (s, 3H, -OAc), 3.64 (t, 2H, J = 7.5 Hz, H-16), 3.66 (d, 1H, J =10.8 Hz, H-18), 3.85 (d, 1H, J =10.8 Hz, H-18'), 5.22 (brs, 1H, H-14), ppm.

*13-epi-Pimar-8(14)-en-16,18-diol* (**13**) :

Mp = 110°C. $[\alpha]^{20}(\lambda)$ : +6.4° (589), +6.7° (578),+7.7 ° (546), +14.8° (436), +27.5° (365), c = 0.46% (EtOH).

IR (KBr) : 3280, 1660, 1050, 1030, 860 $cm^{-1}$.

$^1$H-NMR : 0.80 (s, 3H, $Me_{19}$), 0.81 (s, 3H, $Me_{20}$), 0.96 (s, 3H, $Me_{17}$), 3.11 (d, 1H, J = 10.8 Hz, H-18), 3.39 (d, 1H, J = 10.8 Hz, H-18'), 3.68 (t, 2H, J = 7.4 Hz, H-16), 5.22 (brs, 1H, H-14), ppm.

Acetylation of **12** and **13** gave a further amount of diacetate **7**. Unreacted **7**, together with acetylated **12** and **13**, by the same procedure provided 1.32 g of **8**. The total yield of **8** after two partial saponifications of **7** was 7.22 g (75%).

*16-(Tetrahydropyran-2-yl)oxy-13-epi-pimar-8(14)-en-18-ol, acetate* (**9**) :

Following the procedure described for **5**, **8** (4.20 g, 12.1 mmol) was transformed into **9** (5.06 g, 97%).

IR : 1740, 1650, 1080, 1040, 980, 860 $cm^{-1}$.

$^1$H-NMR (60 MHz) : 0.80 (s, 3H, $Me_{20}$), 0.87 (s, 3H, $Me_{19}$), 0.96 (s, 3H, $Me_{17}$), 3.20-4.20 (m, 10H, H-16,-OTHP), 3.62 (d, 1H, J = 10.6 Hz, H-18), 3.85 (d, 1H, J = 10.6 Hz, H-18'), 4.50 (brs, 1H, -OTHP), 5.19 (brs, 1H, H-14), ppm.

*16-tert-Butyldimethylsilyloxy-13-epi-pimar-8(14)-en-18-ol, acetate* (**10**) :

*t*-Buthylchlorodimethylsilane (120 mg, 0.80 mmol) and imidazole (133 mg) were added to a solution of **8** (233 mg, 0.67 mmol) in dry DMF (4 ml) at 0°C, under $N_2$. The solution was allowed to stand at room temperature for 1 hour. The reaction mixture was worked up in the usual way to give 311 mg of reaction product, which by chromatography column (hexane/EtOAc 9:1) gave **10** (281 mg, 91%).

IR : 1745, 1650, 1250, 1090, 1040, 840, 790 $cm^{-1}$.

$^1$H-NMR : 0.04 (s, 6H, -$SiMe_2$), 0.81 (s, 3H, $Me_{20}$), 0.87 (s, 3H, $Me_{19}$), 0.89 (s, 9H, -Si-*t*-Bu), 0.94 (s, 3H, $Me_{17}$), 3.65 (d, 1H, J = 10.8 Hz, H-18), 3.66 (m, 2H, H-16), 3.86 (d, 1H, J = 10.8 Hz, H-18'), 5.22 (brs, 1H, H-14), ppm.

*16-tert-Butyldiphenylsilyloxy-13-epi-pimar-8(14)-en-18-ol, acetate* (**11**) :

Following the procedure described for **6**, 4.02 g (93%) of **11** were obteined from 2.57 g (7.38 mmol) of **8**.

$[\alpha]^{20}(\lambda)$ : +10.6° (589), +11.2° (578),+12.9 ° (546), +23.4° (436), +39.6° (365), c = 1.40% ($CHCl_3$).

IR (4% $CHCl_3$) : 3060, 1730, 1600, 1500, 1250, 1115, 1040, 1000, 940, 870, 825 $cm^{-1}$.

$^1$H-NMR : 0.78 (s, 3H, $Me_{20}$), 0.86 (s, 3H, $Me_{19}$), 0.88 (s, 3H, $Me_{17}$), 1.04 (s, 9H, -Si-*t*-Bu), 3.64 (d, 1H, J = 10.9 Hz, H-18), 3.70 (m, 2H, H-16), 3.86 (d, 1H, J = 10.9 Hz, H-18'), 5.14 (brs, 1H, H-14), 7.39 and 7.67 (m, 10H, -$Si-Ph_2$), ppm.

HYDROBORATION-OXIDATION REACTIONS :

Method A ($BH_3$/THF) : 4 ml of $BH_3$/THF (1M) were added via syringe to alkene (1 mmol) dissolved in dry THF under $N_2$, and cooled to 0°C; the reaction mixture was allowed to stand at room temperature for 4 hours. Ethanol, 0.6 ml of 6N NaOH and 1.2 ml of $H_2O_2$ (33%) were added cautiously with stirring and ice cooling. The mixture was heated for 1 hour at 50°C, then cooled to room temperature and, after $K_2CO_3$ addition, extracted with ether. The extract was washed with brine, dried and evaporated to give the reaction product.

Method B (B-1 and B-2) ($BF_3$/$NaBH_4$) : A solution containing a mixture of alkene (1 mmol), boron trifluoride ethyl etherate (3 mmol) in dry diglyme (B-1) or THF (B-2) was cooled to 0°C under $N_2$ atmosphere. A solution of sodium borohydride (2 mmol) in dry diglyme (B-1) or THF (B-2) was added dropwise and the mixture was stirred for 9 hours at room temperature. Then, ethanol, 3N NaOH (0.6 ml) and $H_2O_2$ (33%) (1.2 ml) were slowly added . The mixture was stirred at 60°C for 1 hour, after which EtOAc and NaCl were added.

The organic layer was washed with water, dried and evaporated to give the reaction product.

Hydroboration-oxidation of **2** :

Method A. 3.00 g (9.49 mmol) of **2** afforded 3.50 g of crude product. By chromatography of 250 mg of this mixture over silica gel and elution with 7:3 hexane/EtOAc, 155 mg (0.44 mmol, 65%) of **14** + **15** were obtained at a ratio of 3:7.

IR : 3320, 1725, 1250, 1140, 1050 $cm^{-1}$.

$^1$H-NMR of *Methyl 14α,16-dihydroxy-13*-epi-*pimaran-18-oate* (**15**) : 1.04 (s, 3H, $Me_{20}$), 1,05 (s, 3H, $Me_{17}$), 1.19 (s, 3H, $Me_{19}$), 3.53 (d,1H, J = 12.11 Hz, H-14), 3.66 (s, 3H, -0Me), 3.68 (m, 2H, H-16), ppm.

*Diacetate,* **17** : $^1$H-NMR : 0.91 (s, 3H, $Me_{20}$), 1.15 (s, 3H, $Me_{17}$), 1.19 (s, 3H, $Me_{19}$), 2.04 (s, 3H, -OAc), 2.08 (s, 3H, -OAc), 3.63 (s, 3H, -OMe), 4.09 (t, 2H, J =7.4 Hz, H-16), 5.11 (d, 1H, J =12.7 Hz, H-14), ppm.

**14** is described as pure substance in the hydroboration-oxidation of **6.**

Hydroboration-oxidation of **5** :

Method A. 2.88 g of **5** (6.88 mmol) afforded 1.52 g (63%) of **14** and **15** at a ratio of 6:4 by cleavage of the hydroboration-oxidation product with PPTS in Ethanol and chromatography (hexane/EtOAc, 7:3).

Hydroboration-oxidation of **7** :

Method A. 2.23 g of **7** (5.72 mmol) gave 1.02 g (40%) by acetylation ($Ac_2O$/pyr) of the hydroboration-oxidation product. By flash chromatography of the 1.02 g with 8:2 hexane/EtOAc were isolated 328 mg of **20** and 491 mg of **21** (4:6 ratio).

Method B-2. 929 mg (2.38 mmol) of **7** gave 630 mg (59%) of a mixture containing **20** + **21** at a ratio of 4:6 by acetylation of the hydroboration-oxidation product.

*13*-epi-*Pimaran-14β,16,18-triol, triacetate* (**20**) :

$[\alpha]^{20}(\lambda)$ : +6.2° (589), +6.6° (578),+7.5 ° (546), +13.2° (436), +21.5° (365), c = 1.97% ($CHCl_3$)

IR : 3740, 1250, 980 $cm^{-1}$.

$^1$H-NMR : 0.83 (s, 3H, $Me_{19}$), 0.90 (s, 3H, $Me_{20}$), 0.95 (s, 3H, $Me_{17}$), 2.05 (s, 3H, -OAc), 2.06 (s, 3H, -OAc), 2.07 (s,3H, -OAc), 3.58 (d, 1H, J = 10.8 Hz, H-18), 3.83 (d, 1H, J = 10.8 Hz, H-18'), 4.09 (t, 2H, J = 7.5 Hz, H-16), 4.50 (d, 1H, J = 10.1 Hz, H-14), ppm.

*8*-epi-*13*-epi-*Pimaran-14α,16,18-triol, triacetate* (**21**) :

$[\alpha]^{20}(\lambda)$ : +20.0° (589), +20.1° (578),+22.8 ° (546), +38.0° (436), +56.2° (365), c = 1.49% ($CHCl_3$).

IR (4% $CHCl_3$) : 1730, 1250, 1115, 1030, 985 $cm^{-1}$.

$^1$H-NMR : 0.86 (s, 3H, $Me_{19}$), 0.91 (s, 3H, $Me_{20}$), 1.15 (s, 3H, $Me_{17}$), 2.04 (s, 3H, -OAc), 2.05 (s, 3H, -OAc), 2.09 (s, 3H, -OAc), 3.60 (d, 1H, J = 10.9 Hz, H-18), 3.84 (d, 1H, J = 10.9 Hz, H-18'), 4.12 (m, 2H, H-16), 5.13 (d, 1H, J = 12.7 Hz, H-14), ppm.

Hydroboration-oxidation of **9** :

Method A. After acetylation of reaction product, cleavage (PPTS in Ethanol) of tetrahydropyranyl group and chromatography (hexane/EtOAc 8:2), 5.06 g of **9** (11.7 mmol) afforded 2.44 g (51%) of **18** + **19** at a ratio of 6:4. By flash chromatography with 7:3 hexane/EtOAc, 1.04 g of **18** and 690 mg of **19** were isolated .

*14β,18-Diacetoxy-13*-epi-*pimaran-16-ol* (**18**) :

Mp = 101°C. $[\alpha]^{20}(\lambda)$: +0.20°(589), +0.20°(578), +0.20°(546), +0.70°(436), +1.20° (365), c = 0.89% ($CHCl_3$).

IR (4% $CHCl_3$) : 3600,1730,1250, 1040,980 $cm^{-1}$.

$^1$H-NMR : 0.82 (s, 3H, $Me_{19}$), 0.89 (s, 3H, $Me_{20}$), 0.93 (s, 3H, $Me_{17}$), 2.05 (s, 3H, -OAc), 2.07 (s, 3H, -OAc), 3.59 (d,1H, J = 10.9, H-18), 3.69 (t, 2H, J = 7.4 Hz, H-16), 3.82 (d,1H, J = 10.9 Hz, H-18'),4.54 (d, 1H, J = 10.2 Hz, H-14), ppm.

*14α,18-Diacetoxy-8*-epi-*13*-epi-*pimaran-16-ol* (**19**) :

Mp = 138°C.$[\alpha]^{20}(\lambda)$ : +20.6° (589), +21.6° (578),+24.5° (546), +39.4° (436), +58.0° (365), c = 1.45%.

IR (4% $CHCl_3$) : 3600, 1730, 1250, 1040, 985 $cm^{-1}$.

$^1$H-NMR : 0.86 (s, 3H, $Me_{19}$), 0.90 (s, 3H, $Me_{20}$), 1.15 (s, 3H, $Me_{17}$), 2.05 (s, 3H, -OAc), 2.09 (s, 3H,-OAc), 3.61 (d,1H, J = 10.8 Hz, H-18), 3.69 (m, 2H, H-16), 3.83 (d,1H, J = 10.8 Hz, H-18'), 5.13 (d, 1H, J = 12.7 Hz, H-14), ppm.

Hydroboration-oxidation of **10** :

Method A. By cleavage of reaction product (n-tetrabutylammonium fluoride in THF), acetylation and

chromatography, 281 mg of **10** (0.61 mmol) afforded 166 mg (60%) of **20** + **21** at a ratio of 6:4.

Hydroboration-oxidation of **11** :

Metod B-1. By acetylation of the reaction product and chromatography, 4.02 g of **11** (6.86 mmol) afforded 1.91 g (62%) of **20**.

Hydroboration-oxidation of **6** :

Method B-1. 2.47 g (4.32 mmol) of **6** afforded 4.8 g of crude product. By chromatography over silica gel and elution with hexane/EtOAc (1:1) and EtOAc/methanol (9:1), **14** (1.4 g, 50%) and **22** (0.5 g, 20%) were obtained .

*Methyl 14β,16-dihydroxy-13*-epi-*pimaran-18-oate* (**14**) :

Mp = 137°C. $[\alpha]^{20}(\lambda)$ : -16.2° (589), -17.4° (578),-20.2° (546), -31.0° (436), -47.4° (365), c = 0.98% ($CHCl_3$).
IR (4% $CHCl_3$) : 3220, 1720, 1230, 1140, 1100, 1060.
$^1$H-NMR : 0.88 (s, 6H, $Me_{17}$ and $Me_{20}$), 1.17 (s, 3H, $Me_{19}$), 2.96 (d, 1H, J = 9.8 Hz, H-14), 3.64 (s, 3H, -OMe), 3.71 (m, 2H, H-16), ppm.

*13*-epi-*Pimaran-14β,16,18-triol* (**22**) :

Mp = 190°C. $[\alpha]^{20}(\lambda)$ : -21.2° (589), -21.9° (578),-24.6° (546), -39.4° (436), -57.7° (365), c = 0.74% (MeOH).
IR (KBr) 3300, 1080, 1065, 1040, 970, 950, 800 $cm^{-1}$.
$^1$H-NMR (DMSO) : 0.67 (s, 3H, $Me_{19}$), 0.72 (s, 3H, $Me_{17}$), 0.82 (s, 3H, $Me_{20}$), 2.66 (dd, 1H, $J_1$ = 9.5 Hz, $J_2$ = 5.6 Hz, H-14), 2.82 (dd, 1H, $J_1$ = 10.4 Hz, $J_2$ = 5.1 Hz, H-18), 3.16 (dd, 1H, $J_1$ = 10.4 Hz, $J_2$ = 5.1 Hz, H-18'), 3.45 (dt, 2H, $J_1$ = 7.2 Hz, $J_2$ = 5.0 Hz).

By acetylation ($Ac_2O$/pyr) of the hydroboration-oxidation products **14** and **22**, compounds **16** (1.6 g, 95%) and **20** (0.6 g, 95%) were obtained.

*Methyl 14β,16-diacetoxy-13*-epi-*pimaran-18-oate* (**16**) :

Mp = 81°C. $[\alpha]^{20}(\lambda)$ : +12.3° (589), +12.9° (578),+15.1° (546), +26.4° (436), +46.8° (365), c = 1.07%($CHCl_3$).
IR (4% $CHCl_3$) : 1740, 1720, 1240, 1200, 1180, 1140, 1100, 1040 $cm^{-1}$.
$^1$H-NMR : 0.89 (s, 3H, $Me_{20}$), 0.95 (s, 3H, $Me_{17}$), 1.16 (s, 3H, $Me_{19}$), 2.01 (s, 3H, -OAc), 2.06 (s,3H, -OAc), 3.62 (s, 3H, -OMe), 4.10 (t, 2H, J = 7.6 Hz, H-16), 4.50 (d, 1H, J= 10.1 Hz, H-14), ppm.

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## REFERENCES AND NOTES.

1) J. de Pascual Teresa, F. Bermejo Gonzalez, A. Fenández Mateos, F. González Conde and M.E. Romero Alarcón, *An. Quim.* , **79(C)**, 447 (1983).
2) M. Bordell Martín, A. Fernández Mateos, and J. de Pascual Teresa, *An. Quim.*, **84(C)**, 73 (1988).
3) A. Abad, C. Agullo, M. Arnó, L.R. Domingo and R.J. Zaragozá, XII Reunión Bienal del Grupo de Química Orgánica de la R.S.E.Q., Abstracts, p.161, Córdoba (Spain) (1987).
4) J.W. Apsimon, A.S.Y. Chau, W.G. Craig and H. Krehm, *Can. J. Chem.* , **45**, 1439 (1967).
5) P. Ceccherelli, M. Tingoli, M. Curini and R. Pellicciari, *Tetrahedron Lett.* , **40**, 3869 (1978).
6) P. Ceccherelli, M. Curini, M. Tingoli and R. Pellicciari, *J. Chem. Soc. Perkin I* , 1924 (1980).
7) W. Herz, A.K. Pinder and R.N. Mirrington, *J. Org. Chem.* , **31**, 2257 (1966).
8) In the case of methyl sandaracopimarate (reference 1) the ratio 14α/14ß hydroxylation is 7:3.
9) W. Herz, D. Melchior, R.N. Mirrington and P.J.S. Pauwels, *J. Org. Chem.* , **30**, 1873 (1965).
10) H.C. Brown, E.F. Knights and C.G. Scouten, *J. Am. Chem. Soc.* , **96**, 7765 (1974).
11) D.F. Zinkel, L.C. Zank and M.F. Mesolowski, *Diterpene Resin Acids* , p. D31-32, U.S. Department of Agriculture. Madison (Wis.) (1971).
12) D.E. Young and S.G. Shore, *J. Am. Chem. Soc.* , **91**, 3497 (1969).
13) E. Negishi and H.C. Brown, *J. Am. Chem. Soc.* ,**95**, 6757 (1973).