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Remote Hydroxylation of Methyl Groups by Regioselective Cyclopalladation. Partial Synthesis of Hyptatic Acid-A

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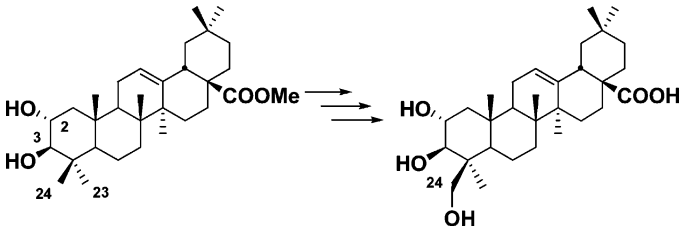
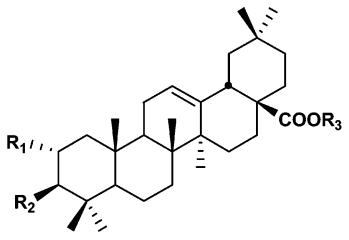


Hyptatic acid-A (24-hydroxymaslinic acid)

Hyptatic acid-A (**32**), a 2α,3*β*,24-trihydroxyolean-12-en-28-oic acid, previously isolated from *Hyptis capitata*, was obtained from maslinic acid (**2**). The regioselective cyclopalladation of the axial methyl group on C-4 of maslinic acid afforded the C-24 hydroxymethylene group due to the presence of a C-2-OR substituent. Nevertheless, hederagenin (**7**) (23-hydroxy derivative) was formed when this oxygenated group was not present.

Introduction

The oxidation of unactivated sp^3 C−H bonds is a process that has found widespread application in synthetic chemistry.[1] These oxidative methods have been applied to the functionalization of several steroids and terpenoids for synthesizing different natural products.[2] Thus, 2-cyano-3,12-dioxooleana-1,9-(11)-dien-28-oic acid (CDDO) and related compounds are potential anti-inflammatory, cancer chemopreventive, and chemotherapeutic agents. Recently, for the synthesis of a new important precursor, 23-hydroxy-CDDO-Me was synthesized from methyl 3,12-dioxooleana-9(11)-en-28-oate by a C-23 oxidation protocol, which involves cyclopalladation of a C-4 methyl group from a 3-one oxime.[3]



1 Oleanolic acid: R_1=H; R_2=OH; R_3=H
2 Maslinic acid: R_1=OH; R_2=OH; R_3=H
3 Methyl oleanate: R_1=H; R_2=OH; R_3=CH_3
4 Methyl maslinate: R_1=OH; R_2=OH; R_3=CH_3

FIGURE 1. Structures of **1**−**4**.

Oximes are among the most useful and versatile synthetic intermediates in organic chemistry, and they also are of considerable theoretical interest. For this reason, the preferred conformation and configuration of oximes has been the subject of extensive investigation for many years. In this sense, the

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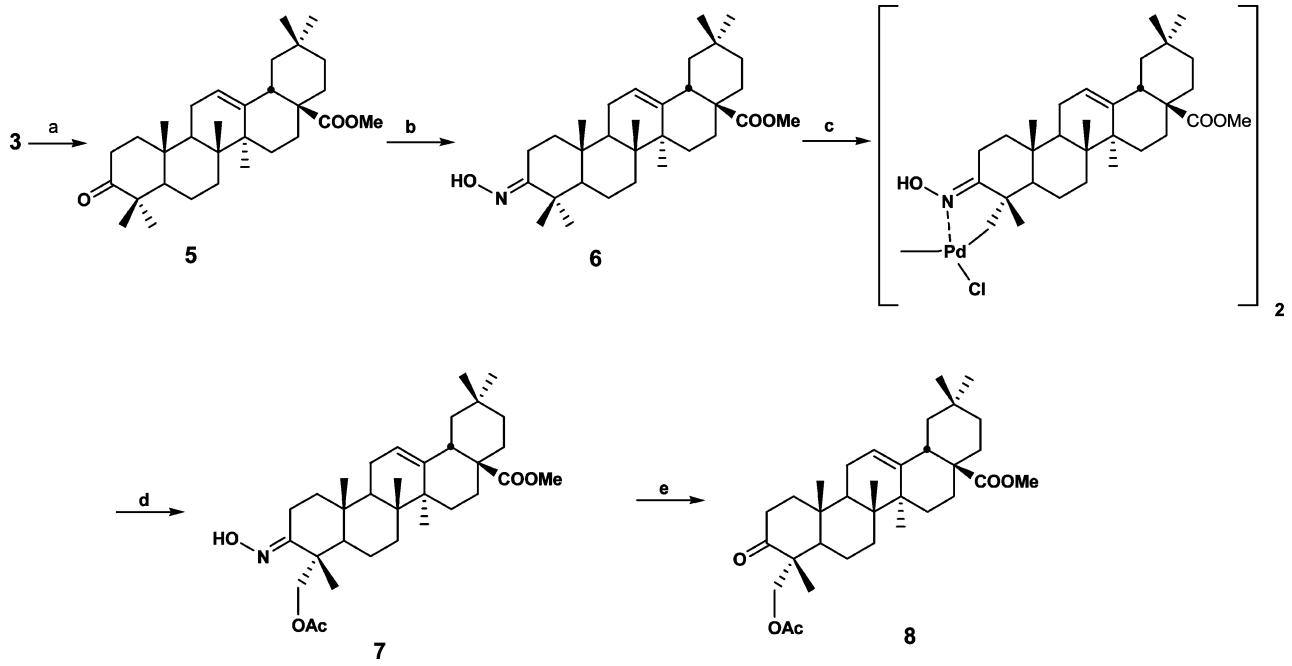
SCHEME 1. Synthesis of the 23-Acetoxy Derivative 8[a]



[a] Reagents and conditions: (a) Jones reagent, acetone, rt, 1 h, 98%. (b) $NH_2OH{\cdot}HCl$, Py, 50 °C, 45 min, 90%. (c) Na_2PdCl_4, HOAc, KOAc, rt, 72 h, 90%. (d) (i) DMAP, Et_3N, Ac_2O, rt, 45 min; (ii) THF, Py, $Pb(OAc)_4$, HOAc, rt, 24 h; (iii) $NaBH_4$, NaOH (1 N), rt, 10 min, 75% (for three steps). (e) $TiCl_3$, NH_4OAc, H_2O, rt, 4 h, 90%.

TABLE 1. ^{13}C NMR Shifts for A-Ring of 3β-Hydroxy-12-Oleanene Derivatives

compound/ carbon	3	10	12	23-hydroxy-erythrodiol[9]	24-hydroxy-methyl oleanate[12]	hederagenin methyl ester[9]
C-1	38.5	38.2	38.4	38.3	38.8	38.1
C-2	27.8	27.8	26.9	26.0	27.6	26.4
C-3	79.1	77.0	76.9	75.7	80.8	76.4
C-4	38.8	41.9	41.9	41.7	41.6	41.7
C-5	55.3	49.9	49.8	49.3	55.9	49.7
C-10	37.1	37.0	36.9	36.8	35.7	36.9
C-23		72.2	72.2	70.3	22.4	71.3
C-24		11.5	11.4	11.6	64.4	11.6

conformationally mobile system of 2-substitued cyclohexanone oximes has been investigated by means of NMR spectroscopy and X-ray crystallography.[4]

Oleanolic acid (**1**) and maslinic acid (**2**) (Figure 1) are oleanene triterpenic acids[5] isolated from the solid wastes of olive oil pressing. A method to obtain large quantities of both compounds from these solid residues has been reported by our group.[6] In previous papers, we have described the conversion of the corresponding esters, **3** and **4**, into several A- and C-ring modified derivatives.[7]

Triterpenoids are a large family of natural products biosynthetically derived from squalene and widely found in nature. Pentacyclic triterpenes and saponins exhibit a wide range of biological activities, and some of them may be used in medicine. Erythrodiol and 23-hydroxyerythrodiol (**12**) are naturally occurring C-28 reduced derivatives of oleanolic acid present in several plants.[8,9] Hederagenin (23-hydroxyoleanolic acid) (**13**)[9,10] has been isolated from various plants and constitutes the aglycone of several triterpenic saponins.[11] Moreover, 24-hydroxyoleanolic acid was isolated from the roots of *Lantana indica*, and its structure was established by chemical and spectroscopic methods.[12] Hyptatic acid-A (2α,3β,24-trihydroxy-olean-12-en-28-oic acid or 24-hydroxymaslinic acid) (**32**) has been isolated as a significant cytotoxic principle of *Hyptis capitata*.[13] Hyptatic acid-B (2α,3β,19α,24-tetrahydroxyurs-12-

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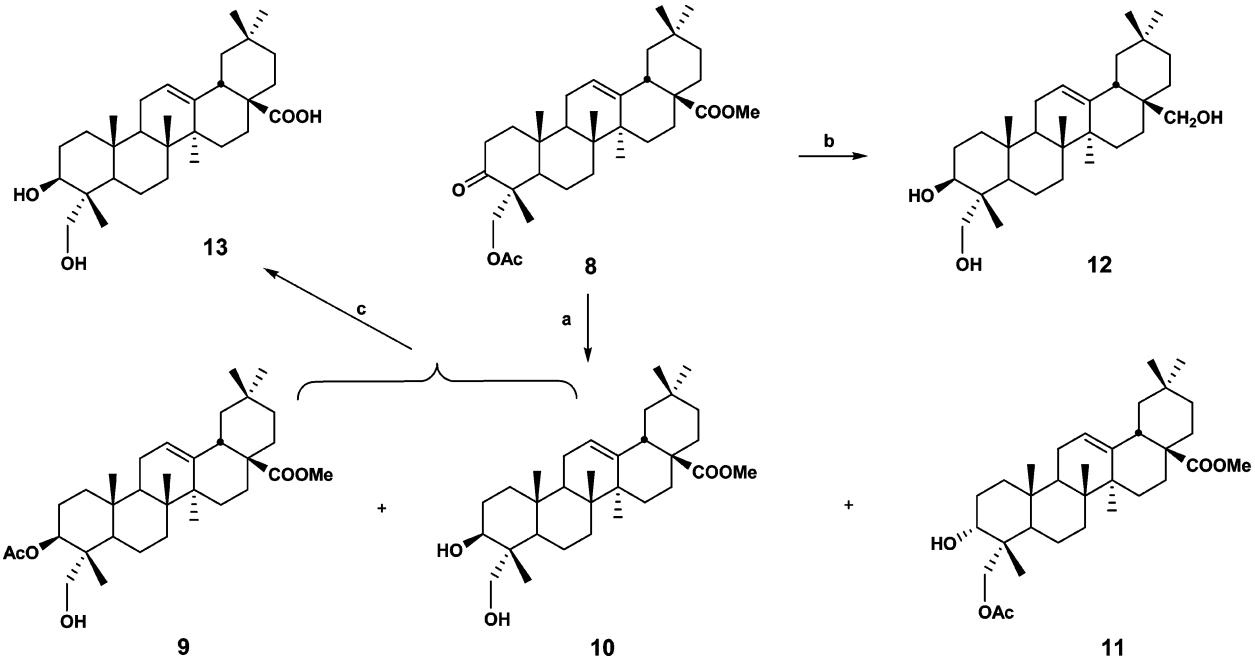
SCHEME 2. Reduction and Demethylation of 23-Hydroxy Derivative 8 and Synthesis of Hederagenin 13[a]



[a] Reagents and conditions: (a) *i*-PrOH, H_2O, $NaBH_4$, reflux, 12 h, **9** (35%), **10** (40%), and **11** (20%). (b) THF, $LiAlH_4$, reflux, 1 h, 94%. (c) LiBr, DMF, reflux, 48 h, 90%.

en-28-oic acid or 24-hydroxytormentic acid) was also isolated from this plant and, as a glucoside, from *Paradrymonia macrophylla*[14] and from the *Rubus* species.[15] On the other hand, arjulonic acid (2α,3β,23-trihydroxyolean-12-en-28-oic acid or 23-hydroxymaslinic acid) was isolated from the trunk wood extracts of *Myrianthus liberecus* together with other pentacyclic triterpenes as their methylesters.[16] Many of these naturally ocurring triterpenoids, together with their structural analogues, have interesting pharmacological profiles, including in vitro anti-HIV, antitumoral, and antioxidant properties.[17] In fact, via a pharmacophore search, 2β,3β-dihydroxyolean-12-en-23,28-dioic acid was identified as being a novel non-peptide HIV-1 protease inhibitor.[18]

In light of these results and our research program into the synthesis of various oleanane triterpenoids to discover new structures with potential pharmacological activities, we carried out several remote functionalizations on the *gem*-dimethyl group on the C-4 of oleanolic acid and maslinic acid. Here, we describe the partial synthesis of 23-hydroxyoleanolic acid (hederagenin) and 24-hydroxymaslinic acid (hyptatic acid-A), two naturally occurring compounds and other related products, using a regioselective cyclopalladation. It is the first reported synthesis of a 24-hydroxy derivative from compounds with a *gem*-dimethyl group on C-4 of the triterpenoid skeleton.

Results and Discussion

Our initial aim was the hydroxylation of the hindered C-4 equatorial methyl group of methyl oleanate (**3**). This functionalization was achieved according to Baldwin's method, which involves cyclopalladation of the methyl group from a 3-oxime functionality.[2] Thus, the oxidation of methyl oleanate yielded the 3-oxoderivative **5**[19] that was oximated to give methyl oleanate 3-oxime **6**. This oxime was palladated with Na_2PdCl_4 to give a dimeric organopalladium complex intermediate. Subsequently, acetylation with Ac_2O, oxidation with $Pb(OAc)_4$, and reductive workup with $NaBH_4$ afforded **7** that was hydrolyzed with $TiCl_3$ to give a 75% overall yield of product **8** (Scheme 1). ^{1}H- and ^{13}C NMR spectra of **7** and **8** demonstrated the existence of an AB system belonging to an acetoxymethylene group (δ 4.11 and 4.06 for product **7** and δ 4.08 and 4.04 for **8**) and the loss of the signal of one angular methyl group on C-4 (C-23 or C-24).

Compound **8** was treated with $NaBH_4$ at reflux in *i*-PrOH/H_2O to afford **9**−**11**, in which the carbonyl group on C-3 was reduced fundamentally from the α-face (**9** and **10**) but also from the β-face (**11**) (Scheme 2). Moreover, the reduction of **8** with $LiAlH_4$ at reflux afforded 23-hydroxyerythrodiol, **12**, the physical and spectral data of which are identical to those given in the literature[9] (Scheme 2). On the other hand, **9** or **10** were demethylated at C-28 by treatment with LiBr at reflux in DMF to produce hederagenin **13** (23-hydroxyoleanolic acid).[9,10] Compounds **12** and **13** showed a downfield shift of the H-3α signal (δ 3.63 for **12** and δ 3.67 for **13**) with respect to a 24-hydroxy derivative described in the literature (δ 3.34).[12]

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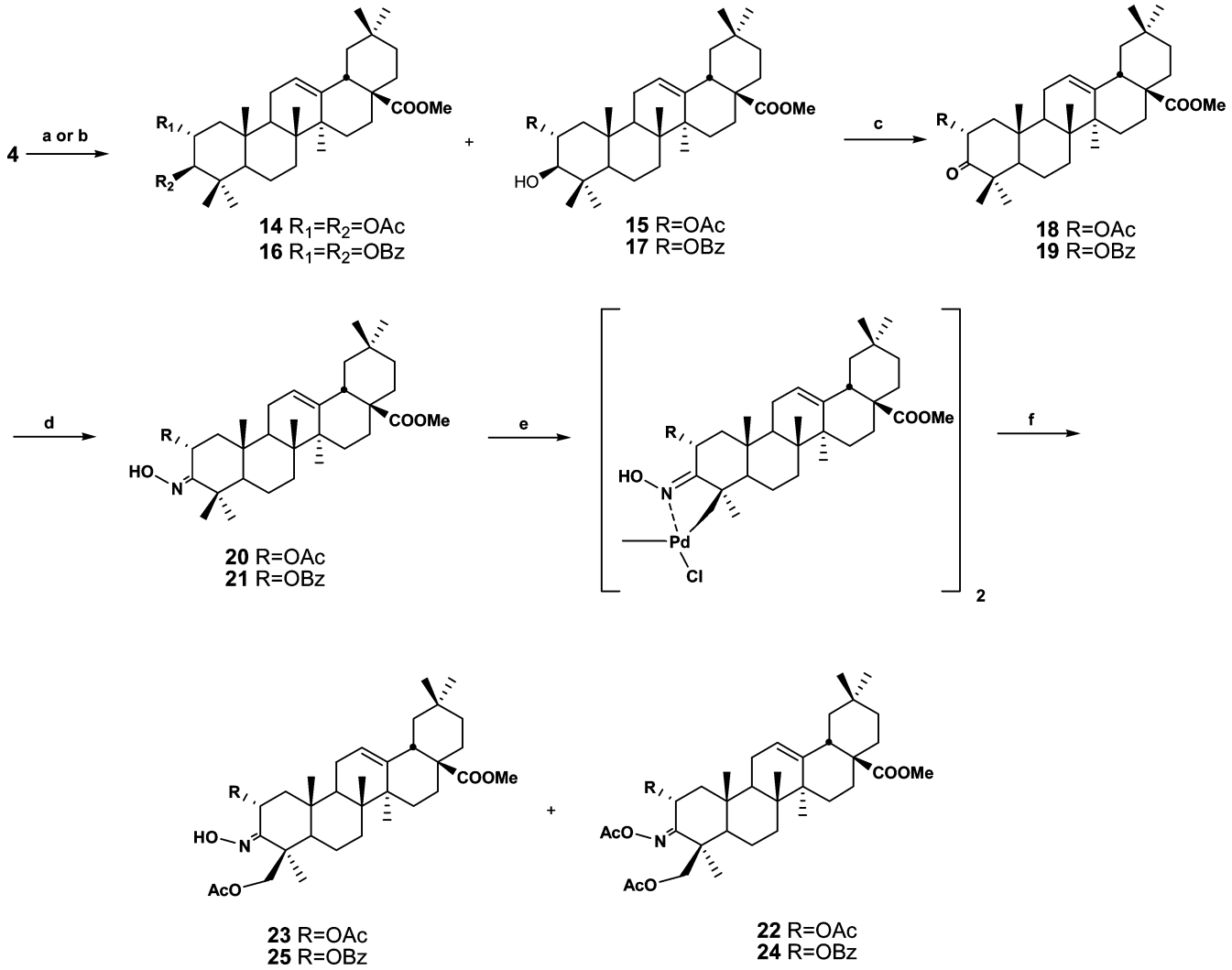
SCHEME 3. Synthesis of the 24-Hydroxy Derivatives 22−25[a]



[a] Reagents and conditions: (a) Ac_2O, Py, rt, 12 h, **14** (30%) and **15** (70%). (b) Benzoyl chloride, rt, 10 min, **16** (20%) and **17** (80%). (c) Jones reagent, acetone, rt, 1 h, **18** (95%) or **19** (98%). (d) $NH_2OH{\cdot}HCl$, Py, 50 °C, 45 min, **20** (75%) or **21** (70%). (e) Na_2PdCl_4, HOAc, KOAc, rt, 72 h, 90%. (f) (i) DMAP, Et_3N, Ac_2O, rt, 45 min; (ii) THF, Py, $Pb(OAc)_4$, HOAc, rt, 24 h; (iii) $NaBH_4$, NaOH (1 N), rt, 10 min, **22** (40%) and **23** (25%) or **24** (35%) and **25** (30%) (for three steps).

This shift can be interpreted as due to the deshielding effect of a hydroxyl group situated in the C-23 methyl group by the cyclopalladation process. This C-23 hydroxylation was also justified by the ^{13}C NMR data of the compound series **7**−**13**. Table 1 shows the ^{13}C NMR shifts for **10** and **12** (23-hydroxymethyl oleanate and 23-hydroxyerythrodiol, respectively), and the data are given in the literature for these compounds[9] and the corresponding 24-hydroxy derivative.[12]

As can be seen from this table, the main difference between the 23-hydroxy derivative (**10** and **12**) and the 24-hydroxy derivative are in C-3, C-5, and C-23 or C-24. Thus, 23-hydroxyderivatives showed considerable shielding γ-effects for C-3 (from −2.2 to −3.4 ppm), C-5 (from −5.4 to −6.0 ppm), and C-24 (around −4.0 ppm) because there were 1,3-diaxial interactions between the hydrogen atoms on C-23 and on the C-3 and C-5 γ-carbons.[20] These shielding γ-effects are not present when the new hydroxylation is situated on the C-24 methyl group, and consequently, these carbons resonated at δ 80.8 (C-3), δ 55.9 (C-5), and δ 64.4 (C-24).[12] The final confirmation of assigning the CH_2OH group to C-23 was provided by the NOE difference spectra of **10**, which showed enhancement between the AB quartet signals of 23-CH_2OH and the H-3 and H-5 signals (Figure 2).

We carried out a similar reaction sequence on methyl maslinate (**4**) (Scheme 3). In this case, the hydroxyl group at C-2 was protected as the acetoxy (**14** and **15**)[21] or benzoyloxy derivatives (**16** and **17**). Products **15** and **17**, which had a free 3β-hydroxyl group, were oxidized, yielding 3-oxo derivatives **18**[21] and **19**, and their oximation processes led to oximes **20** and **21**.

Finally, oximes **20** and **21** were palladated by a process similar to that described previously for **6** to give two 23- or 24-functionalized acetoxy (**22** and **23**) or benzoyloxy (**24** and **25**) derivatives (Scheme 3). In fact, these two pairs of compounds showed the presence of an AB system between δ

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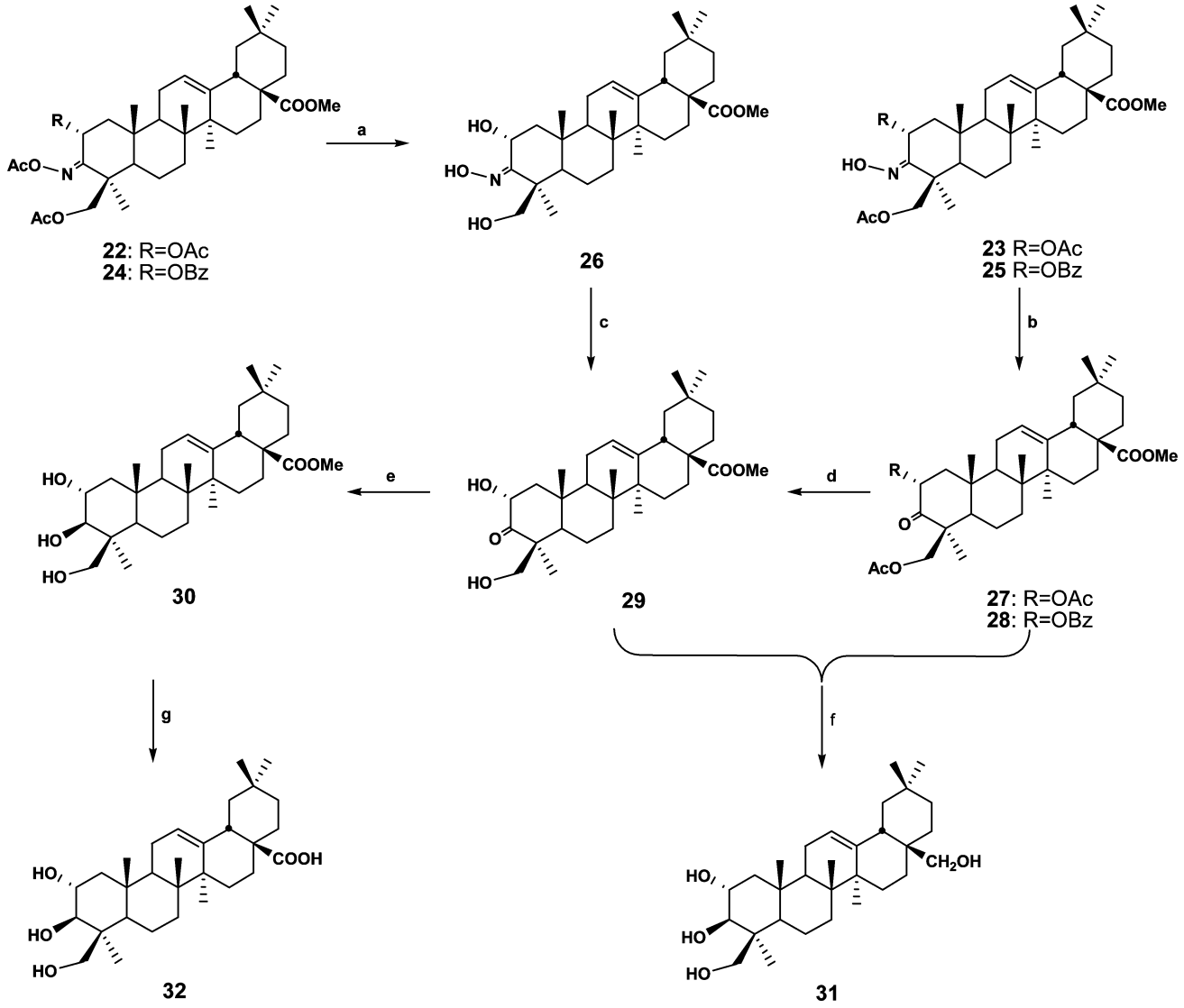
SCHEME 4. Reduction and Demethylation of 24-Hydroxy Derivatives 23−25 and Synthesis of Hyptatic Acid-A 32[a]



[a] Reagents and conditions: (a) MeOH, H_2O, KOH, rt, 2 h, **26** (80%) from **22**, **26** (75%) from **24**. (b) $TiCl_3$, NH_4OAc, H_2O, rt, 4 h, **27** (90%) or **28** (75%). (c) $TiCl_3$, NH_4OAc, H_2O, rt, 4 h, (85%). (d) MeOH, H_2O, KOH, rt, 2 h, **29** (90%) from **27** and **29** (85%) from **28**. (e) *i*-PrOH, H_2O, $NaBH_4$, reflux, 12 h, 80%. (f) THF, $LiAlH_4$, reflux, 1 h, 95%. (g) LiBr, DMF, reflux, 48 h, 90%.

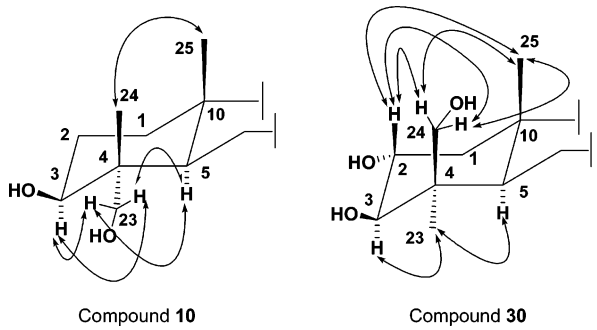


FIGURE 2. Significant NOE correlations for A-ring in **10** and **30**.

4.00 and δ 4.50 due to a new acetoxymethylene group on the methyl groups of C-4.

Complete saponification of **22** and **24** with methanolic KOH afforded trihydroxy derivative **26** (Scheme 4). On the other hand, hydrolysis of oximes **23** and **25** with $TiCl_3$ gave 3-oxo derivatives **27** and **28**, which were treated with KOH/MeOH to obtain the 3-oxo derivative **29**. Compound **29** was also obtained by hydrolysis of oxime **26** (Scheme 4). Reduction of product **29** with $NaBH_4$ at reflux in *i*-PrOH/H_2O afforded **30** in which the carbonyl group on C-3 was reduced from the α-face. Furthermore, the reduction of **29** (or products **27** or **28**) with $LiAlH_4$ at reflux afforded the tetrahydroxy derivative **31** (Scheme 4). Finally, the treatment of **30** with LiBr in refluxing DMF yielded **32**. Compounds **30**−**32** were hydroxymethylene derivatives that showed an upfield shift of the H-3α signal (δ 3.14, 3.14, and 3.04, respectively) as compared with the previously obtained 23-hydroxy derivatives **12** and **13** (δ 3.63 and 3.67, respectively) and with methyl arjulonate[16] (δ 3.39).

These shifts may be due to the loss of the deshielding effect that the 23-CH_2OH function exerts in **12**, **13**, and methyl arjulonate. However, H-3α for several 24-hydroxy derivatives hyptatic acid-B[13] and sericoside[14,15] was more shielded and situated at δ 2.95 and 2.96. Therefore, the cyclopallation process

TABLE 2. ^{13}C NMR Shifts for A-Ring for 2α,3β-Dihydroxy-12-Oleanene Derivatives

carbon	**2**	**30**	**31**	hyptatic acid-B[13a]	sericoside[13,14b]	methyl arjulonate[16]
C-1	46.4	46.5	46.6	46.1	47.5	46.0
C-2	69.0	69.2	69.2	68.7	68.6	68.7
C-3	83.9	85.5	85.5	85.8	85.7	80.1
C-4	39.4	43.4	43.4	43.7	43.9	42.5
C-5	55.3	56.0	55.9	56.0	56.6	48.8
C-10	38.4	39.4	39.4	39.2	38.4	38.2
C-23		23.8	23.8	24.2	24.6	69.9
C-24		68.3	69.7	65.7	65.6	12.9

[a] 24-Hydroxy tormentic acid. [b] 19-Hydroxy-28-glucosyl hyptatic acid-A.

of methyl maslinate had not situated the primary hydroxyl group at C-23 but at C-24; thus, hyptatic acid-A[13] was obtained, and the hoped-for 23-hydroxy derivative (arjulonic acid)[16] was not formed. In this case, the ^{13}C NMR data of **30** and **31** (Table 2) showed positive and lower γ-anti effects for C-3 and C-5 because in this 24-hydroxy derivative, the 1,3-diaxial proton interactions are not possible, and so C-3 and C-5 are more deshielded (δ 85.5 and δ 56.0, respectively). These values are comparable to δ 85.8 and 85.7 for the 24-hydroxy derivatives hyptatic acid-B and sericoside, respectively, and lower than in the corresponding 23-hydroxy derivative, methyl arjulonate (δ 80.1 for C-3 and δ 48.8 for C-5).[16] Finally, the NOE difference spectra in the A-ring of **30** confirmed this 24-hydroxy functionalization, showing a positive NOE effect between 2β-H, 2H of the 24-hydroxymethylene group, and 3H of the 25-methyl group (Figure 2).

A detailed analysis of the NMR spectra of **6** (3-oxime derivative of methyl oleanate) and **20** or **21** (2-acetoxy- or 2-benzoyloxy-3-oxime derivatives of methyl maslinate) can justify the different behaviors of these compounds in the cyclopalladation process. In all cases, the result is a single oxime in which the O−H and C3−C4 bonds are in an anti disposition. Moreover, in the ^{1}H NMR spectrum of **6**, the protons of C-2 are situated at δ 3.06 (1H, ddd, $J_{H2\alpha-H1\beta}$ = 3.3 Hz, $J_{H2\alpha-H1\alpha}$ = 5.2 Hz, and $J_{H2\alpha-H2\beta}$ = 15.4 Hz, H-2α) and δ 2.14 (1H, ddd, $J_{H2\beta-H1\beta}$ = 5.9 Hz, $J_{H2\beta-H1\alpha}$ = 13.9 Hz, and $J_{H2\beta-H2\alpha}$ = 15.4 Hz, H-2β). These coupling constants indicate that the A-ring has a slightly distorted conformation only in the C-3 region because of the presence on this carbon of one C═N exocyclic bond.

However, in **21** from methyl maslinate, in which there was a benzoyloxy group on C-2, H-2β is situated at δ 6.49 (1H, dd, $J_{H2\beta-H1\alpha}$ = 4.6 Hz and $J_{H2\beta-H1\beta}$ = 8.5 Hz) and H-1β at δ 2.33 (1H, dd, $J_{H1\beta-H2\beta}$ = 8.5 Hz and $J_{H1\beta-H1\alpha}$ = 14.4 Hz). From these coupling constants, we can deduce a severely distorted conformation from C-1 to C-4 in the A-ring of the structurally rigid system of the triterpenoid skeleton. In fact, the coupling constant of 8.5 Hz between H-2β and H-1β indicates that both protons are almost eclipsed (dihedral angle of 9.26° according to the Karplus equation), whereas H-2β and H-1α form a dihedral angle of 132.16° (J = 4.6 Hz).

Moreover, theoretical calculations[22] of A-ring conformations for **6** and **21** are in accordance with the experimental results. Thus, the most stable conformation for the A-ring of the C-3 oxime compound with no allyloxy substituent (**6**) is shown in Figure 3. As can be seen from this figure, the A-ring showed a half-chair conformation in which the electron pair of oxime is quite near the C-23 methyl group, which can justify its functionalization in the cyclopalladation process. In addition, the theoretical coupling constants for this conformation of product **6** are very similar to the experimental ones ($J_{H2\alpha-H1\beta}$ = 0.5 Hz, $J_{H2\beta-H1\beta}$ = 7.7 Hz, $J_{H2\alpha-H1\alpha}$ = 8.0 Hz, and $J_{H2\beta-H1\alpha}$ = 10.8 Hz).

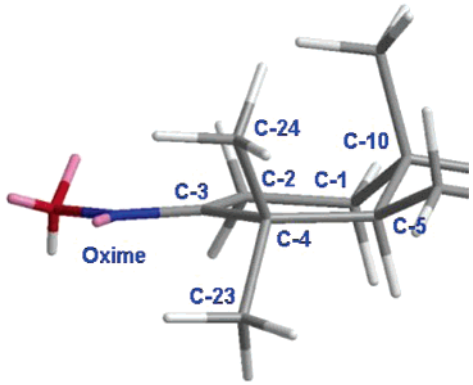


FIGURE 3. A-Ring conformation for **6** with no allyloxy substituent at C-2.

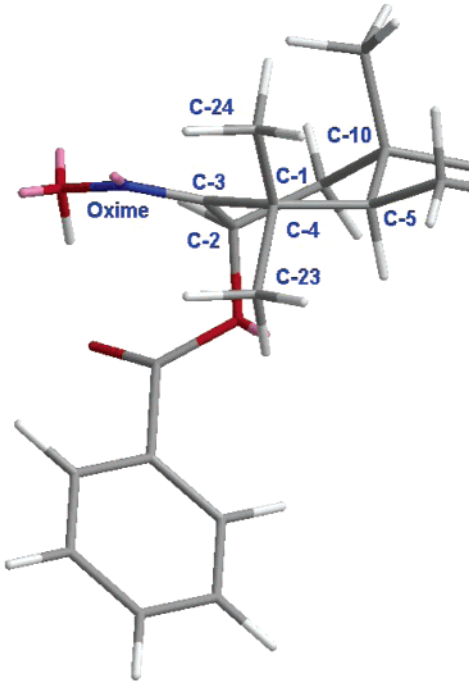


FIGURE 4. A-Ring conformation for **21** with a benzoyloxy substituent at C-2.

Figure 4 shows the most stable conformation for the A-ring of the C-3 oxime compound when there is a benzoyloxy group at C-2 (**21**). This figure confirms that, in this case, the A-ring has a more distorted conformation in which the benzoyloxy group is axially oriented on C-2. Also, in this case, the theoretical coupling constants of H-2 from this conformation ($J_{H2\beta-H1\alpha}$ = 1.2 Hz and $J_{H2\beta-H1\beta}$ = 8.2 Hz) are very similar to the experimental ones. Consequently, the oxime electron pair is now nearest to C-24 and can explain its remote palladium-catalyzed oxygenation.

(22) Obtained by the MM2 option of the program Chem3D Ultra, version 8.0 of CambridgeSoft Corporation.

Conclusion

In conclusion, the presence or absence of a C-2 oxygenated substituent determines which methyl group is functionalized, and the cyclopalladation reaction is a chemically induced oxygenation of the β-position of the *gem*-dimethyl group on C-4 of the terpenoid system. The differing reactivities of methyl oleanate and methyl maslinate in the cyclopalladation process is undoubtedly because of steric hindrance by the C-2 oxygenated group in methyl maslinate derivatives. This behavior is due to different A-ring conformations in methyl oleanate or methyl maslinate derivatives, in which the electron pair of the oxime is quite near the C-23 or C-24 methyl group. Therefore, the presence of a C-2-OR substituent markedly modifies the A-ring conformation of the triterpenoid compounds with this group on C-2, explaining their different regioselectivity in the cyclopalladation process of the methyl groups on C-4.

Experimental Section

Oxidation of Methyl Oleanate (3). Methyl oleanate (**3**) (794 mg, 1.7 mmol) was dissolved in acetone, and Jones reagent was added dropwise at room temperature until an orange color persisted. The excess of reagent was destroyed with MeOH, and the mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was neutralized with $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness at reduced pressure, and the residue was chromatographed to obtain **5** (778 mg, 98%).[19]

Oximation of Methyl 3-Oxooleanate (5). Compound **5** (580 mg, 1.2 mmol) was dissolved in pyridine (7 mL), and $NH_2OH\cdot$HCl (172 mg, 2.4 mmol) was added. The reaction mixture was stirred at 50 °C for 45 min, acidified with 0.1 N HCl solution, neutralized with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The solvent was evaporated at reduced pressure, and the residue was chromatographed to afford **6** (542 mg, 90%) as a white solid: mp 235−237 °C; $[\alpha]^{20}_D$ +19.4 (c 1, $CHCl_3$); IR ($CHCl_3$) 3319, 2947, 1725, 1461, 1165 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.28 (1H, dd, $J_1 = J_2 = 3.5$ Hz), 3.61 (3H, s), 3.06 (1H, ddd, $J_1 = 3.3$ Hz, $J_2 = 5.2$ Hz, $J_3 = 15.4$ Hz), 2.85 (1H, dd, $J_1 = 4.3$ Hz, $J_2 = 13.8$ Hz), 2.14 (1H, ddd, $J_1 = 5.9$ Hz, $J_2 = 13.9$ Hz, $J_3 = 15.4$ Hz), 1.14 (3H, s), 1.10 (3H, s), 1.04 (3H, s), 1.01 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.75 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0, 16.9, 17.1, 19.1, 23.1, 23.3, 23.6, 23.7, 25.9, 27.2, 27.7, 30.8, 32.4, 32.5, 33.2, 33.9, 37.2, 38.5, 39.4, 40.4, 41.4, 41.8, 45.9, 46.8, 47.3, 51.6, 55.9, 122.3, 143.9, 167.1, 178.3; HRMS *m*/*z* calcd for $C_{31}H_{49}NO_3Na$ 506.3618 $[M + Na]^+$, found 506.3620.

Cyclopalladation of Methyl 3-Hydroxyiminoolean-12-en-28-oate (6). To a solution of methyl 3-hydroxyiminoolean-12-en-28-oate (**6**) (524 mg, 1.1 mmol) in HOAc (50 mL), KOAc (128 mg, 1.3 mmol) and Na_2PdCl_4 (383 mg, 1.3 mmol) were added. The solution was stirred for 72 h at room temperature (rt), and cooled water (100 mL) was added to give a yellow precipitate. The palladium complex was filtered through Celite and dried in vacuo at rt for 24 h. To a solution of this yellow solid in dry CH_2Cl_2 (50 mL) were added DMAP (4 mg), Et_3N (0.25 mL), and Ac_2O (0.15 mL). The mixture reaction was stirred at rt for 45 min, washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated at reduced pressure. The crude product was dissolved again in dry THF (40 mL), and pyridine (0.1 mL) was added. The reaction mixture was stirred for 15 min at room temperature and cooled at − 80 °C, and a solution of $Pb(OAc)_4$ (536 mg, 1.2 mmol) in HOAc (10 mL) was added and again stirred at rt for 24 h. To remove the remaining Pd salts, a solution of $NaBH_4$ (40 mg) in 1 N NaOH solution (30 mL) was added to the reaction mixture. The mixture was stirred for 10 min and filtered. The filtrate was diluted with CH_2Cl_2 (75 mL), which was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to give a solid. The crude product was purified on a silica column to obtain **7** (446 mg, 75%) as a white solid: mp 203−205 °C; $[\alpha]^{20}_D$ +32 (c 1, $CHCl_3$); IR ($CHCl_3$) 2948, 2866, 1734, 1719, 1376, 1219 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.29 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.11 (1H, d, $J = 11.0$ Hz), 4.06 (1H, d, $J = 11.0$ Hz), 3.61 (3H, s), 2.83 (2H, m), 2.04 (3H, s), 1.10 (3H, s), 1.05 (3H, s), 0.97 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.75 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 16.9, 19.4, 18.0, 19.5, 21.1, 23.6, 23.1, 23.7, 25.8, 27.7, 30.8, 32.0, 32.4, 33.2, 34.0, 37.0, 36.7, 39.4, 41.5, 41.9, 42.9, 45.9, 46.9, 46.9, 48.7, 51.6, 68.4, 122.3, 143.9, 163.0, 171.1, 178.3; HRMS *m*/*z* calcd for $C_{33}H_{51}NO_5Na$ 564.3660 $[M + Na]^+$, found 564.3664.

Hydrolysis of Methyl 23-Acetoxy-3β-hydroxyiminoolean-12-en-28-oate (7). To a buffered solution of $TiCl_3$ (0.5 mL of 20% aqueous HCl solution containing 19% $TiCl_3$) and NH_4OAc (200 mg, 2.6 mmol) in water (8 mL) was added a solution of oxime **7** (450 mg, 0.8 mmol) in THF (15 mL). The mixture was stirred at rt for 4 h and extracted with CH_2Cl_2. The extract was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to afford a solid that was purified by a silica gel flash chromatography column to give **8** (394 mg, 90%) as a colorless oil: $[\alpha]^{20}_D$ +68 (c 1, $CHCl_3$); IR ($CHCl_3$) 2933, 2863, 1734, 1459, 1234 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 5.30 (dd, 1H, $J_1 = J_2 = 3.6$ Hz), 4.08 (d, 1H, $J = 11.1$ Hz), 4.04 (d, 1H, $J = 11.1$ Hz), 3.62 (s, 3H), 2.85 (dd, 1H, $J_1 = 4.0$ Hz, $J_2 = 13.9$ Hz), 2.42 (m, 2H), 2.01 (s, 3H), 1.13 (s, 3H), 1.04 (s, 3H), 1.00 (s, 3H), 0.92 (s, 3H), 0.89 (s, 3H), 0.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 17.0, 17.6, 19.6, 20.9, 23.6, 23.2, 23.7, 25.8, 27.8, 30.8, 32.4, 32.1, 33.2, 34.0, 35.0, 37.8, 39.4, 36.5, 41.6, 41.9, 45.9, 46.8, 46.9, 48.5, 50.3, 51.6, 67.7, 122.2, 144.1, 170.8, 178.3, 214.5; HRMS *m*/*z* calcd for $C_{33}H_{50}O_5Na$ 549.3553 $[M + Na]^+$, found 549.3556.

Reduction of Methyl 3-oxo-23-Acetoxyolean-12-en-28-oate (8) with $NaBH_4$. Compound **8** (200 mg, 0.37 mmol) was dissolved in *i*-PrOH/H_2O (3:1) (10 mL), and $NaBH_4$ (70 mg, 2 mmol) was added. The reaction mixture was stirred at reflux for 12 h. The excess of reagent was destroyed with $NaHSO_4$, and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The solid residue was purified on a silica gel chromatography column to give **9** (68 mg, 35%), **10** (72 mg, 40%), and **11** (39 mg, 20%). **9**: Colorless oil: $[\alpha]^{20}_D$ +70 (c 1, $CHCl_3$); IR ($CHCl_3$) 3439, 2934, 1732, 1458, 1248 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 5.27 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.87 (dd, 1H, $J_1 = 4.6$ Hz, $J_2 = 12.1$ Hz), 3.61 (3H, s), 3.36 (1H, d, $J = 12.6$ Hz), 2.89 (1H, d, $J = 12.6$ Hz), 2.84 (1H, dd, $J_1 = 4.4$ Hz, $J_2 = 13.9$ Hz), 2.06 (3H, s), 1.12 (3H, s), 0.95 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.71 (3H, s), 0.66 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.0, 16.0, 16.9, 17.8, 21.2, 23.2, 23.5, 23.7, 26.1, 27.8, 30.8, 30.8, 32.4, 32.5, 33.2, 34.0, 36.8, 38.1, 39.4, 41.4, 41.8, 42.4, 46.0, 46.8, 46.8, 47.6, 51.6, 64.6, 74.8, 122.2, 144.1, 172.4, 178.4; HRMS *m*/*z* calcd for $C_{33}H_{52}O_5Na$ 551.3712 $[M + Na]^+$, found 551.3716. **10**: White solid: mp 229−230 °C; $[\alpha]^{20}_D$ +68 (c 1, $CHCl_3$); IR ($CHCl_3$) 3364, 2930, 2857, 1725, 1459 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 5.26 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 3.71 (1H, d, $J = 10.4$ Hz), 3.63 (1H, dd, $J_1 = 4.8$ Hz, $J_2 = 10.1$ Hz), 3.61 (3H, s), 3.41 (d, 1H, $J = 10.4$ Hz), 2.84 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 13.7$ Hz), 1.24 (3H, s), 1.11 (3H, s), 0.94 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.71 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.5, 15.8, 17.0, 18.6, 23.5, 23.2, 23.7, 26.1, 26.9, 27.8, 30.8, 32.5, 32.6, 33.2, 34.0, 37.0, 38.2, 39.4, 41.4, 41.8, 41.9, 46.0, 46.8, 47.7, 49.9, 51.6, 72.2, 77.0, 122.4, 143.9, 178.4; HRMS *m*/*z* calcd for $C_{31}H_{50}O_4Na$ 509.3607 $[M + Na]^+$, found 509.3607. **11**: Colorless oil: $[\alpha]^{20}_D$ +51 (c 1, $CHCl_3$); IR ($CHCl_3$) 3444, 2933, 2863, 1726, 1251 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 5.27 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.18 (1H, d, $J = 11.5$ Hz), 3.81 (1H, d, $J = 11.5$ Hz), 3.61 (3H, s), 3.41 (dd, 1H, $J_1 = 4.8$ Hz, $J_2 = 4.8$ Hz), 2.85 (1H, dd, $J_1 = 4.4$ Hz, $J_2 = 14.3$ Hz), 2.09 (3H, s), 1.11 (3H, s), 0.93 (3H, s), 0.91 (3H, s), 0.89 (3H, s), 0.77 (3H, s), 0.71 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9, 15.9, 17.0, 18.3, 21.1, 23.2, 23.5, 23.7, 26.0, 26.2, 27.8, 30.8, 32.4, 32.5, 33.2,

34.0, 37.0, 38.3, 39.4, 41.4, 41.7, 42.1, 46.0, 46.8, 47.9, 48.4, 51.6, 67.6, 72.8, 122.4, 143.9, 171.5, 178.3; HRMS *m/z* calcd for $C_{33}H_{52}O_5Na$ 551.3712 $[M + Na]^+$, found 551.3712.

Reduction of Methyl 23-Acetoxy-3-oxoolean-12-en-28-oate (8) with $LiAlH_4$. Compound **8** (200 mg, 0.38 mmol) was dissolved in dry THF (10 mL), and a solution of 1 M $LiAlH_4$ in THF (1 mL) was added. The reaction mixture was stirred for 1 h at reflux, the excess of the reagent was destroyed with MeOH, and the solvent was concentrated under reduced pressure. The crude product was purified on a silica column to give (**12**)[9] (164 mg, 94%). IR ($CHCl_3$) 3344, 2930, 2857, 1725, 1459, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.18 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 3.72 (1H, d, $J = 10.3$ Hz), 3.63 (dd, 1H, $J_1 = 6.8$ Hz, $J_2 = 9.0$ Hz), 3.53 (1H, d, $J = 11.0$ Hz), 3.42 (1H, d, $J = 10.3$ Hz), 3.20 (1H, d, $J = 11.0$ Hz), 1.15 (3H, s), 0.97 (3H, s), 0.93 (3H, s), 0.89 (3H, s), 0.87 (3H, s), 0.86 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.4, 16.0, 16.8, 18.6, 22.1, 23.6, 23.7, 25.6, 26.0, 26.9, 31.0, 31.1, 32.5, 33.3, 34.2, 36.9, 37.0, 38.4, 39.9, 41.9, 42.0, 42.4, 46.6, 47.6, 49.8, 69.7, 72.2, 76.9, 122.4, 143.9; HRMS *m/z* calcd for $C_{30}H_{50}O_3Na$ 481. 3714 $[M + Na]^+$, found 481.3720.

Demethylation at C-28 of 23-Hydroxy Derivatives 9 and 10. Compound **9** was dissolved in DMF (3 mL), and LiBr (10 eq) was added. The reaction mixture was stirred at reflux for 48 h, and DMF was removed at reduced pressure. The crude product was purified on a silica column to afford (**13**)[9,10] (157 mg, 90%). IR ($CHCl_3$) 3335, 2928, 2850, 1692, 1457 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 3.67 (1H, dd, $J_1 = 5.0$ Hz, $J_2 = 10.8$ Hz), 3.59 (d, 1H, $J = 10.9$ Hz), 3.36 (d, 1H, $J = 10.9$ Hz), 2.92 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 13.4$ Hz), 1.24 (3H, s), 1.04 (3H, s), 1.01 (3H, s), 0.98 (3H, s), 0.89 (3H, s), 0.77 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.7, 16.3, 17.8, 19.2, 24.0, 24.1, 24.5, 26.4, 27.4, 28.9, 31.6, 33.5, 33.5, 33.8, 34.9, 37.9, 38.5, 40.5, 42.8, 43.0, 43.3, 47.3, 47.7, 48.8, 49.9, 67.6, 74.1, 123.6, 145.3, 181.8; HRMS *m/z* calcd for $C_{30}H_{48}O_4Na$ 495.3450 $[M + Na]^+$, found 495.3451. A similar procedure was followed for **10**.

Acetylation of Methyl Maslinate 4. Methyl maslinate (**4**) (1.2 g, 2.5 mmol) was dissolved in pyridine (5 mL), and Ac_2O (1.2 mL, 10 mmol) was added, stirring the reaction for 12 h at rt. The reaction was diluted with cooled water and extracted with CH_2Cl_2. The organic layer was acidified with aq HCl solution (20 mL, 10%), neutralized with $NaHCO_3$ solution (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified on a silica column to give **14** (427 mg, 30%) and **15** (924 mg, 70%).[21]

Benzoylation of Methyl Maslinate 4. Methyl maslinate (**4**) (1.2 g, 2.5 mmol) was dissolved in pyridine (5 mL), and benzoyl chloride (1.2 mL, 10 mmol) was added. The reaction was stirred for 10 min at rt. The reaction was diluted with cooled water and extracted with CH_2Cl_2. The organic layer was acidified with aq HCl solution (20 mL, 10%), neutralized with $NaHCO_3$ solution (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified on a silica column to afford **16** (348 mg, 20%) and **17** (1160 mg, 80%). **16**: Colorless oil: $[\alpha]^{20}_D$ −12 (c 1, $CHCl_3$); IR ($CHCl_3$) 2946, 1723, 1279, 710 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 7.4−8.2 (10H, m), 5.46 (1H, ddd, $J_1 = 4.6$ Hz, $J_2 = J_3 = 10.4$ Hz), 5.26 (1H, dd, $J_1 = J_2 = 3.4$ Hz), 5.21 (1H, d, $J = 10.4$ Hz), 3.62 (3H, s), 2.86 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.9$ Hz), 2.25 (1H, dd, $J_1 = 4.6$ Hz, $J_2 = 12.3$ Hz), 1.17 (3H, s), 1.14 (3H, s), 1.09 (3H, s), 1.00 (3H, s), 0.91 (3H, s), 0.89 (3H, s), 0.75 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.6, 16.9, 17.9, 18.4, 23.1, 23.6, 23.7, 26.0, 27.7, 28.6, 30.8, 32.4, 32.6, 33.2, 34.0, 38.5, 39.5, 39.9, 41.3, 41.8, 44.0, 45.9, 46.8, 47.7, 51.6, 55.2, 71.1, 81.1, 122.1, 128.3, 128.3, 128.9, 129.6, 129.6, 130.2, 130.3, 130.6, 132.8, 132.9, 134.6, 162.4, 143.9, 166.3, 166.5, 178.3; HRMS *m/z* calcd for $C_{45}H_{58}O_6Na$ 717.4131 $[M + Na]^+$, found 717.4132. **17**: White solid: mp 125−127 °C; $[\alpha]^{20}_D$ +12 (c 1, $CHCl_3$); IR ($CHCl_3$) 3463, 2947, 1720, 1277, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−8.1 (5H, m), 5.25 (1H, dd, $J_1 = J_2 = 3.5$ Hz), 5.19 (1H, ddd, $J_1 = 4.4$ Hz, $J_2 = 10.0$ Hz, $J_3 = 11.3$ Hz), 3.61 (3H, s), 3.37 (1H, d, $J = 10.0$ Hz), 2.84 (1H, dd, $J_1 = 4.3$ Hz, $J_2 = 13.8$ Hz), 2.11 (1H, dd, $J_1 = 4.4$ Hz, $J_2 = 12.1$ Hz), 1.12 (3H, s), 1.08 (3H, s), 1.08 (3H, s), 0.91 (3H, s), 0.90 (3H, s), 0.88 (3H, s), 0.72 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 16.8, 16.9, 18.4, 23.1, 23.6, 23.7, 26.0, 27.7, 28.7, 30.8, 32.4, 32.6, 33.2, 33.9, 38.5, 39.4, 40.0, 41.3, 41.8, 43.8, 45.9, 46.8, 47.7, 51.6, 55.3, 74.1, 81.0, 122.1, 128.4, 128.4, 129.7, 129.7, 130.5, 133.1, 143.9, 167.1, 178.3; HRM *m/z* calcd for $C_{38}H_{54}O_5Na$ 613.3870 $[M + Na]^+$, found 613.3870.

Oxidation of Methyl 2α-Acetoxy-3β-hydroxy-12-en-28-oate (15). Compound **15** (1500 mg, 2.5 mmol) was dissolved in acetone, and Jones reagent was added dropwise at room temperature until an orange color persisted. The excess of reagent was destroyed with MeOH, and the mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was neutralized with $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness at reduced pressure, and the residue was chromatographed to obtain **18** (1250 mg, 95%).[21]

Oxidation of Methyl 2α-Benzoyloxy-3β-hydroxyolean-12-en-28-oate (17). Compound **17** (1200 mg, 2 mmol) was dissolved in acetone, and Jones reagent was added dropwise at room temperature until an orange color persisted. The excess of reagent was destroyed with MeOH, and the mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was neutralized with $NaHCO_3$, dried over anhydrous Na_2SO_4, and evaporated to dryness at reduced pressure, and the residue was chromatographed to obtain **19** (1175 mg, 98%) as colorless oil: $[\alpha]^{20}_D$ +30 (c 1, $CHCl_3$); IR ($CHCl_3$) 2946, 1721, 1460, 1272, 1119, 756, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−8.1 (5H, m), 5.85 (1H, dd, $J_1 = 6.1$ Hz, $J_2 = 13.3$ Hz), 5.29 (1H, dd, $J_1 = J_2 = 3.5$ Hz), 3.63 (3H, s), 2.87 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 13.8$ Hz), 2.35 (1H, dd, $J_1 = 6.1$ Hz, $J_2 = 12.3$ Hz), 1.34 (3H, s), 1.20 (3H, s), 1.14 (3H, s), 1.12 (3H, s), 0.92 (3H, s), 0.89 (3H, s), 0.79 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 17.1, 19.2, 21.4, 23.1, 23.7, 23.7, 25.0, 26.0, 27.8, 30.8, 32.4, 32.4, 33.2, 33.9, 38.1, 39.5, 41.3, 41.8, 45.8, 45.9, 46.8, 47.5, 48.9, 51.6, 57.3, 72.3, 121.8, 128.4, 128.4, 129.9, 129.9, 130.0, 133.1, 144.2, 165.9, 178.3, 209.0; HRMS *m/z* calcd for $C_{38}H_{52}O_5Na$ 611.3712 $[M + Na]^+$, found 611.3714.

Oxidation of Methyl 3-oxo-2α-Acetoxyolean-12-en-28-oate (18). Compound **18** (2000 mg, 3.8 mmol) was dissolved in pyridine (20 mL), and $NH_2OH{\cdot}HCl$ (530 mg, 7.6 mmol) was added. The reaction mixture was stirred at 50 °C for 1 h, acidified with 0.1 N HCl solution, neutralized with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The solvent was evaporated at reduced pressure, and the residue was chromatographed to afford **20** (1540 mg, 75%) as a white solid: mp 194−196 °C; $[\alpha]^{20}_D$ +49 (c 1, $CHCl_3$); IR ($CHCl_3$): 3433, 2948, 1729, 1237, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.20 (1H, dd, $J_1 = 5.2$ Hz, $J_2 = 8.7$ Hz), 5.29 (1H, dd, $J_1 = J_2 = 3.5$ Hz), 3.60 (3H, s), 2.85 (1H, dd, $J_1 = 4.3$ Hz, $J_2 = 14.0$ Hz), 2.24 (1H, dd, $J_1 = 8.7$ Hz, $J_2 = 14.2$ Hz), 2.03 (3H, s), 1.24 (3H, s), 1.15 (3H, s), 1.13 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.83 (3H, s), 0.73 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2, 16.5, 19.9, 21.2, 23.2, 23.6, 23.7, 23.8, 25.8, 27.7, 30.8, 32.0, 32.4, 32.5, 33.2, 34.0, 36.8, 39.2, 39.4, 41.6, 42.0, 45.1, 45.9, 46.4, 46.9, 51.6, 52.4, 62.2, 122.4, 143.6, 162.4, 170.0, 178.3; HRMS *m/z* calcd for $C_{33}H_{51}NO_5$ 542.3840 $[M + H]^+$, found 542.383.

Oxidation of Methyl 3-oxo-2α-Benzoyloxyolean-12-en-28-oate (19). Compound **19** (2400 mg, 4.1 mmol) was dissolved in pyridine (22 mL), and $NH_2OH{\cdot}HCl$ (572 mg, 8.2 mmol) was added. The reaction mixture was stirred at 50 °C for 1 h, acidified with 0.1 N HCl solution, neutralized with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The solvent was evaporated at reduced pressure, and the residue was chromatographed to afford **21** (1.72 g, 70%) as a colorless oil: $[\alpha]^{20}_D$ +42 (c 1, $CHCl_3$); IR ($CHCl_3$) 3436, 2949, 1722, 1270, 756, 712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.4−8.0 (5H, m), 6.49 (1H, dd, $J_1 = 4.6$ Hz, $J_2 = 8.5$ Hz), 5.29 (1H, dd, $J_1 = J_2 = 3.5$ Hz), 3.61 (3H, s), 2.85 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.6$ Hz), 2.33 (1H, dd, $J_1 = 8.5$ Hz, $J_2 = 14.4$ Hz), 1.30 (3H, s), 1.18 (3H, s), 1.12 (3H, s), 0.90 (3H, s), 0.89

(3H, s), 0.87 (3H, s), 0.75 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 16.5, 20.0, 23.0, 23.2, 23.6, 23.6, 25.7, 27.7, 30.7, 32.1, 32.4, 32.5, 33.1, 34.0, 36.8, 39.2, 39.4, 41.6, 42.0, 45.3, 45.8, 46.5, 46.9, 51.6, 52.4, 62.7, 122.4, 128.4, 128.4, 129.7, 129.7, 130.4, 133.0, 143.6, 162.3, 165.6, 178.3; HRMS *m*/*z* calcd for $C_{38}H_{53}NO_5Na$ 626.3821 $[M + Na]^+$, found 626.3818.

Cyclopalladation of Methyl 2α-Acetoxy-3-hydroxyiminoolean-12-en-28-oate (20). To a solution of 2α-acetoxy-3-hydroxyiminoolean-12-en-28-oate (**20**) (1400 mg, 2.5 mmol) in HOAc (160 mL), KOAc (270 mg, 2.8 mmol) and Na_2PdCl_4 (830 mg, 2.8 mmol) were added. The solution was stirred for 72 h at rt, and cooled water (250 mL) was added to give a yellow precipitate. The palladium complex was filtered through Celite and dried in vacuo at rt for 24 h. To a solution of this yellow solid in dry CH_2Cl_2 (120 mL) were added DMAP (6 mg), Et_3N (0.5 mL), and Ac_2O (0.4 mL). The reaction mixture was stirred at rt for 45 min, washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated at reduced pressure. The crude product was dissolved again in dry THF (100 mL), and pyridine (0.2 mL) was added. The reaction mixture was stirred for 15 min at room temperature and cooled at − 80 °C, and a solution of $Pb(OAc)_4$ (1160 mg, 2.6 mmol) in HOAc (40 mL) was added and again stirred at rt for 24 h. To remove the remaining Pd salts, a solution of $NaBH_4$ (105 mg) in 1 N NaOH solution (38 mL) was added to the reaction mixture. The mixture was stirred for 10 min and filtered. The filtrate was diluted with CH_2Cl_2 (200 mL), which was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to give a solid. The crude product was purified on a silica column to obtain **22** (641 mg, 40%) and **23** (387 mg, 25%). **22**: Colorless oil: $[\alpha]^{20}_D$ +55 (c 1, $CHCl_3$); IR ($CHCl_3$) 2947, 1776, 1743, 1233, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96 (1H, dd, $J_1 = J_2 = 8.4$ Hz), 5.27 (1H, dd, $J_1 = J_2 = 3.4$ Hz), 4.42 (1H, d, $J = 11.6$ Hz), 4.23 (1H, d, $J = 11.6$ Hz), 3.59 (3H, s), 2.84 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.6$ Hz), 2.30 (1H, dd, $J_1 = 8.6$ Hz, $J_2 = 13.4$ Hz), 2.09 (3H, s), 2.03 (3H, s), 1.99 (3H, s), 1.32 (3H, s), 1.10 (3H, s), 0.90 (3H, s), 0.89 (3H, s), 0.87 (3H, s), 0.72 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8, 16.7, 19.4, 19.6, 20.9, 21.1, 23.1, 23.6, 24.0, 25.8, 27.6, 28.3, 30.8, 32.3, 32.4, 33.2, 33.9, 36.6, 39.1, 41.5, 41.9, 43.7, 43.8, 45.5, 45.8, 46.8, 51.6, 55.4, 63.6, 66.4, 122.1, 143.9, 166.4, 168.1, 169.4, 170.6, 178.2; HRMS *m*/*z* calcd for $C_{37}H_{55}NO_8Na$ 664.3832 $[M + Na]^+$, found 664.3825. **23**: syrup: $[\alpha]^{20}_D$ +48 (c 1, $CHCl_3$); IR ($CHCl_3$) 2947, 1775, 1743, 1234, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.16 (1H, dd, $J_1 = J_2 = 8.4$ Hz), 5.25 (1H, dd, $J_1 = J_2 = 3.4$ Hz), 4.42 (1H, d, $J = 11.5$ Hz), 4.03 (1H, d, $J = 11.5$ Hz), 3.58 (3H, s), 2.84 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.6$ Hz), 2.29 (1H, dd, $J_1 = 8.5$ Hz, $J_2 = 13.4$ Hz), 2.03 (3H, s), 1.99 (3H, s), 1.20 (3H, s), 1.08 (3H, s), 0.89 (3H, s), 0.88 (3H, s), 0.86 (3H, s), 0.70 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8, 16.7, 19.3, 19.5, 21.1, 23.0, 23.6, 24.0, 25.7, 27.7, 28.4, 30.8, 32.3, 32.4, 33.3, 34.0, 36.7, 39.0, 41.5, 41.9, 42.5, 43.5, 45.5, 45.8, 46.8, 51.6, 54.6, 62.2, 66.7, 122.1, 143.9, 166.4, 169.4, 170.3, 178.2; HRMS *m*/*z* calcd for $C_{35}H_{53}NO_7Na$ 622.3366 $[M + Na]^+$, found 623.3372.

Cyclopalladation of Methyl 2α-Benzoyloxy-3-hydroxyiminoolean-12-en-28-oate (21). To a solution of 2α-benzoyloxy-3-hydroxyiminoolean-12-en-28-oate (**21**) (1800 mg, 3.4 mmol) in HOAc (180 mL), KOAc (324 mg, 3.3 mmol) and Na_2PdCl_4 (1000 mg, 3.4 mmol) were added. The solution was stirred for 72 h at rt, and cooled water (260 mL) was added to give a yellow precipitate. The palladium complex was filtered through Celite and dried in vacuo at rt for 24 h. To a solution of this yellow solid in dry CH_2Cl_2 (150 mL) were added DMAP (8 mg), Et_3N (0.7 mL), and Ac_2O (0.5 mL). The mixture reaction was stirred at rt for 45 min, washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated at reduced pressure. The crude product was dissolved again in dry THF (130 mL), and pyridine (0.25 mL) was added. The reaction mixture was stirred for 15 min at room temperature and cooled at − 80 °C, and a solution of $Pb(OAc)_4$ (1250 mg, 2.8 mmol) in HOAc (52 mL) was added and again stirred at rt for 24 h. To remove the remaining Pd salts, a solution of $NaBH_4$ (140 mg) in 1 N NaOH solution (45 mL) was added to the reaction mixture. It was stirred for 10 min and filtered. The filtrate was diluted with CH_2Cl_2 (250 mL), which was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to give a solid. The crude product was purified on a silica column to afford **24** (738 mg, 35%) and **25** (595 mg, 30%). **24**: Colorless oil: $[\alpha]^{20}_D$ +16 (c 1, $CHCl_3$); IR ($CHCl_3$) 2947, 1725, 1452, 1370, 1267, 1241, 756, 712 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−8.0 (5H, m), 6.21 (1H, dd, $J_1 = J_2 = 8.4$ Hz), 5.29 (1H, dd, $J_1 = J_2 = 3.4$ Hz), 4.46 (1H, d, $J = 11.6$ Hz), 4.33 (1H, d, $J = 11.6$ Hz), 3.61 (3H, s), 2.86 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.6$ Hz), 2.45 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 13.3$ Hz), 2.03 (3H, s), 1.91 (3H, s), 1.44 (3H, s), 1.11 (3H, s), 0.98 (3H, s), 0.91 (3H, s), 0.87 (3H, s), 0.76 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8, 16.8, 19.4, 19.6, 21.1, 23.1, 23.6, 24.0, 25.8, 27.7, 28.3, 30.8, 32.4, 32.4, 33.2, 33.9, 36.7, 39.2, 41.5, 41.9, 43.9, 45.8, 44.1, 45.7, 46.8, 51.6, 55.6, 64.4, 66.5, 122.1, 128.6, 128.6, 129.7, 129.7, 129.7, 133.4, 143.9, 165.2, 166.5, 167.7, 170.7, 178.2; HRMS *m*/*z* calcd for $C_{42}H_{57}NO_8Na$ 726.3982 $[M + Na]^+$, found 726.3984. **25**: Colorless oil: $[\alpha]_D$ +35 (c 1, $CHCl_3$); IR ($CHCl_3$) 3417, 2948, 1722, 1267, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−8.0 (5H, m), 6.38 (1H, dd, $J_1 = 7.1$ Hz, $J_2 = 8.5$ Hz), 5.27 (1H, dd, $J_1 = J_2 = 3.1$ Hz), 4.43 (1H, d, $J = 11.5$ Hz), 4.12 (1H, d, $J = 11.5$ Hz), 3.59 (3H, s), 2.83 (1H, dd, $J_1 = 3.9$ Hz, $J_2 = 13.7$ Hz), 2.46 (1H, dd, $J_1 = 8.5$ Hz, $J_2 = 13.8$ Hz), 1.95 (3H, s), 1.31 (3H, s), 1.08 (3H, s), 0.89 (3H, s), 0.88 (3H, s), 0.85 (3H, s), 0.72 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 16.6, 19.5, 21.0, 23.1, 23.6, 23.9, 25.7, 27.6, 28.2, 30.7, 32.3, 32.3, 33.1, 33.9, 36.4, 39.1, 41.4, 41.9, 42.3, 44.1, 45.7, 45.7, 46.8, 51.6, 54.7, 62.6, 66.9, 122.3, 128.4, 128.4, 129.7, 129.7, 130.2, 133.0, 143.6, 158.5, 165.5, 171.1, 178.3; HRMS *m*/*z* calcd for $C_{40}H_{55}NO_7Na$ 684.3872 $[M + Na]^+$, found 684.3876.

Saponification of Methyl 2α,24-Diacetoxy-3-acetoxyiminoolean-12-en-28-oate (22). Triacetoxy oxime **22** (300 mg, 0.47 mmol) was dissolved in MeOH (5 mL), and MeOH/H_2O (70%) (5 mL) containing KOH (20%) was added. The reaction mixture was stirred at rt for 2 h, neutralized with (20%) HCl solution, and extracted with CH_2Cl_2. The extract was washed with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4, and evaporated in vacuo. Chromatography on a silica gel column yielded **26** (192 mg, 80%) as a colorless oil: $[\alpha]^{20}_D$ +34 (c 1, $CHCl_3$); IR ($CHCl_3$) 3367, 2930, 1726, 1460, 1261, 1035, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.31 (1H, dd, $J_1 = J_2 = 3.3$ Hz), 4.90 (1H, dd, $J_1 = J_2 = 9.2$ Hz), 3.79 (1H, d, $J = 10.9$ Hz), 3.61 (3H, s), 3.51 (1H, d, $J = 10.9$ Hz), 2.86 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.5$ Hz), 1.37 (3H, s), 1.12 (3H, s), 0.91 (3H, s), 0.89 (3H, s), 0.82 (3H, s), 0.73 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.6, 16.8, 19.2, 23.2, 23.7, 23.9, 25.7, 27.4, 27.7, 30.8, 32.5, 32.5, 33.2, 34.0, 36.7, 39.1, 41.5, 42.0, 43.6, 44.1, 45.1, 45.8, 46.9, 51.6, 54.8, 62.5, 67.2, 122.4, 143.8, 168.5, 178.3; HRMS *m*/*z* calcd for $C_{31}H_{49}NO_5$ Na 538.3508 $[M + Na]^+$, found 538.3498.

Saponification of Methyl 2α-Benzoyloxy-24-acetoxy-3-acetoxyiminoolean-12-en-28-oate (24). Benzoyloxydiacetoxyoxime **24** (300 mg, 0.43 mmol) was dissolved in MeOH (5 mL), and MeOH/H_2O (70%) (5 mL) containing KOH (20%) was added. The reaction mixture was stirred at rt for 2 h, neutralized with (20%) HCl solution, and extracted with CH_2Cl_2. The extract was washed with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4, and evaporated in vacuo. Chromatography on a silica gel column yielded **26** (165 mg, 75%).

Hydrolysis of Methyl 2α,24-Diacetoxy-3-hydroxyiminoolean-12-en-28-oate (23). To a buffered solution of $TiCl_3$ (0.15 mL of 20% aqueous HCl solution containing 19% $TiCl_3$) and NH_4OAc (70 mg, 0.9 mmol) in water (3 mL) was added a solution of oxime **23** (150 mg, 0.23 mmol) in THF (5 mL). The mixture was stirred at rt for 4 h and extracted with CH_2Cl_2. The extract was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to afford a solid that was purified by silica gel flash chromatography column to give **27** (124 mg,

90%) as a colorless oil: $[\alpha]^{20}_D$ +62 (c 1, $CHCl_3$); IR ($CHCl_3$) 2947, 1239, 1743, 756 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54 (1H, dd, $J_1 = 6.0$ Hz, $J_2 = 13.2$ Hz), 5.26 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.74 (1H, d, $J = 11.5$ Hz), 3.93 (1H, d, $J = 11.5$ Hz), 3.63 (3H, s), 2.85 (1H, dd, $J_1 = 4.3$ Hz, $J_2 = 13.8$ Hz), 2.22 (1H, dd, $J_1 = 6.1$ Hz, $J_2 = 12.4$ Hz), 2.11 (3H, s), 2.00 (3H, s), 1.32 (3H, s), 1.21 (3H, s), 1.08 (3H, s), 0.90 (3H, s), 0.88 (3H, s), 0.74 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 16.9, 19.7, 20.1, 20.7, 20.8, 23.0, 23.7, 23.8, 25.9, 27.7, 30.8, 32.3, 32.7, 33.1, 33.9, 37.9, 39.4, 41.2, 41.7, 45.9, 46.1, 46.6, 47.7, 51.7, 53.8, 58.3, 66.1, 72.2, 122.5, 144.2, 169.9, 171.1, 178.2, 206.4; HRMS *m*/*z* calcd for $C_{35}H_{52}O_7$-Na 607.3606 $[M + Na]^+$, found 607.3610.

Hydrolysis of Methyl 2α-Benzoyloxy-24-acetoxy-3-hydroxyiminoolean-12-en-28-oate (25). To a buffered solution of $TiCl_3$ (0.15 mL of 20% aqueous HCl solution containing 19% $TiCl_3$) and NH_4OAc (70 mg, 0.9 mmol) in water (3 mL) was added a solution of oxime **25** (150 mg, 0.21 mmol) in THF (5 mL). The mixture was stirred at rt for 4 h and extracted with CH_2Cl_2. The extract was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to afford a solid that was purified by silica gel flash chromatography column to give **28** (103 mg, 75%) as a colorless oil: $[\alpha]^{20}_D = 30$ (c 1, $CHCl_3$); IR ($CHCl_3$) 2947, 1723, 1272, 1234, 756, 712 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−8.1 (5H, m), 5.83 (1H, dd, $J_1 = 6.1$ Hz, $J_2 = 13.2$ Hz), 5.28 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.79 (1H, d, $J = 11.6$ Hz), 4.00 (1H, d, $J = 11.6$ Hz), 3.63 (3H, s), 2.87 (1H, dd, $J_1 = 4.1$ Hz, $J_2 = 13.6$ Hz), 2.41 (1H, dd, $J_1 = 6.1$ Hz, $J_2 = 12.4$ Hz), 2.04 (3H, s), 1.39 (3H, s), 1.24 (3H, s), 1.11 (3H, s), 0.92 (3H, s), 0.89 (3H, s), 0.78 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.9, 17.0, 19.8, 20.1, 20.8, 23.1, 23.7, 23.9, 26.0, 27.8, 30.8, 32.4, 32.8, 33.2, 33.9, 38.1, 39.5, 41.3, 41.8, 45.9, 46.3, 46.7, 47.8, 51.7, 53.3, 58.4, 66.2, 72.7, 121.6, 128.4, 128.4, 129.9, 129.9, 130.3, 133.1, 144.2, 165.5, 171.1, 178.2, 206.1; HRMS *m*/*z* calcd for $C_{40}H_{54}O_7$-Na 669.3768 $[M + Na]^+$, found 669.3767.

Hydrolysis of Methyl 2α,24-Dihydroxy-3-hydroxyiminoolean-12-en-28-oate (26). To a buffered solution of $TiCl_3$ (0.5 mL of 20% aqueous HCl solution containing 19% $TiCl_3$) and NH_4OAc (200 mg, 2.6 mmol) in water (8 mL) was added a solution of oxime **26** (400 mg, 0.78 mmol) in THF (15 mL). The mixture was stirred at rt for 4 h and extracted with CH_2Cl_2. The extract was washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, filtered, and evaporated in vacuo to afford a solid that was purified by silica gel flash chromatography column to give **29** (330 mg, 85%) as a colorless oil: $[\alpha]_D$ +64 (c 1, $CHCl_3$); IR ($CHCl_3$) 3467, 2947, 1720, 1461, 1164, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.26 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.54 (1H, dd, $J_1 = 6.4$ Hz, $J_2 = 12.1$ Hz), 4.12 (1H, d, $J = 11.1$ Hz), 3.60 (3H, s), 3.55 (1H, d, $J = 11.1$ Hz), 2.84 (1H, dd, $J_1 = 4.0$ Hz, $J_2 = 13.8$ Hz), 2.38 (1H, dd, $J_1 = 6.5$ Hz, $J_2 = 12.5$ Hz), 2.24 (1H, dd, $J_1 = J_2 = 6.5$ Hz), 1.25 (3H, s), 1.24 (3H, s), 1.07 (3H, s), 0.90 (3H, s), 0.87 (3H, s), 0.72 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.8, 17.0, 19.3, 19.8, 23.0, 23.7, 23.8, 26.0, 27.7, 30.8, 32.4, 32.9, 33.1, 33.9, 37.7, 39.4, 41.3, 41.7, 45.9, 46.7, 47.6, 49.6, 51.8, 54.7, 58.6, 65.7, 70.0, 121.8, 144.0, 178.3, 214.8; HRMS *m*/*z* calcd for $C_{31}H_{48}O_5Na$ 523.3407 $[M + Na]^+$, found 523.3399.

Saponification of Methyl 2α,24-Diacetoxy-3-oxoolean-12-en-28-oate (27). Diacetoxy ketone **27** (100 mg, 0.47 mmol) was dissolved in MeOH (2 mL), and MeOH/H_2O (70%) (2 mL) containing KOH (20%) was added. The reaction mixture was stirred at rt for 2 h, neutralized with (20%) HCl solution, and extracted with CH_2Cl_2. The extract was washed with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4, and evaporated in vacuo. Chromatography on a silica gel column yielded **29** (77 mg, 90%).

Saponification of Methyl 2α-Benzoyloxy-24-acetoxy-3-oxoolean-12-en-28-oate (28). Benzoyloxyacetoxy ketone **28** (100 mg, 0.15 mmol) was dissolved in MeOH (2 mL), and MeOH/H_2O (70%) (2 mL) containing KOH (20%) was added. The reaction mixture was stirred at rt for 2 h, neutralized with (20%) HCl solution, and extracted with CH_2Cl_2. The extract was washed with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4, and evaporated in vacuo. Chromatography on a silica gel column yielded **29** (66 mg, 85%).

Reduction of Methyl 2α,23-Dihydroxy-3-oxo-olean-12-en-28-oate (29) with $NaBH_4$. Compound **29** (200 mg, 0.40 mmol) was dissolved in *i*-PrOH/H_2O (3:1) (10 mL), and $NaBH_4$ (70 mg, 2 mmol) was added. The reaction mixture was stirred at reflux for 12 h. The excess of reagent was destroyed with $NaHSO_4$, and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The solid residue was purified on a silica gel chromatography column to afford **30** (161 mg, 80%) as a colorless oil: $[\alpha]^{20}_D$ +39 (c 1, $CHCl_3$); IR ($CHCl_3$) 3377, 2932, 1733, 1459, 1164, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.26 (1H, dd, $J_1 = J_2 = 3.6$ Hz), 4.09 (1H, d, $J = 11.1$ Hz), 3.86 (1H, ddd, $J_1 = 4.6$ Hz, $J_2 = 9.4$ Hz, $J_2 = 9.8$ Hz), 3.60 (3H, s), 3.35 (1H, d, $J = 11.1$ Hz), 3.14 (1H, d, $J = 9.4$ Hz) 2.84 (1H, dd, $J_1 = 4.2$ Hz, $J_2 = 14.0$ Hz), 1.26 (3H, s), 1.11 (3H, s), 0.92 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.68 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.9, 17.2, 18.5, 23.0, 23.1, 23.8, 23.8, 26.0, 27.8, 30.8, 32.5, 32.9, 33.1, 34.0, 38.3, 39.4, 41.4, 41.8, 43.4, 46,0, 46.5, 46.8, 47.8, 51.8, 56.0, 68.3, 69.2, 85.5, 122.1, 144.0, 178.3; HRMS *m*/*z* calcd for $C_{31}H_{50}O_5Na$ 525.3556 $[M + Na]^+$, found 525.3557.

Reduction of Methyl 3-oxoMaslinate Derivatives 27, 28, and 29 with $LiAlH_4$. Compound **27** (200 mg, 0.40 mmol) was dissolved in dry THF (10 mL) and a 1 M solution of $LiAlH_4$ in THF (1 mL) was added. The reaction mixture was stirred for 1 h at reflux, the excess of the reagent was destroyed with MeOH, and the solvent was concentrated under reduced pressure. The crude product was purified on a silica column to give **31** (95%) as a colorless oil: $[\alpha]^{20}_D$ +43 (c 1, $CHCl_3$); IR ($CHCl_3$) 3366, 2926, 1459, 1048, 756 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 5.18 (1H, dd, $J_1 = J_2 = 3.3$ Hz), 4.10 (1H, d, $J = 11.4$ Hz), 3.73 (1H, ddd, $J_1 = 4.5$ Hz, $J_2 = 9.8$ Hz, $J_2 = 11.4$ Hz), 3.52 (1H, d, $J = 11.4$ Hz), 3.36 (1H, d, $J = 11.4$ Hz), 3.19 (1H, d, $J = 11.4$ Hz), 3.14 (1H, d, $J = 9.8$ Hz), 1.27 (3H, s), 1.14 (3H, s), 0.94 (3H, s), 0.89 (3H, s), 0.87 (3H, s), 0.86 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 17.5, 18.5, 22.0, 23.0, 23.8, 23.9, 25.6, 26.0, 31.0, 31.1, 32.8, 33.3, 34.2, 37.0, 38.2, 39.4, 41.8, 42.4, 43.4, 46,6, 46.6, 47.7, 55.9, 65.7, 69.2, 69.7, 85.5, 122.1, 144.0; HRMS *m*/*z* calcd for $C_{30}H_{50}O_4Na$ 497.3606 $[M + Na]^+$, found 497.3602. A similar procedure was followed for **28** and **29**.

Demethylation at C-28 of 2α,3β,24-Trihydroxyolean-12-en-28-oate (30). Compound **30** (200 mg, 0.39 mmol) was dissolved in DMF (3 mL), and LiBr (10 eq) was added. The reaction mixture was stirred at reflux for 48 h, and DMF was removed at reduced pressure. The crude product was purified on a silica column to afford **32**[13] (174 mg, 90%). IR ($CHCl_3$) 3412, 2927, 1625, 1458, 756 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 5.24 (1H, dd, $J_1 = J_2 = 3.5$ Hz), 4.01 (1H, d, $J = 11.1$ Hz), 3.77 (1H, ddd, $J_1 = 4.4$ Hz, $J_2 = 9.8$ Hz, $J_2 = 11.5$ Hz), 3.37 (1H, d, $J = 11.1$ Hz), 3.04 (1H, d, $J = 9.8$ Hz), 2.84 (1H, dd, $J_1 = 5.9$ Hz, $J_2 = 13.4$ Hz), 1.22 (3H, s), 1.15 (3H, s), 0.97 (3H, s), 0.93 (3H, s), 0.90 (3H, s), 0.78 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5, 17.6, 19.8, 23.8, 23.8, 24.1, 24.8, 26.4, 28.8, 31.6, 33.5, 33.8, 34.2, 34.9, 39.1, 40.6, 42.7, 42.9, 44.4, 47,2, 47.6, 47.8, 49.2, 57.2, 66.2, 69.6, 86.0, 123.4, 145.3, 181.8; HRMS *m*/*z* calcd for $C_{30}H_{48}O_5Na$ 511.3399 $[M + Na]^+$, found 511.3401.

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Supporting Information Available: Copies of ^{1}H and ^{13}C spectra of all new compounds, theoretical structures and cartesian coordinates for compounds **6** and **21**. This material is avalaible free of charge via the Internet at http://pubs.acs.org.

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