Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron
Tetrahedron 60 (2004) 1491–1503

Partial synthesis of C-ring derivatives from oleanolic and maslinic acids. Formation of several triene systems by chemical and photochemical isomerization processes

Andrés García-Granados, Pilar E. López, Enrique Melguizo, Andrés Parra* and Yolanda Simeó

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Granada, 18071 Granada, Spain

Received 16 September 2003; revised 19 November 2003; accepted 9 December 2003

Abstract—Some triterpenic compounds modified in C-ring were semi-synthesised from oleanolic acid contained in the solid waste of olive-oil pressing. The corresponding esters of oleanolic and maslinic acids rendered products with a diene system, which led to oleantrienes resembling previtamin D_2 by an electrocyclic reaction. Chemical and photochemical isomerization of these compounds yielded two different trienes with similar structure to tachysterol and vitamin D_2.

1. Introduction

Oleanolic acid (3β-hydroxy-12-oleanen-28-oic acid, **1**) and maslinic acid (2α,3β-dihydroxy-12-oleanen-28-oic acid, **2**) are widespread in plants in the form of free acids or derivatives such as methyl esters, acetyl-, oxo-, glycosyl- and other compounds.[1]These triterpenic acids also appear, in large amounts, in olive-oil pressing residues, and our group has developed a procedure for their isolation from these solid waste that renders a 0.4% in weight of oleanolic acid and 0.8% of maslinic acid.[2] The large amounts of both products available allow their use as suitable starting material for the semi-synthesis of other biologically or chemically remarkable compounds.[3] Moreover, these natural oleanene acids and several closely related derivatives exhibit biological and pharmacological properties, such as anti-HIV, hepatoprotective, anti-inflammatory, cytotoxic or antimicrobial activities, which have been summarised in some reviews.[4]

In previous papers, we have described the semi-synthesis of several triterpenic derivatives with the A-ring functionalized from oleanolic and maslinic acids.[5] In this way, contracted A-ring, deoxygenated and halohydrins derivatives, aside from a synthon of A, B-rings of Finasteride® [5α,17β-*N*-(1,1-dimethylethyl)-3-oxo-4-azaandrostan-1-ene-17-carboxamide],[6] were obtained.[7] Finasteride® belongs to the 4-azasteroid structural class of compounds and is being used in the treatment of disorders caused by an excessive production of dihydrotestosterone by the enzyme 5α-reductase, such as prostate disorders, hair growth and pubertal changes. Likewise, we reported recent preliminary results about the formation of several trienes in C-ring from oleanolic and maslinic acids.[8]

In the present paper, above-mentioned trienes and some other derivatives in C-ring of this starting material are semi-synthesised and characterised. Thus, ozonolysis of oleanolic acid (**1**) yielded lactone **7**, the reactivity of which was studied with the aim of forming a homodiene (product **18**), which was finally semi-synthesised by reduction of oleanolic acid (**1**) with $LiAlH_4$ to obtain erythrodiol[9] and subsequent treatment with NBS. On the other hand, the reaction of methyl oleanate, methyl maslinate and their acetyl derivatives with NBS led to dienes **20**–**23** and some brominated and rearranged products. We also described the method of obtaining trienes **30**–**33** with similar structure to preergocalciferol (previtamin D_2) by a photochemical reaction starting from the aforementioned dienes. A chemical isomerization of these compounds with iodine gave trienes **34**–**37** (similar in structure to tachysterol) and a photochemical reaction rendered exocyclic trienes **38**–**41**, resembling ergocalciferol (vitamin D_2). These processes were based on photochemical interconversions of pro-vitamin D_2, lumisterol, previtamin D_2, tachysterol and some derivatives,[10] in addition to photochemical and thermal transformations of some pentacyclic triterpenoids such as methyl dehidroursolate.[11]

2. Results and discussion

Oleanolic (**1**) and maslinic (**2**) acids were obtained from olive-pressing residues by successive extractions with

Keywords: Oleanolic; Maslinic; Triterpene; Diene; Triene; Isomerization.
* Corresponding author. Tel.: +34-58-240480; fax: +34-58-243364; e-mail address: aparra@ugr.es

0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.12.023

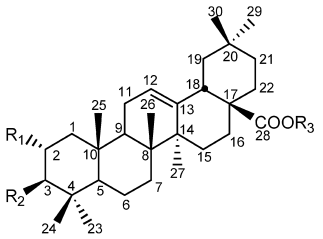


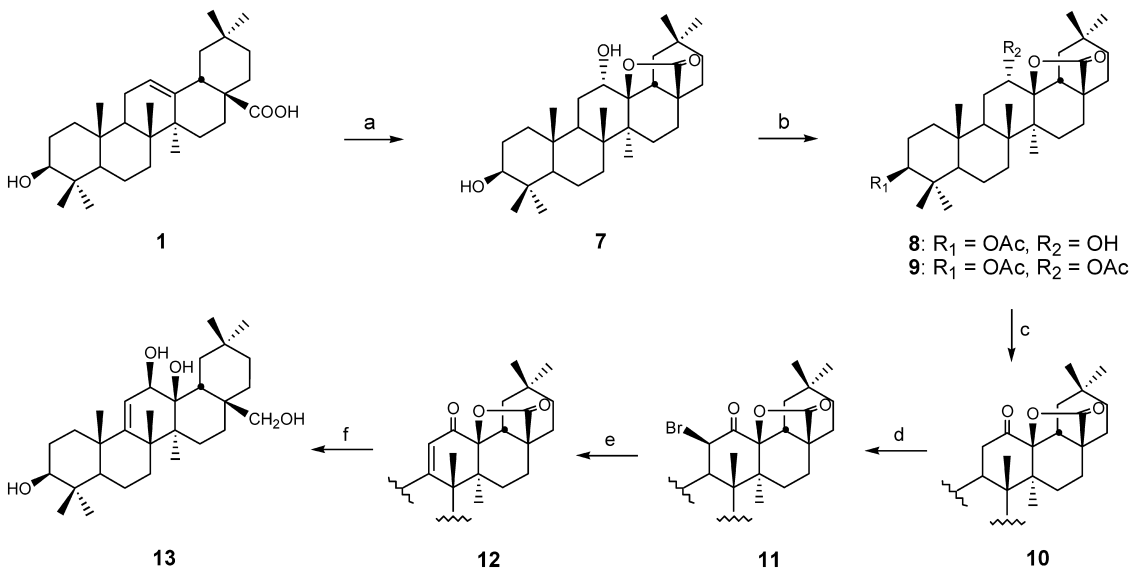
Figure 1. Structures of products **1**–**6**.

hexane and ethyl acetate in soxhlet.[2] 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 starting materials were obtained. The structures of the two oleanene acids (**1** and **2**) were established from their spectroscopic data, which were compared with those in earlier reports.[1] Subsequently, we carried out the esterification of both acids with an ethereal solution of diazomethane or NaOH–MeI, yielding the corresponding methyl alcohol esters, compounds **3** and **4**. Acetylation of these esters with Ac_2O/Py at reflux provided acetylated derivatives **5** and **6** (Fig. 1).

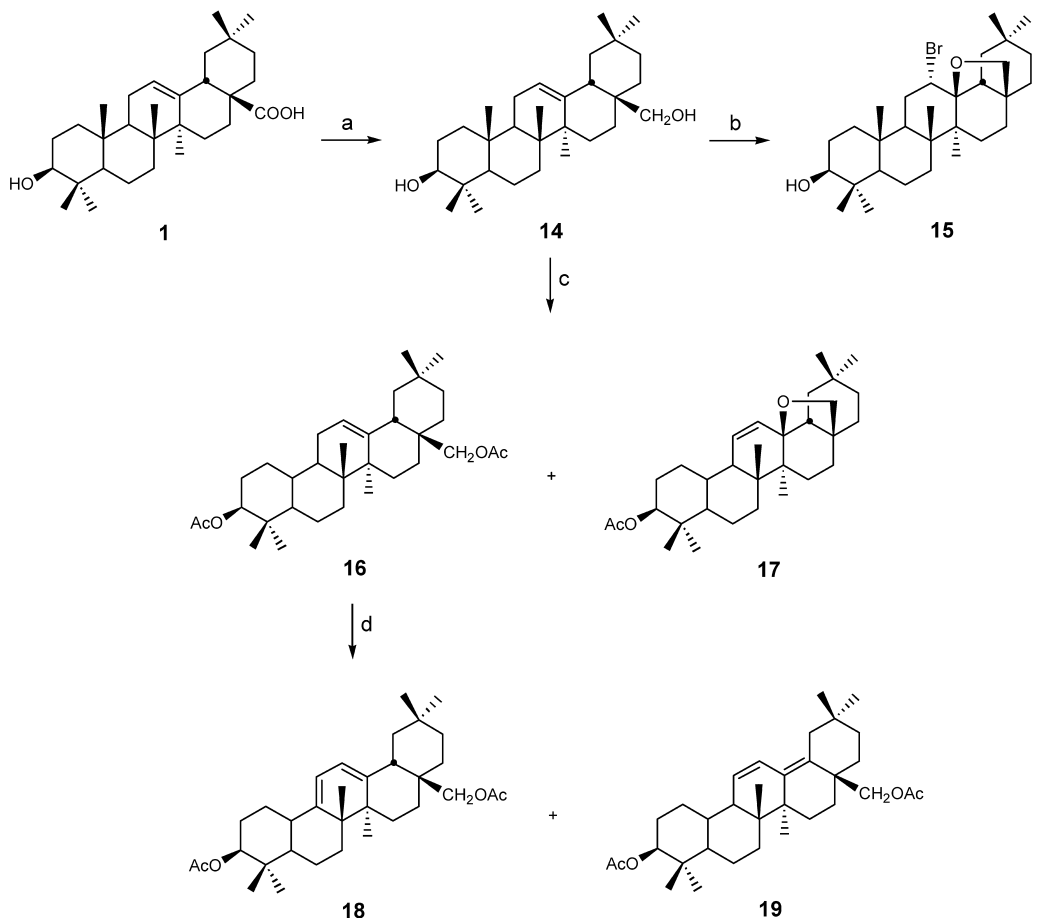
Ozonolysis of oleanolic acid (**1**) in $CHCl_3$:MeOH (1:1) at −78 °C gave lactone **7** (Scheme 1), which was formed by attack of the carboxylic group at C-28 on C-13 and opening of the α-epoxide previously formed by the ozonolysis process between C-12 and C-13. This reaction was similar to the photochemical lactonization of oleanolic acid reported by Misra and Laatsch.[12] Controlled acetylation of product **7** at 0 °C provided compounds **8** and **9**, acetylated in different positions of the molecule. The main product of this reaction, **8** was oxidized with Jones' reagent to obtain the keto lactone **10**. To produce a bromination in α-position to the carbonyl group, we treated product **10** with a solution of Br_2 in CCl_4, rendering compound **11**. The stereochemistry of the halogen atom was established by comparison of the experimental coupling constant between H-9 and H-11 and the theoretical values for the two possible dispositions for H-11. To form a double bond in C-9/C-11, we treated product **11** with Li_2CO_3 and LiBr, obtaining the α,β-unsaturated ketone **12**. Searching to form a diene system in C-ring of triterpene, we opened the lactonic group between C-13 and C-17 by reduction with $LiAlH_4$, yielding tetrol **13** (Scheme 1). In this product, the stereochemistry of the hydroxyl group at C-12 was β, since the hydride ion should enter from the less hindered face, the α face, giving rise to an hydroxyl group in β.

On the other hand, to avoid lactonization, we reduced oleanolic acid (**1**) with $LiAlH_4$ to give product **14**, which was identified as erythrodiol from their NMR data (Scheme 2).[9] Bromination of this compound at C-11 and subsequent dehydrohalogenation could lead to the diene sought. However, treatment of this product with NBS gave compound **15**, resulting from the cyclation of the hydroxyl group at C-28 on C-13 and reaction of negatively charged C-12 with NBS. To avoid the formation of this cyclic ether, we protected the hydroxyl group at C-28. Thus, product **14** was acetylated with Ac_2O/Py, yielding compounds **16** and **17**. The major product of this process, **16**, was the corresponding diacetylated derivative and the minor product had a cyclic ether between C-28 and C-13 and a double bond in C-11/C-12 as a consequence of the cyclation of the hydroxyl group at C-28 before acetylation. Finally, treatment of product **16** with NBS gave diene **18** in one step by bromination in allylic position and subsequent spontaneous dehydrohalogenation, and a minor product, **19**, which is another diene with different positions for the double bonds.

According to the above-described results, in order to avoid the reduction of oleanolic acid and the formation of cyclic ethers or lactones, and to improve the yield of diene, we

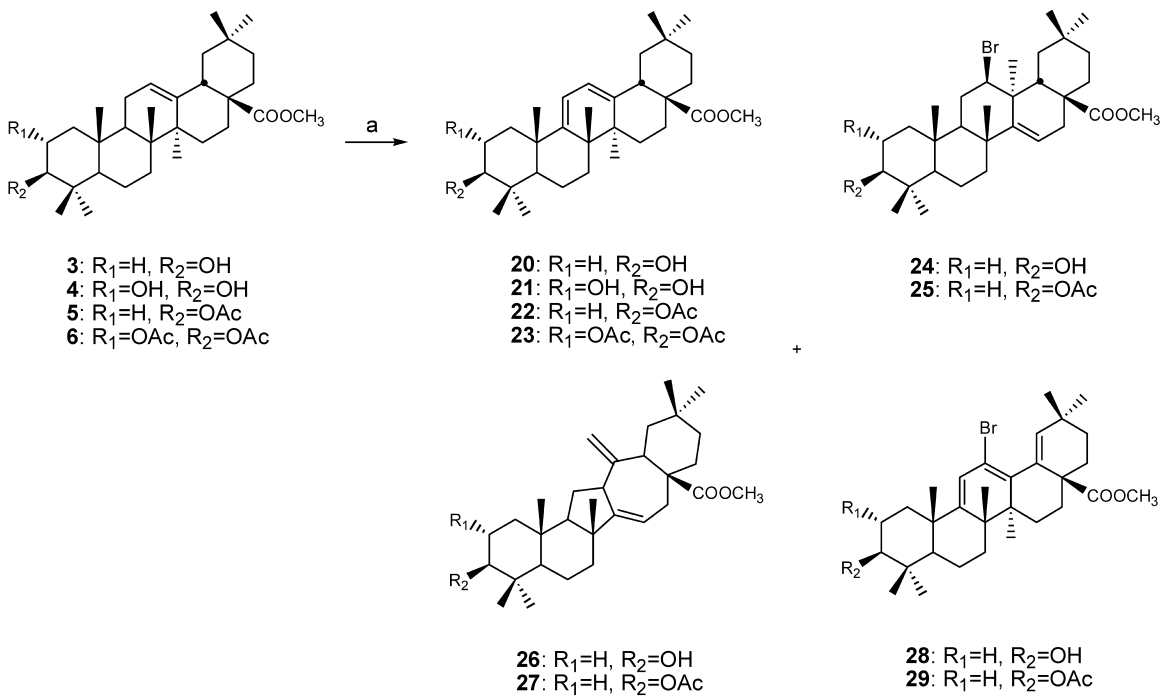


Scheme 1. *Reagents and conditions*: (a) O_3/$CHCl_3$:MeOH/−78 °C/30 min **7** (70%); (b) Ac_2O/Py/0 °C/3 h **8** (70%) and **9** (20%); (c) Jones' reagent/0 °C/1 h **10** (95%); (d) Br_2/CCl_4/rt/5 h **11** (80%); (e) Li_2CO_3/LiBr/reflux/3 h **12** (60%); (f) $LiAlH_4$/THF/reflux/1.5 h **13** (95%).



1 **14** **15** **16** **17** **18** **19**

Scheme 2. *Reagents and conditions*: (a) $LiAlH_4$/THF/reflux/3.5 h **14** (95%); (b) NBS/AIBN/CCl_4/rt/1 h **15** (50%); (c) Ac_2O/Py/reflux/1.5 h **16** (70%) and **17** (20%); (d) NBS/AIBN/CCl_4/rt/1 h **18** (40%) and **19** (5%).



3: R_1=H, R_2=OH
4: R_1=OH, R_2=OH
5: R_1=H, R_2=OAc
6: R_1=OAc, R_2=OAc

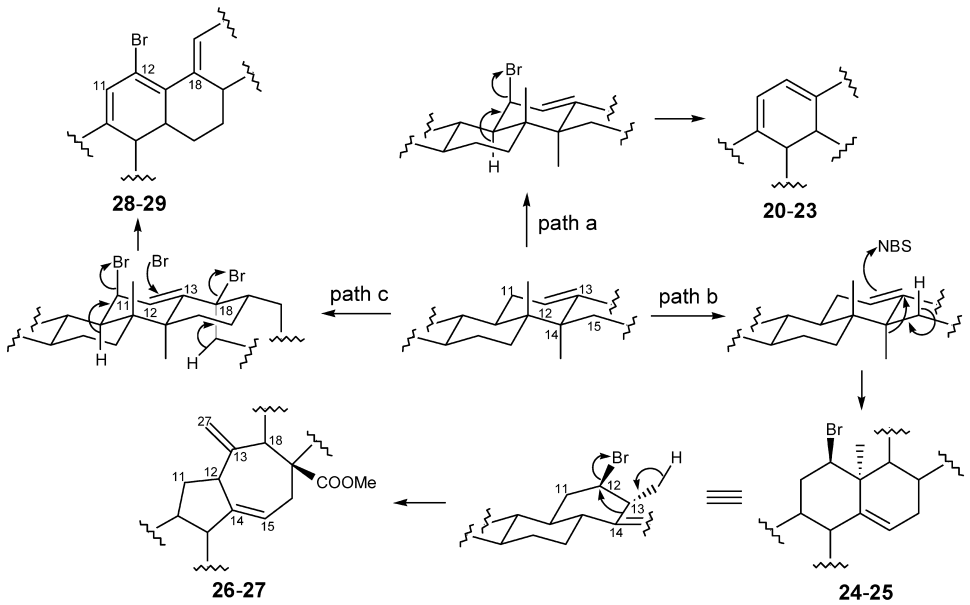
20: R_1=H, R_2=OH
21: R_1=OH, R_2=OH
22: R_1=H, R_2=OAc
23: R_1=OAc, R_2=OAc

24: R_1=H, R_2=OH
25: R_1=H, R_2=OAc

26: R_1=H, R_2=OH
27: R_1=H, R_2=OAc

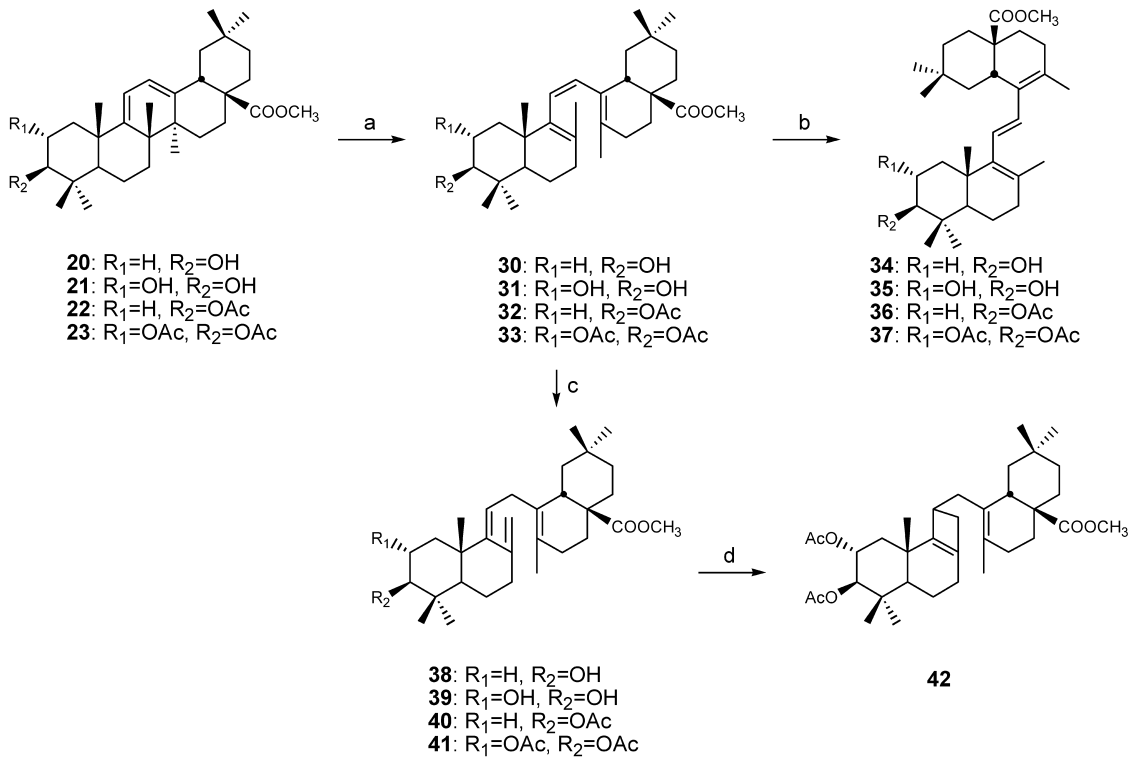
28: R_1=H, R_2=OH
29: R_1=H, R_2=OAc

Scheme 3. *Reagents and conditions*: (a) starting from **3**, NBS/AIBN/CCl_4/rt/2 h **20** (70%), **24** (10%), **26** (5%) and **28** (10%); starting from **4**, NBS/AIBN/CCl_4/reflux/1 h **21** (90%); starting from **5**, NBS/AIBN/CCl_4/rt/2 h **22** (60%), **25** (15%), **27** (5%) and **29** (15%); starting from **6**, NBS/AIBN/CCl_4/reflux/1 h **23** (90%).



Scheme 4. Proposed mechanisms for the obtention of products **20**–**29**.

used methyl oleanate (**3**), methyl maslinate (**4**) and their acetylated derivatives **5** and **6** as starting material for the diene system formation. Thus, treatment of maslinic esters **4** and **6** with NBS at reflux for 1 h rendered an excellent yield of dienes **21** and **23** (90%; Scheme 3). Again, a bromination/dehydrobromination process between C-9 and C-11 had occurred, giving rise to a conjugated double bond in the C-ring of the triterpenic compounds (Scheme 4, path a). However, the reaction of oleanolic esters **3** and **5** with this reagent at rt for 2 h gave dienes **20** and **22**[13], and compounds **24** and **25**, **26** and **27**, and **28** and **29** (Scheme 3), which were characterized by their spectroscopic properties. Products **24** and **25** presented a taraxerene structure and were formed by the loss of a hydrogen of C-15, migration of the methyl group at C-14 to C-13 with the same configuration, and the entry of a halogen atom in C-12 (Scheme 4, path b). This change of skeleton was studied by Corey et al. from a mixture of α-amiryn and β-amiryn.[14] The taraxerene skeleton is more unstable than the olean-12-ene (methyl oleanate) system, and the halogenation in C-12 must provide the required energy to change the skeleton.

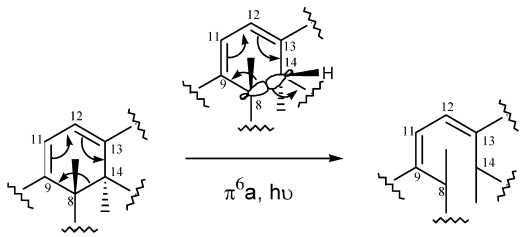


Scheme 5. *Reagents and conditions*: (a) *hν*/EtOH/borosilicate flask/20 min **30**, **31**, **32** and **33** (95%); (b) I_2/hexane/reflux/5 h **34**, **35**, **36** and **37** (60%); (c) *hν*/EtOH/quartz flask/30 min **38**, **39**, **40** and **41** (95%); (d) starting from **41**, *hν*/EtOH/quartz flask/30 min **42** (50%).

Moreover, starting from compounds **24** and **25**, a rearrangement process took place. This transformation could occur due to the transperiplanar disposition of bonds C-12/Br and C-13/C-14, leading to products **26** and **27**, which presented a five-membered ring C and a seven-membered ring D (Scheme 4). The structure of these compounds was established by their spectroscopic characteristics. The appearance of two ethylenic protons each coupled in ^{1}H NMR spectrum, which correlated with the signals of C-12 and C-18 in HMBC spectrum, supports the proposed structure.

Finally, by a double bromination/dehydrobromination process in allylic position and the addition of a halogen atom in C-12, products **28**–**29** were formed (Scheme 4, path c). The presence of four ethylenic quaternary carbon atoms in ^{13}C NMR spectrum confirmed this structure and the low shift for C-12 indicated that the halogen atom was situated in this position.

On the other hand, irradiation of homodienes **20**–**23** with a high pressure Hg street lamp in a borosilicate flask yielded trienes **30**–**33** (95%), respectively (Scheme 5). This C-ring opening occurred by a conrotatory photochemical electrocyclic reaction similar to the transformation of ergosterol in previtamin D. This process could take place due to the *trans*-disposition between Me on C-8 (C-26) and Me on C-14 (C-27), that allowed an antarafacial reaction of the 6π electron system, giving rise to the cleavage of C-8/C-14 bond and thus rendered trienes **30**–**33** (Scheme 6). The structure of compound **33** was established by their mono- and bidimensional spectra and an X-ray experience, that showed an helicolidal disposition of D, E-rings over A, B-rings.

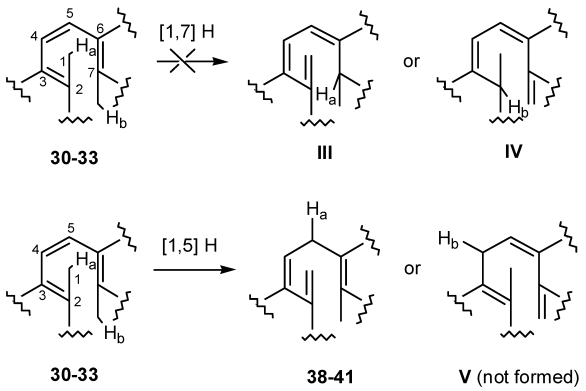


Scheme 6. Electrocyclic reaction of products **20**–**23**.

After separation by column chromatography, purification and characterization, products **30**–**33** were independently treated with different oxidative reagents (ozone, OsO_4/$NaIO_4$, $RuCl_3$/$NaIO_4$), rendering a mixture of various epoxy or methylketone compounds resulting from oxidation in the most substituted double bonds while the central double bond (C-11/C-12 double bond) remained unaltered. Subsequently, we carried out the chemical isomerization of *cis*-trienes **30**–**33** to *trans*-trienes **34**–**37** by treatment with iodine in hexane in acceptable yield (60%) (Scheme 5). The *trans*-disposition of the double bond between C-11 and C-12 was verified mainly by comparison of ^{1}H NMR and ^{13}C NMR data. Thus, compounds **30**–**33** (*cis*-trienes) had moderately high coupling constants (Table 1). However, compounds **34**–**37** (*trans*-trienes) presented similar shifts for H-11 and H-12, but had higher coupling constants between these two protons. Furthermore, products **34**–**37** had lower ^{13}C NMR shifts for C-11 and C-12 than compounds **30**–**33**.

Table 1. Comparison of some remarkable shifts of products **30**–**37**

	30	**31**	**32**	**33**	**34**	**35**	**36**	**37**
$J_{11/12}$ (Hz)	12.9	12.8	12.9	12.6	16.2	16.2	16.2	16.0
C-11 (ppm)	127.3	126.8	127.3	127.2	123.2	122.7	123.0	122.4
C-12 (ppm)	132.9	133.1	132.9	133.3	131.3	131.8	131.4	131.7



Scheme 7. Possible [1,5]H and [1,7]H displacements for products **30**–**33**.

Hypothetically, although the *trans* disposition of the central double bond was fixed, there were four possible stereochemical dispositions for the double bonds between C-9 and C-11 or C-12 and C-13 due to the possible rotation around these bonds. However, it was verified experimentally that mainly one product was obtained. Data from NOE experiments confirmed that one of the ethylenic protons (H-11 or H-12) was located between the two allylic methyl groups (Fig. 2). Therefore, we discarded *cis*–*cis* and *trans*–*trans* dispositions, since in these structures each ethylenic proton correlated with only one allylic methyl group. Finally, to distinguish between the *cis*–*trans* (I) or *trans*–*cis* (II) disposition, we examined the results of HMBC and HMQC experiments. These spectra showed that the ethylenic proton located between the two allylic methyls in NOE spectrum correlated in the HMBC spectrum with C-18, leading us to deduce that this ethylenic hydrogen was H-12 and products **34**–**37** presented a *cis*–*trans* structure. Therefore, *trans* trienes had a $S_{9,11}Z$ $S_{12,13}E$ disposition (Fig. 3).

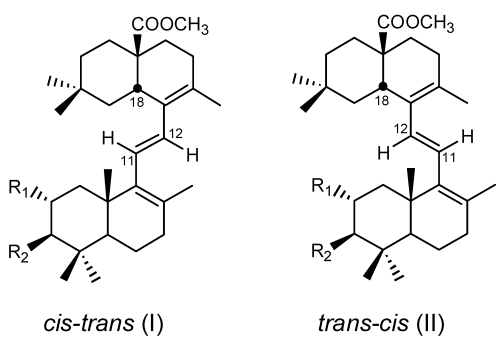
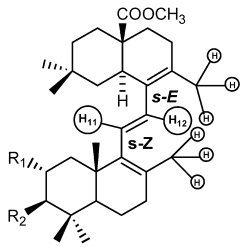


Figure 2. Two possible dispositions for products **34**–**37**.



34: R_1=H, R_2=OH
35: R_1=OH, R_2=OH
36: R_1=H, R_2=OAc
37: R_1=OAc, R_2=OAc

Figure 3. Structures of products **34**–**37**.

Moreover, irradiation of products **30**–**33** (*cis*-trienes) independently in a quartz flask for 30 min yielded exocyclic trienes **38**–**41** in very high yield (95%) (Scheme 5). The appearance of an exocyclic double bond was confirmed by the spectroscopic characteristic of the methylene group. This product was formed by a [1,5]H displacement, since a suprafacial migration of one hydrogen from C-26 methyl group to C-12 took place (Scheme 7). However, a spontaneous or photochemical [1,7]H sigmatropic rearrangement did not occur as in the transformation of provitamin D_2 to vitamin D_2,[10,15] because C-26 and C-27 methyls in trienes **30**–**33** distorted the molecular conformation, impeding any antarafacial or suprafacial migration between 1 and 7 positions of the H sigmatropic shift.

Thus, the molecular disposition allowed only one of the two possible [1,5]H displacements, since experimentally only trienes **38**–**41**, which presented two conjugated double bonds between C-8/C-26 and C-9/C-11 and another isolated double bond between C-13 and C-14 atoms, were formed.

Finally, when exocyclic triene **41** was isolated and irradiated again under the same conditions for an extra time of 30 min, product **42** was obtained (Scheme 5). Analogous compounds to diene **42** were described as over-irradiation products by Barton et al. in the photochemical reaction of a triene obtained from methyl dehydroursolate acetate.[11] This compound **42** could be formed by an electrocyclic reaction of a 4π electron system, giving rise to a C-26/C-11 bond and a double bond between C-8 and C-9. The structure was deduced from spectroscopic data, which showed four ethylenic quaternary carbon atoms and no methylene group.

3. Conclusion

Oleanolic and maslinic acids were suitable starting material for the semi-synthesis of several remarkable derivatives modified in C and/or D rings of the oleanene skeleton. Treatment of the esters of aforementioned acids with NBS gave rise to a promising diene system in C-ring by a spontaneous bromination/dehydrobromination process.

The cleveage of the C-8/C-14 bond of the diene by an electrocyclic reaction was achieved, yielding a triene with the C-ring opened. Starting from this compound, an exocyclic triene was obtained by a photochemical reaction, while a chemical isomerization led to a *trans*-triene, whose stereochemical disposition was determined accurately. These triene products will be used in future research as starting material for the semi-synthesis of significant sesquiterpene chiral synthons by cleavage of the central double bonds.

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 polarization 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). Mps 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 μm) 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 starting materials

Oleanolic acid (**1**)[1,2] and maslinic acid (**2**)[1,2] were isolated from solid wastes resulting from olive-oil production, which were extracted in a Soxhlet 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 column chromatography over silica gel, eluting with a $CHCl_3$–MeOH or CH_2Cl_2–Acetone 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 3β-hydroxy-12-oleanen-28-oate (**3**)[5] and methyl 2α,3β-dihydroxy-12-oleanen-28-oate (**4**)[5] were obtained. Acetylation of these esters with Ac_2O/Py at reflux provided acetylated derivatives **5**[5] and **6**[5].

4.2.1. Ozonolysis of 1. Product **1** (1.5 g, 3.3 mmol), after being dissolved in 15 mL of $CHCl_3$ and 15 mL of MeOH, was stirred at −78 °C and passed through an O_3 flow of 0.1 L/min (10% O_2–90% O_3). After 30 min, excess ozone was removed with argon. The mixture was maintained with stirring while being cooled down for 4 h. Then it was evaporated and purified over silica gel, yielding 1.08 g (70%) of **7**: white solid; mp 247–249 °C; $[\alpha]_D^{25}$=26 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3472, 2949, 1751 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.87 (1H, dd, J_1=J_2=2.9 Hz, H-12), 3.21 (1H,

dd, J_1=5.4 Hz, J_2=10.9 Hz, H-3), 1.29 (3H, s, 3H-27), 1.13 (3H, s, 3H-26), 0.98 (3H, s, 3H-23), 0.97 (3H, s, 3H-29), 0.88 (3H, s, 3H-30), 0.86 (3H, s, 3H-25), 0.76 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.4 (C-24), 16.4 (C-25), 17.8 (C-6), 18.6 and 18.7 (C-26 and C-27), 21.3 (C-16), 24.0 (C-30), 27.3, 27.5, 28.1 and 28.8 (C-2, C-11, C-15 and C-22), 28.1 (C-23), 31.6 (C-20), 33.3 (C-29), 34.0 and 34.2 (C-7 and C-21), 36.5 (C-10), 38.9 (C-1), 39.0 (C-4), 39.5 (C-19), 42.1 (C-14), 42.4 (C-8), 44.6 (C-9), 44.8 (C-17), 51.2 (C-18), 55.2 (C-5), 76.4 (C-12), 78.9 (C-3), 90.7 (C-13), 180.0 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 495.3454 ($C_{30}H_{48}O_4Na$, calcd 495.3450).

4.2.2. Acetylation of 7. Product **7** (650 mg, 1.4 mmol) was dissolved in 20 mL of pyridine and 10 mL of Ac_2O and stirred for 3 h at 0 °C. The reaction mixture was diluted with water, extracted with CH_2Cl_2, washed with saturated aqueous $KHSO_4$ solution and dried with anhydrous Na_2SO_4. The solvent was evaporated at reduced pressure and the residue was chromatographed on a silica gel column to give 65 mg (10%) of **7**, 495 mg (70%) of product **8**: white solid; mp 261–263 °C; $[\alpha]_D^{25}$=37 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3487, 2928, 2360, 1739, 1247 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.48 (1H, dd, J_1=5.7 Hz, J_2=9.7 Hz, H-3), 3.87 (1H, dd, J_1=J_2=2.5 Hz, H-12), 2.04 (3H, s, CO*CH*$_3$), 1.29 (3H, s, Me), 1.13 (3H, s, Me), 0.97 (3H, s, Me), 0.89 (3H, s, Me), 0.89 (3H, s, Me), 0.86 (3H, s, Me), 0.84 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.5 (C-24), 16.5 (C-25), 17.7 (C-6), 18.6 and 18.7 (C-26 and C-27), 21.3 (C-16), 21.4 (CO*CH*$_3$), 23.6 (C-2), 24.0 (C-30), 27.6, 28.1 and 28.9 (C-11, C-15 and C-22), 28.0 (C-23), 31.6 (C-20), 33.3 (C-29), 34.0 and 34.2 (C-7 and C-21), 36.4 (C-10), 37.9 (C-4), 38.6 and 39.4 (C-1 and C-19), 42.1 (C-14), 42.4 (C-8), 44.6 (C-9), 44.8 (C-17), 51.2 (C-18), 55.4 (C-5), 76.3 (C-12), 80.9 (C-3), 90.7 (C-13), 171.2 (*COCH*$_3$), 180.1 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 537.3557 ($C_{32}H_{50}O_5Na$, calcd 537.3556); and 150 mg (20%) of **9**: white solid; mp 241–243 °C; $[\alpha]_D^{25}$=57 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2928, 2360, 1776, 1743, 1246 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.01 (1H, dd, J_1=J_2= 2.9 Hz, H-12), 4.47 (1H, dd, J_1=6.2 Hz, J_2=10.0 Hz, H-3), 2.09 (3H, s, CO*CH*$_3$), 2.04 (3H, s, CO*CH*$_3$), 1.26 (3H, s, Me), 1.15 (3H, s, Me), 0.96 (3H, s, Me), 0.87 (3H, s, Me), 0.86 (3H, s, Me), 0.84 (3H, s, Me), 0.81 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.3 and 16.5 (C-24 and C-25), 17.7 (C-6), 18.4 and 18.6 (C-26 and C-27), 21.1 (C-16), 21.4 (CO*CH*$_3$), 21.5 (CO*CH*$_3$), 23.6 (C-2), 23.9 (C-30), 25.2 (C-15), 27.4 and 27.9 (C-11 and C-22), 28.0 (C-23), 31.6 (C-20), 33.4 (C-29), 33.9 (C-7), 33.9 (C-21), 36.4 (C-10), 37.9 (C-4), 38.5 (C-1), 39.5 (C-19), 42.2 (C-14), 42.3 (C-8), 44.6 (C-17), 45.4 (C-9), 50.3 (C-18), 55.4 (C-5), 76.8 (C-12), 80.7 (C-3), 89.5 (C-13), 169.4 (*CO*CH_3), 171.2 (*CO*CH_3), 179.1 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 579.3664 ($C_{34}H_{52}O_6Na$, calcd 579.3662).

4.2.3. Oxidation of 8. Jones' reagent was added dropwise to a stirred solution of product **8** (450 mg, 0.9 mmol) in acetone at 0 °C until an orange-brown colour persisted. Methanol was added and the reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 425 mg (95%) of **10**: white solid; mp 287–289 °C; $[\alpha]_D^{25}$=8 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2951, 1780, 1727, 1247 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.46 (1H, dd, J_1=5.0 Hz, J_2=10.8 Hz, H-3), 2.69 (1H, dd, J_1=J_2=13.9 Hz, H-11a), 2.52 (1H, dd, J_1=J_2=8.2 Hz, H-18), 2.35 (1H, dd, J_1=3.0 Hz, J_2= 13.9 Hz, H-11b), 2.03 (3H, s, CO*CH*$_3$), 1.30 (3H, s, 3H-25), 0.96 (3H, s, 3H-29), 0.94 (3H, s, 3H-26), 0.94 (3H, s, 3H-27), 0.92 (3H, s, 3H-23), 0.85 (3H, s, 3H-30), 0.85 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.9 and 18.2 (C-26 and C-27), 16.4 (C-24), 17.5 (C-6), 18.6 (C-25), 20.7 (C-16), 21.3 (CO*CH*$_3$), 23.4 (C-2), 23.8 (C-30), 25.9 (C-15), 27.3 (C-22), 27.9 (C-23), 31.6 (C-20), 32.9 (C-1), 33.2 (C-29), 34.2 (C-7), 37.2 and 37.9 (C-4 and C-10), 37.3 and 37.4 (C-11 and C-21), 38.1 (C-19), 42.5 (C-8), 43.7 (C-14), 44.0 (C-18), 44.0 (C-17), 51.0 (C-9), 55.0 (C-5), 80.3 (C-3), 91.0 (C-13), 171.0 (*CO*CH_3), 178.5 (C-28), 206.0 (C-12); HRLSIMS, *m/z*: $[M+Na]^+$ 535.3391 ($C_{32}H_{48}O_5Na$, calcd 535.3399).

4.2.4. Treatment of 10 with bromine. Product **10** (405 mg, 0.8 mmol) was dissolved in 10 mL of CH_2Cl_2 and 4 mL of a 0.1 M solution of Br_2 in CCl_4 were added.The reaction mixture was maintained at room temperature for 5 h, and then diluted with CH_2Cl_2, neutralized with a $NaHCO_3$ solution, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography over silica gel yielded 374 mg (80%) of **11**: white solid; mp 252–254 °C; $[\alpha]_D^{25}$=4 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2949, 1780, 1719, 1247 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.47 (1H, dd, J_1=4.5 Hz, J_2=11.1 Hz, H-3), 4.32 (1H, d, J=6.6 Hz, H-11), 2.67 (1H, dd, J_1= 2.7 Hz, J_2=13.7 Hz, H-18), 2.03 (3H, s, CO*CH*$_3$), 1.46 (3H, s, Me), 0.98 (3H, s, Me), 0.97 (3H, s, Me), 0.90 (3H, s, Me), 0.87 (3H, s, Me), 0.85 (3H, s, Me), 0.84 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.3 (Me), 16.7 (Me), 17.3 (C-6), 19.4 (Me), 20.3 (Me), 21.3 (CO*CH*$_3$), 21.5 (C-16), 23.4 (C-2), 23.5 (C-30), 26.5 and 26.8 (C-15 and C-22), 27.8 (C-23), 31.5 (C-1), 31.7 (C-20), 33.3 (C-29), 34.3 (C-7), 37.1 (C-21), 38.0 (C-4), 39.0 (C-19), 39.1 (C-10), 41.7 and 42.2 (C-8 and C-14), 44.6 (C-17), 46.1 and 48.4 (C-9 and C-18), 55.1 (C-5), 57.4 (C-11), 80.1 (C-3), 90.6 (C-13), 171.0 (*CO*CH_3), 177.7 (C-28), 200.3 (C-12); HRLSIMS, *m/z*: $[M+Na]^+$ 613.2510 ($C_{32}H_{47}O_5BrNa$, calcd 613.2505).

4.2.5. Dehydrohalogenation of 11. Product **11** (318 mg, 0.5 mmol) was dissolved in 10 mL of anhydrous DMF, and LiBr (116 mg, 1.3 mmol) and Li_2CO_3 (155 mg, 2.1 mmol) were added. After 3 h at reflux, the reaction mixture was extracted with an acetic acid solution and CH_2Cl_2, neutralized with $NaHCO_3$, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 95 mg (30%) of **11** and 166 mg (60%) of **12**: white solid; mp 274–276 °C; $[\alpha]_D^{25}$=74 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2951, 1778, 1735, 1667, 1246 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.97 (1H, s, H-11), 4.47 (1H, dd, J_1=5.0 Hz, J_2=11.3 Hz, H-3), 2.94 (1H, dd, J_1=2.7 Hz, J_2=13.5 Hz, H-18), 2.06 (3H, s, CO*CH*$_3$), 1.44 (3H, s, Me), 1.27 (3H, s, Me), 0.98 (3H, s, Me), 0.95 (3H, s, Me), 0.95 (3H, s, Me), 0.92 (3H, s, Me), 0.90 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.7 (Me), 17.2 (C-6), 20.3 (C-16), 21.3 (CO*CH*$_3$), 23.1 (Me), 23.9 (C-2), 23.9 (Me), 24.5 (Me), 25.9 (C-15), 27.2 (C-22), 28.1 (Me), 30.1 (Me), 31.7 (C-20), 33.2 (C-29), 34.0 and 34.1 (C-1 and C-7), 36.1 and 36.7 (C-19 and C-21), 38.3 (C-4), 40.3 (C-10), 41.7 (C-8), 43.6 (C-14), 44.0 (C-18), 46.0 (C-17), 50.4 (C-5), 79.6 (C-3), 87.9 (C-13), 121.8 (C-11), 171.0 (*CO*CH_3), 178.8 (C-28), 183.6 (C-9), 192.4

(C-12); HRLSIMS, *m/z*: $[M+Na]^+$ 533.3249 ($C_{32}H_{46}O_5Na$, calcd 533.3243).

4.2.6. Reduction of 12. 140 mg (0.3 mmol) of product **12** were dissolved in 2 mL of dry THF and 1 mL of a solution of $LiAlH_4$ in THF (1 M) was added. The reaction mixture was maintained at reflux for 1.5 h, and then diluted with aqueous ether, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography over silica gel yielded 124 mg (95%) of **13**: white solid; mp 233–235 °C; $[\alpha]_D^{25}$=23 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3371, 2938 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.25 (1H, d, *J*=2.3 Hz, H-11), 4.24 (1H, d, *J*=2.3 Hz, H-12), 3.93 (1H, d, *J*=10.9 Hz, H-28a), 3.42 (1H, d, *J*=10.9 Hz, H-28b), 3.17 (1H, dd, J_1=4.8 Hz, J_2=11.3 Hz, H-3), 1.42 (3H, s, Me), 1.17 (3H, s, Me), 1.02 (3H, s, Me), 0.97 (3H, s, Me), 0.89 (3H, s, Me), 0.89 (3H, s, Me), 0.80 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.5 (Me), 18.0 (C-6), 22.3 (Me), 24.1 (Me), 24.4 (Me), 25.5 (Me), 26.1 (C-15), 26.1 (C-16), 27.9 (C-2), 28.1 (Me), 31.2 (C-20), 32.7 (C-29), 33.2, 34.0 and 34.3 (C-7, C-21 and C-22), 36.7 and 39.4 (C-4 and C-10), 38.2 (C-1), 39.8 (C-18), 39.9 (C-8), 40.1 (C-19), 44.1 (C-14), 44.5 (C-17), 53.2 (C-5), 68.5 (C-12), 70.6 (C-28), 77.8 (C-13), 78.5 (C-3), 119.2 (C-11), 154.8 (C-9); HRLSIMS, *m/z*: $[M+Na]^+$ 497.3600 ($C_{30}H_{50}O_4Na$, calcd 497.3607).

4.2.7. Reduction of 1. Product **1** (500 mg, 1.1 mmol) was dissolved in 20 mL of dry THF and 8 mL of a 1 M solution of $LiAlH_4$ in THF were added. After 3.5 h at reflux, the reaction mixture was diluted with aqueous ether, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed over silica gel to obtain 478 mg (95%) of product **14**.[9]

4.2.8. Bromination of 14. Product **14** (228 mg, 0.5 mmol) was dissolved in 15 mL of CCl_4, and 90 mg (0.5 mmol) of NBS and a catalytic amount of AIBN were added. The reaction mixture was maintained at room temperature for 1 h and then extracted with a solution of $NaHCO_3$, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography over silica gel yielded 113 mg (50%) of **14** and 130 mg (50%) of **15**: white solid; mp 124–126 °C; $[\alpha]_D^{25}$=78 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3422, 2927 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.24 (1H, dd, J_1=2.5 Hz, J_2=3.5 Hz, H-12), 3.73 (1H, d, *J*=7.0 Hz, H-28a), 3.28 (1H, d, *J*=7.0 Hz, H-28b), 3.24 (1H, dd, J_1=4.9 Hz, J_2=11.2 Hz, H-3), 1.30 (3H, s, Me), 1.25 (3H, s, Me), 0.98 (3H, s, Me), 0.97 (3H, s, Me), 0.89 (3H, s, Me), 0.87 (3H, s, Me), 0.76 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.5 (Me), 17.1 (Me), 17.8 (C-6), 19.3 (Me), 21.8 (Me), 23.7 (Me), 25.0 (C-16), 27.3 (C-2), 28.1 (C-23), 29.2 (C-15), 31.1 (C-7), 31.1 (C-11), 32.0 (C-20), 33.7 (C-29), 34.3 (C-21), 35.0 (C-22), 36.7 (C-4), 38.4 (C-1), 39.0 (C-10), 40.2 (C-19), 42.7 and 43.0 (C-8 and C-17), 45.7 (C-14), 46.0 (C-9), 53.2 (C-18), 55.3 (C-5), 60.6 (C-12), 77.5 (C-28), 78.9 (C-3), 87.5 (C-13); HRLSIMS, *m/z*: $[M+Na]^+$ 543.2812 ($C_{30}H_{49}O_2BrNa$, calcd 543.2814).

4.2.9. Acetylation of 14. Product **14** (138 mg, 0.3 mmol) was dissolved in 6 mL of pyridine and 3 mL of Ac_2O and stirred for 1.5 h at reflux. The reaction mixture was diluted with water, extracted with CH_2Cl_2, washed with saturated aqueous $KHSO_4$ solution and dried with anhydrous Na_2SO_4. The solvent was evaporated at reduced pressure and the residue was chromatographed on a silica gel column to give 111 mg (70%) of **16**: white solid; mp 168–170 °C; $[\alpha]_D^{25}$=56 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2948, 1737, 1245 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.18 (1H, dd, J_1=J_2=3.6 Hz, H-12), 4.48 (1H, dd, J_1=7.3 Hz, J_2=9.1 Hz, H-3), 4.01 (1H, d, *J*=11.0 Hz, H-28a), 3.68 (1H, d, *J*=11.0 Hz, H-28b), 2.03 (3H, s, COO*CH*$_3$), 2.03 (3H, s, COO*CH*$_3$), 1.14 (3H, s, Me), 0.93 (3H, s, Me), 0.93 (3H, s, Me), 0.87 (3H, s, Me), 0.85 (3H, s, Me), 0.85 (3H, s, Me), 0.84 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.6 (C-26), 16.7 (C-24), 16.7 (C-25), 18.3 (C-6), 21.0 (CO*CH*$_3$), 21.4 (CO*CH*$_3$), 21.4 (C-30), 22.3 (C-16), 23.6 (C-2), 23.6 (C-11), 25.6 (C-15), 26.0 (C-27), 28.1 (C-23), 30.9 (C-20), 31.4 (C-22), 32.5 (C-7), 33.2 (C-29), 34.0 (C-21), 35.8, 36.9, 37.8 and 39.8 (C-4, C-8, C-10 and C-17), 38.3 (C-1), 41.7 (C-14), 42.6 (C-18), 46.3 (C-19), 47.6 (C-9), 55.3 (C-5), 70.8 (C-28), 80.9 (C-3), 122.9 (C-12), 143.7 (C-13), 171.1 (*CO*CH_3), 171.4 (*CO*CH_3); HRLSIMS, *m/z*: $[M+Na]^+$ 549.3913 ($C_{34}H_{54}O_4Na$, calcd 549.3920); and 29 mg (20%) of **17**: white solid; mp 205–207 °C; $[\alpha]_D^{25}$=74 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2925, 1737, 1244 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.83 (1H, d, *J*=10.3 Hz, H-12), 5.36 (1H, dd, J_1=3.2 Hz, J_2=10.2 Hz, H-11), 4.47 (1H, dd, J_1=8.3 Hz, J_2=9.2 Hz, H-3), 3.69 (1H, d, *J*=6.7 Hz, H-28a), 3.25 (1H, d, *J*=6.7 Hz, H-28b), 2.04 (3H, s, CO*CH*$_3$), 1.07 (3H, s, Me), 0.95 (3H, s, Me), 0.92 (3H, s, Me), 0.91 (3H, s, Me), 0.85 (3H, s, Me), 0.84 (3H, s, Me), 0.84 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.1 (Me), 17.6 (C-6), 18.0 (Me), 19.4 (Me), 19.5 (Me), 21.4 (CO*CH*$_3$), 23.5 (C-16), 23.6 (Me), 25.3 and 25.7 (C-2 and C-15), 27.8 (C-27), 30.9 (C-7), 31.3 (C-21), 31.7 (C-20), 33.7 (C-29), 34.9 (C-22), 36.4, 37.9, 41.6, 41.6 and 43.8 (C-4, C-8, C-10, C-14 and C-17), 37.1 and 38.0 (C-1 and C-19), 51.1 (C-9), 53.2 (C-18), 54.9 (C-5), 77.0 (C-28), 80.9 (C-3), 84.8 (C-13), 131.0 and 132.1 (C-11 and C-12), 171.1 (*CO*CH_3); HRLSIMS, *m/z*: $[M+Na]^+$ 505.3669 ($C_{32}H_{50}O_3Na$, calcd 505.3658).

4.2.10. Treatment of 16 with NBS. Product **16** (81 mg, 0.15 mmol) was dissolved in 8 mL of CCl_4, and 27 mg (0.15 mmol) of NBS and a catalytic amount of AIBN were added. The reaction mixture was maintained at room temperature for 1 h and then extracted with a solution of $NaHCO_3$, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography over silica gel yielded 32 mg (40%) of **18**: syrup; $[\alpha]_D^{25}$=210 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2948, 1738, 1244 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.55 (1H, d, *J*=5.8 Hz, H-11), 5.49 (1H, d, *J*=5.8 Hz, H-12), 4.50 (1H, dd, J_1=5.8 Hz, J_2=10.6 Hz, H-3), 4.06 (1H, d, *J*=11.0 Hz, H-28a), 3.76 (1H, d, *J*=11.1 Hz, H-28b), 2.04 (3H, s, CO*CH*$_3$), 2.04 (3H, s, CO*CH*$_3$), 1.19 (3H, s, 3H-25), 1.11 (3H, s, 3H-26), 0.99 (3H, s, 3H-27), 0.89 (3H, s, 3H-23), 0.89 (3H, s, 3H-30), 0.88 (3H, s, 3H-24), 0.86 (3H, s, 3H-29); ^{13}C NMR ($CDCl_3$): δ 16.8 (C-24), 18.2 (C-6), 20.0 (C-27), 20.9 (CO*CH*$_3$), 21.1 (CO*CH*$_3$), 21.4 (C-26), 22.7 (C-16), 23.6 (C-30), 24.3 (C-2), 25.1 (C-15), 25.3 (C-25), 28.2 (C-23), 31.0 (C-20), 31.4 (C-22), 32.0 (C-7), 33.1 (C-29), 33.9 (C-21), 35.6 (C-17), 36.9 (C-1), 37.9 (C-4), 38.7 (C-10), 40.7 (C-14), 40.9 (C-18), 42.7 (C-8), 46.4 (C-19), 51.2 (C-5), 71.1 (C-28), 80.6 (C-3), 115.9 (C-11), 121.5 (C-12), 145.2 (C-13), 154.5 (C-9), 171.1 (*CO*CH_3), 171.4 (*CO*CH_3); HRLSIMS, *m/z*: $[M+Na]^+$ 547.3762 ($C_{34}H_{52}O_4Na$, calcd 547.3763); and 4 mg (5%) of **19**: white solid; mp 139–141 °C; $[\alpha]_D^{25}$=−6 (*c* 0.4, $CHCl_3$); IR

($CHCl_3$): ν 2929, 1737, 1242 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.39 (1H, dd, J_1=3.1 Hz, J_2=10.6 Hz, H-11), 5.57 (1H, d, J=10.6 Hz, H-12), 4.50 (1H, dd, J_1=6.2 Hz, J_2=10.0 Hz, H-3), 4.16 (1H, d, J=11.2 Hz, H-28a), 3.98 (1H, d, J=11.2 Hz, H-28b), 2.05 (3H, s, COCH_3), 2.04 (3H, s, COCH_3), 0.95 (3H, s, Me), 0.94 (3H, s, Me), 0.91 (3H, s, Me), 0.85 (3H, s, Me), 0.84 (3H, s, Me), 0.77 (3H, s, Me), 0.71 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.2 (Me), 16.7 (Me), 18.1 (Me), 18.3 (C-6), 20.4 (Me), 21.2 (COCH_3), 21.4 (COCH_3), 23.5 and 24.3 (C-2 and C-15), 24.4 (Me), 27.9 (C-23), 30.0 (C-16), 32.3 (C-29), 32.4, 33.0 and 35.0 (C-7, C-21 and C-22), 33.0 (C-20), 36.7, 37.9 and 38.0 (C-4, C-8 and C-10), 37.8 and 38.2 (C-1 and C-19), 40.4 and 42.3 (C-14 and C-17), 54.2 (C-9), 55.0 (C-5), 65.8 (C-28), 80.9 (C-3), 125.5 and 126.6 (C-11 and C-12), 133.2 and 137.1 (C-13 and C-18), 171.1 (*CO*CH_3), 171.4 (*CO*CH_3); HRLSIMS, *m/z*: $[M+Na]^+$ 547.3764 ($C_{34}H_{52}O_4Na$, calcd 547.3763).

4.2.11. Treatment of 3 with NBS. Product **3** (1.4 g, 3 mmol) was dissolved in 30 mL of CCl_4, and 535 mg (3 mmol) of NBS and a catalytic amount of AIBN were added. After 2 h at room temperature, the reaction mixture was extracted with a solution of $NaHCO_3$, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 989 mg (70%) of **20**: white solid; mp 133–135 °C; $[\alpha]_D^{25}$=258 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3457, 2947, 1723 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.57 (1H, d, J=5.9 Hz, H-11), 5.54 (1H, d, J=5.9 Hz, H-12), 3.62 (3H, s, COOCH_3), 3.21 (1H, dd, J_1=4.9 Hz, J_2=11.2 Hz, H-3), 2.99 (1H, dd, J_1=3.7 Hz, J_2=13.2 Hz, H-18), 1.14 (3H, s, 3H-25), 1.00 (3H, s, 3H-23), 0.99 (3H, s, 3H-27), 0.92 (3H, s, 3H-30), 0.92 (3H, s, 3H-26), 0.88 (3H, s, 3H-29), 0.78 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.7 (C-24), 18.3 (C-6), 20.2 (C-26), 20.2 (C-27), 23.7 (C-30), 23.8 (C-16), 25.1 (C-25), 27.00 (C-15), 27.9 (C-2), 28.3 (C-23), 30.7 (C-20), 32.2 (C-7), 32.2 (C-22), 33.0 (C-29), 33.8 (C-21), 37.1 (C-1), 38.9 (C-10), 39.0 (C-4), 39.7 (C-18), 40.7 (C-14), 42.4 (C-8), 45.9 (C-19), 46.1 (C-17), 51.2 (C-5), 51.8 (COOCH_3), 78.7 (C-3), 115.7 (C-11), 120.6 (C-12), 145.2 (C-13), 154.6 (C-9), 178.4 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 491.3500 ($C_{31}H_{48}O_3Na$, calc. 491.3501); 165 mg (10%) of **24**: white solid; mp 173–175 °C; $[\alpha]_D^{25}$=31 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3330, 2945, 1723 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.66 (1H, dd, J_1=3.3 Hz, J_2=8.1 Hz, H-15), 4.84 (1H, dd, J_1=J_2=9.4 Hz, H-12), 3.55 (3H, s, COOCH_3), 3.17 (1H, dd, J_1=5.2 Hz, J_2=10.8 Hz, H-3), 2.71 (1H, dd, J_1=6.0 Hz, J_2=13.5 Hz, H-18), 1.07 (3H, s, 3H-27), 0.96 (3H, s, 3H-30), 0.94 (3H, s, 3H-23), 0.91 (3H, s, 3H-29), 0.87 (3H, s, 3H-25), 0.83 (3H, s, 3H-26), 0.75 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.4 (C-24), 15.7 (C-25), 18.8 (C-6), 20.7 (C-27), 25.7 (C-30), 27.1 (C-2), 27.6 (C-26), 27.9 (C-23), 29.2 (C-11), 30.9 (C-20), 31.9, 32.4 and 33.9 (C-7, C-21 and C-22), 32.3 (C-29), 37.1 (C-1), 37.8 (C-10), 37.8 (C-16), 38.8 (C-4), 39.6 (C-8), 41.1 (C-19), 41.4 (C-18), 43.7 (C-13), 51.2 (C-17), 51.4 (C-9), 51.7 (COOCH_3), 55.4 (C-5), 66.2 (C-12), 78.8 (C-3), 121.5 (C-15), 157.5 (C-14), 178.2 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 571.2761 ($C_{31}H_{49}O_3BrNa$, calcd 571.2763); 75 mg (5%) of **26**: white solid; mp 143–145 °C; $[\alpha]_D^{25}$=5 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3356, 2930, 1728, 1451, 1196 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.96 (1H, dd, J_1=4.7 Hz, J_2=7.6 Hz, H-15), 4.79 (1H, d, J=1.8 Hz, H-27a), 4.73 (1H, d, J=1.8 Hz, H-27b), 3.63 (3H, s, COOCH_3), 3.40 (1H, dd, J_1=0.0 Hz, J_2=9.0 Hz, H-12), 3.30 (1H, dd, J_1=2.4 Hz, J_2=12.5 Hz, H-18), 3.17 (1H, dd, J_1=6.5 Hz, J_2=9.2 Hz, H-3), 2.17 (1H, dd, J_1=2.2 Hz, J_2=4.7 Hz, H-16), 0.95 (3H, s, 3H-23), 0.95 (3H, s, 3H-29), 0.93 (3H, s, 3H-26), 0.86 (3H, s, 3H-30), 0.83 (3H, s, 3H-25), 0.78 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.3 and 15.4 (C-24 and C-25), 19.1 (C-6), 22.3 (C-30), 27.1 and 27.2 (C-2 and C-7), 27.5 and 28.2 (C-23 and C-29), 29.7 (C-20), 31.9 (C-26), 31.9 (C-16), 33.6 and 34.7 (C-21 and C-22), 36.9 (C-10), 38.1, 38.2 and 38.6 (C-1, C-11 and C-19), 38.9 (C-4), 41.0 (C-18), 42.0 (C-12), 46.2 (C-8), 50.4 (C-17), 51.9 (COOCH_3), 56.3 (C-5), 59.7 (C-9), 79.3 (C-3), 105.2 (C-27), 113.0 (C-15), 155.7 (C-13), 157.3 (C-14), 179.9 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 491.3492 ($C_{31}H_{48}O_3Na$, calcd 491.3501); and 167 mg (10%) of **28**: white solid; mp 148–150 °C; $[\alpha]_D^{25}$=83 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3469, 2949, 1724, 1458, 1217, 1033 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.93 (1H, s, H-19), 5.81 (1H, s, H-11), 3.64 (3H, s, COOCH_3), 3.22 (1H, dd, J_1=4.9 Hz, J_2=11.3 Hz, H-3), 1.24 (3H, s, Me), 1.09 (3H, s, Me), 1.06 (3H, s, Me), 1.00 (3H, s, Me), 0.97 (3H, s, Me), 0.88 (3H, s, Me), 0.79 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.8 (C-24), 16.8 (C-27), 18.2 (C-6), 21.9 (C-26), 25.5 (C-25), 27.0 (C-15), 27.8 (C-2), 28.3 (C-23), 28.3 (C-30), 29.4 (C-29), 32.5 (C-22), 33.3 (C-7), 33.3 (C-20), 33.5 (C-21), 34.3 (C-16), 37.1 (C-1), 39.0 (C-10), 39.0 (C-4), 42.3 (C-8), 46.0 (C-14), 47.6 (C-17), 51.3 (C-5), 52.1 (COOCH_3), 78.5 (C-3), 113.2 (C-12), 123.0 (C-11), 131.6 (C-18), 139.3 (C-13), 141.4 (C-19), 156.5 (C-9), 177.1 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 567.2447 ($C_{31}H_{45}O_3BrNa$, calcd 567.2450).

4.2.12. Treatment of 4 with NBS. Product **4** (1.2 g, 2.5 mmol) was dissolved in 30 mL of CCl_4, and 446 mg (2.5 mmol) of NBS and a catalytic amount of AIBN were added. The reaction mixture was maintained at reflux for 1 h, and then extracted with a solution of $NaHCO_3$, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 1.1 g (90%) of **21**: white solid; mp 221–223 °C; $[\alpha]_D^{25}$=107 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3433, 2946, 1727 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.59 (1H, d, J=5.8 Hz, H-11), 5.53 (1H, d, J=5.8 Hz, H-12), 3.71 (1H, ddd, J_1=4.3 Hz, J_2=9.6 Hz, J_3=11.6 Hz, H-2), 3.61 (3H, s, COOCH_3), 2.98 (1H, d, J=9.6 Hz, H-3), 2.29 (1H, dd, J_1=4.4 Hz, J_2=12.5 Hz, H-18), 1.18 (3H, s, Me), 1.02 (3H, s, Me), 0.97 (3H, s, Me), 0.91 (3H, s, Me), 0.90 (3H, s, Me), 0.86 (3H, s, Me), 0.80 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.9 (Me), 18.3 (C-6), 20.3 (Me), 20.4 (Me), 23.7 (Me), 23.8 (C-16), 26.1 (Me), 26.9 (C-15), 28.8 (Me), 30.7 (C-20), 32.1 (C-7), 32.2 (C-22), 33.0 (Me), 33.8 (C-21), 39.1 (C-4), 39.7 (C-18), 40.0 (C-8), 40.8 (C-10), 42.3 (C-14), 45.1 (C-1), 45.9 (C-19), 46.1 (C-17), 51.3 (C-5), 51.8 (COOCH_3), 69.5 (C-2), 83.6 (C-3), 116.0 (C-11), 120.5 (C-12), 145.5 (C-13), 153.4 (C-9), 178.4 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 507.3446 ($C_{31}H_{48}O_4Na$, calcd 507.3450).

4.2.13. Treatment of 5 with NBS. Product **5** (1 g, 2 mmol) was dissolved in 30 mL of CCl_4, and 357 mg (2 mmol) of NBS and a catalytic amount of AIBN were added. After 2 h at room temperature, the reaction mixture was extracted with a solution of $NaHCO_3$, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 668 mg (60%) of product **22**,[13] 195 mg (15%) of product **25**: white solid; mp 178–180 °C;

$[\alpha]_D^{25}$=40 (*c* 0.9, $CHCl_3$); IR ($CHCl_3$): ν 2947, 1729, 1245 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.66 (1H, dd, J_1=3.3 Hz, J_2=8.1 Hz, H-15), 4.84 (1H, dd, J_1=J_2=9.3 Hz, H-12), 4.44 (1H, dd, J_1=5.8 Hz, J_2=10.4 Hz, H-3), 3.55 (3H, s, COO*CH*$_3$), 2.71 (1H, dd, J_1=6.0 Hz, J_2=13.5 Hz, H-18), 2.02 (3H, s, CO*CH*$_3$), 1.57 (3H, s, Me), 1.07 (3H, s, Me), 0.96 (3H, s, Me), 0.92 (3H, s, Me), 0.90 (3H, s, Me), 0.83 (3H, s, Me), 0.82 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.8 (C-25), 16.5 (C-24), 18.6 (C-6), 20.6 (C-27), 21.4 (CO*CH*$_3$), 23.4 (C-2), 25.7 (C-30), 27.6 (C-26), 27.9 (C-23), 29.2 (C-11), 30.9 (C-20), 31.9, 32.3 and 33.9 (C-7, C-21 and C-22), 32.3 (C-29), 37.1 (C-1), 37.5 (C-16), 37.7 (C-4), 37.7 (C-10), 39.6 (C-8), 41.0 (C-19), 41.4 (C-18), 43.7 (C-13), 51.2 (C-17), 51.3 (C-9), 51.7 (COO*CH*$_3$), 55.6 (C-5), 66.0 (C-12), 80.7 (C-3), 121.6 (C-15), 157.4 (C-14), 171.0 (*CO*CH$_3$), 178.3 (C-28); HRLSIMS, *m*/*z*: $[M+Na]^+$ 613.2874 ($C_{33}H_{51}O_4BrNa$, calcd 613.2868); 53 mg (5%) of **27**: white solid; mp 168–170 °C; $[\alpha]_D^{25}$=15 (*c* 0.6, $CHCl_3$); IR ($CHCl_3$): ν 2928, 1728, 1244 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.97 (1H, dd, J_1=4.9 Hz, J_2=7.7 Hz, H-15), 4.78 (1H, d, *J*=1.7 Hz, H-27a), 4.74 (1H, d, *J*=1.7 Hz, H-27b), 4.44 (1H, dd, J_1=6.0 Hz, J_2=9.5 Hz, H-3), 3.64 (3H, s, COO*CH*$_3$), 3.40 (1H, dd, J_1=0.0 Hz, J_2=9.4 Hz, H-12), 3.30 (1H, dd, J_1=2.4 Hz, J_2=12.5 Hz, H-18), 2.18 (1H, dd, J_1=2.1 Hz, J_2=4.9 Hz, H-16), 0.96 (3H, s, Me), 0.93 (3H, s, Me), 0.86 (3H, s, Me), 0.86 (3H, s, Me), 0.86 (3H, s, Me), 0.83 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.5 (C-25), 16.4 (C-24), 19.0 (C-6), 21.4 (CO*CH*$_3$), 22.3 (C-30), 23.5 (C-2), 27.1 (C-7), 27.5 and 28.2 (C-23 and C-29), 29.7 (C-20), 31.9 (C-26), 31.9 (C-16), 33.7 and 34.7 (C-21 and C-22), 36.8 (C-10), 37.8 (C-4), 37.9, 38.0 and 38.6 (C-1, C-11 and C-19), 41.1 (C-18), 42.0 (C-12), 46.2 (C-8), 50.4 (C-17), 51.9 (COO*CH*$_3$), 56.4 (C-5), 59.6 (C-9), 81.2 (C-3), 105.4 (C-27), 113.1 (C-15), 155.5 (C-13), 157.1 (C-14), 171.0 (*CO*CH$_3$), 179.9 (C-28); HRLSIMS, *m*/*z*: $[M+Na]^+$ 533.3612 ($C_{33}H_{50}O_4Na$, calcd 533.3607); and 191 mg (15%) of **29**: white solid; mp 185–187 °C; $[\alpha]_D^{25}$=96 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2951, 1729, 1461, 1369, 1246, 1031 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.89 (1H, s, H-19), 5.76 (1H, s, H-11), 4.44 (1H, dd, J_1=5.2 Hz, J_2=11.0 Hz, H-3), 3.58 (3H, s, COO*CH*$_3$), 1.99 (3H, s, CO*CH*$_3$), 1.21 (3H, s, 3H-25), 1.04 (3H, s, 3H-29), 1.01 (3H, s, 3H-26), 0.92 (3H, s, 3H-30), 0.83 (3H, s, 3H-23), 0.82 (3H, s, 3H-27), 0.82 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 16.5 (C-27), 16.7 (C-24), 17.9 (C-6), 21.2 (CO*CH*$_3$), 21.8 (C-26), 24.0 (C-2), 25.4 (C-25), 26.8 (C-15), 28.0 (C-23), 28.1 (C-30), 29.3 (C-29), 32.3 (C-22), 33.1 (C-7), 33.1 (C-20), 33.4 (C-21), 34.1 (C-16), 36.7 (C-1), 37.8 (C-4), 38.7 (C-10), 42.1 (C-8), 45.8 (C-14), 47.4 (C-17), 51.2 (C-5), 51.9 (COO*CH*$_3$), 80.0 (C-3), 113.0 (C-12), 123.0 (C-11), 131.4 (C-18), 139.3 (C-13), 141.2 (C-19), 155.9 (C-9), 170.8 (*COCH*$_3$), 176.8 (C-28); HRLSIMS, *m*/*z*: $[M+Na]^+$ 609.2548 ($C_{33}H_{47}O_4BrNa$, calcd 609.2555).

4.2.14. Treatment of 6 with NBS. Product **6** (1.2 g, 2.1 mmol) was dissolved in 30 mL of CCl_4, and 374 mg (2.1 mmol) of NBS and a catalytic amount of AIBN were added. The reaction mixture was maintained at reflux for 1 h, and then extracted with a solution of $NaHCO_3$, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 1.1 g (90%) of **23**: white solid; mp 191–193 °C; $[\alpha]_D^{25}$=152 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2948, 1741, 1369, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.53 (1H, d, J_1=5.9 Hz, H-11), 5.51 (1H, d, J_1=5.9 Hz, H-12), 5.11 (1H, ddd, J_1=4.5 Hz, J_2=10.4 Hz, J_3=11.7 Hz, H-2), 4.72 (1H, d, *J*=10.4 Hz, H-3), 3.60 (3H, s, COO*CH*$_3$), 2.97 (1H, dd, J_1=4.3 Hz, J_2=14.2 Hz, H-18), 2.02 (3H, s, CO*CH*$_3$), 1.96 (3H, s, CO*CH*$_3$), 1.25 (3H, s, Me), 0.95 (3H, s, Me), 0.90 (3H, s, Me), 0.89 (3H, s, Me), 0.88 (3H, s, Me), 0.87 (3H, s, Me), 0.86 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 17.7 (Me), 18.2 (C-6), 20.3 (Me), 20.3 (Me), 21.0 (CO*CH*$_3$), 21.2 (CO*CH*$_3$), 23.7 (Me), 23.7 (C-16), 25.9 (Me), 26.9 (C-15), 28.6 (Me), 30.7 (C-20), 32.0 (C-7), 32.2 (C-22), 33.0 (Me), 33.8 (C-21), 39.2 (C-4), 39.7 (C-18), 39.8 (C-8), 40.7 (C-10), 42.3 (C-14), 42.5 (C-1), 45.8 (C-19), 46.1 (C-17), 51.0 (C-5), 51.7 (COO*CH*$_3$), 70.4 (C-2), 80.4 (C-3), 116.3 (C-11), 120.5 (C-12), 145.8 (C-13), 152.8 (C-9), 170.6 (*CO*CH$_3$), 170.9 (*CO*CH$_3$), 178.3 (C-28); HRLSIMS, *m*/*z*: $[M+Na]^+$ 591.3664 ($C_{35}H_{52}O_6Na$, calcd 591.3661).

4.2.15. Photolysis of 20. Product **20** (325 mg, 0.7 mmol) was dissolved in 65 mL of ethanol and irradiated in a borosilicate flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. After 20 min, the solvent was evaporated and the residue chromatographed on a silica gel column to obtain 308 mg (95%) of **30**: white solid; mp 196–198 °C; $[\alpha]_D^{25}$=145 (*c* 0.7, $CHCl_3$); IR ($CHCl_3$): ν 3442, 2945, 1727 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.98 (1H, d, *J*=12.8 Hz, H-12), 5.80 (1H, d, *J*=12.8 Hz, H-11), 3.60 (3H, s, COO*CH*$_3$), 3.24 (1H, dd, J_1=4.9 Hz, J_2=11.3 Hz, H-3), 2.77 (1H, dd, J_1=3.6 Hz, J_2=12.7 Hz, H-18), 1.47 (3H, s, 3H-27), 1.25 (3H, s, 3H-26), 1.08 (3H, s, 3H-25), 1.00 (3H, s, 3H-23), 0.86 (3H, s, 3H-30), 0.85 (3H, s, 3H-29), 0.81 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.6 (C-24), 18.8 (C-6), 20.8 (C-27), 21.5 (C-26), 21.9 (C-25), 22.7 (C-16), 25.0 (C-30), 28.0 (C-2), 28.3 (C-23), 29.8 (C-7), 30.7 (C-20), 32.8 (C-22), 33.0 (C-29), 34.1 (C-21), 34.3 (C-15), 36.0 (C-1), 37.1 (C-18), 38.6 and 39.0 (C-4 and C-10), 43.0 (C-19), 45.4 (C-17), 50.7 (C-5), 51.7 (COO*CH*$_3$), 79.0 (C-3), 127.3 (C-11), 127.8 (C-14), 129.8 (C-8), 132.9 (C-12), 134.5 (C-13), 138.0 (C-9), 178.4 (C-28); HRLSIMS, *m*/*z*: $[M+Na]^+$ 491.3511 ($C_{31}H_{48}O_3Na$, calcd 491.3501).

4.2.16. Photolysis of 21. A solution of 325 mg (0.7 mmol) of product **21** in 65 mL of ethanol was irradiated for 20 min in a borosilicate flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. The reaction mixture was evaporated. Chromatography over silica gel yielded 310 mg (95%) of **31**: syrup; $[\alpha]_D^{25}$=48 (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3423, 2946, 1729, 1459, 1255, 1170, 1046 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.03 (1H, d, *J*=12.8 Hz, H-12), 5.80 (1H, d, *J*=12.8 Hz, H-11), 3.72 (1H, ddd, J_1=4.6 Hz, J_2=10.6 Hz, J_3=10.6 Hz, H-2), 3.61 (3H, s, COO*CH*$_3$), 3.05 (1H, d, *J*=10.6 Hz, H-3), 2.79 (1H, dd, J_1=4.0 Hz, J_2=12.5 Hz, H-18), 1.50 (3H, s, Me), 1.41 (3H, s, Me), 1.29 (3H, s, Me), 1.14 (3H, s, Me), 1.05 (3H, s, Me), 0.86 (3H, s, Me), 0.86 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.7 (Me), 18.8 (C-6), 20.9 (Me), 21.5 (Me), 22.7 (C-16), 23.2 (Me), 25.0 (Me), 28.8 (Me), 29.7 and 29.9 (C-7 and C-22), 30.8 (C-20), 32.9 (C-15), 33.0 (Me), 34.1 (C-21), 37.1 (C-18), 39.1 and 39.7 (C-4 and C-10), 43.0 (C-1), 43.9 (C-19), 45.5 (C-17), 50.5 (C-5), 51.7 (COO*CH*$_3$), 69.7 (C-2), 83.8 (C-3), 126.8 (C-11), 128.3 (C-14), 129.5 (C-13), 133.1 (C-12), 134.4 (C-8), 137.6 (C-9), 178.5 (C-28);

HRLSIMS, *m/z*: $[M+Na]^+$ 507.3444 ($C_{31}H_{48}O_4Na$, calcd 507.3450).

4.2.17. Photolysis of 22. A solution of 350 mg (0.7 mmol) of product **22** in 65 mL of ethanol was irradiated for 20 min in a borosilicate flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. The reaction mixture was evaporated. Chromatography over silica gel yielded 332 mg (95%) of **32**: syrup; $[\alpha]_D^{25}=157$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2946, 1731, 1247 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.90 (1H, d, $J=12.8$ Hz, H-12), 5.80 (1H, d, $J=12.8$ Hz, H-11), 4.52 (1H, dd, $J_1=5.0$ Hz, $J_2=11.3$ Hz, H-3), 3.62 (3H, s, COO*CH*$_3$), 2.79 (1H, dd, $J_1=3.9$ Hz, $J_2=12.7$ Hz, H-18), 2.04 (3H, s, CO*CH*$_3$), 1.48 (3H, s, 3H-27), 1.27 (3H, s, 3H-26), 1.10 (3H, s, 3H-25), 0.89, 0.88 and 0.88 (3H each, s, 3H-23, 3H-24 and 3H-30), 0.85 (3H, s, 3H-29); ^{13}C NMR ($CDCl_3$): δ 16.7 (C-24), 18.8 (C-6), 20.8 (C-27), 21.4 and 21.5 (C-26 and CO*CH*$_3$), 22.0 (C-25), 22.7 (C-16), 24.4 (C-2), 25.0 (C-30), 28.3 (C-23), 29.8 (C-7), 30.8 (C-20), 32.9 (C-22), 33.0 (C-29), 34.1 (C-15), 34.1 (C-21), 35.5 (C-1), 37.1 (C-18), 37.9 and 38.6 (C-4 and C-10), 43.1 (C-19), 45.4 (C-17), 50.6 (C-5), 51.7 (COO*CH*$_3$), 81.0 (C-3), 127.3 (C-11), 128.0 (C-14), 129.7 (C-8), 132.9 (C-12), 134.5 (C-13), 137.8 (C-9), 171.1 (*CO*CH$_3$), 178.4 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 533.3600 ($C_{33}H_{50}O_4Na$, calcd 533.3607).

4.2.18. Photolysis of 23. Product **23** (400 mg, 0.7 mmol) was dissolved in 65 mL of ethanol and irradiated in a borosilicate flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. After 20 min, the solvent was evaporated and the residue chromatographed on a silica gel column to obtain 381 mg (95%) of **33**: white solid; mp 169–171 °C; $[\alpha]_D^{25}=29$ (*c* 0.7, $CHCl_3$); IR ($CHCl_3$): ν 2948, 1740, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.02 (1H, d, $J=12.6$ Hz, H-12), 5.78 (1H, d, $J=12.6$ Hz, H-11), 5.09 (1H, ddd, $J_1=4.5$ Hz, $J_2=10.5$ Hz, $J_3=15.0$ Hz, H-2), 4.82 (1H, d, $J=10.5$ Hz, H-3), 3.66 (3H, s, COO*CH*$_3$), 2.81 (1H, dd, $J_1=3.4$ Hz, $J_2=12.3$ Hz, H-18), 2.03 (3H, s, CO*CH*$_3$), 1.96 (3H, s, CO*CH*$_3$), 1.44 (3H, s, Me), 1.23 (3H, s, Me), 1.16 (3H, s, Me), 0.92 (3H, s, Me), 0.91 (3H, s, Me), 0.87 (3H, s, Me), 0.85 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 17.6 (C-24), 18.6 (C-6), 20.7 (C-27), 21.0 (C-26), 21.2 (CO*CH*$_3$), 21.7 (CO*CH*$_3$), 22.7 (C-16), 22.7 (C-25), 24.9 (C-30), 28.5 (C-23), 29.8 (C-7), 30.7 (C-20), 32.9 (C-22), 33.0 (C-29), 34.2 (C-15), 34.2 (C-21), 37.0 (C-18), 39.3 (C-4), 39.6 (C-10), 40.7 (C-1), 43.0 (C-19), 45.4 (C-17), 51.8 (C-5), 51.8 (COO*CH*$_3$), 70.9 (C-2), 80.7 (C-3), 127.2 (C-11), 128.1 (C-14), 133.3 (C-12), 133.5 (C-8), 134.4 (C-13), 136.9 (C-9), 170.6 (*CO*CH$_3$), 170.9 (*CO*CH$_3$), 178.3 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 591.3668 ($C_{35}H_{52}O_6Na$, calcd 591.3662).

4.2.19. Isomerization of 30 with I_2. Product **30** (45 mg, 0.1 mmol) was dissolved in 50 mL of hexane and 5 mg (0.02 mmol) of I_2 were added. After 5 h at light reflux, 0.5 mL of sodium bisulfite were added. The reaction mixture was washed with water, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 9 mg (20%) of **30** and 27 mg (60%) of **34**: syrup; $[\alpha]_D^{25}=52$ (*c* 0.6, $CHCl_3$); IR ($CHCl_3$): ν 3349, 1639 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.16 (1H, d, $J=16.3$ Hz, H-12), 5.97 (1H, d, $J=16.3$ Hz, H-11), 3.61 (3H, s, COO*CH*$_3$), 3.24 (1H, dd, $J_1=4.7$ Hz, $J_2=11.3$ Hz, H-3), 3.13 (1H, dd, $J_1=3.1$ Hz, $J_2=12.7$ Hz, H-18), 1.66 (3H, s, 3H-26), 1.64 (3H, s, 3H-27), 1.01 (3H, s, Me), 1.01 (3H, s, Me), 1.00 (3H, s, Me), 0.88 (3H, s, Me), 0.81 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 15.5 (C-24), 18.7 (C-6), 19.1 (C-27), 20.4 (C-25), 21.4 (C-26), 22.5 (C-16), 24.1 (C-30), 28.0 (C-2), 28.1 (C-23), 30.7 (C-7), 30.9 (C-20), 32.1 (C-22), 32.9 (C-18), 33.3 (C-29), 33.8 and 34.2 (C-15 and C-21), 36.6 (C-1), 38.1 (C-10), 39.0 (C-4), 42.2 (C-19), 45.7 (C-17), 50.6 (C-5), 51.7 (COO*CH*$_3$), 79.0 (C-3), 123.2 (C-11), 126.8 (C-8), 129.5 (C-14), 131.3 (C-12), 132.5 (C-13), 141.6 (C-9), 178.2 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 491.3509 ($C_{31}H_{48}O_3Na$, calcd 491.3501).

4.2.20. Isomerization of 31 with I_2. 5 mg (0.02 mmol) of iodine were added to a solution of 50 mg (0.1 mmol) of product **31** in 50 mL of hexane. After 5 h at light reflux, 0.5 mL of sodium bisulfite were added. The reaction mixture was washed with water, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography over silica gel yielded 10 mg (20%) of starting material and 31 mg (60%) of product **35**: syrup; $[\alpha]_D^{25}=69$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3422, 2946, 1727, 1456, 1257, 1171 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.17 (1H, d, $J=16.2$ Hz, H-12), 5.96 (1H, d, $J=16.2$ Hz, H-11), 3.71 (1H, ddd, $J_1=4.2$ Hz, $J_2=9.5$ Hz, $J_3=11.5$ Hz, H-2), 3.62 (3H, s, COO*CH*$_3$), 3.13 (1H, dd, $J_1=3.0$ Hz, $J_2=12.7$ Hz, H-18), 3.03 (1H, d, $J=9.5$ Hz, H-3), 1.66 and 1.64 (3H each, s, 3H-26 and 3H-27), 1.08 (3H, s, Me), 1.05 (3H, s, Me), 1.02 (3H, s, Me), 0.89 (3H, s, Me), 0.85 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.6 (Me), 18.7 (C-6), 19.1 (Me), 21.4 (Me), 21.6 (Me), 22.5 (C-16), 24.2 (Me), 28.6 (Me), 30.7 (C-7), 30.9 (C-20), 32.1 (C-22), 33.0 (Me), 33.4 (C-18), 33.6 and 34.2 (C-15 and C-21), 39.1 and 39.2 (C-4 and C-10), 42.3 and 44.6 (C-1 and C-19), 45.7 (C-17), 50.6 (C-5), 51.7 (COO*CH*$_3$), 69.6 (C-2), 83.8 (C-3), 122.7 (C-11), 127.0 (C-8), 129.8 (C-14), 131.8 (C-12), 132.4 (C-13), 141.1 (C-9), 178.2 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 507.3450 ($C_{31}H_{48}O_4Na$, calcd 507.3450).

4.2.21. Isomerization of 32 with I_2. Product **32** (50 mg, 0.1 mmol) was dissolved in 50 mL of hexane and 5 mg (0.02 mmol) of I_2 were added. After 5 h at light reflux, 0.5 mL of sodium bisulfite were added. The reaction mixture was washed with water, dried over anhydrous Na_2SO_4, evaporated to dryness and chromatographed on a silica gel column to obtain 10 mg (20%) of **32** and 30 mg (60%) of **36**: syrup; $[\alpha]_D^{25}=80$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2948, 1729, 1247, 756 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.15 (1H, d, $J=16.3$ Hz, H-12), 5.94 (1H, d, $J=16.3$ Hz, H-11), 4.48 (1H, dd, $J_1=4.5$ Hz, $J_2=11.4$ Hz, H-3), 3.59 (3H, s, COO*CH*$_3$), 3.11 (1H, dd, $J_1=3.3$ Hz, $J_2=13.1$ Hz, H-18), 2.03 (3H, s, CO*CH*$_3$), 1.65 (3H, s, 3H-26), 1.62 (3H, s, 3H-27), 1.02 (3H, s, 3H-25), 0.98 (3H, s, 3H-30), 0.87, 0.87 and 0.86 (3H each, s, 3H-23, 3H-24 and 3H-29); ^{13}C NMR ($CDCl_3$): δ 16.6 (C-24), 18.6 (C-6), 19.0 (C-27), 20.5 (C-25), 21.4 (C-26), 21.4 (CO*CH*$_3$), 22.4 (C-16), 24.1 (C-30), 24.2 (C-2), 28.1 (C-23), 30.6 (C-7), 30.9 (C-20), 32.1 (C-22), 32.9 (C-18), 33.3 (C-29), 33.6 and 34.1 (C-15 and C-21), 36.2 (C-1), 37.9 (C-4), 37.9 (C-10), 42.2 (C-19), 45.7 (C-17), 50.7 (C-5), 51.7 (COO*CH*$_3$), 81.0 (C-3), 123.0 (C-11), 126.8 (C-8), 129.5 (C-14), 131.4 (C-12), 132.4 (C-13), 141.3 (C-9), 171.0 (*CO*CH$_3$), 178.2 (C-28);

HRLSIMS, *m/z*: $[M+Na]^+$ 533.3602 ($C_{33}H_{50}O_4Na$, calcd 533.3607).

4.2.22. Isomerization of 33 with I_2. 5 mg (0.02 mmol) of iodine were added to a solution of 55 mg (0.1 mmol) of product **33** in 50 mL of hexane. After 5 h at light reflux, 0.5 mL of sodium bisulfite were added. The reaction mixture was washed with water, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography over silica gel yielded 11 mg (20%) of starting material and 34 mg (60%) of **37**: syrup; $[\alpha]_D^{25}=1$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2949, 1739, 1369, 1249 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.19 (1H, d, J=16.0 Hz, H-12), 5.91 (1H, d, J=16.0 Hz, H-11), 5.14 (1H, ddd, J_1=4.0 Hz, J_2=11.3 Hz, J_3=11.3 Hz, H-2), 4.75 (1H, d, J=11.3 Hz, H-3), 3.60 (3H, s, COO*CH*$_3$), 3.10 (1H, dd, J_1=2.8 Hz, J_2=13.0 Hz, H-18), 2.04 (3H, s, CO*CH*$_3$), 1.96 (3H, s, CO*CH*$_3$), 1.69 (3H, s, Me), 1.63 (3H, s, Me), 1.17 (3H, s, Me), 0.98 (3H, s, Me), 0.93 (3H, s, Me), 0.91 (3H, s, Me), 0.86 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 17.5 (Me), 18.6 (C-6), 19.1 (Me), 21.0 (CO*CH*$_3$), 21.2 (CO*CH*$_3$), 21.5 (Me), 21.5 (Me), 22.4 (C-16), 24.0 (Me), 28.4 (Me), 29.8 (C-7), 30.6 and 33.4 (C-21 and C-22), 30.9 (C-20), 33.0 (Me), 33.3 (C-18), 34.1 (C-15), 38.9 and 39.4 (C-4 and C-10), 42.2 (C-19), 42.3 (C-1), 45.7 (C-17), 50.1 (C-5), 51.7 (COO*CH*$_3$), 70.4 (C-2), 80.6 (C-3), 122.4 (C-11), 127.1 (C-8), 130.0 (C-14), 131.7 (C-12), 132.3 (C-13), 140.3 (C-9), 170.3 (*CO*CH$_3$), 170.9 (*CO*CH$_3$), 178.1 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 591.3664 ($C_{35}H_{52}O_6Na$, calcd 591.3662).

4.2.23. Photolysis of 30. Product **30** (325 mg, 0.7 mmol) was dissolved in 65 mL of ethanol and irradiated in a quartz flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. After 30 min, the solvent was evaporated and the residue chromatographed on a silica gel column to obtain 309 mg (95%) of **38**: syrup; $[\alpha]_D^{25}=20$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3445, 2945, 1726 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.99 (1H, d, J=2.3 Hz, H-26a), 4.93 (1H, dd, J_1=4.5 Hz, J_2=9.4 Hz, H-11), 4.53 (1H, d, J=2.3 Hz, H-26b), 3.60 (3H, s, COO*CH*$_3$), 3.23 (1H, dd, J_1=4.9 Hz, J_2=10.0 Hz, H-3), 1.51 (3H, s, 3H-27), 0.97 (3H, s, 3H-25), 0.94 (3H, s, 3H-23), 0.89 (3H, s, 3H-30), 0.87 (3H, s, 3H-29), 0.81 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 15.5 (C-24), 19.0 (C-27), 20.8 (C-25), 23.0 and 23.2 (C-6 and C-16), 24.3 (C-30), 27.9 (C-2), 28.4 (C-23), 29.9 and 30.5 (C-12 and C-15), 30.7 (C-20), 32.2 (C-22), 33.0 (C-29), 34.1 (C-21), 35.2 (C-1), 36.0 (C-18), 37.3 (C-7), 39.5 (C-4), 40.6 (C-10), 41.5 (C-19), 45.8 (C-17), 51.7 (COO*CH*$_3$), 52.7 (C-5), 79.1 (C-3), 112.1 (C-26), 117.2 (C-11), 125.0 (C-14), 133.5 (C-13), 145.4 (C-8), 151.0 (C-9), 178.3 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 491.3502 ($C_{31}H_{48}O_3Na$, calcd 491.3501).

4.2.24. Photolysis of 31. A solution of 325 mg (0.7 mmol) of product **31** in 65 mL of ethanol was irradiated for 30 min in a quartz flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. The reaction mixture was evaporated. Chromatography over silica gel yielded 311 mg (95%) of **39**: syrup; $[\alpha]_D^{25}=32$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 3412, 2945, 1727, 1462, 1255, 1170 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.02 (1H, d, J=2.3 Hz, H-26a), 4.95 (1H, dd, J_1=4.3 Hz, J_2=9.6 Hz, H-11), 4.56 (1H, d, J=2.3 Hz, H-26b), 3.78 (1H, ddd, J_1=4.0 Hz, J_2=9.5 Hz, J_3=11.6 Hz, H-2), 3.62 (3H, s, COO*CH*$_3$), 3.03 (1H, d, J=9.5 Hz, H-3), 2.90 (1H, dd, J_1=9.6 Hz, J_2=15.4 Hz, H-12a), 2.75 (1H, dd, J_1=4.3 Hz, J_2=15.4 Hz, H-12b), 1.51 (3H, s, Me), 1.02 (3H, s, Me), 1.00 (3H, s, Me), 0.89 (3H, s, Me), 0.87 (3H, s, Me), 0.84 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 16.7 (Me), 19.0 (Me), 20.8 (Me), 22.9 and 23.1 (C-6 and C-16), 24.4 (Me), 28.9 (Me), 30.0 (C-15), 30.7 and 32.2 (C-12 and C-22), 30.7 (C-20), 33.0 (Me), 34.1 (C-21), 36.2 (C-18), 37.1 (C-7), 39.7 and 41.6 (C-4 and C-10), 41.5 (C-1), 43.3 (C-19), 45.8 (C-17), 51.8 and 52.7 (C-5 and COO*CH*$_3$), 69.5 (C-2), 83.9 (C-3), 112.7 (C-26), 117.8 (C-11), 125.2 (C-14), 133.4 (C-13), 144.9 (C-9), 150.1 (C-8), 178.4 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 507.3444 ($C_{31}H_{48}O_4Na$, calcd 507.3450).

4.2.25. Acetylation of 38. Product **38** (100 mg, 0.2 mmol) was dissolved in 4 mL of pyridine and 2 mL of Ac_2O and stirred for 1 h at reflux. The reaction mixture was diluted with water, extracted with CH_2Cl_2, washed with saturated aqueous $KHSO_4$ solution and dried with anhydrous Na_2SO_4. The solvent was evaporated at reduced pressure and the residue was chromatographed on a silica gel column to give 104 mg (95%) of **40**: syrup; $[\alpha]_D^{25}=38$ (*c* 0.6, $CHCl_3$); IR ($CHCl_3$): ν 2946, 1730, 1242 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.00 (1H, d, J=2.4 Hz, H-26a), 4.96 (1H, dd, J_1=4.5 Hz, J_2=9.5 Hz, H-11), 4.55 (1H, d, J=2.4 Hz, H-26b), 4.50 (1H, dd, H-3), 3.63 (3H, s, COO*CH*$_3$), 2.05 (3H, s, CO*CH*$_3$), 1.51 (3H, s, 3H-27), 0.97 (3H, s, 3H-25), 0.90 (3H, s, 3H-23), 0.89 (3H, s, 3H-30), 0.88 (3H, s, 3H-29), 0.86 (3H, s, 3H-24); ^{13}C NMR ($CDCl_3$): δ 16.7 (C-24), 19.0 (C-27), 20.9 (C-25), 21.4 (CO*CH*$_3$), 23.1 (C-6), 23.1 (C-16), 24.4 (C-30), 24.4 (C-2), 28.3 (C-23), 30.0 and 30.8 (C-12 and C-15), 30.7 (C-20), 32.2 (C-22), 33.0 (C-29), 34.1 (C-21), 34.9 (C-1), 36.4 (C-18), 37.1 (C-7), 38.4 (C-4), 40.4 (C-10), 41.6 (C-19), 45.8 (C-17), 51.8 (COO*CH*$_3$), 52.8 (C-5), 81.1 (C-3), 112.2 (C-26), 117.6 (C-11), 125.2 (C-14), 133.5 (C-13), 145.3 (C-8), 150.6 (C-9), 171.0 (*COCH*$_3$), 178.2 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 533.3601 ($C_{33}H_{50}O_4Na$, calcd 533.3607).

4.2.26. Photolysis of 33. Product **33** (390 mg, 0.7 mmol) was dissolved in 65 mL of ethanol and irradiated in a quartz flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. After 30 min, the solvent was evaporated and the residue chromatographed on a silica gel column to obtain 370 mg (95%) of **41**: white solid; mp 71–73 °C; $[\alpha]_D^{25}=28$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2946, 2356, 1743, 1251 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.19 (1H, ddd, J_1=3.9 Hz, J_2=11.2 Hz, J_3=11.2 Hz, H-2), 5.04 (1H, d, J=2.1 Hz, H-26a), 4.88 (1H, dd, J_1=4.3 Hz, J_2=9.5 Hz, H-11), 4.76 (1H, d, J=11.2 Hz, H-3), 4.58 (1H, d, J=2.1 Hz, H-26), 3.64 (3H, s, COO*CH*$_3$), 2.89 (1H, dd, J_1=9.5 Hz, J_2=15.5 Hz, H-12a), 2.73 (1H, dd, J_1=4.3 Hz, J_2=15.5 Hz, H-12b), 2.05 (3H, s, CO*CH*$_3$), 2.00 (3H, s, CO*CH*$_3$), 1.51 (3H, s, Me), 1.08 (3H, s, Me), 0.93 (3H, s, Me), 0.90 (3H, s, Me), 0.89 (3H, s, Me), 0.88 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 17.6 (Me), 19.0 (Me), 21.0 (Me), 21.2 (CO*CH*$_3$), 21.6 (CO*CH*$_3$), 22.9 (C-6), 23.0 (C-16), 24.3 (Me), 28.6 (Me), 29.8 (C-15), 29.9 (C-20), 30.6 (C-12), 30.7 (C-22), 33.0 (Me), 34.1 (C-21), 36.2 (C-18), 36.8 (C-7), 39.7 (C-4), 40.8 (C-1), 41.4 (C-10), 41.6 (C-19), 45.8 (C-17), 51.8 (COO*CH*$_3$), 52.3 (C-5), 70.6 (C-2), 80.6 (C-3), 113.0 (C-26), 117.9 (C-11), 125.3 (C-14), 133.2 (C-13),

144.4 (C-9), 149.5 (C-8), 170.5 (COCH$_3$), 170.8 (COCH$_3$), 178.2 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 591.3670 ($C_{35}H_{52}O_6Na$, calcd 591.3662).

4.2.27. Photolysis of 41. A solution of 340 mg (0.6 mmol) of product **41** in 55 mL of ethanol was irradiated for 30 min in a quartz flask using a 125 W high-pressure Hg street lamp with the outermost glass shell removed. The reaction mixture was evaporated. Chromatography over silica gel yielded 175 mg (50%) of starting material and 154 mg (45%) of **42**: white solid; mp 100–102 °C; $[\alpha]_D^{25}=-5$ (*c* 1, $CHCl_3$); IR ($CHCl_3$): ν 2947, 1733, 1249 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.15 (1H, ddd, J_1=4.6 Hz, J_2=10.7 Hz, J_3=11.3 Hz, H-2), 4.78 (1H, d, J=10.7 Hz, H-3), 3.59 (3H, s, COOCH_3), 3.05 (1H, m, H-11), 2.65 (1H, dd, J_1=3.7 Hz, J_2=10.3 Hz, H-18), 2.27 (1H, dd, J_1=4.2 Hz, J_2=13.0 Hz, H-26), 2.05 (3H, s, COCH_3), 2.00 (3H, s, COCH_3), 1.52 (3H, s, Me), 1.12 (3H, s, Me), 0.97 (3H, s, Me), 0.90 (3H, s, Me), 0.90 (3H, s, Me), 0.90 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 17.3 (C-24), 19.3 (C-6), 19.6 (C-27), 21.0 (C-25), 21.0 (COCH_3), 21.3 (COCH_3), 22.6 (C-16), 24.3 (C-30), 26.6 (C-15), 28.3 (C-23), 29.9 (C-21), 30.8 (C-20), 32.2 (C-22), 32.9 (C-29), 34.0 (C-12), 34.5 (C-7), 35.2 (C-18), 35.3 (C-26), 37.7 (C-4), 38.9 (C-11), 39.5 (C-10), 40.0 (C-1), 41.9 (C-19), 45.8 (C-17), 51.1 (C-5), 51.6 (COOCH_3), 70.1 (C-2), 80.9 (C-3), 125.4 (C-14), 132.8 (C-13), 136.8 (C-8), 152.8 (C-9), 170.7 (COCH$_3$), 170.8 (COCH$_3$), 178.4 (C-28); HRLSIMS, *m/z*: $[M+Na]^+$ 591.3669 ($C_{35}H_{52}O_6Na$, calcd 591.3662).

Acknowledgements

This work was supported by a grant from the Comisión Interministerial de Ciencia y Tecnología and by a project from the Ministerio de Educación y Cultura (No. PM98-0213). We thank David Nesbitt for reviewing the language of the original English manuscript.

References and notes

1. Dictionary of Natural Products on CD-ROM, Chapman and Hall, ISSN 0966-2146 ver. 5.1 (1996), oleanolic acid CAS (508-02-01), maslinic acid CAS (4373-41-5).
2. Garcia-Granados, A.; Martinez, A.; Parra, A.; Rivas, F. P.C.T. Int. Appl. W0 043331, 1998; (*Chem. Abstr.* **1998**, *128*, 179706).
3. Manna, S.; Yadagiri, P.; Falck, *J. Chem. Soc., Chem. Commun.* **1987**, 1324–1325.
4. Liu, *J. Ethnopharmacol.* **1995**, *49*, 57–68.
5. Garcia-Granados, A.; Dueñas, J.; Moliz, J. N.; Parra, A.; Perez, F. L.; Dobado, J. A.; Molina, J. *J. Chem. Res. (S)* **2000**, 56–57. Garcia-Granados, A.; Dueñas, J.; Moliz, J. N.; Parra, A.; Perez, F. L.; Dobado, J. A.; Molina, J. *J. Chem. Res. (M)* **2000**, *2*, 0326–0339. Garcia-Granados, A.; Dueñas, J.; Melguizo, E.; Moliz, J. N.; Parra, A.; Perez, F. L.; Dobado, J. A.; Molina, J. *J. Chem. Res. (S)* **2000**, 212–213. Garcia-Granados, A.; Dueñas, J.; Melguizo, E.; Moliz, J. N.; Parra, A.; Perez, F. L.; Dobado, J. A.; Molina, J. *J. Chem. Res. (M)* **2000**, *2*, 0653–0670.
6. Rasmusson, G. H.; Reynolds, G. F.; Steinberg, N. G.; Walton, E.; Patel, G. F.; Liang, T.; Cascieri, M. A.; Cheung, A. H.; Brooks, J. R.; Berman, C. *J. Med. Chem.* **1986**, *29*, 2298. Spera, G.; Lubrano, C. *Int. J. Immunopathol. Pharmacol.* **1996**, *91*, 33. Ling, Y. Z.; Li, J. S.; Kato, K.; Liu, Y.; Wang, X.; Klus, G. T.; Marat, K.; Nnane, I. P.; Brodie, A. M. H. *Bioorg. Med. Chem.* **1998**, *6*, 1683.
7. Garcia-Granados, A.; Lopez, P. E.; Melguizo, E.; Moliz, J. N.; Parra, A.; Simeo, Y. *J. Org. Chem.* **2003**, *68*, 4833–4844.
8. Garcia-Granados, A.; Lopez, P. E.; Melguizo, E.; Parra, A.; Simeo, Y. *Tetrahedron Lett.* **2003**, *44*, 6673–6677.
9. Monaco, P.; Caputo, R.; Palumbo, G.; Mangoni, L. *Phytochemistry* **1973**, *12*, 939.
10. Havinga, E.; de Kock, R. J.; Rappoldt, M. P. *Tetrahedron* **1960**, *11*, 276–284. Lugtenburg, J.; Havinga, E. *Tetrahedron Lett.* **1969**, *28*, 2391–2394. Gottfried, N.; Kaiser, W.; Braun, M.; Fuss, W.; Kompa, K. L. *Chem. Phys. Lett.* **1984**, *110*, 335–339. Schönecker, B.; Reichenbächer, M.; Gliesing, S.; Gonschior, M.; Griebenow, S.; Scheddin, D.; Mayer, H. *Steroids* **1998**, *63*, 28–36.
11. Autrey, R. L.; Barton, D. H. R.; Ganguly, A. K.; Reusch, W. H. *J. Chem. Soc.* **1961**, *3*, 3313–3319.
12. Misra, L.; Laatsch, H. *Phytochemistry* **2000**, *54*, 969–974.
13. Lampasona, M. E. P.; Catalan, C. A. N.; Gedris, T. E.; Herz, W. *Phytochemistry* **1998**, *49*, 2061–2064.
14. Agata, I.; Corey, E. J.; Hortmann, A. G.; Klein, J.; Proskow, S.; Ursprung, J. J. *J. Org. Chem.* **1965**, *30*, 1698–1710.
15. Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. Organic Chemistry. *Pericyclic reactions 2: sigmatropic and electrocyclic reactions*; Oxford University Press: Oxford, 2001; Chapter 36.