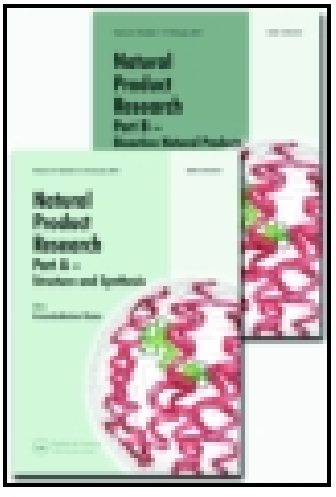

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# Different pathways for the deoxygenation of the A-ring of natural triterpene compounds

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# Different pathways for the deoxygenation of the A-ring of natural triterpene compounds

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Some deoxygenation pathways were tested to remove the hydroxyl groups of the natural triterpenes oleanolic acid and maslinic acid to obtain a practical starting material for the semisynthesis of other interesting organic synthons. Different deoxygenation processes were carried out starting from these triterpenic acids or from several derivatives such as methyl esters and epoxy derivatives. The hydroxyl groups were transformed into some intermediate compounds including xanthyl, thiocarbonyl or tosyl derivatives. The opening of the oxirane ring between C-2 and C-3 was also achieved through different methods using deoxygenating reagents such as $Me_3SiCl/NaI$, $WCl_4/n$-BuLi and $Cp_2TiCl$.

**Keywords:** oleanolic acid; maslinic acid; triterpene; deoxygenation



## 1. Introduction

In several areas of natural product chemistry, it is frequently necessary to replace a secondary hydroxyl with a hydrogen atom without the possibility of rearrangement. Deoxygenation of alcohols and epoxides is a useful and important process in organic synthesis which is often conducted efficiently using free radical chemistry. Thus, one of the most well-known methods with which to deoxygenate hydroxyl compounds was described by Barton and co-workers forming the corresponding thiocarbonates and xanthates which were treated with $Bu_3SnH$ as a reducing agent (Barton & McCombie, 1975). Afterwards, considerable efforts have been made to improve this procedure and to avoid the use of the tin hydride because of its toxic properties (Barton, Dorchak, & Jaszberenyi, 1992b; Barton, Jang, & Jaszberenyi, 1991a, 1991b, 1991c, 1992a, 1993; Lopez, Hays, & Fu, 1997). The hydroxyl group can also be converted into the corresponding tosylate or mesylate, which is later eliminated. However, when the $S_N2$ process is hindered, the deoxygenation of some secondary hydroxyl groups is very difficult and several rearrangement processes can occur. A new procedure to deoxygenate hydroxyl groups is via their trifluoroacetate derivatives with diphenylsilane (Jang, Kim, Cho, & Chung, 2001; Kim, Cho, & Jang, 2004). The process is quite simple and appropriate for the deoxygenation of tertiary alcohol without side reactions and with high yields of reaction products. Another typical

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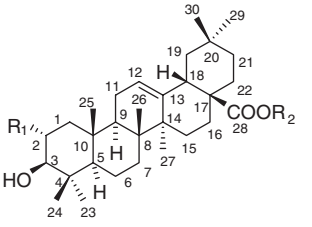
procedure to eliminate hydroxyl groups is the method of Wolff–Kishner modified by Huang-Minlon through the corresponding hydrazone under basic medium (Abad, Agullo, Arno, Marin, & Zaragoza, 1997; Huang-Minlon, 1946, 1949; Hutchins & Hutchins, 1991). Moreover, epoxides are versatile intermediates in organic chemistry and relatively few general methods exist for removing oxygen atoms from the epoxy compounds. Generally, these procedures require expensive reagents and severe reaction conditions, which may affect other functional groups present in the molecule. In this sense, epoxides have been deoxygenated by several protocols using $Me_3SiCl/NaI$, $Ph_3P/I_2$, $ZrCl_4/NaI$, $WCl_4/n$-BuLi, $Cp_2TiCl$ (Caputo, Mangoni, Neri, & Palumbo, 1981; Cuerva et al., 2006; Gansäuer, Pierobon, & Bluhm, 1998; Nugent & Rajanbabu, 1988, 1989, 1994; Nugent, Rajanbabu, & Beattie, 1990; Paryzek & Wydra, 1984).




| Name | Number | $R_1$ | $R_2$ |
|---|---|---|---|
| Oleanolic acid | **1** | H | H |
| Maslinic acid | **2** | OH | H |
| Methyl oleanoate | **3** | H | $CH_3$ |
| Methyl maslinate | **4** | OH | $CH_3$ |

Figure 1. Structures of compounds **1**–**4**.

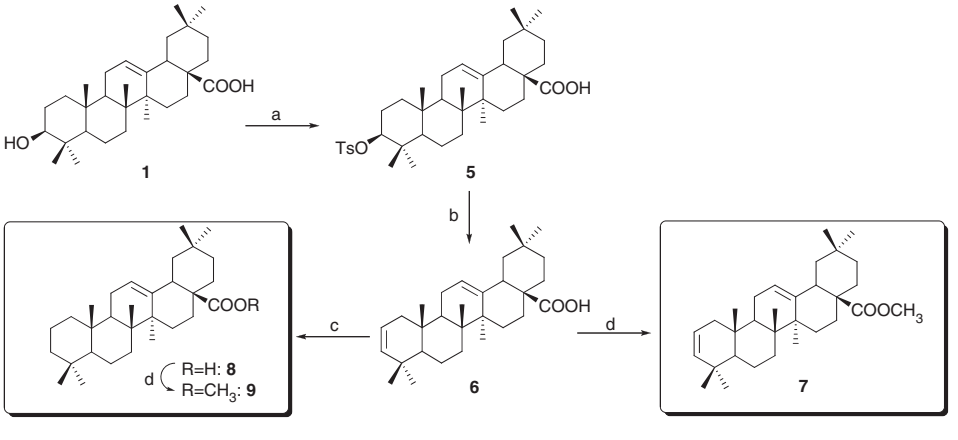
On the other hand, oleanolic acid (**1**) (3$\beta$-hydroxy-12-oleanen-28-oic acid) and maslinic acid (**2**) (2$\alpha$,3$\beta$-dihydroxy-12-oleanen-28-oic acid) (Figure 1) are natural triterpene acids widespread in plants in the form of free acids or derivatives such as methyl esters, acetyl-, oxo-, glycosyl- and other compounds (Bianchi, Pozzi, & Vlahov, 1994; Garcia-Granados, Martinez, Moliz, Parra, & Rivas, 1998a, 1998b). Previously, our research group reported a general isolation method that allowed us to obtain large quantities of both compounds from olive-oil pressing residues (Garcia-Granados, Martinez, Parra, & Rivas, 1998c). Deoxygenation of these compounds was initially studied via reduction of the corresponding thionoformates (Garcia-Granados et al., 2000a) and, although giving the desired A-ring deoxygenated products in good yield, these processes were very expensive due to requiring high amounts of starting material to semisynthesise other chemically useful compounds. On the other hand, in previous papers, we have also described the conversion of the corresponding esters, **3** and **4** (Figure 1), into several A-ring and C-ring modified derivatives. In this sense, our preliminary work has shown that, when these compounds were treated with phosphorus pentachloride or mesyl chloride, several rearrangements occurred and different A-ring contracted compounds were obtained (Garcia-Granados et al., 2000a, 2000b). Similarly, when methyl 2$\beta$,3$\beta$-epoxy-12-oleanen-28-oate was deoxygenated with $Ph_3P/I_2$, a minor A-ring deoxygenated product and several halohydrin derivatives were semisynthesised (Garcia-Granados et al., 2003a). We have also reported on the initial study of the formation of several C-ring derivatives from oleanolic and maslinic acids, and the cleavage of the triterpene molecule (Garcia-Granados, Lopez, Melguizo, Parra, & Simeo 2003b, 2004a, 2004b, 2006). Our research group has also described the remote hydroxylation of the C-23 and C-24 methyl groups of these natural triterpene compounds by a regioselective cyclopalladation process, producing other

natural compounds with potentially useful biological activities (Garcia-Granados, Lopez, Melguizo, Parra, & Simeo, 2007). Recently, we have reported the preparation of several maslinic acid derivatives containing amino acids and peptides as potent anti-HIV agents (Parra et al., 2009).

In the light of these results, in this article, we explore the scope of some of these deoxygenation protocols of the A-ring of these natural oleanene compounds with the aim to optimise these procedures and to obtain A-ring deoxygenated compounds, which will be a useful starting material for the semisynthesis of other interesting organic synthons.

## 2. Results and discussion

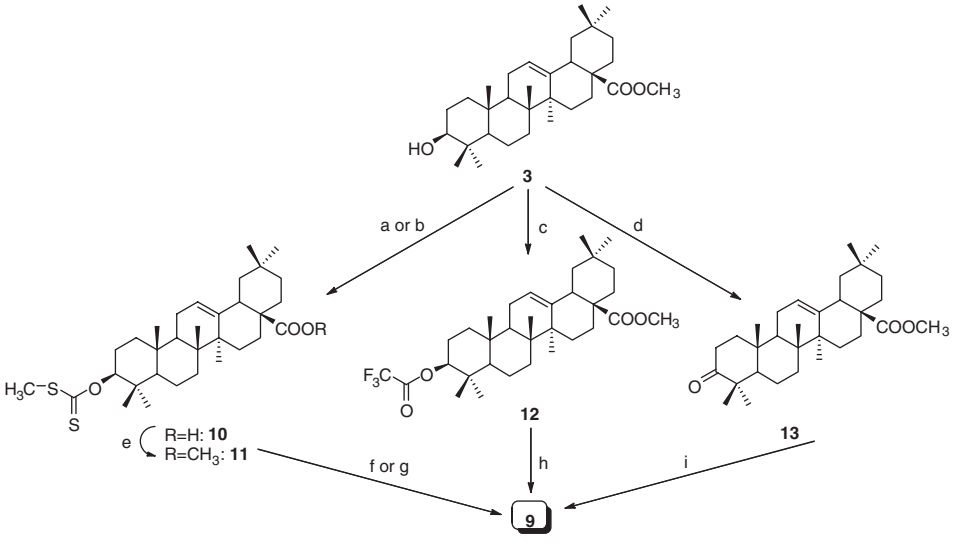
Oleanolic acid (**1**) and maslinic acid (**2**) were obtained from olive-pressing residues by successive extractions with hexane and ethyl acetate in a Soxhlet apparatus (Garcia-Granados et al., 1998c). The hexane extract contained mostly oleanolic acid (**1**) (80–85%), whereas the EtOAc extract contained mostly maslinic acid (**2**) (80–85%). After flash chromatography on a silica gel column, large amounts of these compounds were obtained and our principal goal was its A-ring deoxygenation, starting from several derivatives. Firstly, we used oleanolic acid (**1**) as the starting material, which was deoxygenated via its 3-tosyl derivative (Scheme 1). This tosyl derivative **5** was deoxygenated in an acceptable yield (42%) by treatment with sodium acetate in DMF at 120°C, giving compound **6**, which had a double bond between C-2 and C-3. The esterification of the C-28 carboxylic group of 3,12-oleandien-28-oic acid (**6**) was carried with NaOH/MeI and thus the desired final product (**7**), 3-deoxy $\Delta^{2,3}$ methyl oleanoate (Garcia-Granados et al., 2000a), was formed (Scheme 1). Finally, catalytic hydrogenation of the 2,12-oleandiene compound **6** with $H_2$/Pt gave 3-deoxyoleanolic acid (**8**), and its esterification with NaOH/MeI yielded 3-deoxymethyl oleanoate (**9**) (Garcia-Granados et al., 2000a). Therefore, the key and limiting process for the deoxygenation procedure starting with oleanolic acid (**1**), given in Scheme 1, was the tosyl elimination (42%), because the other steps are practically quantitative.




Scheme 1. Deoxygenation of oleanolic acid (**1**). Reagents and conditions: (a) PTSCl, py, rt, 24 h; (b) NaAcO, DMF, 120°C, 24 h; (c) $H_2$, Pt, 12 h; (d) (i) NaOH 5N, THF, reflux, 3 h; (ii) $CH_3I$, THF, 2 h.

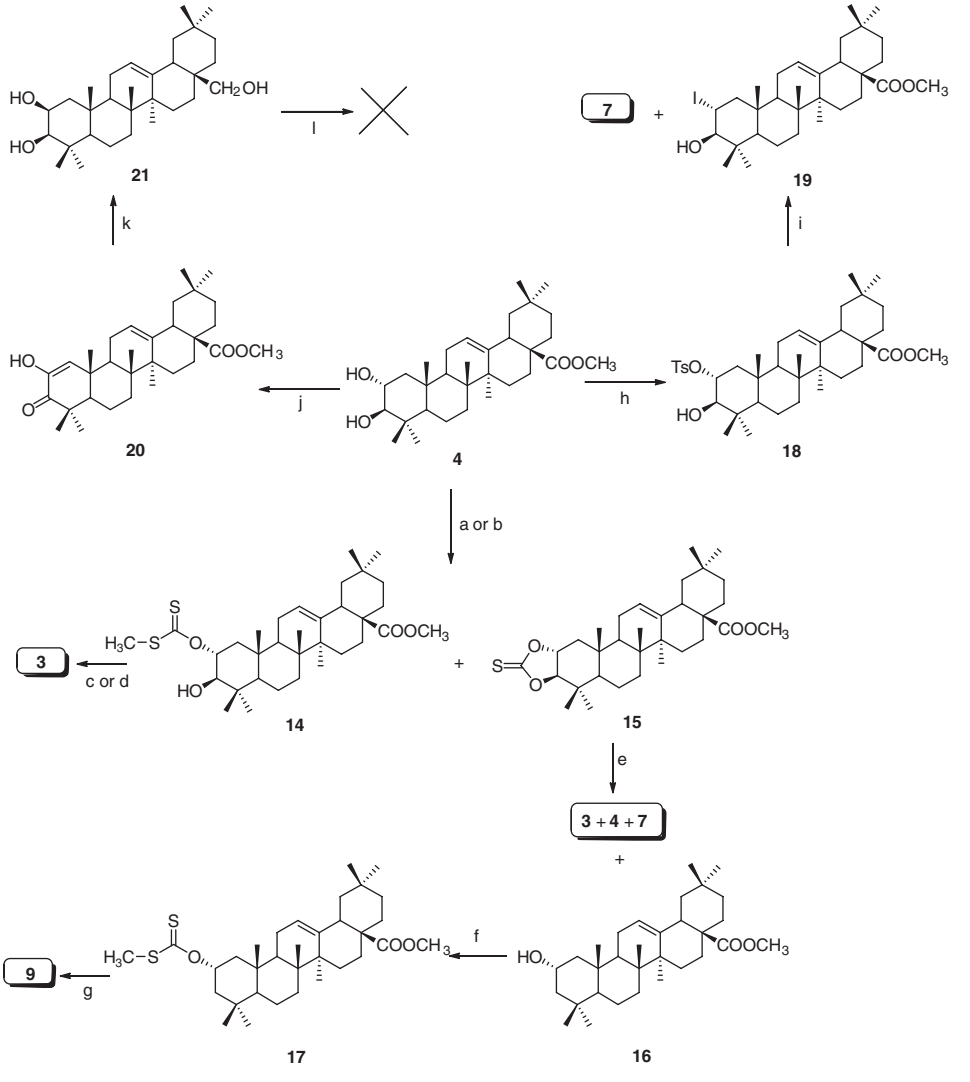
Subsequently, we started from the methyl oleanoate (**3**) which was deoxygenated at the A-ring through several pathways (Scheme 2). Thus, when compound **3** was treated with *sec*-butyllithium/$CS_2$/MeI, the corresponding C-28 demethylated-xanthate derivative (**10**) and the xanthyl methyl ester (**11**) were obtained. Xanthate (**11**) was only formed in a good yield (80%) when the deprotonation process was carried out with NaH instead of *sec*-butyllithium (Scheme 2, treatment b). The trifyl derivative (**12**) was also prepared by treatment with trifluoroacetic anhydride. Finally, the 3-oxoderivative (**13**) (Garcia-Granados et al., 2000a) was also formed by treatment of methyl oleanoate (**3**) with Jones' reagent. 3-Xanthyl (**11**), 3-trifyl (**12**) and 3-oxo (**13**) derivatives were deoxygenated by different procedures and with diverse yields (see Scheme 2 and Section 4) to give the desired compound **9**, 3-deoxymethyl oleanoate. The best route to deoxygenate methyl oleanoate **3** was through its 3-xanthyl derivative (**11**), since this pathway gave a global yield of 70%.

Deoxygenation of methyl maslinate (**4**) was more complex, because of the presence of two hydroxyl groups in the A-ring of the skeleton. In Scheme 3, two deoxygenation pathways are shown through its xanthyl or tosyl derivatives, which led us to the two desired A-ring deoxygenated compounds, **7** and/or **9**. First, methyl maslinate (**4**) was treated with *sec*-butyllithium/$CS_2$/MeI or NaH/MeI to give (in similar yields) the C-2 monosubstituted xanthyl derivative **14** (40% or 60%, respectively) and the cyclic thiocarbonate **15** (50% or 30%, respectively). Compound **14** was deoxygenated at C-2 by the xanthyl group, yielding the reusable methyl oleanoate (**3**). Reductive treatment of thiocarbonate (**15**) gave a mixture of the previously known compounds **3**, **4**, **7** and the 3-deoxygenated compound **16**, which was also deoxygenated through its 2-xanthyl




Scheme 2. Deoxygenation of methyl oleanoate (**3**). Reagents and conditions: (a) (i) *sec*-BuLi, THF, reflux, 2 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux 2 h; (b) (i) NaH, THF, reflux, 3 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux, 2 h; (c) $(CF_3)_2O$, py, rt, 24 h; (d) Jones reagent, acetone, rt, 30 min; (e) (i) NaOH 5N, THF, reflux, 3 h; (ii) $CH_3I$, THF, reflux, 2 h; (f) $H_3PO_2$, AIBN, $Et_3N$, dioxane, reflux, 3 h; (g) $(Bu_3Sn)_2O$, toluene, PMHS, AIBN, 80°C, 3h; (h) $Ph_2SiH_2$, $(^tBuO)_2$, 130°C, 24 h; (i) $N_2H_4$, KOH, ethylene glycol, reflux, 5 h.

derivative **17**. Methyl maslinate (**4**) was also deoxygenated through selective tosylation, forming the 2-tosyl methyl maslinate **18** (Garcia-Granados et al., 2000b), but its treatment with KI/TMSCl at reflux in DMF led us mainly to the iodohydrin **19**. Deoxygenation of methyl maslinate (**4**) was also attempted by epimerisation at C2 by oxidation/reduction treatments (compounds **20** and **21**) but the final triol did not form the corresponding thiocarbonate.

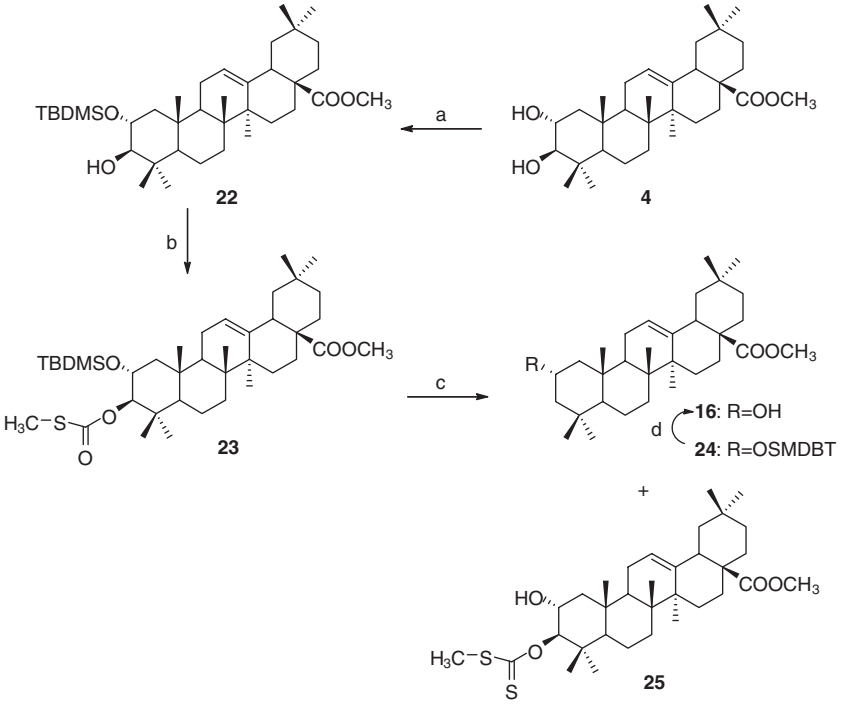



Scheme 3. Deoxygenation of methyl maslinate (**4**). Reagents and conditions: (a) (i) *sec*-BuLi, THF, reflux, 2 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux 2 h; (b) (i) NaH, THF, reflux, 3 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux, 2 h; (c) $(Bu_3Sn)_2O$, toluene, PMHS, AIBN, 80°C, 3 h; (d) $H_3PO_2$, AIBN, $Et_3N$, dioxane, reflux, 3 h; (e) $(Bu_3Sn)_2O$, toluene, PMHS, AIBN, 80°C, 3 h; (f) (i) NaH, THF, reflux, 3 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux, 1 h; (g) $H_3PO_2$, AIBN, $Et_3N$, dioxane, reflux, 3 h; (h) TsCl, py, rt, 24 h; (i) KI, TMSCl, DMF, reflux, 12 h; (j) Dess–Martin reagent, DCM, rt, 2 h; (k) $LiAlH_4$, THF, reflux, 3 h; (l) (a) (i) NaH, THF, reflux, 3 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux, 1 h.

As methyl maslinate (**4**) had two A-ring hydroxyl groups its deoxygenation was also tested by a sequential process protecting selectively the less hindered C-2 hydroxyl group (Scheme 4). Thus, methyl maslinate (**4**) was selectively silylised at C-2 by treatment with TBDMSCl in pyridine yielding a good yield of 2-tertbutyldimethylsilyl methyl maslinate (**22**) which was transformed into the 2$\alpha$-silyl 3$\beta$-xanthyl methyl maslinate (**23**). The typical reduction of **23** gave 2-deprotected 3-desulphured compound **16**, the corresponding 2-tertbutyldimethylsilyl derivative (**24**) and the 2-deprotected 3-xanthyl derivative (**25**). On the other hand, compounds **16** and **24** were usable to an efficient total deoxygenation of the A-ring through the corresponding 2-xanthyl derivative according to the previously detailed reaction conditions. Therefore, the deoxygenation procedure established for the A-ring of methyl maslinate (**4**) in Scheme 4 was accomplished with an acceptable global yield and can be considered as a viable method for this aim.

The last method tested for the total A-ring deoxygenation of methyl maslinate (**4**) was through its 2$\beta$,3$\beta$-epoxy derivative **26** (Scheme 5) (Garcia-Granados et al., 2003a) which was obtained from **4** by Mitsunobu reaction or via tosylation and, later, it was deoxygenated following different pathways (Scheme 5, treatments c, d and e). Initially, compound **26** was treated with trimethylchlorosilane/potassium iodide, giving **7**, and mainly the iodohydrins **19** and **27**. An unsuccessful deoxygenation process of the epoxide **26** was also carried out with tungsten chloride/*n*-butyllithium because the chlorohydrin **28** was the major compound of this reaction (Scheme 5, treatment d).

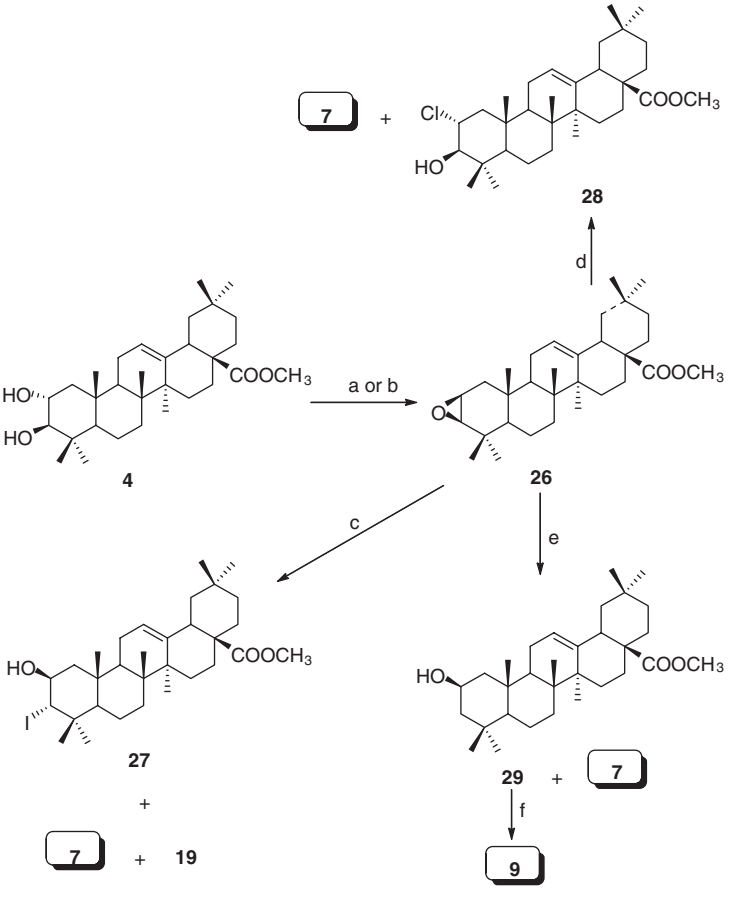





Scheme 4. Controlled deoxygenation of methyl maslinate (**4**). Reagents and conditions: (a) TBDMSCl, py, reflux, 2 h; (b) (i) NaH, THF, reflux, 3 h; (ii) $CS_2$, reflux, 30 min; (iii) $CH_3I$, reflux, 2 h; (c) $H_3PO_2$, AIBN, $Et_3N$, dioxane, reflux, 3 h; (d) $BF_3$, DCM, rt, 3 h.

Lastly, the epoxy derivative (**26**) was treated with titanocene chloride ($Cp_2TiCl$) formed *in situ* by treatment of dicyclopentadienyl titanium dichloride, $Cp_2TiCl_2$, with Mn in THF by a stoichiometric or catalytic procedure (see Section 4). Both methods gave a high yield (around 80%) of the desired 3-deoxy$\Delta^{2,3}$methyl oleanoate, **7** and a small amount of the reutilisable compound **29**. The axial configuration of the hydroxyl group at C-2 of compound **29** was corroborated by the easy dehydration that this compound underwent when treated with phosphorus trichloride oxide in pyridine. The diaxial disposition of the hydroxyl group at C-2 and a hydrogen atom at C-3 allowed easy water elimination and thus the objective compound, 3-deoxymethyl oleanoate (**9**), was obtained in very high yield. Consequently, a complete and valuable deoxygenation of methyl maslinate (**4**) was achieved when its 2$\beta$,3$\beta$-epoxy derivative of methyl was treated with titanocene chloride in both stoichiometric and catalytic conditions.






Scheme 5. Deoxygenation of methyl maslinate (**4**) through its 2$\beta$,2$\beta$-epoxy derivative (**26**). Reagents and conditions: (a) (i) PTSCl, py, rt, 24 h; (ii) Na, MeOH, reflux, 1 h; (b) DEAD, $PPh_3$, DMF, reflux, 2 h; (c) $Me_3SiCl$, KI, 1 h, 0°C or rt or reflux; (d) $WCl_6$, *n*-BuLi, rt, 20 min; (e) $Cp_2TiCl_2$, Mn, THF, rt, 3 h or $Cp_2TiCl_2$, Mn, collidine, $Me_3SiCl$, THF, 3 h, rt; (f) $POCl_3$, py, reflux, 30 min.

## 3. Conclusions

Starting with several derivatives of natural triterpene acids, oleanolic acid and maslinic acid, from the waste products of the olive industry, a deoxygenation of their A-ring was attempted using different procedures. Direct deoxygenation of oleanolic acid (**1**) was achieved with acceptable yield (around 50%) by means of the elimination of its 3-tosyl derivative, whereas methyl oleanoate (**3**) was efficiently deoxygenated through its 3-xanthyl derivative (approximately 70%).

Methyl maslinate (**4**) showed some complexity for the complete deoxygenation of its A-ring because there are two equatorial hydroxyl groups at C-2 and C-3 that were difficult to eliminate. Methyl maslinate (**4**) was satisfactorily deoxygenated (about 60%) through the successive xanthyl derivatives obtained by controlled semisynthesis or using an appropriate protecting group. However, the best procedure with which to deoxygenate methyl maslinate (**4**) was through its 2$\beta$,3$\beta$-epoxy derivative (**26**), which was treated with titanocene chloride in catalytic proportion to give a high yield (around 90%) of 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) and 3-deoxymethyl oleanoate (**9**).



## 4. Experimental

### 4.1. *General*

Measurements of NMR spectra (300.13 MHz $^1$H and 75.47 MHz $^{13}$C) were made in $CDCl_3$ (which also provided the lock signal) using BRUKER AM-300 or ARX-400 spectrometers. The assignments of $^{13}$C chemical shifts were made with the aid of distortionless enhancement by polarisation transfer (DEPT) using a flip angle of 135°. Bruker's programs were used for COSY (45°) and C/H and C/C correlation. IR spectra were recorded on a MATTSON SATELLITE FTIR spectrometer. High-resolution mass spectra were made in a MICROMASS AUTOSPEC-Q spectrometer (EBE geometry). Melting points were determined using a Kofler (Reichter) apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 25°C. All reaction solvents were dried and distilled immediately prior to use; chromatography solvents were distilled prior to use. Commercially available reagents were used without further purification. Silica gel Scharlau 60 (40–60 mm) was used for flash chromatography. $CH_2Cl_2$ or $CHCl_3$ containing increasing amounts of $Me_2CO$ were used as eluents. Analytical plates (silica gel, Merck 60 G) were rendered visible by spraying with $H_2SO_4$-AcOH, followed by heating to 120°C.

### 4.2. *Isolation of oleanolic acid (1) and maslinic acid (2) and obtention of their methyl esters (3) and (4)*

Oleanolic acid (**1**) and maslinic acid (**2**) were isolated from the solid wastes resulting from olive-oil production (Garcia-Granados et al., 1998c), which were macerated and extracted in a Soxhlet apparatus with hexane and EtOAc successively. Hexane extracts were a mixture of oleanolic acid and maslinic acid (80 : 20), whereas this relationship was (20 : 80) for the EtOAc extracts. Both products were purified from these mixtures by CC over silica gel, eluting with a $CHCl_3$-MeOH or $CH_2Cl_2$-$Me_2CO$ mixtures of increasing polarity. Oleanolic acid (**1**) and maslinic acid (**2**) were transformed into the corresponding methyl

esters with ethereal $CH_2N_2$ or NaOH-MeI, and thus methyl 3$\beta$-hydroxy-12-oleanen-28-oate (**3**) and methyl 2$\alpha$,3$\beta$-dihydroxy-12-oleanen-28-oate (**4**) were obtained (Garcia-Granados et al., 2000a).

### 4.3. *Tosylation of oleanolic acid (1)*

To a solution of oleanolic acid (**1**) (500 mg, 1.1 mmol) in py (20 mL), *p*-toluenesulfonyl chloride (731 mg, 3.8 mmol) was added. The reaction mixture was stirred at room temperature for 24 h, diluted with water and extracted with DCM. The organic layer was washed with saturated $KHSO_4$ solution and dried over anhydrous $Na_2SO_4$. The solvent was evaporated at reduced pressure and the residue was chromatographed on a silica gel column to give **5** (625 mg, 95%).



### 4.4. *Tosyl oleanolic acid (5)*

White solid, m.p. 110–112°C; $[\alpha]_D^{25} + 48^\circ$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2930, 2862, 1745, 1690; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.30 and 7.80 (4H each, m, OTs), 5.24 (1H, dd, $J = 3.5$ Hz, H-12), 4.21 (1H, dd, $J_1 = 5.1$ Hz, $J_2 = 11.5$ Hz, H-3), 2.83 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.9$ Hz, H-18), 2.42 (3H, s, OTs), 1.09 (3H, s, Me), 0.90 (3H, s, Me), 0.88 (3H, s, Me), 0.87 (3H, s, Me), 0.78 (3H, s, Me), 0.78 (3H, s, Me), 0.67 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 433.3648 $[M + Na]^+$ (Calcd for $C_{37}H_{54}O_5SNa$, 633.3646).

### 4.5. *Detosylation of tosyl oleanolic acid (5)*

To a solution of compound **5** (600 mg, 0.80 mmol) in DMF (5 mL), sodium acetate (300 mg, 2.2 mmol) was added and the mixture was heated at 120°C for 24 h. The solvent was removed in vacuum and the resultant residue was washed with water and extracted three times with DCM ($3 \times 20$ mL). The organic layer was dried on anhydrous $Na_2SO_4$, concentrated in vacuum and chromatographed on a silica gel column, yielding **6** (205 mg, 42%).

### 4.6. *Deoxyoleanolic acid (6)*

Syrup; $[\alpha]_D^{25} + 74$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3421, 2947, 1693, 146, 758; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.36 (3H, m, H-1, H-2, H-12), 2.82 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.9$ Hz, H-18), 1.25 (3H, s, Me), 1.13 (3H, s, Me), 0.94 (3H, s, Me), 0.93 (3H, s, Me), 0.92 (3H, s, Me), 0.89 (3H, s, Me), 0.77 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 461.3398 $[M + Na]^+$ (Calcd for $C_{30}H_{46}O_2Na$, 461.3395).

### 4.7. *Esterification of 3,12-oleandien-28-oic acid (6)*

To a solution of compound **6** (150 mg, 0.34 mmol) in THF (10 mL), a solution of NaOH (1 mL, 5N) was added and the mixture was refluxed for 3 h. After this time, $CH_3I$ (2 mL) was added and the reaction mixture was shaken for 2 h at rt. The solvent was removed in vacuum and the residue was washed with aqueous 1 N HCl solution and extracted with

Table 1. $^{13}C$ chemical shifts (in $Cl_3CD$, $\delta$ in ppm) for compounds **5**, **6**, **8**, **10**–**12**, **14**–**16**.

| | Compound no. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Carbon | **5** | **6** | **8** | **10** | **11** | **12** | **14** | **15** | **16** |
| 1 | 38.3 | 40.7 | 40.1 | 37.9 | 38.0 | 38.0 | 42.6 | 40.9 | 51.2 |
| 2 | 24.7 | 121.5 | 18.6 | 22.5 | 22.6 | 23.0 | 80.6 | 81.0 | 65.2 |
| 3 | 91.0 | 138.0 | 42.1 | 91.4 | 91.4 | 86.3 | 83.5 | 95.0 | 51.2 |
| 4 | 36.7 | 34.5 | 33.2 | 37.0 | 37.0 | 37.9 | 38.8 | 40.8 | 39.6 |
| 5 | 55.5 | 52.1 | 56.3 | 55.4 | 55.4 | 55.2 | 55.3 | 56.0 | 55.7 |
| 6 | 18.4 | 19.6 | 18.6 | 18.1 | 18.2 | 18.2 | 18.3 | 17.6 | 18.5 |
| 7 | 32.5 | 32.1 | 32.7 | 32.5 | 32.6 | 32.5 | 32.5 | 32.3 | 32.5 |
| 8 | 39.5 | 39.5 | 39.5 | 39.3 | 39.3 | 41.3 | 40.2 | 38.1 | 39.6 |
| 9 | 47.5 | 46.2 | 47.8 | 47.5 | 47.6 | 47.6 | 47.6 | 47.9 | 47.8 |
| 10 | 38.5 | 36.3 | 37.4 | 38.7 | 38.7 | 38.7 | 39.4 | 39.8 | 39.6 |
| 11 | 23.3 | 23.3 | 23.5 | 23.4 | 23.5 | 23.1 | 23.6 | 23.7 | 23.6 |
| 12 | 122.1 | 122.9 | 123.0 | 122.5 | 122.3 | 122.1 | 122.0 | 121.4 | 122.4 |
| 13 | 143.5 | 143.5 | 143.6 | 143.7 | 143.9 | 143.9 | 144.0 | 144.3 | 143.9 |
| 14 | 41.6 | 41.9 | 41.7 | 41.6 | 41.7 | 41.3 | 41.7 | 41.8 | 41.8 |
| 15 | 27.7 | 27.8 | 27.7 | 27.7 | 27.7 | 27.7 | 27.7 | 27.7 | 27.7 |
| 16 | 23.0 | 23.3 | 23.5 | 22.8 | 23.1 | 23.5 | 23.6 | 23.0 | 23.2 |
| 17 | 46.7 | 46.7 | 46.6 | 46.6 | 46.8 | 46.7 | 46.8 | 46.7 | 46.8 |
| 18 | 41.8 | 41.1 | 41.0 | 40.9 | 41.3 | 41.2 | 41.3 | 41.3 | 41.4 |
| 19 | 45.9 | 46.0 | 46.0 | 45.9 | 45.9 | 45.9 | 45.9 | 45.9 | 45.9 |
| 20 | 30.7 | 30.7 | 30.8 | 30.7 | 30.7 | 30.7 | 30.8 | 30.7 | 30.8 |
| 21 | 33.9 | 33.9 | 33.9 | 33.8 | 33.9 | 33.9 | 33.9 | 33.9 | 34.0 |
| 22 | 32.5 | 32.5 | 32.7 | 32.5 | 32.6 | 32.5 | 32.4 | 32.6 | 32.7 |
| Me | 15.1 | 15.6 | 15.3 | 15.4 | 15.4 | 15.4 | 16.3 | 16.1 | 16.5 |
| Me | 16.4 | 16.9 | 17.3 | 17.2 | 16.9 | 16.4 | 16.8 | 17.1 | 17.0 |
| Me | 16.8 | 22.8 | 21.8 | 17.4 | 17.5 | 16.8 | 16.9 | 17.2 | 22.7 |
| Me | 23.7 | 23.6 | 27.7 | 23.6 | 23.7 | 23.7 | 23.7 | 23.7 | 23.7 |
| Me | 25.7 | 25.9 | 26.1 | 26.0 | 26.0 | 25.9 | 26.0 | 26.0 | 26.0 |
| Me | 27.8 | 31.9 | 33.2 | 28.1 | 28.1 | 27.9 | 28.6 | 27.9 | 33.2 |
| Me | 33.2 | 33.2 | 33.2 | 33.1 | 33.2 | 33.1 | 33.2 | 33.1 | 33.2 |
| 28 | 180.9 | 180.7 | 180.6 | 180.8 | 178.4 | 178.4 | 178.3 | 178.1 | 178.3 |
| COO*Me* | | | | | 51.6 | 51.6 | 51.6 | 51.5 | 51.6 |
| Groups in A-ring | 21.5 | | | 18.7 | 18.6 | 114.2 | 19.1 | 193.4 | |
| | 127.7 | | | 215.8 | 215.8 | 158.0 | 216.6 | | |
| | 129.7 | | | | | | | | |
| | 134.9 | | | | | | | | |
| | 134.9 | | | | | | | | |



DCM. The organic layer was neutralised with saturated solution of $NaHCO_3$, dried with anhydrous $Na_2SO_4$, filtered, concentrated in vacuum and chromatographed on a silica gel column to give 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) (135 mg, 90%) (Garcia-Granados et al., 2000a).

### 4.8. *Hydrogenation of 3,12-oleandien-28-oic acid (6)*

Compound **6** (200 mg, 0.46 mmol) in DCM (10 mL) was hydrogenated on Pt/C at rt for 12 h at 4 atm of $H_2$. The mixture reaction was filtered, concentrated in vacuum and chromatographed on a silica gel column to give **8** (199 mg, 98%).

### 4.9. *12-Oleanen-28-oic acid (8)*

White solid, m.p. 233–235°C; $[\alpha]_D^{25} + 69$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2923, 2360, 1689; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.26 (1H, dd, $J_1 = 3.5$ Hz, $J_2 = 3.5$ Hz, H-12), 2.80 (1H, dd, $J_1 = 3.6$ Hz, $J_2 = 13.9$ Hz, H-18), 1.12 (3H, s, Me), 0.91 (3H, s, Me), 0.90 (3H, s, Me), 0.89 (3H, s, Me), 0.84 (3H, s, Me), 0.79 (3H, s, Me), 0.79 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 463.3557 $[M + Na]^+$ (Calcd for $C_{30}H_{48}O_2Na$, 463.3552).

Compound **8** was esterificated under the above mentioned conditions to give 3-deoxy methyl oleanoate (**9**, 93%) (Garcia-Granados et al., 2000a).

### 4.10. *Xanthylation of methyl oleanoate (3) with* sec*-butyllithium*

To a solution of methyl oleanoate (**3**) (500 mg, 1.1 mmol) in THF (25 mL), a solution of *sec*-BuLi (2 mL, 1.4 M in cyclohexane) was added and the reaction was refluxed with stirring for 2 h. After that, $S_2C$ (2 mL, 33 mmol) was added, the reaction mixture stirred for 30 min at reflux, MeI (1 mL, 16 mmol) was added and the mixture was again refluxed for 2 h. The mixture was neutralised with aqueous 1 N HCl solution and extracted with DCM. The organic layer was dried with anhydrous $Na_2SO_4$ and concentrated in vacuum. The residue was chromatographed on a silica gel column to provide **10** (58 mg, 10%) and **11** (357 mg, 60%).

### 4.11. *Xanthyl-12-oleanen-28-oic acid (10)*

White solid, m.p. 177–179°C; $[\alpha]_D^{25} + 29$ (c 0.6, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2946, 2863, 1694, 1238, 1058; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.25 (1H, dd, $J_1 = 4.9$ Hz, $J_2 = 12.0$ Hz, H-3), 5.20 (1H, dd, $J_1 = 3.4$ Hz, $J_2 = 3.4$ Hz, H-12), 2.81 (1H, dd, $J_1 = 4.1$ Hz, $J_2 = 13.8$ Hz, H-18), 2.54 (3H, s, $CSSCH_3$), 1.12 (3H, s, Me), 0.96 (3H, s, Me), 0.95 (3H, s, Me), 0.92 (3H, s, Me), 0.92 (3H, s, Me), 0.90 (3H, s, Me), 0.74 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 569.3099 $[M + Na]^+$ (Calcd for $C_{32}H_{50}O_3S_2Na$, 569.3099).

### 4.12. *Xanthyl methyl oleanoate (11)*

White solid, m.p. 202–204°C; $[\alpha]_D^{25} + 48$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2922, 1724, 1233, 1058; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.31 (1H, dd, $J_1 = 4.6$ Hz, $J_2 = 10.8$ Hz, H-3), 5.26 (1H, dd, $J_1 = 3.6$ Hz, $J_2 = 3.6$ Hz, H-12), 3.61 (3H, s, COO*Me*), 2.84 (1H, dd, $J_1 = 4.6$ Hz, $J_2 = 13.6$ Hz, H-18), 2.53 (3H, s, CSS*Me*), 1.11 (3H, s, Me), 0.95 (3H, s, Me), 0.95 (3H, s, Me), 0.91 (3H, s, Me), 0.91 (3H, s, Me), 0.88 (3H, s, Me), 0.71 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 583.3258 $[M + Na]^+$ (Calcd for $C_{33}H_{52}O_3S_2Na$, 583.3255).

### 4.13. *Xanthylation of methyl oleanoate (3) with sodium hydride*

Methyl oleanoate (**3**) (450 mg, 0.96 mmol) in THF (20 mL) was treated with NaH (110 mg, 4.8 mmol) at reflux for 3 h. After that, $S_2C$ (2 mL, 33 mmol) was added, the reaction mixture shaken for 30 min at reflux, MeI (1 mL, 16 mmol) was added and the mixture was again refluxed for 2 h. The mixture was neutralised with aqueous 1 N HCl solution and

extracted with DCM. The organic layer was dried with anhydrous $Na_2SO_4$, concentrated in vacuum and purified on a silica gel column to obtain **11** (415 mg, 77%).

Xanthate (**10**) was esterificated according to the previously mentioned reaction conditions to obtain **11** (95%).

### 4.14. *Trifylation of methyl oleanoate (12)*

Methyl oleanoate (**3**) (500 mg, 1.1 mmol) in py (10 mL) was treated with trifluoroacetic anhydride (0.5 mL, 2.75 mmol) and the reaction mixture was stirred at rt for 24 h. The mixture was washed with aqueous 1N HCl solution, neutralised with saturated solution of $NaHCO_3$, and extracted with DCM. The organic layer was dried on anhydrous $Na_2SO_4$ and concentrated in vacuum. The residue was purified on a silica gel column to obtain **12** (579 mg, 93%).



### 4.15. *Trifyl methyl oleanoate (12)*

White solid, m.p. 171–172°C; $[\alpha]_D^{25} + 48$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2950, 1777, 1724, 1218, 773; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.24 (1H, dd, $J_1 = J = 3.4$ Hz, H-12), 4.65 (1H, dd, $J_1 = 4.9$ Hz, $J_2 = 11.3$ Hz, H-3), 3.58 (3H, s, COO*Me*), 2.83 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 13.8$ Hz, H-18), 1.09 (3H, s, Me), 0.91 (3H, s, Me), 0.88 (3H, s, Me), 0.87 (3H, s, Me), 0.86 (3H, s, Me), 0.69 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 589.3483 $[M + Na]^+$ (Calcd for $C_{33}H_{49}O_2F_3Na$, 589.3481).

### 4.16. *Oxidation of methyl oleanoate (3)*

Jones reagent was added dropwise to a stirred solution of methyl oleanoate (**3**) (200 mg, 0.42 mmol) in acetone at 0°C until an orange-brown colour persisted. Methanol was then added and the reaction mixture was diluted with water and extracted with DCM. The organic layer was dried over anhydrous $Na_2SO_4$, evaporated to dryness and chromatographed on a silica gel column to obtain **13** (196 mg, 95%) (Garcia-Granados et al., 2000a).

### 4.17. *Reduction of xanthate (11) with $H_3PO_2$*

Xanthate (**11**) (95 mg, 0.17 mmol) in dioxane (5 mL), was treated with $Et_3N$ (0.05 mL, 0.3 mmol), $H_3PO_2$ (0.1 mL, 0.9 mmol) and AIBN (15 mg in 3 mL of dioxane) with stirring at reflux for 3 h. The reaction mixture was washed with water and extracted with diethyl ether. The organic layer was dried with anhydrous $Na_2SO_4$, concentrated in vacuum and purified on a silica gel column giving 3-deoxy methyl oleanoate (**9**) (67 mg, 87%).

### 4.18. *Reduction of xanthate (11) with $(Bu_3Sn)_2O$/PMHS*

To a solution of xanthate (**11**) (150 mg, 0.3 mmol) in toluene (3 mL), PMHS (0.1 mL, 1.006 g $mL^{-1}$), AIBN (10 mg), *n*-butanol (0.2 mL) and $(Bu_3Sn)_2O$ (0.01 mL, 1.170 g $mL^{-1}$) were added. The mixture was stirred under argon atmosphere at 80°C for 3 h, after that AIBN (20 mg) and $(Bu_3Sn)_2O$ (0.01 mL) were again added and the reaction mixture was

stirred at rt for 3 h. The reaction mixture was diluted with THF and an aqueous 2N NaOH solution (2 mL) was added. The mixture was extracted with ethyl ether, the organic layer was dried with anhydrous $Na_2SO_4$ and the solvent concentrated in vacuum. The residue was purified on a silica gel column to give **9** (110 mg, 80%).

### 4.19. *Reduction of triflate (12) with $Ph_2SiH_2$*

A mixture of triflate (**12**) (200 mg, 0.37 mmol), $Ph_2SiH_2$ (211 mg, 1.11 mmol) and ($^tBuO)_2$ (0.07 mL, 0.37 mmol) was heated at 130°C and stirred for 24 h. The reaction mixture was diluted with water and extracted with DCM. The organic extract was dried with anhydrous $Na_2SO_4$, concentrated in vacuum and purified on a silica gel column to obtain methyl 3-deoxyoleanoate (**9**) (55 mg, 30%).



### 4.20. *Huang-Minlon reduction of 3-oxomethyl oleanoate (13)*

A mixture of 3-oxoderivative **13** (50 mg, 0.11 mmol), KOH (12 mg, 0.33 mmol) and $N_2H_2$ (1 mL in 15 mL of ethyleneglycol) was stirred and refluxed for 5 h. The reaction mixture was diluted with DCM, washed with water and neutralised with a saturated solution of $KHSO_3$. The organic layer was dried with anhydrous $Na_2SO_4$ and concentrated in vacuum. The residue was purified on a silica gel column to provide methyl 3-deoxyoleanoate (**9**) (6 mg, 11%).

### 4.21. *Xanthylation of methyl maslinate (4) and reduction of its derivatives*

Methyl maslinate (**4**, 500 mg, 1.1 mmol) was xanthylated under similar conditions and after work-up, compounds **14** (237 mg, 40%) and **15** (272 mg, 50%) were obtained. Similarly, when the xanthylation of **4** was carried out with sodium hydride and after work-up, products **14** (355 mg, 60%) and **15** (165 mg, 30%) were formed.

Compound **14**: White solid, m.p. 164–166°C; $[\alpha]_D^{25} + 4$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2947, 2360, 1724, 1232, 1053; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.83 (1H, ddd, $J_1 = 4.5$ Hz, $J_2 = 10.0$ Hz, $J_3 = 10.7$ Hz, H-2), 5.25 (1H, dd, $J_1 = 3.6$ Hz, $J_2 = 3.6$ Hz, H-12), 3.61 (3H, s, COO$CH_3$), 3.44 (1H, d, $J = 10.0$ Hz, H-3), 2.84 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 13.8$ Hz, H-18), 2.55 (1H, s, CSS$CH_3$), 1.11 (3H, s, Me), 1.07 (3H, s, Me), 0.94 (3H, s, Me), 0.91 (3H, s, Me), 0.88 (3H, s, Me), 0.88 (3H, s, Me), 0.71 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 599.3206 $[M + Na]^+$ (Calcd for $C_{33}H_{52}O_4S_2Na$, 599.3204).

Compound **15**: White solid, m.p. 245–247°C; $[\alpha]_D^{25} + 85$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2948, 1802, 1724, 1290; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.25 (1H, dd, $J_1 = 3.6$ Hz, $J_2 = 3.6$ Hz, H-12), 4.50 (1H, ddd, $J_1 = 4.4$ Hz, $J_2 = 11.5$ Hz, $J_3 = 12.4$ Hz, H-2), 3.88 (1H, d, $J = 12.4$ Hz, H-3), 3.59 (3H, s, COO$CH_3$), 2.84 (1H, dd, $J_1 = 4.4$ Hz, $J_2 = 13.9$ Hz, H-18), 2.24 (1H, dd, $J_1 = 4.1$ Hz, $J_2 = 11.5$ Hz, H-1$\beta$, 1.13 (3H, s, Me), 1.11 (3H, s, Me), 1.02 (3H, s, Me), 0.95 (3H, s, Me), 0.90 (3H, s, Me), 0.87 (3H, s, Me), 0.72 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS (*m*/*z*) 551.3171 $[M + Na]^+$ (Calcd for $C_{32}H_{48}O_4SNa$, 551.3171).

Reduction of xanthate (**14**) with $H_3PO_2$ and $(Bu_3Sn)_2O$ gave similar yields of methyl oleanoate (**3**) (80–85%). Reduction of thiocarbonate (**15**) with $(Bu_3Sn)_2O$ yielded methyl

oleanoate (**3**, 29%), methyl maslinate (**4**, 33%), 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**, 20%) and (**16**, 9%).

Compound **16**: Syrup; $[\alpha]_D^{25}+23$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3385, 2947, 2874, 1725, 1458; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.28 (1H, dd, $J_1=3.6$ Hz, $J_2=3.6$ Hz, H-12), 3.87 (1H, dddd, $J_1=4.3$ Hz, $J_2=4.3$ Hz, $J_3=11.2$ Hz, $J_4=11.2$ Hz, H-2), 3.60 (3H, s, COO$CH_3$), 2.85 (1H, dd, $J_1=4.2$ Hz, $J_2=13.8$ Hz, H-18), 1.12 (3H, s, Me), 0.93 (3H, s, Me), 0.92 (3H, s, Me), 0.92 (3H, s, Me), 0.89 (3H, s, Me), 0.85 (3H, s, Me), 0.71 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 1; HRLSIMS ($m/z$) 493.3652 $[M+Na]^+$ (Calcd for $C_{33}H_{50}O_5Na$, 493.3658).

Likewise, compound **16** was xanthylated at C-2 to form derivative **17** (80%) and its reduction with $H_3PO_2$ led to compound **9** (80%).

Compound **17**: White solid, m.p. 192–194°C; $[\alpha]_D^{25}$ +11 (c 0.7, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2946, 1728, 1460, 1230, 1053; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.88 (1H, dddd, $J_1=4.2$ Hz, $J_2=8.4$ Hz, $J_3=11.6$ Hz, $J_4=15.9$ Hz, H-2), 5.26 (1H, dd, $J_1=J_2=3.6$ Hz, H-12), 3.61 (3H, s, COO$CH_3$), 2.85 (1H, dd, $J_1=4.5$ Hz, $J_2=14.0$ Hz, H-18), 2.52 (3H, s, $CH_3$S–), 1.12 (3H, s, Me), 1.01 (3H, s, Me), 0.96 (3H, s, Me), 0.92 (3H, s, Me), 0.89 (3H, s, Me), 0.89 (3H, s, Me), 0.71 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS $m/z$ 583.3253 $[M+Na]^+$ (Calcd for $C_{33}H_{52}O_3S_2Na$, 583.3256).

### 4.22. *Tosylation of methyl maslinate (4) and deoxygenation of its derivative*

Methyl maslinate (**4**, 500 mg, 1.02 mmol) was dissolved in py (10 mL) and treated with TsCl (300 mg) at rt with stirring for 24 h. The reaction mixture was diluted with water and extracted with DCM. The organic layer was washed with saturated $KHSO_4$ solution and dried over anhydrous $Na_2SO_4$. The solvent was evaporated at reduced pressure and the residue was chromatographed on a silica gel column to give **18** (600 mg, 90%) (Garcia-Granados et al., 2000b). Treatment of **18** with TMSCl/KI yielded 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) (70 mg, 20%) and **19** (349 mg, 75%).

Compound **19**: Syrup; $[\alpha]_D^{25}+22$ (c 0.5, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3424, 2946, 1722, 1162; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.26 (1H, dd, $J_1=3.6$ Hz, $J_2=3.6$ Hz, H-12), 4.57 (1H, ddd, $J_1=4.2$ Hz, $J_2=10.7$ Hz, $J_3=12.8$ Hz, H-2), 3.60 (3H, s, COO$CH_3$), 3.32 (1H, dd, $J=3.4$ Hz, $J_2=10.7$ Hz, H-3), 2.84 (1H, dd, $J_1=4.2$ Hz, $J_2=13.8$ Hz, H-18), 2.41 (1H, dd, $J_1=4.2$ Hz, $J_2=12.9$ Hz, H-1$\beta$), 1.11 (3H, s, Me), 1.08 (3H, s, Me), 0.94 (3H, s, Me), 0.91 (3H, s, Me), 0.86 (3H, s, Me), 0.82 (3H, s, Me), 0.69 (3H, s, Me). $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS ($m/z$) 619.2628 $[M+Na]^+$ (Calcd for $C_{31}H_{49}O_3INa$, 619.2624).

Methyl maslinate (**4**) was also oxygenated with Dess–Martin reagent to give **20** (79%) (Garcia-Granados et al., 2000b); its reduction with $LiAlH_4$ gave **21** (95%), which could not be deoxygenated.

Compound **21**: White solid, m.p. 133–135°C; $[\alpha]_D^{25}+23$ (c 0.5, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3421, 2948, 2865, 1733, 1460, 1364; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.18 (1H, dd, $J_1=3.5$ Hz, $J_2=3.5$ Hz, H-12), 3.67 (1H, ddd, $J_1=6.7$ Hz, $J_2=6.7$ Hz, $J_3=6.7$ Hz, H-2), 3.53 (1H, d, $J=11.0$ Hz, H-28a), 3.19 (1H, d, $J=6.7$ Hz, H-3), 3.18 (1H, d, $J=11.0$ Hz, H-28b), 1.23 (3H, s, Me), 1.13 (3H, s, Me), 0.99 (3H, s, Me), 0.98 (3H, s, Me), 0.93

Table 2. $^{13}C$ chemical shifts (in $Cl_3CD$, $\delta$ in ppm) for compounds **17**, **19**, **21**–**24**, **27**–**29**.

| | Compound no. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Carbon | **17** | **19** | **21** | **22** | **23** | **24** | **27** | **28** | **29** |
| 1 | 44.5 | 52.8 | 46.5 | 46.0 | 45.9 | 46.0 | 47.3 | 48.9 | 45.9 |
| 2 | 79.9 | 41.8 | 71.1 | 70.8 | 67.9 | 79.6 | 69.2 | 64.1 | 67.7 |
| 3 | 44.5 | 83.6 | 78.5 | 83.2 | 93.3 | 38.5 | 64.9 | 82.9 | 47.3 |
| 4 | 35.3 | 39.5 | 41.9 | 39.5 | 40.6 | 31.0 | 38.3 | 40.4 | 32.8 |
| 5 | 55.9 | 55.5 | 55.2 | 55.3 | 55.0 | 55.4 | 51.6 | 55.3 | 53.6 |
| 6 | 18.4 | 18.4 | 18.2 | 18.2 | 18.2 | 18.6 | 21.6 | 18.3 | 19.0 |
| 7 | 32.5 | 32.4 | 32.6 | 32.4 | 32.6 | 32.8 | 32.4 | 32.4 | 32.5 |
| 8 | 39.5 | 40.7 | 38.2 | 38.5 | 38.0 | 37.0 | 37.5 | 39.4 | 39.7 |
| 9 | 47.8 | 47.4 | 48.1 | 47.6 | 48.3 | 47.8 | 48.2 | 47.5 | 48.1 |
| 10 | 39.6 | 41.5 | 37.0 | 38.8 | 39.4 | 39.4 | 39.6 | 39.6 | 37.9 |
| 11 | 23.1 | 23.1 | 23.1 | 23.1 | 23.1 | 23.2 | 23.2 | 23.1 | 23.2 |
| 12 | 122.2 | 122.0 | 122.5 | 122.1 | 122.0 | 122.5 | 122.4 | 122.0 | 122.7 |
| 13 | 143.9 | 144.0 | 144.3 | 144.1 | 144.1 | 143.9 | 143.8 | 144.0 | 143.8 |
| 14 | 41.8 | 41.8 | 40.0 | 41.4 | 41.8 | 41.7 | 41.9 | 41.8 | 41.9 |
| 15 | 27.7 | 27.7 | 25.5 | 27.7 | 27.7 | 27.7 | 27.7 | 27.7 | 27.7 |
| 16 | 23.6 | 23.5 | 23.7 | 23.6 | 23.5 | 23.5 | 23.4 | 23.5 | 23.5 |
| 17 | 46.8 | 46.8 | 46.8 | 46.8 | 46.8 | 46.8 | 46.9 | 46.8 | 46.8 |
| 18 | 41.4 | 41.3 | 42.4 | 41.4 | 41.4 | 41.4 | 41.5 | 41.3 | 41.5 |
| 19 | 46.0 | 45.9 | 44.3 | 47.2 | 47.5 | 46.0 | 45.9 | 45.9 | 46.6 |
| 20 | 30.8 | 30.8 | 31.0 | 30.7 | 30.8 | 30.8 | 30.8 | 30.8 | 30.8 |
| 21 | 32.5 | 32.5 | 31.1 | 32.6 | 32.4 | 32.5 | 32.4 | 32.4 | 32.5 |
| 22 | 33.6 | 33.9 | 34.2 | 33.9 | 33.9 | 34.0 | 34.0 | 33.9 | 34.0 |
| Me | 16.3 | 15.6 | 16.5 | 16.6 | 16.7 | 14.1 | 16.5 | 16.1 | 16.8 |
| Me | 17.0 | 16.2 | 16.8 | 16.9 | 16.9 | 15.4 | 16.5 | 16.6 | 18.5 |
| Me | 22.5 | 17.0 | 17.4 | 17.0 | 18.4 | 16.2 | 20.4 | 17.0 | 23.7 |
| Me | 23.7 | 23.7 | 23.7 | 23.7 | 23.7 | 16.9 | 23.7 | 23.7 | 24.7 |
| Me | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 23.7 | 24.2 | 26.0 | 26.0 |
| Me | 33.2 | 29.3 | 31.8 | 28.8 | 28.8 | 28.6 | 26.0 | 29.0 | 33.2 |
| Me | 33.4 | 33.2 | 33.32 | 33.2 | 33.2 | 33.2 | 33.2 | 33.2 | 33.2 |
| 28 | 178.3 | 178.3 | 69.7 | 178.3 | 178.3 | 178.3 | 178.4 | 178.3 | 178.3 |
| COO*Me* | 51.6 | 51.7 | | 51.6 | 51.6 | 51.5 | 51.6 | 51.6 | 51.6 |
| Groups in A-ring | 18.8 | | | −4.5 | −4.8 | −4.8 | | | |
| | 215.2 | | | −3.8 | −4.3 | −3.7 | | | |
| | | | | 18.1 | 19.0 | 18.2 | | | |
| | | | | 25.9 | 18.9 | 26.0 | | | |
| | | | | | 25.7 | | | | |
| | | | | | 216.8 | | | | |

(3H, s, Me), 0.86 (3H, s, Me), 0.85 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS (*m*/*z*) 481.3659 $[M + Na]^+$ (Calcd for $C_{30}H_{50}O_3Na$, 481.3658).

### 4.23. *Silylation and xanthylation of methyl maslinate (4)*

Methyl maslinate (**4**) (1.45 g, 3 mmol) was dissolved in py (10 mL) and TBDMSCl (900 mg, 6 mmol) was added. The reaction mixture was refluxed for 2 h and extracted with DCM. The organic layer was washed with aqueous 1 N HCl solution, neutralised with saturated $NaHCO_3$ solution and dried over anhydrous $Na_2SO_4$. The solvent was evaporated at

reduced pressure and the residue was chromatographed on a silicagel column to give **22** (1.7 g, 95%). This compound was xanthylated in the usual manner to give **23** (70%).

Compound **22**: White solid, m.p. 180–182°C; $[\alpha]_D^{25}$ +17 (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3596, 2949, 1726, 1462, 1258, 1078, 838, 758; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.27 (1H, dd, $J_1 = J_2 = 3.7$ Hz, H-12), 3.67 (1H, ddd, $J_1 = 4.5$ Hz, $J_2 = 9.2$ Hz, $J_3 = 11.1$ Hz, H-2), 3.60 (3H, s, COO$CH_3$), 2.99 (1H, d, $J = 9.2$ Hz, H-3), 2.84 (1H, dd, $J_1 = 4.4$ Hz, $J_2 = 13.9$ Hz, H-18), 1.11 (3H, s, 3H-27), 1.03 (3H, s, 3H-23), 0.94 (3H, s, 3H-25), 0.91 (3H, s, 3H-30), 0.87 (3H, s, 3H-29), 0.87 (9H, s, $(CH_3)_3$C–), 0.81 (3H, s, 3H-24), 0.70 (3H, s, 3H-26), 0.08 (3H, s, $CH_3$Si–), 0.06 (3H, s, $CH_3$Si–); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS $m/z$ 623.4480 $[M + Na]^+$ (Calcd for $C_{37}H_{64}SiO_4Na$, 623.4472).

Compound **23**: White solid, m.p. 256–258°C; $[\alpha]_D^{25}$ + 10 (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2948, 1728, 1462, 1236, 1054; $^1H$ RMN (300 MHz, $CDCl_3$): $\delta$ 5.60 (1H, d, $J = 9.6$ Hz, H-3), 5.27 (1H, dd, $J_1 = J_2 = 3.7$ Hz, H-12), 3.98 (1H, ddd, $J_1 = 4.7$ Hz, $J_2 = 9.6$ Hz, $J_3 = 11.0$ Hz, H-2), 3.61 (3H, s, COO$CH_3$), 2.85 (1H, dd, $J_1 = 4.1$ Hz, $J_2 = 14.0$ Hz, H-18), 2.54 (3H, S, $CH_3$S–), 1.11 (3H, s, Me), 0.99 (3H, s, Me), 0.91 (3H, s, Me), 0.91 (3H, s, Me), 0.89 (3H, s, Me), 0.88 (3H, s, Me), 0.81 (9H, s, $(CH_3)_3$C–), 0.71 (3H, s, Me), 0.03 (3H, s, $CH_3$Si–), 0.01 (3H, s, $CH_3$Si–); $^{13}C$ RMN (75 MHz, $CDCl_3$): Table 2; HRLSIMS $m/z$ 713.4069 $[M + Na]^+$ (Calcd for $C_{39}H_{66}O_4SiNaS_2$, 713.4061).

### 4.24. *Reduction of xanthate (23) with $H_3PO_2$*

The usual reduction of xanthate (**23**) gave **16** (85 mg, 40%), **24** (77 mg, 33%) and **25** (23 mg, 10%).

Compound **24**: White solid, m.p. 268–270°C; $[\alpha]_D^{25}$ +31 (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2928, 1732, 1463, 1254, 1162, 1099, 1073, 836; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.27 (1H, dd, $J_1 = J_2 = 3.5$ Hz, H-12), 3.61 (3H, s, COO$CH_3$), 3.17 (1H, dd, $J_1 = 4.6$ Hz, $J_2 = 11.0$ Hz, H-2), 2.85 (1H, dd, $J_1 = 4.5$ Hz, $J_2 = 13.8$ Hz, H-18), 1.11 (3H, s, Me), 0.91 (3H, s, Me), 0.89 (3H, s, Me), 0.89 (3H, s, Me), 0.89 (3H, s, $(CH_3)_3$C–), 0.87 (3H, s, Me), 0.87 (6H, s, $(CH_3)_3$C–), 0.73 (3H, s, Me), 0.70 (3H, s, Me), 0.02 (6H, s, $CH_3$Si–); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS, $m/z$ 607.4519 $[M + Na]^+$ (Calcd for $C_{37}H_{64}O_3SiNa$, 607.4522).

Compound **25**: Syrup; $[\alpha]_D^{25}$ +58 (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3439, 2947, 1727, 1457, 1235, 1055, 758; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.54 (1H, d, $J = 9.9$ Hz, H-3), 5.27 (1H, dd, $J_1 = J_2 = 3.5$ Hz, H-12), 4.01 (1H, ddd, H-2), 3.61 (3H, s, COO$CH_3$), 2.85 (1H, dd, $J_1 = 4.3$ Hz, $J_2 = 13.9$ Hz, H-18), 2.59 (3H, s, $CH_3$S–), 1.12 (3H, s, Me), 1.00 (3H, s, Me), 0.95 (3H, s, Me), 0.92 (3H, s, Me), 0.91 (3H, s, Me), 0.89 (3H, s, Me), 0.71 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS $m/z$ 599.3209 $[M + Na]^+$ (Calcd for $C_{33}H_{52}O_4NaS_2$, 599.3198).

### 4.25. *Epoxidation of methyl maslinate (4)*

Epoxy derivative **26** was obtained by Mitsunobu reaction or via tosylation according to the routes given in the literature (Garcia-Granados et al., 2003a) in a very good yield. Deoxygenation of **26** with $Me_3SiCl$-KI gave 3-deoxy$\Delta^{2,3}$methyl oleanoate **7**, (12%), **19** (80%) and **27** (7%).

Compound **27**: Syrup; $[\alpha]_D^{25}$ +66 (c 0.5, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3402, 2943, 1723, 1124: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.29 (1H, dd, $J_1 = 3.6$ Hz, $J_2 = 3.6$ Hz, H-12), 4.73 (1H, d, $J = 4.8$ Hz, H-3), 4.01 (1H, ddd, $J_1 = 4.8$ Hz, $J_2 = 9.4$ Hz, $J_3 = 10.5$ Hz, H-2), 3.61 (3H, s, COO$CH_3$), 2.85 (1H, dd, $J_1 = 4.5$ Hz, $J_2 = 14.4$ Hz, H-18), 1.14 (3H, s, Me), 1.12 (3H, s, Me), 1.09 (3H, s, Me), 1.03 (3H, s, Me), 0.91 (3H, s, Me), 0.89 (3H, s, Me), 0.71 (3H, s, Me). $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS (*m*/*z*) 619.2623 $[M + Na]^+$ (Calcd for $C_{31}H_{49}O_3INa$, 619.2624).

Deoxygenation of **26** with $WCl_6$/n-BuLi yielded 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) (8 mg, 8%) and **28** (50 mg, 46%).

Compound **28**: Yellow solid, m.p. 185–187°C; $[\alpha]_D^{25} + 50$ (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$ 3404, 2947, 1724, 1125; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.27 (1H, dd, $J_1 = J_2 = 3.6$ Hz, H-12), 4.12 (1H, ddd, $J_1 = 4.3$ Hz, $J_2 = 10.2$ Hz, $J_3 = 12.2$ Hz, H-2), 3.61 (3H, s, COO$CH_3$), 3.17 (1H, d, $J = 10.2$ Hz, H-3), 2.85 (1H, dd, $J_1 = 4.5$ Hz, $J_2 = 13.8$ Hz, H-18), 1.12 (3H, s, Me), 1.08 (3H, s, Me), 0.96 (3H, s, Me), 0.91 (3H, s, Me), 0.89 (3H, s, Me), 0.83 (3H, s, Me), 0.70 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS *m*/*z* 527.3269 $[M + Na]^+$ (Calcd for $C_{31}H_{49}O_3ClNa$, 527.3268).



### 4.26. *Deoxygenation of 2β,3β-epoxy methyl maslinate (26) with $Cp_2TiCl$*

*A. Stoichiometric procedure*: To a solution of $Cp_2TiCl_2$ (700 mg, 3 equiv) and Mn (1000 mg, 8 equiv) in THF (20 mL), compound **26** (468 mg, 1 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 3 h at rt, washed with aqueous 1N HCl solution and extracted with DCM. The organic layer was dried over anhydrous $Na_2SO_4$, concentrated in vacuum and purified on a silica gel column yielding 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) (370 mg, 82%) and **29** (28 mg, 6%).

### 4.27. *2-Epi 3-deoxy methyl maslinate (29)*

White solid, m.p. 190–192°C; $[\alpha]_D^{25}$ +22 (c 1, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3423, 2947, 2865, 1723, 1462, 1034; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.27 (1H, dd, $J_1 = 3.8$ Hz, $J_2 = 7.4$ Hz, H-12), 4.05 (1H, dddd, $J_1 = 5.4$ Hz, $J_2 = 5.4$ Hz, $J_3 = 5.4$, $J_4 = 5.4$ Hz, H-2), 3.59 (3H, s, COO$CH_3$), 2.83 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.8$ Hz, H-18), 1.15 (3H, s, Me), 1.10 (3H, s, Me), 0.98 (3H, s, Me), 0.90 (3H, s, Me), 0.90 (3H, s, Me), 0.87 (3H, s, Me), 0.71 (3H, s, Me); $^{13}C$ NMR (75 MHz, $CDCl_3$): Table 2; HRLSIMS (*m*/*z*) (Calcd for $C_{31}H_{50}O_3Na$ 493.3657 $[M + Na]^+$, found 493.3659).

*B. Catalytic procedure*: A solution of $Cp_2TiCl_2$ (22 mg, 0.0086 mmol) and Mn (186 mg, 8 equiv) in THF (5 mL) was maintained at rt for 15 min until it gave a green colour. After that, compound **26** (200 mg, 0.42 mmol) in THF (5 mL) and a mixture of $Me_3SiCl$ (0.2 mL, 0.17 mmol) and collidine (0.4 mL, 0.29 mmol) in THF (2 mL) were added. The reaction mixture was stirred for 3 h at rt in argon atmosphere, washed with aqueous 1N HCl solution and extracted with DCM. The organic layer was dried over anhydrous $Na_2SO_4$, concentrated in vacuum and purified on a silica gel column yielding 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) (146 mg, 77%) and **29** (22 mg, 11%).

### 4.28. *Dehydration of compound 29 with $POCl_3$*

Compound **29** (200 mg, 0.4 mmol) was dissolved in py (5 mL) and 1 mL de $POCl_3$ was added. The reaction mixture was refluxed for 30 min, washed with cold water and an aqueous saturated solution of $NaHSO_4$, and then extracted with DCM. The organic layer was dried over anhydrous $Na_2SO_4$, concentrated in vacuum and purified on a silica gel column, yielding 3-deoxy$\Delta^{2,3}$methyl oleanoate (**7**) (166 mg, 92%).

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## References

Abad, A., Agullo, C., Arno, M., Marin, M.L., & Zaragoza, R.J. (1997). First diastereoselective synthesis of (−)-thyrsiflorin A methyl ester. *Synlett,* 574–576.

Barton, D.H.R., Dorchak, J., & Jaszberenyi, J.Cs. (1992b). The invention of radical reactions. Part XXIV. Relative rates of acylation and radical deoxygenation of secondary alcohols. *Tetrahedron, 48*, 7435–7446.

Barton, D.H.R., Jang, D.O., & Jaszberenyi, J.Cs. (1991a). Towards dideoxynucleosides: The silicon approach. *Tetrahedron Letters, 32*, 2569–2572.

Barton, D.H.R., Jang, D.O., & Jaszberenyi, J.Cs. (1991b). Radical deoxygenation of secondary and primary alcohols with phenylsilane. *Synlett,* 435–438.

Barton, D.H.R., Jang, D.O., & Jaszberenyi, J.Cs. (1991c). Radical deoxygenation of secondary and primary alcohols with phenylsilane. *Tetrahedron Letters, 32*, 7187–7190.

Barton, D.H.R., Jang, D.O., & Jaszberenyi, J.Cs. (1992a). Hypophosphorous acid and its salts: New reagents for radical chain deoxygenation, dehalogenation and deamination. *Tetrahedron Letters, 33*, 5709–5712.

Barton, D.H.R., Jang, D.O., & Jaszberenyi, J.Cs. (1993). The invention of radical reactions. Part XXXI. Diphenylsilane: A reagent for deoxygenation of alcohols via their thiocarbonyl derivatives, deamination via isonitriles, and dehalogenation of bromo and iodo compounds by radical chain chemistry. *Tetrahedron, 33*, 7193–7214.

Barton, D.H.R., & McCombie, S.W. (1975). New method for the deoxygenation of secondary alcohols. *Journal of the Chemical Society, Perkin Transactions I, 5*, 1574–1585.

Bianchi, G., Pozzi, N., & Vlahov, G. (1994). Pentacyclic triterpene acids in olives. *Phytochemistry, 37*, 205–207.

Caputo, R., Mangoni, L., Neri, O., & Palumbo, G. (1981). Direct conversion of oxiranes to alkenes by chlorotrimethylsilane and sodium iodide. *Tetrahedron Letters, 22*, 3551–3552.

Cuerva, J.M., Campaña, A.G., Justicia, J., Rosales, A., Oller-Lopez, J.L., Robles, R., et al. (2006). Water: The ideal hydrogen-atom source in free-radical chemistry mediated by Ti III and other single-electron-transfer metals? *Angewandte Chemie International Edition, 45*, 5522–5526.

Gansäuer, A., Pierobon, M., & Bluhm, H. (1998). Catalytic, highly regio- and chemoselective generation of radicals from epoxides: Titanocene dichloride as an electron transfer catalyst in transition metal catalyzed radical reactions. *Angewandte Chemie International Edition, 37*, 101–103.

Garcia-Granados, A., Dueñas, J., Moliz, J.N., Parra, A., Perez, F.L., Dobado, J.A., et al. (2000a). Semi-synthesis of triterpene A-ring derivatives from oleanolic and maslinic acids. Theoretical and experimental $^{13}C$ chemical shifts. *Journal of Chemical Research, Miniprint, 2*, 326–339.

Garcia-Granados, A., Dueñas, J., Moliz, J.N., Parra, A., Perez, F.L., Dobado, J.A., et al. (2000b). Semi-synthesis of triterpene A-ring derivatives from oleanolic and maslinic acids. Part II. Theoretical and experimental $^{13}C$ chemical shifts. *Journal of Chemical Research, Miniprint, 5*, 653–670.

Garcia-Granados, A., Lopez, P.E., Melguizo, E., Moliz, J.N., Parra, A., & Simeo, Y. (2003a). Epoxides, cyclic sulfites, and sulfate from natural pentacyclic triterpenoids: Theoretical calculations and chemical transformations. *Journal of Organic Chemistry, 68*, 4833–4844.

Garcia-Granados, A., Lopez, P.E., Melguizo, E., Parra, A., & Simeo, Y. (2003b). Degradation of triterpenic compounds from olive-pressing residues. Synthesis of trans-decalin type chiral synthons. *Tetrahedron Letters, 44*, 6673–6677.

Garcia-Granados, A., Lopez, P.E., Melguizo, E., Parra, A., & Simeo, Y. (2004a). Partial synthesis of C-ring derivatives from oleanolic and maslinic acids. Formation of several triene systems by chemical and photochemical isomerization processes. *Tetrahedron, 60*, 1491–1503.

Garcia-Granados, A., Lopez, P.E., Melguizo, E., Parra, A., & Simeo, Y. (2004b). Oxidation of several triterpenic diene and triene systems. Oxidative cleavage to obtain chiral intermediates for drimane and phenanthrene semi-synthesis. *Tetrahedron, 60*, 3831–3845.

Garcia-Granados, A., Lopez, P.E., Melguizo, E., Parra, A., & Simeo, Y. (2006). Reactivity of chiral sesquiterpene synthons obtained by the degradation of maslinic acid from olive-pressing residues. *Synthetic Communications, 36*, 3001–3018.

Garcia-Granados, A., Lopez, P.E., Melguizo, E., Parra, A., & Simeo, Y. (2007). Remote hydroxylation of methyl groups by regioselective cyclopalladation. Partial synthesis of hyptatic acid-A. *Journal of Organic Chemistry, 72*, 3500–3509.

Garcia-Granados, A., Martinez, A., Moliz, J.N., Parra, A., & Rivas, F. (1998a). 3$\beta$-hydroxyolean-12-en-28-oic acid (oleanolic acid). *Molecules, 3*, M87.

Garcia-Granados, A., Martinez, A., Moliz, J.N., Parra, A., & Rivas, F. (1998b). 2$\alpha$,3$\beta$-dihydroxyolean-12-en-28-oic acid (maslinic acid). *Molecules, 3*, M88.

Garcia-Granados, A., Martinez, A., Parra, A., & Rivas, F. (1998c). Process for the industrial recovery of oleanolic and maslinic acids contained in the olive milling subproducts. *Chemical Abstracts*, International Patent: 128:179706.

Huang-Minlon, J. (1946). Simple modification of the Wolff–Kishner reduction. *Journal of American Chemical Society, 68*, 2487–2488.

Huang-Minlon, J. (1949). Reduction of steroid ketones and other carbonyl compounds by modified Wolff-Kishner method. *Journal of American Chemical Society, 71*, 3301–3303.

Hutchins, R.O., & Hutchins, M.K. (1991). Reduction of C=X to CH2 by Wolff–Kishner and other hydrazone methods. In B.M. Trost & I. Fleming (Eds.), *Comprehensive organic synthesis* (Vol. 8, pp. 327–343). Oxford: Pergamon Press.

Jang, D.O., Kim, J., Cho, D.H., & Chung, C.M. (2001). Radical deoxygenation of alcohols via their trifluoroacetate derivatives with diphenylsilane. *Tetrahedron Letters, 42*, 1073–1075.

Kim, J., Cho, D.H., & Jang, D.O. (2004). Radical deoxygenation of tertiary alcohols via trifluoroacetates. *Tetrahedron Letters, 45*, 3031–3033.

Lopez, R.M., Hays, D.S., & Fu, G.C. (1997). $Bu_3SnH$-Catalyzed Barton–McCombie deoxygenation of alcohols. *Journal of American Chemical Society, 119*, 6949–6950.

Nugent, W.A., & Rajanbabu, T.V. (1988). Transition-metal-centered radicals in organic synthesis. Titanium(III)-induced cyclization of epoxy olefins. *Journal of American Chemical Society, 110*, 8561–8562.

Nugent, W.A., & Rajanbabu, T.V. (1989). Intermolecular addition of epoxides to activated olefins: A new reaction. *Journal of American Chemical Society, 111*, 4525–4527.

Nugent, W.A., & Rajanbabu, T.V. (1994). Selective generation of free radicals from epoxides using a transition-metal radical. A powerful new tool for organic synthesis. *Journal of American Chemical Society, 116*, 986–997.

Nugent, W.A., Rajanbabu, T.V., & Beattie, M.S. (1990). Free radical-mediated reduction and deoxygenation of epoxides. *Journal of American Chemical Society, 112*, 6408–6409.

Parra, A., Rivas, F., Lopez, P.E., Garcia-Granados, A., Martinez, A., Albericio, F., et al. (2009). Solution- and solid-phase synthesis and anti-HIV activity of maslinic acid derivatives containing amino acids and peptides. *Bioorganic and Medicinal Chemistry, 17*, 1139–1145.

Paryzek, Z., & Wydra, R. (1984). Reaction of some trisubstituted steroid epoxides with triphenylphosphine-iodine complex. Deoxygenation of epoxides. *Tetrahedron Letters, 25*, 2601–2604.