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Formation of an Endoperoxide upon Chromium-Catalyzed Allylic Oxidation of a Triterpene by Oxygen

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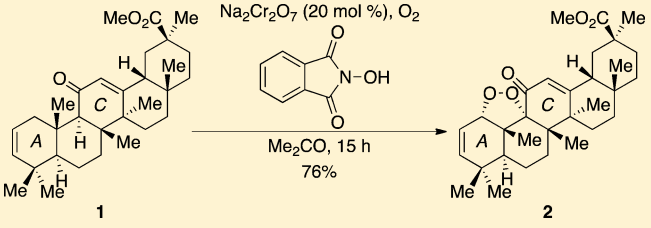
Supporting Information

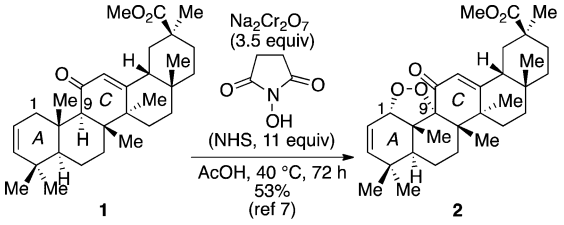
ABSTRACT: The chromium-catalyzed allylic oxidation of triterpene **1** with O_2 and *N*-hydroxyphthalimide (NHPI, 5 equiv) formed endoperoxide **2** in 76% yield at ambient temperature. Unlike standard allylic oxidations, this oxidation is catalytic in chromium because oxygen, not the chromium reagent, is the oxidant. This oxidation is sensitive to the precise structure of the substrate. The endoperoxide is only formed if ring A is unsaturated and ring C contains an enone. A mechanism is proposed that involves the coupling of two stabilized radicals on rings A and C to form endoperoxide **2**.



INTRODUCTION

Allylic oxidation is an important method for the functionalization of alkenes. Although generally used to convert alkenes to allylic alcohols and enones,[1,2] allylic oxidation reactions have been developed to prepare allylic hydroperoxides,[3,4] including enantioenriched substrates.[5,6] Recently, an allylic oxidation that formed two new C–O bonds was reported for the triterpene **1** and structural relatives (Scheme 1).[7,8] The formation of

Scheme 1. Allylic Oxidation To Form Endoperoxide

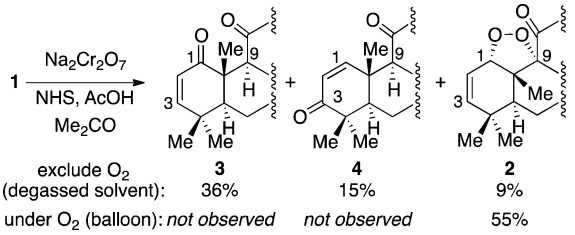


endoperoxides such as **2**, which are of interest because of their potent antitumor activity,[7,8] requires stereoselective oxidation of both C-1 and C-9. Although few examples have been reported, the value of this biologically active compound justifies an improved synthetic method. We report experiments that suggest the reaction involves generation and coupling of two stabilized radicals, an alkylperoxyl radical and an α-acyl radical. We also demonstrate that the formation of endoperoxide **2** requires O_2 as the terminal oxidant, and because chromium reagents serve only to generate radicals from an *N*-hydroxylamine,[9] chromium reagents can be used catalytically.

RESULTS AND DISCUSSION

Initial experiments revealed that O_2 was the source of the two new oxygen atoms of the endoperoxide **2**. The oxidation with sodium dichromate and *N*-hydroxysuccinimide (NHS) was performed under an inert atmosphere in a glovebox using degassed solvents to exclude oxygen. These conditions formed isomeric allylic oxidation products, enones **3** and **4**, accompanied by small amounts of the endoperoxide **2** (Scheme 2). The identities of the enone **4** and peroxide **2** were

Scheme 2. Formation of Dienediones without Oxygen



established by X-ray crystallography, and the structure of enone **3** was assigned by spectroscopic methods.[10] The regioisomeric enones **3** and **4** are the products expected from allylic oxidation reactions[1,2] and are similar to those observed upon oxidation of triterpenes related to **1**.[11−13] Because O_2 appeared to be required to form endoperoxide **2**, the oxidation was repeated under an atmosphere of O_2 supplied by a balloon. Under these conditions, endoperoxide **2** was formed from triterpene **1** in 55% yield after only 6 h at 40 °C (compared to 72 h, Scheme 1). These results indicate that O_2 from the atmosphere, not the chromium oxide source, must be the terminal oxidant for the formation of peroxide **2**.[14,15]

Because the oxidant was found to be O_2, an attractive oxidant for the functionalization of organic compounds,[9] conditions were developed to improve the efficiency of the peroxidation reaction (Table 1). The radical precursor NHS was replaced

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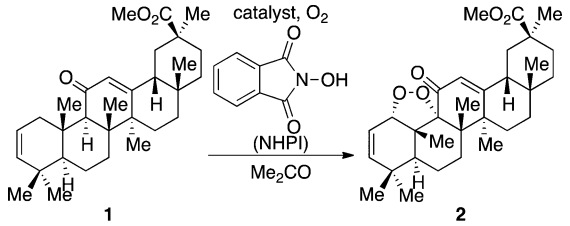
Table 1. Optimization of Oxidation Conditions



entry	catalyst	NHPI (equiv)	time (h)	yield (%)
1	$Na_2Cr_2O_7{\cdot}2H_2O$[a]	10	15	76
2	**$Na_2Cr_2O_7{\cdot}2H_2O$[a]**	**5**	**15**	**73**
3	$Na_2Cr_2O_7{\cdot}2H_2O$[a]	10	8[c]	73
4	$Na_2Cr_2O_7{\cdot}2H_2O$[a]	3	15	0
5	**CrO_3[b]**	**5**	**15**	**73**
6	CrO_3[a]	10	35	68
7	PCC[a]	10	42	51
8	MnO_2[b]	10	48[c]	15

[a]Catalyst loading: 20 mol %. [b]Catalyst loading: 40 mol %. [c]Reaction temp: 40 °C.

with the more reactive reagent *N*-hydroxyphthalimide (NHPI),[16] which afforded endoperoxide **2** in only 15 h at room temperature (compared to 24 h for NHS) and in higher yields (76% compared to 42%). More than 3 equiv of NHPI was necessary to conduct the reaction (entries 2 and 4, Table 1),[17] likely due to the decomposition of NHPI to inert phthalimide and phthalic anhydride under the reaction conditions.[18] Oxidation could be performed using only catalytic amounts (20–40 mol %) of CrO_3 and $Na_2Cr_2O_7$, decreasing the loading of toxic chromium[1] (entries 1–6, Table 1). Some metal complexes, such as pyridinium chlorochromate (PCC, entry 7) and MnO_2 (entry 8), provided the product, but the reactions were less efficient. The use of other allylic oxidation catalysts, such as $Co(OAc)_2{\cdot}4H_2O$, $Co(acac)_2$, $Mn(OAc)_2{\cdot}2H_2O$, and $[Cu(MeCN)_4]ClO_4$, led to little or no product. Contrary to observations with other allylic oxidation conditions,[1] acetic acid was not needed for the peroxidation reaction. A variety of solvents can be used, including acetone, acetonitrile, nitromethane, ethyl acetate, and chloroform, but the oxidation does not work in trifluorotoluene, trifluoroethanol, dichloroethane, dimethyl sulfoxide, and benzene.

The allylic oxidation appears to be specific to the triterpene **1** and its close structural relatives.[7,8] The triterpene **5** (Figure 1),

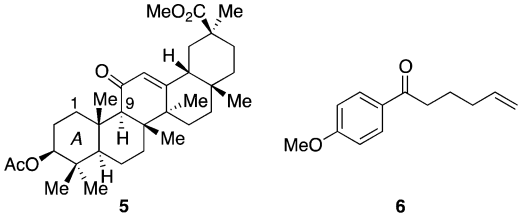
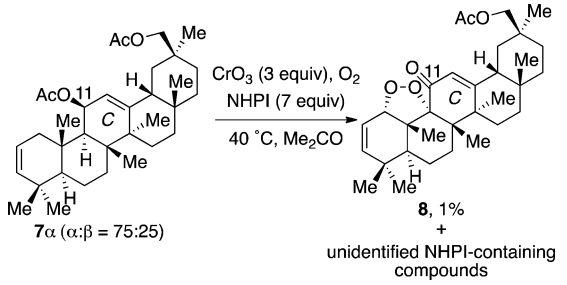


Figure 1. Substrates of unsuccessful attempted oxidations.

which lacks the carbon–carbon double bond in the A ring, was recovered unchanged upon attempted oxidation. This result indicates that activation of a carbon–hydrogen bond at C-1, the less sterically hindered carbon, must occur to give a stabilized radical,[19] which is presumably trapped by O_2 at a diffusion-limited rate.[20–22] It is also not sufficient for a compound to contain both the ketone and alkene functional groups of the triterpene; those functional groups must be properly positioned. The δ,ε-unsaturated ketone **6** (Figure 1), which possesses the key functional groups at the appropriate distance but different orientation in space, did not undergo oxidation under either stoichiometric or catalytic conditions.

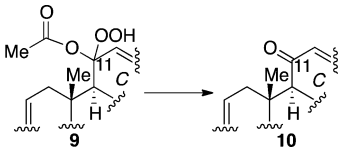
The enone functional group in ring C is also necessary for the formation of the endoperoxide. Oxidation of the acetylated triterpenes **7**α and **7**β, formed by reduction and acetylation of triterpene **1**,[10] resulted in the endoperoxide **8** in 1% yield along with unidentified NHPI-containing compounds (Scheme 3).[23]

Scheme 3. Oxidation of Protected Triterpene



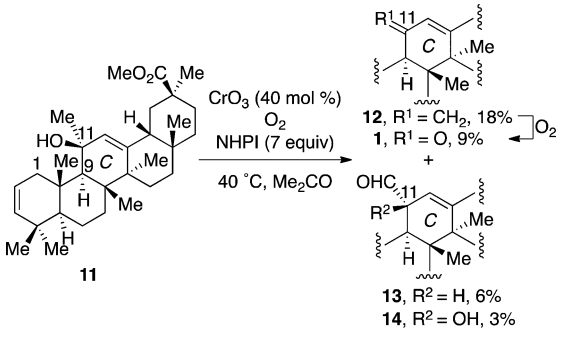
This reaction may involve activation of the carbon–hydrogen bond at C-11, trapping with O_2, and hydrolysis of the mixed peroxyketal **9** to form a small amount of enone **10** (Scheme 4). Subsequent peroxidation would occur as for triterpene **1**.

Scheme 4. Oxidative Deacetylation



Reactions of a tertiary alcohol derived from triterpene **1** reinforce the conclusion that the enone moiety in the C ring is necessary for oxidation (Scheme 5). The alkylated triterpene

Scheme 5. Oxidation of Alkylated Triterpene



11, formed by addition of MeMgBr to enone **1**, gave several products upon exposure to the optimized conditions using catalytic chromium reagents, none of which were peroxides (Scheme 5). Triene **12** was formed by elimination of the tertiary hydroxyl group of triterpene **11** by the acidic chromium reagent.[24,25] The structure of triene **12** was assigned by ^{1}H NMR spectroscopy and mass spectrometry, but the isolated sample was unstable to air, forming dienone **1** upon handling. The dienone **1** was also formed (9% yield) in the course of

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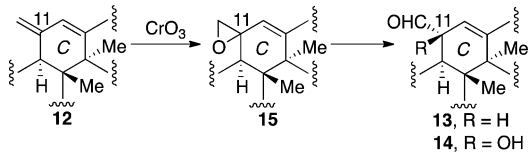
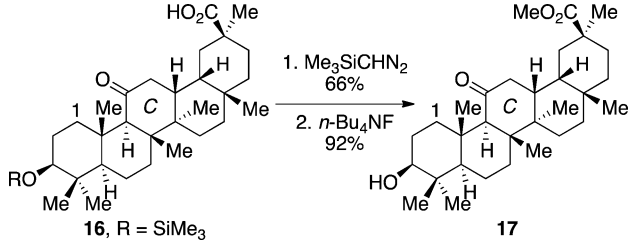
oxidation of allylic alcohol **11**, presumably by conversion of the triene **12** to a dioxetane and subsequent cleavage.[26] When the oxidation was repeated with stoichiometric quantities of the chromium complex (3 equiv), the dienone **1** formed in situ was further oxidized to form endoperoxide **2** (17% yield). Two other products, aldehydes **13** and **14**, were formed in small quantities during the attempt to oxidize allylic alcohol **11** under catalytic conditions (Scheme 5). The identity of the aldehyde **13** was established by X-ray crystallography, and the structure of its oxidized analogue, **14**, was determined by spectroscopic methods.[10] The aldehyde **13** could be formed by chromium-mediated oxidation of triene **12** (Scheme 6),[27−30] a reaction that would proceed via epoxide **15**.[27] The more oxidized aldehyde, **14**, may result from allylic oxidation of aldehyde **13** or hydroxylation of its enol form.[31]

Scheme 6. Mechanism of Formation of Aldehydes 13 and 14



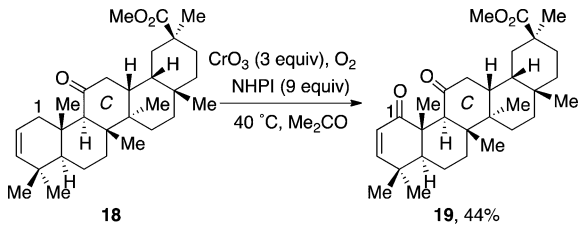
Not only must the carbonyl group be present on the C ring to form endoperoxide **2** but it must also be an unsaturated carbonyl group. To saturate the C ring, Birch reduction was performed on a silyl-protected glycyrrhetinic acid[10,32] to give ketone **16**, followed by esterification, and deprotection of the alcohol to afford ketone **17** (Scheme 7). Oxidation of the

Scheme 7. Saturation of Ring C



saturated ketone **18**, formed by elimination of **17** under Mitsunobu conditions, gave enone **19** as a single regioisomer (Scheme 8). The regioselective introduction of the oxygen

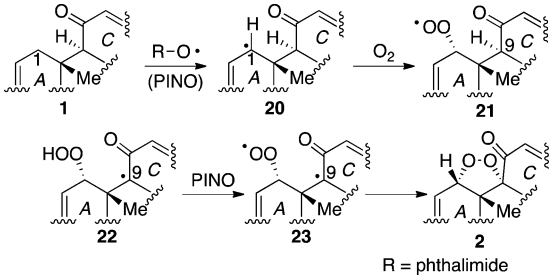
Scheme 8. Oxidation of Saturated Ring C



atom at C-1 is consistent with the allylic oxidation reaction in the presence of O_2 but not the reaction in the absence of O_2 (Scheme 2). This result suggests that the allylic radical formed by activation of the carbon−hydrogen bond at C-1 occurred first, and that this allylic radical was trapped by O_2 to form an allylic hydroperoxide. Because this intermediate cannot proceed to the cyclic peroxide, it was converted to the enone by metal-promoted decomposition of the allylic hydroperoxide.[33,34]

The experiments described here give insight into the mechanism of the formation of the cyclic peroxide **2** illustrated in Scheme 1 and Table 1. It is expected that a chromium-coordinated peroxide abstracts the hydrogen atom of NHPI to generate PINO.[35,36] PINO then removes the allylic hydrogen atom at C-1 of **1** (Scheme 9). Following activation of the

Scheme 9. Allylic Oxidation Mechanism



carbon−hydrogen bond, an allylic peroxyl group is formed at C-1 of **20** by trapping with O_2.[20−22,37] The axial orientation of the peroxyl group likely results from attack of O_2 to the allylic radical from an orientation that maximizes orbital overlap in the transition state.[38] This peroxyl radical is persistent[39−41] and could perform radical translocation by a 1,5-hydrogen atom abstraction[42,43] at C-9 to form the stabilized radical **22** (Scheme 9). PINO could regenerate the persistent peroxyl radical group of **23**, which could then couple to the radical on C-9.[44−48] The coupling of persistent radicals has been suggested[39,49] as the key step in related intermolecular coupling reactions of ketones with hydroperoxides, a preparatively useful transformation[44,50] first reported by Kharasch.[2] Mechanistically related couplings of persistent peroxyl radicals and benzylic radicals have been reported.[40] An alternative mechanism has been suggested involving the addition of peroxyl radical **21** to the enol tautomer of the ring C carbonyl group.[51] The enol form, however, is strongly disfavored in both aromatic and non-aromatic ketones,[52] and the cyclization is likely to be considerably slower than related reactions with carbon radicals.[53]

The preference for oxidation of the unsaturated ketone **1** (Scheme 1) over the saturated ketone **18** (Scheme 8) may reflect the orientation of the α-hydrogen atom at C-9 (Figure 2). Computational studies (HF/6-31G*) indicate that the two

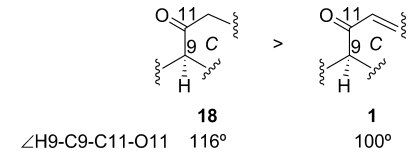


Figure 2. Dihedral angle of interest.

types of ketones have subtly different structures in the region undergoing oxidation. In both the saturated and unsaturated ketones, the pentacyclic ring systems have few possible conformations available to them.[10] Saturation of the C ring of **18** alters the orientation of this ring compared to the unsaturated system (**1**). The calculated dihedral angle ∠H9−C9−C11−O11 (Figure 2) of the saturated ketone **18** is much larger (116°) than that for the unsaturated ketone **1** (100°).

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The smaller dihedral angle for the unsaturated ketone is closer to the angle calculated (105°) for the transition state for removal of an allylic hydrogen atom by the hydroxyl radical.[54] Consequently, it may be easier to remove the hydrogen atom from the unsaturated ketone **1**, thus increasing the likelihood that the radical **22** (Scheme 9) would be formed.

CONCLUSION

In conclusion, we have demonstrated that the peroxidations of triterpenes related to **1** require O_2 to install the peroxide functional group. These reactions can be conducted with only catalytic quantities of chromium complexes, which significantly simplifies the isolation and purification of the biologically active products. The reaction is sensitive to the precise nature and orientation of the functional groups present in this triterpene because the mechanism appears to involve two stabilized radicals that combine in the key ring-forming step.

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR spectra were recorded at 400, 500, or 600 MHz at ambient temperature, and ^{13}C NMR spectra were recorded at 100, 125, or 150 MHz at ambient temperature, as indicated. ^{1}H and ^{13}C NMR spectroscopic data are reported as follows: chemical shifts are reported in parts per million on the δ scale, referenced to internal tetramethylsilane (δ 0.00) or residual solvent (^{1}H NMR: δ 7.26 for $CDCl_3$; ^{13}C NMR: δ 77.2 for $CDCl_3$),[55] multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, m = multiplet), coupling constants (Hz), and integration. For products that are difficult to purify, distinguishable peaks are listed in ^{1}H NMR and ^{13}C NMR spectral data, as indicated. Multiplicity of carbon peaks was determined using HSQC. Infrared (IR) spectra were obtained by a FT-IR using attenuated total reflectance. High-resolution mass spectra (HRMS) were acquired on an accurate-mass time-of-flight spectrometer using peak matching. Melting points were reported uncorrected. Analytical thin layer chromatography was performed on silica gel 60 Å F254 plates. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on silica gel (SiO_2) 60 (230–400 mesh). Tetrahydrofuran, methylene chloride, diethyl ether, and triethylamine were dried by filtration through alumina following the method of Grubbs.[56]

Preparation of Substrates. Triterpene **1**[7] was prepared according to the previously reported procedures.

Representative Procedure for the Preparation of Oxidized Triterpenes. *Methyl 2,3-Dihydro-1α,9α-peroxo-11-oxoolean-12-en-30-oate **2** (Table 1, entry 1).* Modifying a reported procedure,[7] to an oxygen-flushed solution of **1** (0.085 g, 0.18 mmol) in acetone (5 mL) were added *N*-hydroxyphthalimide (0.148 g, 0.905 mmol) and sodium dichromate dihydrate (0.011 g, 0.036 mmol). The reaction mixture was stirred under O_2 (balloon) at ambient temperature for 15 h, filtered through silica gel with $CHCl_3$ (20 mL), and concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded **2** as a white solid (0.070 g, 76%). The spectral data are consistent with the data reported:[7] ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (d, J = 9.9, 1H), 5.80 (s, 1H), 5.51 (dd, J = 9.9, 5.2, 1H), 4.92 (dd, J = 5.2, 1H), 3.69 (s, 3H), 2.13–1.97 (m, 6H), 1.79 (td, J = 13.4, 4.2, 1H), 1.69–1.63 (m, 2H), 1.52 (dd, J = 13.1, 2.9, 1H), 1.47 (dd, J = 12.7, 2.8, 1H), 1.43–1.40 (m, 1H), 1.38 (s, 3H), 1.35 (s, 3H), 1.32–1.30 (m, 2H), 1.26 (s, 3H), 1.25–1.23 (m, 1H), 1.15 (s, 3H), 1.06 (s, 3H), 1.02–0.98 (m, 1H), 0.96 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.0 (C), 177.1 (C), 169.3 (C), 144.8 (CH), 126.5 (CH), 117.8 (CH), 90.7 (C), 80.5 (CH), 51.9 (CH_3), 49.9 (CH), 46.8 (C), 44.5 (C), 44.2 (C), 43.1 (CH), 40.7 (CH_2), 37.8 (CH_2), 35.4 (C), 32.7 (C), 31.36 (CH_3), 31.35 (CH_2), 31.34 (C), 30.0 (CH_2), 28.8 (CH_3), 28.4 (CH_3), 28.0 (CH_2), 26.6 (CH_2), 26.3 (CH_3), 21.9 (CH_3), 20.4 (CH_3), 17.7 (CH_2), 15.8 (CH_3). Suitable crystals for X-ray crystallography were obtained by slow evaporation of 10% EtOAc in hexanes. Crystallographic data are included in Supporting Information.

*Methyl 2,3-Dihydro-1α,9α-peroxo-11-oxoolean-12-en-30-oate **2** (Table 1, entry 5).* Following the representative procedure for the preparation of oxidized triterpenes, to **1** (0.047 g, 0.10 mmol) in acetone (5 mL) were added *N*-hydroxyphthalimide (0.082 g, 0.50 mmol) and chromium(VI) oxide (0.002 g, 0.02 mmol) to afford **2** as a white solid (0.036 g, 73%). The spectral data match the data reported (vide supra).[7]

*Methyl 1,11-Dioxoolean-2,12-dien-30-oate **3** and Methyl 3,11-Dioxoolean-1,12-dien-30-oate **4**.* Modifying a reported procedure,[7] each of the components of the reaction were carefully dried and degassed to remove H_2O and oxygen before performing the oxidation reaction in a glovebox. For drying acetic acid, AcOH (10 mL) was treated with Ac_2O (20 μL), followed by the addition of chromium(VI) oxide (0.200 g, 2.00 mmol). After being heated (100 °C) for 1 h, the AcOH was fractionally distilled, freeze–pump–thawed (3× at 50 mTorr) in a Schlenk bomb, and transferred into a glovebox under vacuum. For drying acetone, acetone (40 mL) was dried overnight over 4 Å molecular sieves, filtered, distilled (short path), freeze–pump–thawed (3× at 50 mTorr) in a Schlenk bomb, and transferred into a glovebox under vacuum. Enone **1**, sodium dichromate dihydrate, and *N*-hydroxysuccinimide were dried in Schlenk flasks under vacuum (50 mTorr) for 24 h, flushed with argon (3×), and transferred into a glovebox under vacuum. Enone **1** (0.192 g, 0.411 mmol), sodium dichromate dihydrate (0.424 g, 1.42 mmol), and *N*-hydroxysuccinimide (0.521 g, 4.53 mmol) in acetone (20 mL) and AcOH (4.0 mL) were stirred in the glovebox at ambient temperature for 4 days. After the the reaction mixture was removed from the glovebox under argon, saturated aqueous $NaHSO_3$ (10 mL) was added. The reaction mixture was opened to air and diluted with CH_2Cl_2 (40 mL) and saturated aqueous $NaHCO_3$ (10 mL). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (10 mL), dried over $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded dienedione **3** as a white solid (0.072 g, 36%), dienedione **4** as a white solid (0.029 g, 15%), and endoperoxide **2** as a white solid (0.019 g, 9%). The spectral data of endoperoxide **2** match the data reported (vide supra). **3**: mp 205–207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.22 (d, J = 10.2, 1H), 5.78 (d, J = 10.2, 1H), 5.75 (s, 1H), 3.68 (s, 3H), 3.07 (s, 1H), 2.10–2.06 (m, 1H), 2.03–1.97 (m, 3H), 1.83 (td, J = 13.6, 4.5, 1H), 1.66–1.59 (m, 4H), 1.55 (s, 3H), 1.46–1.40 (m, 1H), 1.39 (s, 3H), 1.37–1.29 (m, 2H), 1.24–1.17 (m, 2H), 1.14 (s, 6H), 1.12 (s, 3H), 1.04 (s, 3H), 1.02–0.98 (m, 1H), 0.87–0.81 (m, 1H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, diagnostic peaks) δ 205.2 (C), 197.7 (C), 176.9 (C), 167.8 (C), 152.9 (CH), 128.5 (CH), 124.0 (CH), 51.8 (CH_3), 51.6 (CH), 51.4 (CH), 48.7 (CH), 47.0 (C), 45.0 (C), 44.0 (C), 43.5 (C), 40.9 (CH_2), 37.7 (CH_2), 36.2 (C), 31.9 (CH_2), 31.6 (CH_2), 31.2 (CH_3), 28.5 (CH_3), 28.3 (CH_3), 26.5 (CH_2), 23.0 (CH_3), 22.4 (CH_3), 18.6 (CH_3), 18.5 (CH_2), 16.0 (CH_3); IR 2926, 1724, 1683, 1458 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{31}H_{45}O_4$ $(M + H)^+$ 481.3312, found 481.3324. **4**: mp 175–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 10.1, 1H), 5.79 (d, J = 10.2, 1H), 5.76 (s, 1H), 3.69 (s, 3H), 2.67 (s, 1H), 2.14 (dd, J = 13.8, 3.7, 1H), 2.08–1.81 (m, 5H), 1.72–1.45 (m, 6H), 1.41 (s, 3H), 1.38 (s, 3H), 1.33–1.30 (m, 2H), 1.17 (s, 3H), 1.152 (s, 3H), 1.148 (s, 3H), 1.11 (s, 3H), 1.06–0.99 (m, 1H), 0.87–0.85 (m, 1H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.5 (C), 199.0 (C), 176.9 (C), 170.7 (C), 161.5 (CH), 128.2 (CH), 124.6 (CH), 55.6 (CH), 52.8 (CH), 51.8 (CH_3), 48.5 (CH), 45.6 (C), 44.8 (C), 44.0 (C), 43.5 (C), 41.1 (CH_2), 38.8 (C), 37.7 (CH_2), 32.1 (CH_2), 31.9 (C), 31.1 (CH_2), 28.6 (CH_3), 28.3 (CH_3), 27.6 (CH_3), 26.5 (CH_2), 26.3 (CH_2), 23.4 (CH_3), 21.6 (CH_3), 20.1 (CH_3), 18.9 (CH_3), 18.2 (CH_2); IR 2948, 1730, 1659, 1453 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{31}H_{45}O_4$ $(M + H)^+$ 481.3312, found 481.3327. Suitable crystals for X-ray crystallography were obtained by slow evaporation of EtOAc in hexanes. Crystallographic data are included in Supporting Information.

*3β-(Acetyloxy)-11-oxo-18β-olean-12-en-30-oic Acid Methyl Ester **5**.* The precursor of **5**, the methyl ester of glycyrrhetinic acid, was

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prepared according to a reported procedure,[7] and the spectral data are consistent with the data reported. To a solution of acetic anhydride (0.05 mL, 0.5 mmol) and DMAP (0.0003 g, 0.002 mmol) in NEt_3 (0.05 mL) was added a solution of methylated glycyrrhetinic acid (0.051 g, 0.10 mmol) in CH_2Cl_2 (0.7 mL). After 20 h, C_6H_6 (5 mL) and HCl (4 mL, 2 M in H_2O) were added. The organic layer was washed with saturated aqueous $NaHCO_3$ (4 mL). The combined aqueous layers were extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded **5** as a white solid (0.043 g, 80%). The spectral data are consistent with the data reported:[57] ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.56 (s, 1H), 4.50 (dd, J = 11.8, 4.7, 1H), 3.67 (s, 3H), 2.78 (dt, J = 13.7, 3.6, 1H), 2.34 (s, 1H), 2.08−1.89 (m, 4H), 2.03 (s, 3H), 1.80 (td, J = 13.8, 4.5, 1H), 1.72−1.56 (m, 6H), 1.47−1.37 (m, 4H), 1.34 (s, 3H), 1.30−1.29 (m, 2H), 1.14 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.06−0.98 (m, 2H), 0.863 (s, 3H), 0.860 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.2 (C), 177.0 (C), 171.1 (C), 169.3 (C), 128.6 (CH), 80.7 (CH), 61.8 (CH), 55.1 (C), 51.9 (CH_3), 48.5 (CH_3), 45.5 (C), 44.1 (C), 43.3 (CH_2), 41.2 (CH_2), 38.9 (CH), 38.1 (CH_2), 37.8 (C), 37.0 (C), 32.8 (CH_2), 31.9 (CH_2), 31.2 (CH_2), 28.6 (CH_3), 28.4 (CH_3), 28.2 (CH_3), 26.6 (C), 26.5 (CH), 23.7 (CH_2), 23.4 (CH_2), 21.4 (CH_2), 18.8 (CH_3), 17.5 (CH_3), 16.8 (CH_3), 16.5 (CH_3).

1-(4-Methoxyphenyl)hex-5-en-1-one ***6***. The alcohol precursor to ketone **6** was synthesized according to a reported procedure,[58] and the spectral data are consistent with the data reported. To a solution of this alcohol (0.19 g, 0.93 mmol) in CH_2Cl_2 (5 mL) was added Celite (0.5 g) followed by PCC (0.30 g, 1.4 mmol). After 18 h, the reaction mixture was filtered through Celite and concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded **6** as a colorless oil (0.17 g, 90% yield). The spectral data are consistent with the data reported:[59] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, J = 8.9, 2H), 6.92 (d, J = 8.9, 2H), 5.82 (ddt, J = 16.9, 10.3, 6.7, 1H), 5.03 (dq, J = 17.1, 1.6, 1H), 4.99 (m, 1H), 3.86 (s, 3H), 2.92 (t, J = 7.3, 2H), 2.14 (m, 2H), 1.83 (qu, J = 7.3, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.0 (C), 163.5 (C), 138.3 (CH), 130.4 (CH), 130.3 (C), 115.3 (CH_2), 113.8 (CH), 55.6 (CH_3), 37.5 (CH_2), 33.4 (CH_2), 23.7 (CH_2).

11α,30-(Acetyloxy)-18β,20β-olean-2,12-dienol ***7α*** *and 11β,30-(Acetyloxy)-18β,20β-olean-2,12-dienol* ***7β***. To a cooled (0 °C) solution of dienone **1** (0.501 g, 1.07 mmol) in THF (10 mL) was added lithium aluminum hydride (0.124 g, 3.27 mmol). The reaction mixture was warmed to ambient temperature for 15 h, and then H_2O (10 mL) was added. The reaction mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (30:70 EtOAc/hexanes) afforded a mixture of alcohol diastereomers as a white solid (0.473 g, quantitative, α/β = 88:12 ≈ 7:1). The stereochemistry was determined by correlation of the alkene ^{1}H NMR shifts and J values to a similar allylic alcohol triterpene:[60] mp 120−125 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.48 (ddd, J = 10.1, 6.0, 1.9, 7H), 5.43 (ddd, J = 10.0, 6.1, 1.8, 1H), 5.39 (dd, J = 10.1, 2.2, 7H), 5.36 (d, J = 2.4, 1H), 5.35 (d, J = 4.1, 7H), 5.25 (d, J = 3.4, 1H), 4.29−4.27 (m, 8H), 3.56 (d, J = 10.7, 8H), 3.49 (d, J = 10.7, 8H), 2.39 (dd, J = 17.3, 6.2, 1H), 2.31 (dd, J = 17.1, 6.0, 7H), 2.04−1.97 (m, 14H), 1.92−1.88 (m, 2H), 1.85−1.77 (m, 14H), 1.73−1.71 (m, 2H), 1.67−1.61 (m, 21H), 1.55−1.50 (m, 14H), 1.44 (s, 21H), 1.42−1.40 (m, 7H), 1.39 (s, 3H), 1.38−1.34 (m, 18H), 1.32−1.26 (m, 24H), 1.25 (s, 24H), 1.23−1.21 (m, 2H), 1.19−1.16 (m, 2H), 1.11 (s, 24H), 1.10−1.08 (m, 14H), 1.05 (s, 6H), 1.02−0.99 (m, 4H), 0.97 (s, 3H), 0.95 (s, 21H), 0.93 (s, 24H), 0.91 (s, 3H), 0.90 (s, 21H), 0.87 (s, 21H), 0.84 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, major diastereomer α) δ 147.8 (C), 137.8 (CH), 126.4 (CH), 121.3 (CH), 67.0 (CH), 66.8 (CH_2), 52.8 (CH_2), 51.4 (CH_2), 46.7 (CH_2), 42.8 (C), 42.1 (CH_2), 40.4 (CH), 39.8 (C), 37.7 (C), 36.5 (CH_2), 35.7 (C), 34.4 (C), 33.1 (CH_2), 32.5 (CH_3), 32.2 (C), 29.7 (CH), 28.5 (CH_3), 27.5 (CH_3), 27.4 (CH_3), 26.5 (CH), 25.2 (CH_3), 23.2 (CH_2), 19.9 (CH_2), 19.5 (CH_3), 18.3 (CH_3); IR 3369, 2950, 2865, 1455, 1382 cm^{-1}; HRMS (TOF MS ES +) m/z calcd for $C_{30}H_{47}O$ $(M - OH)^+$ 423.3621, found 423.3634.

To a solution of acetic anhydride (0.1 mL, 1.0 mmol) and DMAP (0.0006 g, 0.005 mmol) in NEt_3 (0.3 mL) was added a diastereomeric mixture of this dienol (0.051 g, 0.10 mmol, α/β = 88:12). After 19 h, C_6H_6 (5 mL) and HCl (4 mL, 2 M in H_2O) were added. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (4 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded a diastereomeric mixture of **7** as a colorless oil (0.051 g, 80%, α/β = 75:25 ≈ 3:1). Characterization was performed using the mixture of diastereomers, but only the major diastereomer showed distinguishable peaks by ^{13}C NMR spectroscopy: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.51 (dd, J = 9.0, 2.5, 1H), 5.48−5.46 (m, 3H), 5.44−5.42 (m, 3H), 5.39−5.37 (m, 3H), 5.36−5.35 (m, 2H), 5.19−5.17 (m, 4H), 4.05 (d, J = 10.9, 1H), 4.00 (d, J = 10.9, 3H), 3.93 (d, J = 10.9, 3H), 3.89 (d, J = 10.7, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 2.047 (s, 9H), 2.045 (s, 9H), 2.022−2.021 (m, 5H), 2.00−1.99 (m, 6H), 1.96−1.92 (m, 7H), 1.88−1.80 (m, 4H), 1.77−1.75 (m, 6H), 1.70 (d, J = 5.5, 3H), 1.66−1.60 (m, 10H), 1.56−1.54 (m, 8H), 1.39−1.37 (m, 14H), 1.34−1.28 (m, 8H), 1.27−1.26 (m, 3H), 1.25 (s, 3H), 1.23 (s, 9H), 1.22 (s, 9H), 1.18−1.16 (m, 2H), 1.12 (s, 9H), 1.08 (s, 3H), 1.07 (s, 6H), 0.97 (s, 3H), 0.95 (s, 9H), 0.92 (s, 9H), 0.90 (s, 12H), 0.87 (s, 9H), 0.83 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$, major diastereomer α) δ 171.6 (C), 170.7 (C), 149.5 (C), 137.8 (CH), 122.1 (CH), 121.0 (CH), 68.7 (CH), 68.0 (CH_2), 52.9 (CH_2), 50.3 (CH), 46.4 (CH), 42.4 (C), 42.0 (CH_2), 40.2 (CH_2), 39.7 (C), 37.1 (CH_3), 36.5 (CH_2), 34.4 (C), 34.3 (C), 32.3 (CH_3), 32.2 (CH_2), 30.3 (CH_3), 28.4 (CH_3), 28.0 (C), 27.1 (CH_2), 27.0 (CH), 26.4 (CH_2), 25.4 (CH_3), 23.2 (C), 22.1 (CH_3), 21.1 (CH_3), 19.9 (CH_2), 18.5 (CH_3), 17.8 (CH_3); IR 2953, 2867, 1731, 1465, 1386 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{32}H_{49}O_2$ $(M - OAc)^+$ 465.3727, found 465.3741.

2,3-Dihydro-1α,9α-peroxo-11-oxoolean-12-en-30-(acetyloxy)ol ***8***. Following the representative procedure for the preparation of oxidized triterpenes, to **7** (0.029 g, 0.056 mmol, α/β = 75:25 ≈ 3:1) in acetone (0.6 mL) were added *N*-hydroxyphthalimide (0.062 g, 0.38 mmol) and chromium(VI) oxide (0.021 g, 0.21 mmol) at 40 °C under O_2 to afford **8** as a white solid (0.0004 g, 1%): mp 137−140 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.83 (d, J = 9.8, 1H), 5.72 (s, 1H), 5.52 (dd, J = 9.8, 5.2, 1H), 4.92 (d, J = 5.3, 1H), 4.07 (d, J = 11.0, 1H), 3.90 (d, J = 10.9, 1H), 2.15−2.09 (m, 2H), 2.08 (s, 3H), 2.02−1.98 (m, 2H), 1.82−1.78 (m, 1H), 1.71−1.66 (m, 2H), 1.50−1.49 (m, 1H), 1.48−1.45 (m, 1H), 1.44−1.41 (m, 1H), 1.40 (s, 3H), 1.36 (s, 3H), 1.34−1.30 (m, 2H), 1.27 (s, 3H), 1.26−1.24 (m, 2H), 1.23−1.21 (m, 1H), 1.15−1.13 (m, 1H), 1.07 (s, 3H), 0.97 (s, 3H), 0.94 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, diagnostic peaks) δ 193.7 (C), 171.4 (C), 169.4 (C), 144.7 (CH), 126.3 (CH), 117.6 (CH), 90.6 (C), 80.4 (CH), 67.5 (CH_2), 55.3 (CH), 48.3 (CH_2), 46.7 (C), 44.5 (C), 43.0 (CH), 39.5 (CH_2), 35.9 (CH_2), 35.3 (C), 34.1 (CH_2), 33.0 (C), 31.2 (CH_3), 30.3 (C), 29.8 (CH_2), 28.6 (CH_3), 27.8 (CH_3), 26.5 (CH_2), 26.4 (CH_3), 21.8 (CH_3), 20.9 (CH_3), 20.3 (CH_3), 17.6 (CH_2), 15.6 (CH_3); IR 2928, 1738, 1669, 1462 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{32}H_{47}O_5$ $(M + H)^+$ 511.3418, found 511.3421.

11β-Hydroxy-11α-methyl-18β-olean-2,12-dien-30-oic Acid Methyl Ester ***11***. To a cooled (0 °C) solution of dienone **1** (0.080 g, 0.17 mmol) in THF (0.7 mL) was added MeMgBr (0.3 mL, 3 M in THF, 0.9 mmol). The reaction mixture was warmed to ambient temperature for 12 h, and then H_2O (5 mL) was added. The reaction mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (10:90 EtOAc/hexanes) afforded **11** as a white solid (0.044 g, 57%). The stereochemistry was determined by correlation to a similar alkylated triterpene[61] and correlation to the X-ray structure of **13** in Supporting Information: mp 120−124 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.47−5.45 (m, 1H), 5.37 (d, J = 10.1, 1H), 5.08 (s, 1H), 3.69 (s, 3H), 2.45 (dd, J = 16.1, 6.2, 1H), 2.06 (d, J = 16.1, 1H), 1.96−1.92 (m, 3H), 1.84−1.81 (m, 1H), 1.70 (td, J = 13.9, 4.5, 1H), 1.63 (s, 1H), 1.55−1.47 (m, 4H), 1.44 (s, 3H), 1.41 (s, 3H), 1.37−1.26 (m, 4H), 1.22−1.21 (m, 1H), 1.19 (s, 3H), 1.16−1.14 (m, 1H), 1.12 (s, 3H), 1.06 (s, 3H), 1.04−1.02 (m, 1H), 0.95 (s, 3H), 0.92 (s, 3H), 0.90−0.85 (m, 1H), 0.82 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ

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177.7 (C), 143.5 (C), 137.3 (CH), 134.7 (CH), 121.6 (CH), 73.3 (C), 55.9 (CH), 53.3 (CH_3), 51.8 (CH_3), 47.0 (CH), 44.4 (C), 43.13 (CH), 43.10 (CH_2), 41.8 (C), 41.7 (C), 40.3 (C), 38.5 (CH_2), 34.6 (CH_2), 34.3 (C), 32.4 (CH_3), 32.3 (CH_2), 31.6 (CH_2), 31.4 (CH_2), 28.61 (CH_3), 28.58 (CH_3), 27.2 (CH_2), 27.0 (C), 24.1 (CH_3), 23.5 (CH_3), 20.3 (CH_2), 18.8 (CH_3), 18.3 (CH_3); IR 3531, 2949, 1720, 1457, 1383 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{32}H_{50}NaO_3$ $(M + Na)^+$ 505.3652, found 505.3642.

11-Methylene-18β-olean-2,12-dien-30-oic Acid Methyl Ester **12**, *11α-Formyl-18β-olean-2,12-dien-30-oic Acid Methyl Ester* **13**, *and 11α-Formyl-11β-hydroxy-18β-olean-2,12-dien-30-oic Acid Methyl Ester* **14**. Following the representative procedure for the preparation of oxidized triterpenes, to **11** (0.061 g, 0.13 mmol) in acetone (1 mL) were added *N*-hydroxyphthalimide (0.160 g, 0.978 mmol) and chromium(VI) oxide (0.005 g, 0.05 mmol) at 40 °C under O_2. Purification by flash chromatography (5:95−10:90 EtOAc/hexanes) afforded triene **12** as a white solid (0.0106 g, 18%), dienone **1** as a white solid (0.006 g, 9%), **13** as a white solid (0.004 g, 6%), and **14** as a white solid (0.002 g, 3%). The spectral data of dienone **1** match the data reported.[7] **12**: ^1H NMR (600 MHz, $CDCl_3$) δ 5.72 (s, 1H), 5.42−5.41 (m, 2H), 5.08−5.06 (m, 2H), 3.70 (s, 3H), 2.72 (dd, J = 17.2, 4.7, 1H), 2.37 (s, 1H), 1.99−1.91 (m, 4H), 1.81−1.78 (m, 1H), 1.74 (td, J = 13.6, 4.2, 1H), 1.63−1.58 (m, 2H), 1.51−1.49 (m, 1H), 1.43−1.40 (m, 1H), 1.37−1.25 (m, 4H), 1.22 (s, 3H), 1.21 (s, 3H), 1.151−1.146 (m, 1H), 1.13 (s, 3H), 1.09−1.08 (m, 1H), 0.99 (s, 3H), 0.98 (s, 3H), 0.94 (s, 3H), 0.91−0.88 (m, 1H), 0.79 (s, 3H); IR 2952, 2925, 2854, 1733, 1593, 1463 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{32}H_{49}O_2$ $(M + H)^+$ 465.3727, found 465.3719. This compound was found to be air-sensitive, undergoing extensive decomposition before a ^{13}C NMR spectrum and melting point were acquired. **13**: ^1H NMR (600 MHz, $CDCl_3$) δ 9.26 (d, J = 4.9, 1H), 5.38 (dd, J = 10.2, 2.3, 1H), 5.34 (ddd, J = 10.0, 5.6, 1.5, 1H), 4.95 (d, J = 4.0, 1H), 3.67 (s, 3H), 3.15 (qu, J = 3.5, 1H), 2.07−2.05 (m, 1H), 2.02−1.99 (m, 1H), 1.98−1.93 (m, 1H), 1.80−1.76 (m, 2H), 1.68 (dd, J = 16.0, 5.9, 1H), 1.61−1.57 (m, 2H), 1.51−1.46 (m, 1H), 1.44−1.39 (m, 1H), 1.37−1.32 (m, 2H), 1.30−1.27 (m, 3H), 1.26−1.25 (m, 1H), 1.23 (s, 3H), 1.11 (s, 3H), 1.03 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.96−0.92 (m, 2H), 0.90 (s, 3H), 0.89−0.87 (m, 1H), 0.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.8 (CH), 177.6 (C), 153.7 (C), 138.2 (CH), 120.6 (CH), 116.9 (CH), 52.2 (CH), 52.1 (CH), 51.8 (CH_3), 48.4 (CH), 47.4 (CH), 44.4 (C), 43.7 (CH_2), 42.0 (CH_2), 41.9 (C), 40.3 (C), 38.4 (CH_2), 37.8 (C), 34.7 (C), 31.9 (CH_3), 31.6 (CH_2), 31.4 (CH_2), 29.8 (CH_2), 28.6 (CH_3), 28.5 (CH_3), 26.9 (C), 26.8 (CH_3), 26.7 (CH_2), 22.8 (CH_3), 19.7 (CH_2), 17.9 (CH_3), 17.2 (CH_3); IR 2951, 2866, 1720, 1458 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{32}H_{49}O_3$ $(M + H)^+$ 481.3676, found 481.3677. Suitable crystals for X-ray crystallography were obtained by slow evaporation of $CHCl_3$. Crystallographic data are included in Supporting Information. Not enough material was available to determine a melting point. **14**: ^1H NMR (600 MHz, $CDCl_3$) δ 9.85 (d, J = 1.0, 1H), 5.38 (ddd, J = 10.1, 6.2, 1.9, 1H), 5.31 (dd, J = 10.2, 2.4, 1H), 4.65 (s, 1H), 3.79 (d, J = 1.0, 1H), 3.67 (s, 3H), 2.37 (s, 1H), 2.13−2.10 (m, 1H), 2.01−1.94 (m, 5H), 1.84−1.79 (m, 1H), 1.71−1.66 (m, 1H), 1.62−1.57 (m, 1H), 1.49−1.45 (m, 1H), 1.38 (s, 3H), 1.33 (s, 3H), 1.32−1.27 (m, 3H), 1.25 (s, 2H), 1.24−1.19 (m, 1H), 1.17−1.15 (m, 1H), 1.12 (s, 3H), 1.06 (s, 3H), 0.96 (s, 3H), 0.92−0.90 (m, 1H), 0.88 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, diagnostic peaks) δ 177.5 (C), 136.7 (CH), 122.1 (CH), 121.9 (CH), 81.4 (C), 58.2 (CH), 52.7 (CH), 51.8 (CH_3), 47.7 (CH), 44.3 (C), 43.7 (C), 42.5 (CH_2), 42.4 (CH_2), 41.8 (CH_2), 38.7 (C), 38.3 (CH_2), 34.4 (C), 33.6 (CH_2), 32.2 (CH_3), 31.8 (CH_2), 31.4 (CH_2), 28.5 (CH_3), 28.4 (CH_3), 26.8 (C), 25.8 (CH_3), 23.0 (CH_3), 20.4 (CH_3), 19.7 (CH_2), 19.6 (CH_3); IR 3484, 2929, 2869, 1730, 1462 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{32}H_{48}NaO_4$ $(M + Na)^+$ 519.3445, found 519.3434. Not enough material was available to determine a melting point.

3β-Trimethylsiloxy-11-oxo-18β-olean-30-oic Acid **16**. The silyl-protected glycyrrhetinic acid precursor to ketone **16** was synthesized according to a reported procedure,[57] and the spectral data are consistent with the data reported. Following a reported procedure,[32] to a cooled (−78 °C) solution of lithium (3.5 g, 0.50 mol) in ammonia (800 mL), which was dried over lithium (6 g) at −78 °C, was added a solution of the silyl-protected glycyrrhetinic acid (5.30 g, 9.76 mmol) in THF (150 mL) dropwise by addition funnel over 1 h under argon. After 1 h, to the cold (−78 °C) reaction mixture was added acetone (100 mL) dropwise by addition funnel over 45 min. The cooling bath was removed from the reaction mixture, and when the blue color vanished, ammonium chloride (33 g) was added portionwise over 15 min. After the ammonia was allowed to evaporate overnight, the reaction mixture was dissolved in THF (500 mL) and concentrated in vacuo. Purification by flash chromatography (20:80−50:50 EtOAc/hexanes) afforded **16** as a white solid (0.296 g, 6%): mp 230 °C dec; ^1H NMR (500 MHz, $CDCl_3$) δ 3.15 (dd, J = 11.6, 4.2, 1H), 2.46−2.44 (m, 1H), 2.25−2.22 (m, 1H), 2.11 (s, 1H), 1.95−1.85 (m, 4H), 1.73−1.64 (m, 2H), 1.59−1.51 (m, 2H), 1.48−1.39 (m, 4H), 1.36−1.24 (m, 6H), 1.22 (s, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 1.11−1.06 (m, 1H), 0.98 (s, 3H), 0.93 (s, 3H), 0.87 (s, 3H), 0.83−0.79 (m, 1H), 0.75 (s, 3H), 0.54−0.52 (m, 1H), 0.09 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.2 (C), 182.3 (C), 79.7 (CH), 64.6 (CH), 54.7 (CH), 46.3 (C), 45.4 (CH_2), 44.0 (C), 43.0 (CH), 40.9 (C), 39.4 (C), 38.6 (CH_2), 38.5 (CH_2), 36.5 (C), 35.8 (CH), 33.5 (CH_2), 32.9 (CH_2), 32.0 (CH_2), 31.2 (CH_2), 29.1 (CH_3), 28.6 (CH_3), 27.9 (CH_3), 27.6 (CH_2), 27.1 (CH_2), 26.5 (C), 18.8 (CH_3), 18.4 (CH_2), 17.4 (CH_3), 16.3 (CH_3), 16.1 (CH_3), 0.63 (CH_3); IR 2954, 2869, 1720, 1700, 1466, 1387 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{33}H_{57}O_4Si$ $(M + H)^+$ 545.4021, found 545.4023.

3β-Hydroxy-11-oxo-18β-olean-30-oic Acid Methyl Ester **17**. Following a reported procedure for a related triterpene,[62] to a cooled (0 °C) solution of saturated ketone **16** (0.071 g, 0.13 mmol) in toluene (0.93 mL) and MeOH (0.33 mL) was added trimethylsilyl diazomethane (0.17 mL, 2.0 M in hexanes, 0.26 mmol). After 1.5 h, aqueous AcOH (3 drops) was added, followed by EtOAc (35 mL). The phases were separated, and the organic layer was washed with saturated aqueous $NaHCO_3$ (5 mL) and H_2O (5 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification by flash chromatography (5:95 EtOAc/hexanes) afforded the corresponding methyl ester as a white solid (0.048 g, 66%): mp 235−237 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 3.62 (s, 3H), 3.14 (dd, J = 11.6, 4.4, 1H), 2.48−2.39 (m, 2H), 2.23 (dt, J = 13.3, 3.5, 1H), 2.10 (s, 1H), 1.95−1.83 (m, 4H), 1.72−1.63 (m, 3H), 1.58−1.53 (m, 2H), 1.45−1.38 (m, 2H), 1.34−1.25 (m, 5H), 1.17 (s, 3H), 1.16 (s, 3H), 1.13 (s, 3H), 1.08−1.05 (m, 1H), 0.97 (s, 3H), 0.92−0.91 (m, 1H), 0.89 (s, 3H), 0.86 (s, 3H), 0.80−0.77 (m, 1H), 0.74 (s, 3H), 0.52 (dd, J = 11.9, 1.7, 1H), 0.08 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.2 (C), 177.4 (C), 79.7 (CH), 64.5 (CH), 54.7 (CH), 51.7 (CH_3), 46.2 (C), 45.5 (CH_2), 44.2 (C), 43.1 (CH), 40.9 (C), 39.4 (C), 38.6 (CH_2), 38.4 (CH_2), 36.5 (C), 35.8 (CH), 33.7 (CH_2), 32.8 (CH_2), 32.0 (CH_2), 31.4 (CH_2), 29.0 (CH_3), 28.6 (CH_3), 27.9 (CH_3), 27.6 (CH_2), 27.1 (CH_2), 26.5 (C), 18.8 (CH_3), 18.4 (CH_2), 17.4 (CH_3), 16.3 (CH_3), 16.1 (CH_3), 0.61 (CH_3); IR 2961, 2868, 1729, 1697, 1465, 1366 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{34}H_{59}O_4Si$ $(M + H)^+$ 559.4177, found 559.4189.

To a solution of this methyl ester (0.044 g, 0.079 mmol) in THF (1.5 mL) was added tetrabutylammonium fluoride (0.17 mL, 1.0 M in THF, 0.12 mmol). After 23 h, brine (10 mL) was added. The reaction mixture was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (30:70 EtOAc/hexanes) afforded **17** as a white solid (0.035 g, 92%): mp 225−227 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 4.30 (q, J = 7.1, 1H), 3.62 (s, 3H), 3.16 (dd, J = 11.6, 4.7, 1H), 2.46−2.39 (m, 2H), 2.27 (dt, J = 13.3, 3.5, 1H), 2.10 (s, 1H), 1.94−1.85 (m, 4H), 1.70−1.65 (m, 1H), 1.63−1.59 (m, 1H), 1.57−1.54 (m, 2H), 1.46−1.38 (m, 2H), 1.33−1.24 (m, 6H), 1.17 (s, 3H), 1.16 (s, 3H), 1.13 (s, 3H), 1.08−1.05 (m, 1H), 0.97 (s, 3H), 0.96 (s, 3H), 0.92−0.91 (m, 1H), 0.89 (s, 3H), 0.84−0.80 (m, 1H), 0.77 (s, 3H), 0.54 (dd, J = 12.1, 1.8, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.1 (C), 177.4 (C), 79.0 (CH), 64.4 (CH), 54.6 (CH), 51.7 (CH_3), 46.2 (C), 45.5 (CH_2), 44.2 (C), 43.1 (CH), 40.9 (C), 39.0 (C), 38.6 (CH_2), 38.4 (CH_2), 36.5 (C), 35.8 (CH), 33.7 (CH_2), 32.8 (CH_2), 31.9 (CH_2), 31.4 (CH_2), 28.9 (CH_3), 28.2 (CH_3), 27.9 (CH_3), 27.2 (CH_2), 26.5 (C), 18.8 (CH_3), 18.1 (CH_2), 17.4 (CH_3), 16.2 (CH_3),

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15.6 (CH_3), 14.2 (CH_2); IR 3348, 2937, 2870, 1723, 1699, 1465 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{31}H_{51}O_4$ $(M + H)^+$ 487.3782, found 487.3788.

11-Oxo-18β-olean-2-en-30-oic Acid Methyl Ester ***18***. Following a reported procedure for the related unsaturated ketone **1** (vide supra),[7] to a cooled (0 °C) solution of alcohol **17** (0.035 g, 0.072 mmol), PPh_3 (0.104 g, 0.397 mmol), and 3,3-dimethylglutarimide (0.055 g, 0.39 mmol) in THF (1.2 mL) was added diethyl azodicarboxylate (0.06 mL, 0.4 mmol). The reaction mixture was warmed to ambient temperature for 10 h and then was concentrated in vacuo. Purification by flash chromatography (2:98 EtOAc/hexanes) afforded **18** as a white solid (0.004 g, 10%): mp 195−197 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.41−5.35 (m, 2H), 4.63 (dd, J = 13.4, 6.4, 1H), 3.64 (s, 3H), 2.59 (dd, J = 16.9, 5.0, 1H), 2.51−2.44 (m, 2H), 2.10 (s, 1H), 1.96−1.86 (m, 4H), 1.72 (t, J = 12.9, 1H), 1.65−1.61 (m, 1H), 1.53−1.43 (m, 3H), 1.34−1.27 (m, 6H), 1.24 (s, 3H), 1.18 (s, 3H), 1.15 (s, 3H), 1.12−1.10 (m, 1H), 1.02 (s, 3H), 0.98−0.96 (m, 1H), 0.94 (s, 3H), 0.91 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.6 (C), 177.6 (C), 137.5 (CH), 121.6 (CH), 76.2 (CH), 63.5 (CH), 51.7 (CH), 51.4 (CH_3), 46.2 (C), 45.4 (CH_2), 44.3 (C), 43.1 (CH), 40.9 (C), 40.4 (C), 38.7 (CH_2), 35.8 (CH_2), 35.7 (C), 33.8 (CH_2), 32.9 (CH_2), 32.0 (CH_2), 31.4 (CH_2), 31.1 (CH_3), 29.0 (CH_3), 28.0 (CH_3), 27.1 (CH_2), 26.6 (C), 23.4 (CH_3), 19.3 (CH_3), 18.3 (CH_2), 17.3 (CH_3), 16.1 (CH_3); IR 2950, 2867, 1729, 1701, 1463 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{31}H_{49}O_3$ $(M + H)^+$ 469.3676, found 469.3680.

1,11-Dioxo-18β-olean-2-en-30-oic Acid Methyl Ester ***19***. Following the representative procedure for the preparation of oxidized triterpenes, to **18** (0.004 g, 0.007 mmol) in acetone (0.2 mL) were added *N*-hydroxyphthalimide (0.010 g, 0.063 mmol) and chromium(VI) oxide (0.002 g, 0.02 mmol) at 40 °C under O_2 to afford **19** as a white solid (0.0016 g, 44%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.30 (d, J = 10.1, 1H), 5.75 (d, J = 10.2, 1H), 3.64 (s, 3H), 2.78 (t, J = 13.5, 1H), 2.66 (s, 1H), 2.46−2.42 (m, 1H), 1.97−1.92 (m, 2H), 1.91−1.88 (m, 2H), 1.66 (s, 3H), 1.63−1.58 (m, 4H), 1.38−1.33 (m, 2H), 1.32−1.28 (m, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.12 (s, 3H), 1.05 (s, 3H), 1.03 (s, 3H), 0.90 (s, 3H), 0.88−0.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, diagnostic peaks) δ 177.6 (C), 154.6 (CH), 123.7 (CH), 54.0 (C), 51.7 (CH_3), 51.0 (CH), 48.0 (CH), 46.5 (C), 45.5 (CH_2), 44.3 (C), 43.6 (C), 41.5 (CH_2), 38.6 (CH_2), 36.9 (CH), 36.0 (C), 33.9 (CH_2), 32.9 (C), 31.5 (CH_2), 31.4 (CH_3), 30.9 (CH_2), 29.8 (CH_3), 29.0 (CH_3), 28.0 (CH_3), 26.7 (CH_2), 22.5 (CH_3), 19.1 (CH_2), 18.2 (CH_3), 17.5 (CH_3), 15.9 (CH); IR 2929, 1730, 1700, 1682, 1462 cm^{-1}; HRMS (TOF MS ES+) m/z calcd for $C_{31}H_{47}O_4$ $(M + H)^+$ 483.3469, found 483.3478. Not enough material was available to determine a melting point.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Computational data, X-ray crystallographic data (CIF), and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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