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Total synthesis of the tricyclic skeleton of the natural Celastraceae sesquiterpenoids and related synthetic analogs

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Abstract—A concise and efficient synthesis of the C_{13} tricyclic core of the dihydro-β-agarofuran skeleton common to the natural Celastraceae sesquiterpenoids is described. The strategy entails a Mukaiyama aldol reaction of a tetrahydronaphthalene enol silane with acetone, epoxidation, ketone reduction, and acid-catalyzed cyclization. This key scaffold was converted into diverse polyhydroxylated derivatives, which were tested for insecticidal activity.
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1. Introduction

The Celastraceae family is a rich source of sesquiterpenoids of remarkably diverse structures ranging from small alkaloids and oligopeptides to very complex macrocyclic arrays. In addition to their skeletal diversity and complexity, many such natural products show broad ranging bioactivities. Of particular note are their cytotoxic,[1] antitumor,[2] immunosupressive,[3] and anti-HIV[4] activities.

Several Celastraceae species have a long history of use in traditional Chinese agriculture to protect crops from insect attack and are commonly known as the bittersweet family.[5] A number of secondary metabolites exhibit insect antifeedant activity, providing the possibility of their application as alternatives to existing synthetic insecticides.[6] Since the discovery of wilforine,[7] which is very potent against cabbage leaf worm, considerable efforts have been directed toward the discovery of other active compounds. However, although considerable numbers of antifeedant terpenoids have been isolated, few synthetic approaches toward these unique structures have been reported to date.[8] All the Celastraceae sesquiterpenoids are based on the C_{15} tricyclic dihydro-β-agarofuran skeleton (Fig. 1). Their high bioactivity is attributed to the presence of polyhydroxy functionalities, partially or totally esterified. These features make these sesquiterpenoids challenging synthetic targets particularly with

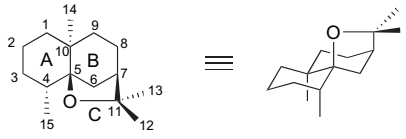

Figure 1.

the need to devise concise, economically viable synthetic routes. Herein, we report a new and efficient synthetic route to the tricyclic core **6** of the dihydro-β-agarofuran skeleton and late oxygenation reactions to produce several classes of analogs. Considering their potential bioactivity, synthetic efforts were specifically focused on introducing different degrees of hydroxylation with varied stereochemistry, as well as with variable degrees of alcohol esterification.

2. Results and discussion

Our first goal was to develop a concise method for the preparation of the tricyclic compound **6**, which was chosen as a pivotal intermediate for further derivatization. The Mukaiyama reaction of enol silane **1**[9] with acetone gave the silylated aldol product **2** (Scheme 1). Subsequent regioselective epoxidation of diene **2** by reaction with *m*-chloroperoxybenzoic acid (*m*CPBA) gave monoepoxide **3** (71%) as a separable 1:4 mixture of *syn*- and *anti*-diastereoisomer. Subsequent reduction of ketone **3** using sodium borohydride gave alcohol **4** (41%) as the sole stereoisomer. An X-ray structure of the alcohol **4** confirmed the relative *anti*-configuration between the epoxide group and silylated alcohol functionality. Deprotection using tetrabutylammonium

Keywords: Sesquiterpenoid; Celastraceae; Polyhydroxylation; Epoxidation; Insecticide.
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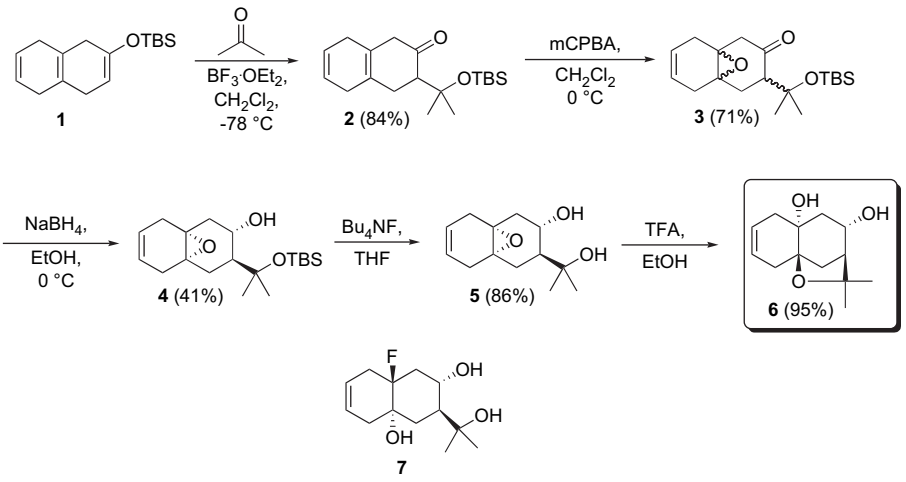


Scheme 1.

fluoride gave diol **5** (86%). In contrast, desilylation using HF–pyridine gave a complex mixture containing the tricyclic diol **6** (38%) and fluoride **7** (42%). The relative configuration of the fluoride **7** was assigned by an X-ray crystallographic study. Attention at this point was directed toward the construction of the tetrahydrofuran ring system of diol **6**. The optimum cyclization via opening of epoxide **5** was catalyzed by trifluoroacetic acid (TFA) in ethanol at room temperature and this gave diol **6** in excellent yield (95%). The structure of the diol **6** was confirmed by an X-ray crystallographic structure determination of the derived 4-nitrobenzoate ester (Fig. 2).

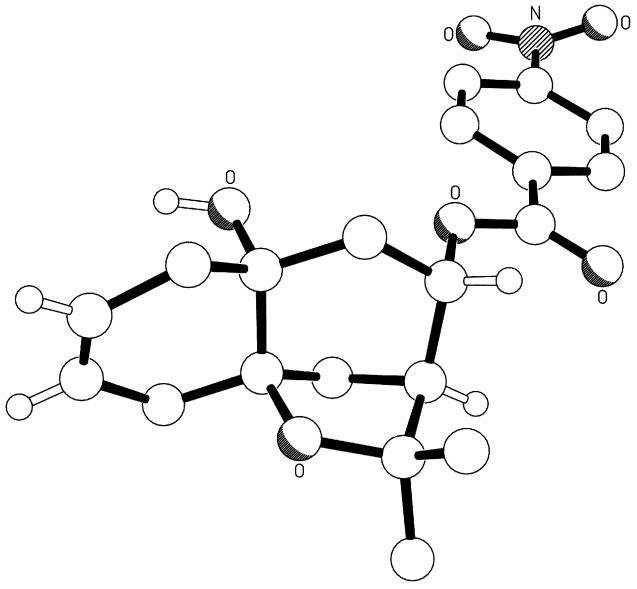
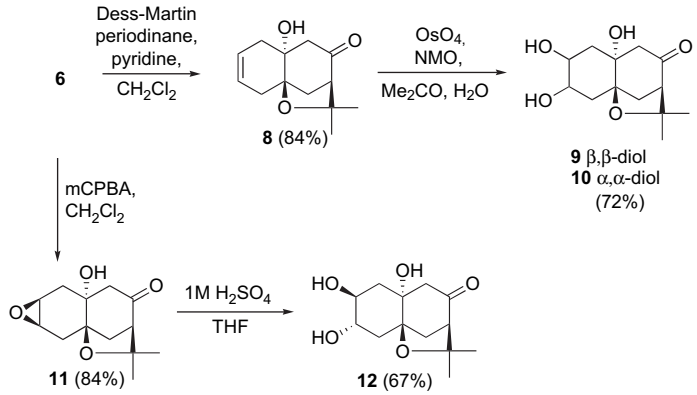


Figure 2. The molecular structure of 4-nitrobenzoate ester from diol **6**.

With tricycle **6** in hand, we sought to functionalize the alkene entity to prepare more heavily oxygenated derivatives. González et al. have shown that the presence of a C-8 keto residue in dihydro-β-agarofuran derivatives tends to favor insecticidal activity.[10] Thus, alcohol **6** was oxidized using the Dess–Martin reagent to provide ketone **8** (84%) (Scheme 2). Hydroxylation of alkene **8** using *N*-methylmorpholine-*N*-oxide in the presence of a catalytic amount of osmium tetroxide gave the *syn*-β,β-diol **9** and α,α-diol **10** (72%, 1:1). In parallel, reaction of alkene **6** with *m*CPBA gave the epoxide **11** (84%), which was tentatively assigned as β by comparison with the phenylselenylation reaction in Scheme 7, vide infra. Subsequent reaction of epoxide **11** with sulfuric acid (1 M) gave the trans-diequatorial diol **12** (67%), which was presumably formed via a pseudo-boat conformation of the epoxide. The structural assignment of diol **12** was carried out following the assignment of stereochemistry of dienone **14** (vide infra).



Scheme 2.

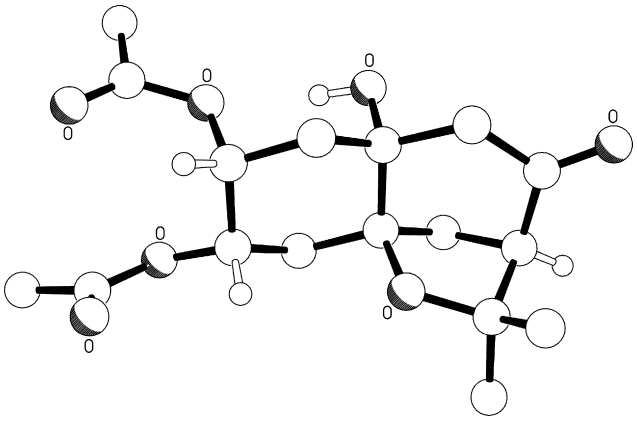
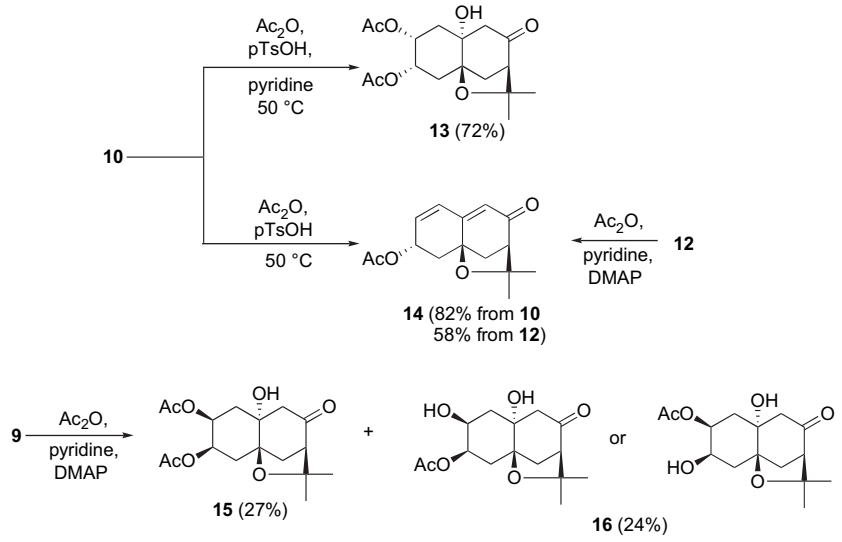


Figure 3. The molecular structure of diacetate **13**.

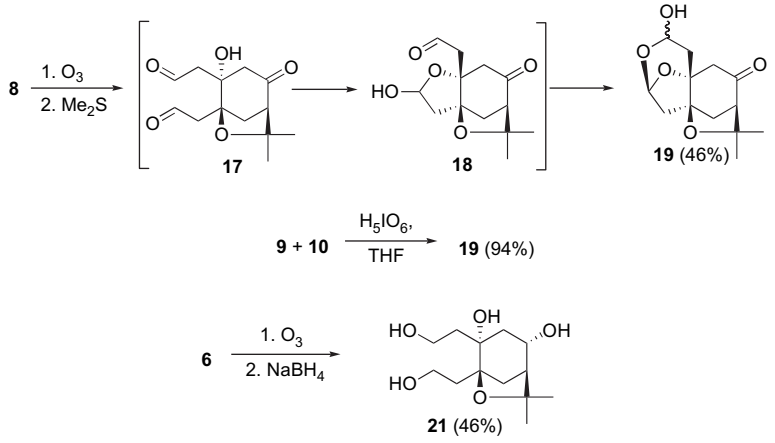
Acetylation of diol **10** in pyridine containing *p*-toluenesulfonic acid gave diester **13** (72%), the structure of which was confirmed by an X-ray crystallographic study. This also allowed for the unambiguous assignment of the relative configuration of both alcohols **9** and **10** (Fig. 3). In contrast, acetylation without pyridine as a solvent gave the dienone **14** (82%) (Scheme 3). Acetylation of diol **9** gave a mixture of di-**15** and mono-ester **16**. In contrast, esterification of triol **12** gave only the dienone **14** (58%). All attempted acetylations of the tertiary alcohol residue were unsuccessful presumably due to the steric hindrance at this position.

Ozonolysis of the tricyclic ketone **8** in dichloromethane with a dimethyl sulfide work-up gave the tetracyclic lactol **19**, which was presumably formed from dialdehyde **17** and lactol **18** (Scheme 4). The same product **19** was alternatively synthesized by the periodate cleavage of diols **9** and **10** (94%). Fortunately, the 4-nitrobenzoate ester **20** was crystalline and an X-ray structural analysis allowed for the structural assignment (Fig. 4). Ozonolysis of tricyclic alkene **6** in methanol and dichloromethane followed by sodium borohydride reduction gave tetraol **21** (46%).

We next sought to prepare isomers of pentaol **24** from the cyclohexadiene **23** as a pivotal building block (Scheme 5). Bromination of enone **8** gave an unstable intermediate possibly the dibromide **22** or the corresponding bromohydrin, which was unstable and directly dehydrohalogenated using *N*″-*tert*-butyl-*N*,*N*,*N*′,*N*′-tetramethylguanidine in dichloromethane, DABCO in acetonitrile, or DBU in DMSO to provide dienone **25** (65, 26, 76%, respectively) (Scheme 6).



Scheme 3.



Scheme 4.

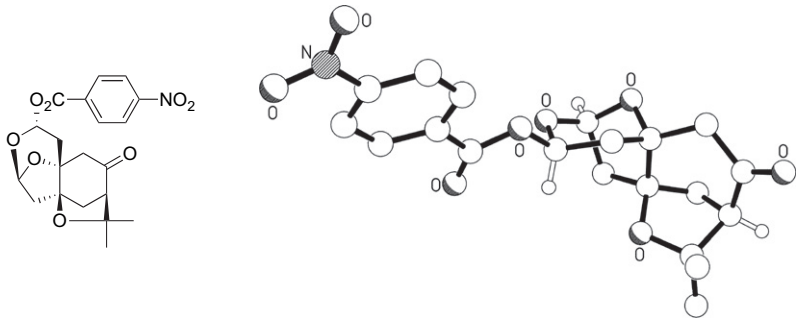
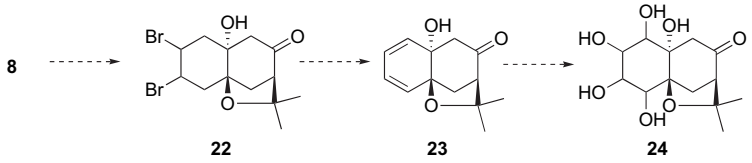
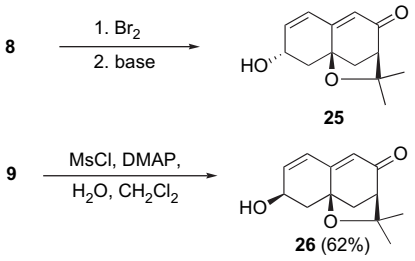


Figure 4. The molecular structure of 4-nitrobenzoate ester **20**.



Scheme 5.

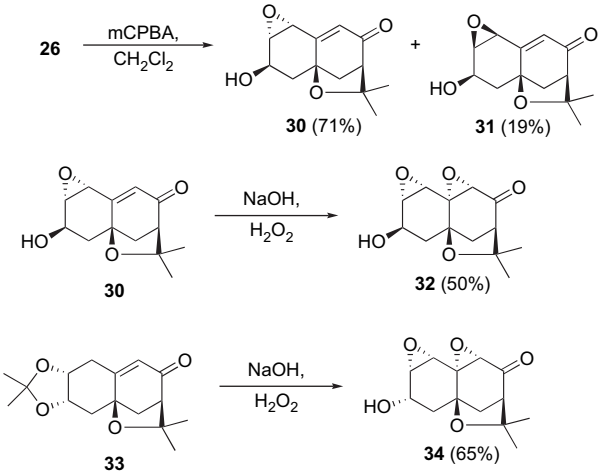


Scheme 6.

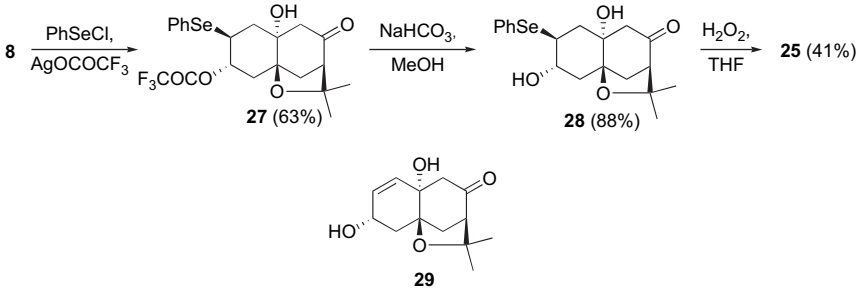
Alternatively, triol **9** was allowed to react with methanesulfonyl chloride and DMAP in dichloromethane and water[11] to give dienone **26** (62%), the structure of which was confirmed by an X-ray structural determination.

Reaction of phenylselenenyl chloride and silver trifluoroacetate with alkene **8** gave trifluoroacetate **27**, which was hydrolyzed to give selenide **28**.[12] Subsequent oxidation with hydrogen peroxide gave dienone **25** rather than the target alkenediol **29** (the configurational assignment of **27** and **28** was based on the structure of the product **25**) (Scheme 7).

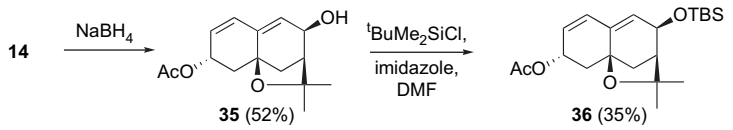
Since, by this stage, we had prepared more dienones **25** and **26** than we originally planned, we chose to examine these substrates in further oxidation reactions. Epoxidation of **26** using *m*CPBA gave a readily separable mixture of diastereoisomeric mono-epoxides **30** and **31** (4:1). The relative configurations of **30** and **31** were established on the basis of an X-ray crystallographic structural determination of **31**. Further epoxidation of alkene **30**, by reaction with hydrogen peroxide under basic conditions, gave the diepoxide **32** (50%). In parallel, epoxidation of ketal **33** (vide infra) under alkaline conditions gave the isomeric diepoxide **34**. The structure of isomer **34** was established by an X-ray crystallographic structural determination (Scheme 8).



Scheme 8.



Scheme 7.

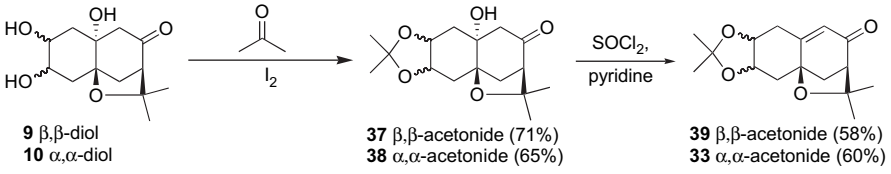


Scheme 9.

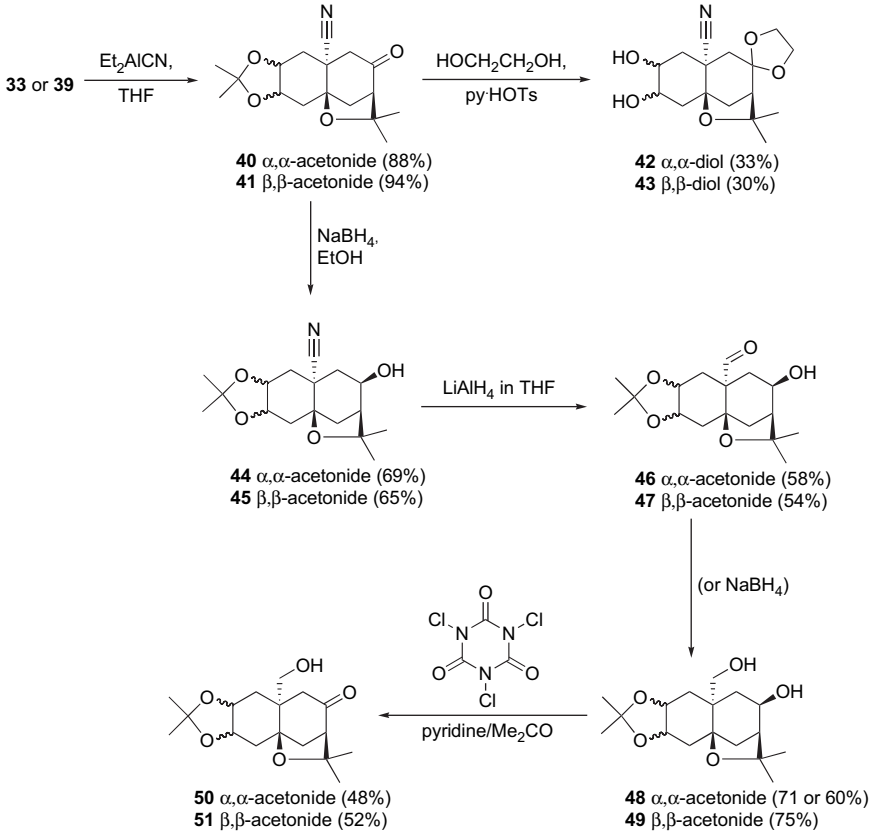
Attempted ring opening reactions of epoxide **30** or **32** under acidic, Lewis acidic or basic conditions gave either intractable mixtures of products or only unreacted starting material. Reduction of ketone **14** and protection gave the silyl ether **36**, which was tentatively assigned as having the β-stereochemistry on the basis of expected steric approach control in the reduction step. Unfortunately, attempted dihydroxylation of **36** using osmium tetroxide[13] gave only complex mixture of products (Scheme 9).

At this stage, we thought to explore the addition of C-1 and C-2 species followed by oxidation to generate additional terpenoid analogs for bioassays. Acetonide protection of diol **9** or **10** gave ketal **37** or **38**. Subsequent dehydration using thionyl chloride in pyridine gave ketal **39** or **33**, respectively (Scheme 10).

Attempted Michael addition of nitromethane to **33** in the presence of DBU or triethylamine or tetrabutylammonium fluoride gave only the elimination product **25**. Alternatively, attempted Michael addition of the cuprate derived from vinylmagnesium bromide to **33** gave unreacted starting material. Following ample precedent from the steroid literature, reaction of diethylaluminum cyanide with the Michael acceptor **33** or **39** gave nitrile **40** or **41** (88, 94%, respectively). The configuration at C-10 was tentatively assigned as presented below on the basis of literature precedent for this reagent and expected steric approach control of the addition (Scheme 11).[14] trans-Ketalization of ketal **40** or **41** proceeded in only modest yields to provide adduct **42** or **43**. Alternatively, ketone **40** or **41** was reduced using sodium borohydride to provide alcohol **44** or **45** (69, 65%, respectively), which were subsequently reduced to provide the



Scheme 10.



Scheme 11.

corresponding aldehydes. The optimum synthesis of aldehyde **46** or **47** utilized lithium aluminum hydride in THF at room temperature (58, 54%, respectively). Further reduction of **46** or **47** using lithium aluminum hydride or sodium borohydride gave alcohol **48** or **49**. In contrast, direct reduction of nitrile **40** or **41** to diol **48** or **49** was accompanied with significant lowering of the overall yields due to the formation of more side products. Subsequent selective mono-oxidation of diol **48** or **49** using trichloroisocyanuric acid[15] gave the target ketone **50** or **51** (48, 52%, respectively) (Scheme 11). Again in this sequence, the stereochemistry of the secondary alcohol was assigned as β on the basis of expected steric approach control in the initial sodium borohydride reduction step.

Deprotection of acetonide **51** followed by in situ esterification of the resulting diol **52** gave diester **53** (31% over two steps) (Scheme 12).

Having aldehyde **46** in hand, a complementary route to synthesize multihydroxy sesquiterpenoids was examined. Wittig reaction of aldehyde **46** with methylenetriphenylphosphorane gave alkene **54** (66%). Oxidation of the secondary alcohol, followed by cleavage of the *iso*-propylidene protection group gave diol **56**, which was acetylated to provide diester **57**. Dihydroxylation of alkene **57** was inefficient, probably due to the rigidity of the skeleton and steric hindrance of the double bond, but gave diol **58** as a single diastereoisomer. Finally, exhaustive acetylation of diol **58** gave the corresponding tetra-ester **59** (75%) (Scheme 13).

Many advanced derivatives were tested for their insecticidal activities. Several compounds showed activity against a variety of insects, including silverleaf whiteflies (*Bemisia argentifolii*), orchid thrips (*Dichromothrips corbetti*), boll weevils (*Anthonomus grandis*), and several species of aphids and hoppers.

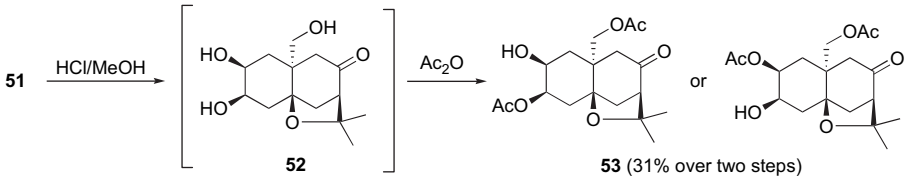
3. Conclusion

We developed a new efficient multigram synthesis of the key sesquiterpenoid analog **6**, which was converted into a range of polyoxygenated derivatives. Structures of selected intermediates were unambiguously established by X-ray crystallographic structural determinations. This initial broad insecticidal activity combined with the efficient chemical access described herein offers an attractive opportunity to further investigate the potential of the Celastraceae sesquiterpenoids class for the development of new and selective insecticides.

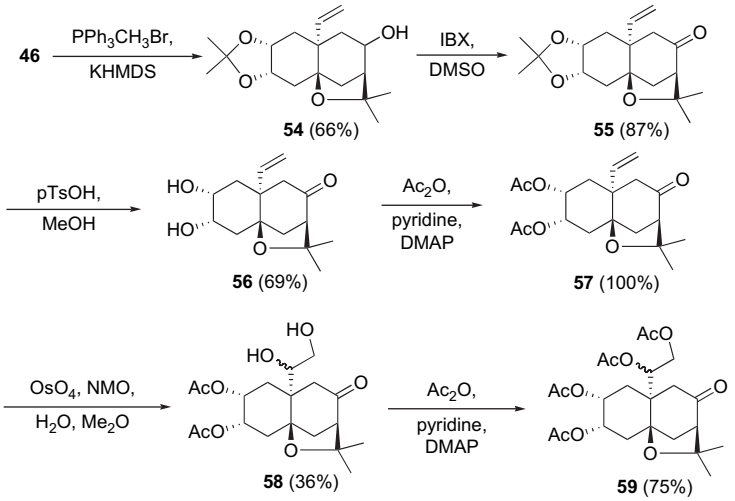
4. Experimental section

4.1. General procedures

Unless otherwise stated, reaction solvents were dried by distillation under N_2 from CaH_2 (CH_2Cl_2, PhMe, pyridine), Na–Ph_2CO (Et_2O, THF), K_2CO_3 (MeOH) or obtained commercially anhydrous (DMF, MeCN, Et_3N, *i*-Pr_2NEt, EtOH). Other solvents and all reagents were obtained from commercial suppliers and used without further purification unless otherwise stated. Reactions were performed in oven-dried glassware under N_2 unless otherwise stated. Chromatographed refers to flash column chromatography on silica gel (eluants are given in parenthesis). Thin layer chromatography (TLC) was performed on pre-coated glass backed



Scheme 12.



Scheme 13.

silica plates and visualized with a UV lamp (215 or 254 nm), potassium permanganate, or vanillin stains.

4.2. 3-(2-(*tert*-Butyldimethylsilyloxy)-2-propyl)-1,2,3,4,5,8-hexahydro-2-naphthalen-one (2)

Me_2CO (1.8 mL, 24 mmol) followed by $BF_3 \cdot OEt_2$ (2.5 mL, 20 mmol) were added dropwise to triene **1** (5.52 g, 20 mmol) in anhydrous CH_2Cl_2 (50 mL) at −75 °C. After 4 h, saturated aqueous $NaHCO_3$ (25 mL) was added, the layers were separated, and the aqueous phase was extracted with Et_2O (2×80 mL). The combined organic extracts were washed with H_2O (20 mL), dried ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexane/Et_2O 19:1) gave silyl ether **2** (5.60 g, 87%) as a colorless oil: R_f (hexane/Et_2O 9:1) 0.70; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.86 (s, 9H), 1.32 (s, 3H), 1.38 (s, 3H), 2.30–2.82 (m, 9H), 5.53–5.56 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −2.0, 18.1, 25.8, 26.2, 29.6, 30.7, 30.8, 32.4, 46.0, 59.1, 74.1, 123.1, 123.7, 124.2, 126.4, 210.3; MS (EI) *m*/*z* 320 ($M^{+\bullet}$); HRMS (EI) *m*/*z* calcd for $C_{19}H_{32}O_2Si$: 320.2171; found: 320.2172.

4.3. 4-(2-(*tert*-Butyldimethylsilyloxy)-2-propyl)-11-oxabicyclo[4.4.1]undecan-2-one (3)

*m*CPBA (0.56 g, 2.52 mmol) was added in one portion to diene **2** (0.62 g, 1.94 mmol) in dry CH_2Cl_2 (9.7 mL) at 0 °C. After 2 h, the mixture was diluted with saturated aqueous $NaHCO_3$ (20 mL), extracted with EtOAc (3×50 mL), dried ($MgSO_4$), and rotary evaporated. The crude product was chromatographed (silica, hexane/EtOAc 19:1) to give a mixture of diastereoisomeric epoxides **3** (*syn*/*anti* 1:4 by ^{1}H NMR) (0.53 g, 81%) as a colorless oil: R_f (pentane/Et_2O 4:1) 0.43. An aliquot of the isomer mixture was separated by chromatography (silica, hexane/CH_2Cl_2/EtOAc 7:3:5) to give analytically pure samples of each epoxide **3** isomer.

syn-**3**: IR (film) 3442, 1713, 1669, 1471, 1381, 1363, 1254, 1036, 835, 773 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.88 (s, 9H), 1.28 (s, 3H), 1.36 (s, 3H), 2.22–76 (m, 9H), 5.45–5.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −2.0, 18.1, 24.5, 25.8, 29.6, 30.4, 31.2, 33.2, 47.8, 56.6, 60.9, 64.3, 74.2, 121.6, 122.5, 207.2; MS (CI) *m*/*z* 337 $(M+H)^+$; HRMS (CI) *m*/*z* calcd for $C_{19}H_{33}O_3Si$: 337.2198; found: 337.2197.

anti-**3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.13 (s, 3H), 0.88 (s, 9H), 1.32 (s, 3H), 1.33 (s, 3H), 2.22–2.64 (m, 7H), 2.68–2.88 (m, 2H), 5.42–5.58 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −2.1, 18.2, 25.9, 27.5, 29.8, 30.0, 30.3, 46.0, 56.0, 60.4, 60.5, 74.7, 121.7, 122.5, 207.8.

4.4. (3*SR*,6*RS*,11*SR*)-4-(2-(*tert*-Butyldimethylsilyloxy)-2-propyl)-11-oxabicyclo[4.4.1]undecan-2-ol (4)

$NaBH_4$ (2.2 g, 58.2 mmol) was added in one portion to epoxide **3** (*syn*/*anti* 1:4, 9.8 g, 29.1 mmol) in EtOH (100 mL) at 0 °C. After 45 min, saturated aqueous NH_4Cl and saturated aqueous NaCl were added and the mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$) and rotary evaporated. Chromatography (silica, hexane/Et_2O 4:1 to 7:3) gave alcohol **4** (4.08 g, 41%) as a white solid: R_f (hexane/Et_2O 7:3) 0.25; mp 122–124 °C (EtOAc); IR (film) 3480, 1637, 1254, 835 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 6H), 0.88 (s, 9H), 1.32 (s, 6H), 1.36–1.43 (m, 1H), 1.77–1.88 (m, 1H), 1.94–2.10 (m, 2H), 2.13–2.23 (m, 1H), 2.25–2.36 (m, 2H), 2.40–2.65 (m, 2H), 3.70–3.82 (m, 1H), 5.10 (br s, 1H), 5.40–5.50 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.9, −1.8, 18.0, 24.4, 25.8, 29.2, 30.9, 31.7, 31.8, 39.2, 47.3, 60.3, 61.4, 68.8, 78.7, 122.5, 122.3; MS (CI) *m*/*z* 339 $(M+H)^+$; HRMS (CI) *m*/*z* calcd for $C_{19}H_{35}O_3Si$: 339.2355; found: 339.2370.

4.5. (1*RS*,3*SR*,4*SR*,6*SR*)-4-(1-Hydroxy-1-methylethyl)-11-oxatricyclo[4.4.1.0^{1,6}]undec-8-en-3-ol (5)

Bu_4NF in THF (1 M, 19.3 mL, 19.2 mmol) was added with stirring to alcohol **4** (5.43 g, 16.0 mmol) in THF (45 mL) at room temperature. After 35 min, saturated aqueous NH_4Cl and saturated aqueous NaCl were added, and the mixture was extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 3:2 to 1:1) to give diol **5** (3.09 g, 86%) as a colorless oil: R_f (hexanes/EtOAc 2:3) 0.20; IR (film) 3441, 1698, 1384, 1139, 1038 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.22 (s, 3H), 1.26–1.39 (m, 1H), 1.70–1.83 (m, 1H), 1.89–2.63 (m, 7H), 3.71–3.82 (m, 1H), 4.20 (br s, 1H), 4.93 (br, 1H), 5.32–5.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.3, 29.4, 30.7, 32.0, 32.2, 39.7, 45.6, 60.4, 61.5, 69.5, 74.4, 122.3, 122.3; MS (CI) *m*/*z* 242 $(M+NH_4)^+$; HRMS (CI) *m*/*z* calcd for $C_{13}H_{24}O_3N$: 242.1756; found: 242.1760. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.56; H, 8.95.

4.6. (1*RS*,6*RS*,8*SR*,9*SR*)-10,10-Dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodec-3-ene-6,8-diol (6)

Epoxide **5** (3.09 g, 13.8 mmol) and TFA (0.20 mL, 2.7 mmol) in EtOH (140 mL) were stirred for 25 min at room temperature. The mixture was washed with saturated aqueous $NaHCO_3$ and NaCl, and extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, CH_2Cl_2/MeOH 97:3) to give alcohol **6** (2.94 g, 95%) as a light yellow oil: R_f (CH_2Cl_2/MeOH 95:5) 0.22; IR (film) 3420, 1520, 1301, 1062, 890 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.30 (s, 3H), 1.71–1.84 (m, 2H), 1.99–2.16 (m, 4H), 2.28–2.38 (m, 1H), 2.45–2.73 (m, 4H), 4.02–4.13 (m, 1H), 5.51–5.71 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 30.8, 31.5, 34.1, 36.7, 41.7, 49.7, 67.7, 71.8, 81.6, 82.3, 123.4, 125.0; MS (CI) *m*/*z* 242 $(M+NH_4)^+$; HRMS (CI) *m*/*z* calcd for $C_{13}H_{24}O_3N$: 242.1756; found: 242.1756. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.79; H, 8.92.

4.7. (1*RS*,6*RS*,8*SR*,9*SR*)-6-Hydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodec-3-en-8-yl 4-nitrobenzoate

p-Nitrobenzoyl chloride (39 mg, 0.214 mmol) was added to alcohol **6** (40 mg, 0.178 mmol) in anhydrous pyridine (0.36 mL) at room temperature. After 5.5 h, saturated aqueous NH_4Cl and NaCl were added, and the mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$) and rotary evaporated. Chromatography (silica, hexanes/EtOAc 3:2) gave the *p*-nitrobenzoate ester (51 mg, 77%)

as a white solid: R_f (hexanes/EtOAc 2:3) 0.67; mp 185–187 °C (EtOAc); IR (film) 1717, 1526, 1281, 955 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.44 (s, 3H), 1.80–2.61 (m, 9H), 2.74–2.82 (m, 1H), 5.40–5.47 (m, 1H), 5.62–5.82 (m, 2H), 8.13–8.34 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 30.5, 32.3, 34.1, 37.0, 39.1, 47.1, 71.1, 72.5, 81.6, 82.3, 123.5, 123.5, 125.4, 130.7, 136.0, 150.5, 164.0; MS (CI) *m/z* 356 (M+H−H_2O); HRMS (CI) *m/z* calcd for $C_{20}H_{22}NO_5$: 356.1498; found: 356.1486.

4.8. (2*SR*,3*SR*,4a*SR*,8a*SR*)-8a-Fluoro-3-(1-hydroxy-1-methylethyl)-1,3,4,5,8,8a-hexahydronaphthalene-2,4a(2*H*)-diol (7)

HF–pyridine (0.56 mL, 21.5 mmol) was added to epoxide **4** (182 mg, 0.537 mmol) in dry THF (5.4 mL) at 0 °C. After 2 days at room temperature, saturated aqueous $NaHCO_3$ and brine were added, and the mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, CH_2Cl_2/MeOH 97:3) to give alcohol **6** (46 mg, 38%) and fluoride **7** (55 mg, 42%), respectively, as a colorless oil and a white crystalline solid. Data for **7**: R_f (CH_2Cl_2/MeOH 95:5) 0.36; mp 111–115 °C (EtOAc); ^1H NMR (300 MHz, CD_3OD) δ 1.22 (s, 3H), 1.23 (s, 3H), 1.23–1.47 (m, 1H), 1.53–2.50 (m, 8H), 3.87–4.15 (m, 1H), 5.20–5.75 (m, 2H); MS (CI) *m/z* 244 $(M+H)^+$.

4.9. (1*RS*,6*RS*,9*RS*)-6-Hydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.$0^{1,6}$]dodec-3-en-8-one (8)

Pyridine (2.4 mL, 29.80 mmol) and Dess–Martin periodinane (6.32 g, 14.90 mmol) were added to alcohol **6** (1.67 g, 7.44 mmol) in dry CH_2Cl_2 (37 mL). After 1.5 h, saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ (5:1) were added, and the mixture was extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give ketone **8** (1.39 g, 84%) as a colorless oil: R_f (hexanes/EtOAc 40:60) 0.44; IR (film) 3416, 1709, 1672, 1457, 1384, 1265, 1202, 738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.32 (s, 3H), 1.82–2.02 (m, 1H), 2.08–2.36 (m, 3H), 2.40–2.75 (m, 6H), 5.60–5.95 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 29.3, 33.7, 34.8, 37.1, 50.5, 60.4, 71.9, 81.8, 82.5, 123.8, 125.6, 208.9; MS (CI) *m/z* 240 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{22}O_3N$: 240.1599; found: 240.1593.

4.10. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-3,4,6-Trihydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.$0^{1,6}$]dodecan-8-one (9) and (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3,4,6-trihydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.$0^{1,6}$]dodecan-8-one (10)

N-Methylmorpholine-*N*-oxide (163 mg, 1.390 mmol) and OsO_4 in ^{t}BuOH (2.5 wt %, 0.58 mL, 5 mol %) were added with stirring to ketone **8** (206 mg, 0.927 mmol) in Me_2CO and H_2O (4:1, 13.2 mL) at room temperature. After 13 h, the mixture was diluted with saturated aqueous Na_2SO_4 and stirred for a further 45 min. The suspension was extracted with EtOAc and the extract was dried ($MgSO_4$) and rotary evaporated. Chromatography (silica, hexanes/EtOAc 1:9) gave diols **9** (86 mg, 36%) and **10** (86 mg, 36%) both as colorless oils.

Data for **9**: R_f (hexanes/EtOAc 1:9) 0.17; IR (film) 3425, 1711, 1670, 1296, 1140, 1032, 892, 734 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 1.20 (s, 3H), 1.30 (s, 3H), 1.62–1.78 (m, 1H), 1.82–2.03 (m, 2H), 2.12–2.28 (m, 2H), 2.28–2.50 (m, 2H), 2.50–2.68 (m, 2H), 3.80–4.08 (m, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 23.2, 28.2, 34.7, 34.8, 36.7, 50.8, 60.3, 68.3, 69.8, 74.3, 81.8, 85.1, 210.1; MS (CI) *m/z* 274 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{24}O_5N$: 274.1654; found: 274.1644.

Data for **10**: R_f (hexanes/EtOAc 1:9) 0.07; ^1H NMR (300 MHz, CD_3OD) δ 1.28 (s, 3H), 1.32 (s, 3H), 1.62–1.77 (m, 1H), 1.79–1.93 (m, 1H), 1.97–2.12 (m, 1H), 2.16–2.43 (m, 3H), 2.46–2.67 (m, 3H), 3.70–3.94 (m, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 23.2, 28.0, 34.6, 35.9, 37.0, 51.7, 59.5, 67.3, 70.1, 74.5, 83.3, 84.0, 209.3; MS (CI) *m/z* 274 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{24}O_5N$: 274.1654; found: 274.1646.

4.11. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3,4-Epoxy-6-hydroxy-10,10-dimethyl-11-oxatetracyclo[7.2.1.$0^{1,6}$]dodecan-8-one (11)

*m*CPBA (133 mg, 0.594 mmol) was added with stirring to alcohol **6** (110 mg, 0.495 mmol) in dry CH_2Cl_2 (1.2 mL) at room temperature. After 13 h, saturated aqueous $NaHCO_3$ was added and the resultant mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 3:2) to give epoxide **11** (99 mg, 84%) as an oil: R_f (hexanes/EtOAc 2:3) 0.35; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.28 (s, 3H), 2.05–2.60 (m, 9H), 3.30–3.45 (m, 2H), 3.58–3.75 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.9, 29.1, 32.5, 33.0, 34.9, 50.8, 51.4, 54.3, 60.2, 72.8, 81.1, 82.7, 208.1; MS (CI) *m/z* 256 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{22}NO_4$: 256.1549; found: 256.1545. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.43; H, 7.71.

4.12. (1*SR*,3*SR*,4*SR*,6*RS*,9*RS*)-3,4,6-Trihydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.$0^{1,6}$]dodecan-8-one (12)

Epoxide **11** (114 mg, 0.478 mmol) and H_2SO_4 (1 M, 0.6 mL) in THF (9.6 mL) were stirred at room temperature for 17 h. Saturated aqueous $NaHCO_3$ was added, the suspension was extracted with EtOAc, dried ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexanes/EtOAc 2:3) gave diol **12** (82 mg, 67%) as a colorless oil: R_f (hexanes/EtOAc 1:9) 0.32; ^1H NMR (300 MHz, CD_3OD) δ 1.25 (s, 3H), 1.32 (s, 3H), 1.60–1.82 (m, 2H), 2.12–2.31 (m, 2H), 2.31–2.68 (m, 5H), 3.73–4.00 (m, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 23.3, 28.0, 32.0, 32.9, 35.2, 51.2, 59.6, 69.9, 70.0, 74.5, 83.3, 84.9, 209.4; MS (CI) *m/z* 274 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{24}O_5N$: 274.1654; found: 274.1652.

4.13. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3-(Acetoxy)-6-hydroxy-10,10-dimethyl-8-oxo-11-oxatricyclo[7.2.1.$0^{1,6}$]dodec-4-yl acetate (13)

Ac_2O (0.078 mL, 0.84 mmol) and *p*-TsOH (106.5 mg, 0.56 mmol) were added in one portion to diol **10** (71 mg, 0.28 mmol) in pyridine (2 mL) at room temperature. After 4 h at 50 °C, the mixture was cooled to room temperature,

diluted with H_2O (2 mL), and basified to pH 9 with saturated aqueous NH_3. The aqueous phase was extracted with $CHCl_3$ (3×15 mL) and the combined organic layers were dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 4:1 to 7:3) to give diester **13** (68.8 mg, 72%) as a white solid: R_f (hexanes/EtOAc 7:3) 0.31; mp 125–130 °C (EtOAc); IR (film) 3453, 1740, 1714, 1368, 1242, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.26 (s, 3H), 1.77 (m, 1H), 1.99 (m, 3H), 2.11 (m, 3H), 2.21 (m, 2H), 2.67 (m, 6H), 3.13 (br s, 1H), 5.26 (m, 1H), 5.50 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 21.1, 24.3, 29.1, 32.4, 34.9, 35.9, 51.0, 60.4, 69.2, 73.6, 82.4, 84.3, 168.9, 170.1, 208.4; MS (CI) *m/z* 358 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{28}NO_7$: 358.1866; found: 358.1869.

4.14. (1*SR*,3*SR*,9*RS*)-10,10-Dimethyl-8-oxo-11-oxatricyclo[7.2.1.0^{1,6}]dodeca-4,6-dien-3-yl acetate (14)

Method A: diol **10** (51 mg, 0.19 mmol), *p*-TsOH (76 mg, 0.39 mmol), and Ac_2O (2 mL) were heated at 50 °C for 4.5 h. The mixture was basified to pH 9 with saturated aqueous NH_3 and the resultant suspension was extracted with $CHCl_3$. After rotary evaporation, the crude product was chromatographed (silica, hexanes/EtOAc 4:1) to give dienone **14** (41 mg, 82%) as a yellow oil. *Method B*: diol **12** (28 mg, 0.11 mmol), Ac_2O (26 μL, 0.28 mmol), and DMAP (2 mg) in dry pyridine (0.7 mL) were stirred at room temperature for 13 h. Saturated aqueous $NaHCO_3$ and NH_4Cl were added, and the suspension was extracted with EtOAc, dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 4:1) to give dienone **14** (17 mg, 58%) as an oil: R_f (hexanes/EtOAc 7:3) 0.31; IR (film) 3430, 1738, 1673, 1370, 1240, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.36 (s, 3H), 2.10 (s, 3H), 2.23 (m, 4H), 2.85 (s, 1H), 5.75 (m, 2H), 6.23 (s, 1H), 6.24 (s, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 21.1, 25.7, 29.9, 37.4, 42.7, 60.1, 68.0, 78.1, 81.8, 123.7, 126.5, 138.7, 155.3, 170.3, 201.1; MS (EI) *m/z* 262 ($M^{\bullet}$); MS (CI) *m/z* 263 $(M+H)^+$, 280 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{15}H_{19}O_4$: 263.1283; found: 263.1288.

4.15. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-3-(Acetoxy)-6-hydroxy-10,10-dimethyl-8-oxo-11-oxatricyclo[7.2.1.0^{1,6}]dodec-4-yl acetate (15)

Diol **9** (107 mg, 0.40 mmol), Ac_2O (98 μL, 1.0 mmol), and DMAP (2 mg) in dry pyridine (2 mL) were stirred at room temperature for 13 h, the mixture was diluted with saturated aqueous NH_4Cl and extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 4:1 to 7:3) to give diester **15** (39 mg, 27%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.68; IR (film) 3437, 1710, 1650, 1369, 1241, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.26 (s, 3H), 2.06 (s, 3H), 2.13 (s, 3H), 2.16 (m, 1H), 2.57 (m, 8H), 5.07 (m, 1H), 5.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 21.2, 24.5, 29.3, 33.6, 35.0, 35.3, 52.4, 59.9, 68.6, 69.5, 75.8, 81.4, 82.1, 170.7, 171.1, 208.7; MS (CI) *m/z* 341 $(M+H)^+$, 358 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{28}NO_7$: 358.1866; found: 358.1870. Further elution during chromatography gave the diol **16** (30 mg, 24%) as a colorless oil; R_f (hexanes/EtOAc 1:1) 0.42; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 3H), 1.33 (s, 3H), 1.95 (m, 2H), 2.12 (s, 3H), 2.50 (m, 7H), 2.99 (br s, 1H), 4.09 (m, 1H), 4.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 24.4, 29.1, 34.4, 35.2, 36.3, 52.3, 59.4, 67.9, 71.3, 75.3, 83.9, 171.2, 207.7; MS (CI) *m/z* 299 $(M+H)^+$, 316 $(M+NH_4)^+$.

4.16. (3*RS*,9*RS*,9a*SR*)-7-Hydroxy-2,2-dimethyl-5a,9-epoxy-3,9a-methano-decahydro-5*H*-heptalen-4-one (19)

Method A: ozone was bubbled through ketone **8** (88 mg, 0.39 mmol) in CH_2Cl_2 (10 mL) at −75 °C until the blue color persisted (30 min) when the excess of ozone was removed by bubbling oxygen at −75 °C. The reaction was quenched with Me_2S (1 mL) at −75 °C and allowed to warm to room temperature. After 13 h, the mixture was rotary evaporated and chromatographed (silica, hexanes/EtOAc 1:1) to give lactol **19** (46 mg, 46%) as a colorless oil containing both diastereoisomers (4:1 by ^1H NMR). *Method B*: periodic acid (10 mg, 0.05 mmol) in dry THF (1 mL) was added to diols **9** and **10** (11.8 mg, 0.045 mmol) in dry THF (1 mL) at 0 °C. After 80 min, the mixture was allowed to warm to room temperature and diluted with brine. The suspension was extracted with EtOAc and the extract was dried ($MgSO_4$) and rotary evaporated to give lactol **19** (10.8 mg, 94%) as a colorless oil containing both diastereoisomers (4:1 by ^1H NMR): R_f (hexanes/EtOAc 7:3) 0.27; IR (film) 3407, 1715, 1665, 1278, 1119, 968 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (data for the major diastereoisomer) δ 1.19 (s, 3H), 1.32 (s, 3H), 1.60 (m, 1H), 2.37 (m, 6H), 2.63 (m, 2H), 3.45 (br s, 1H), 5.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.4, 30.0, 36.7, 39.8, 42.8, 47.3, 58.4, 79.7, 83.2, 84.9, 89.2, 98.9, 208.8; MS (CI) *m/z* 254 $(M+H)^+$, 272 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{22}NO_5$: 272.1498; found: 272.1508.

4.17. (3*RS*,7*RS*,9*RS*,9a*SR*)-2,2-Dimethyl-5a,9-epoxy-3,9a-methano-7-(4-nitrobenzoyloxy)-decahydro-5*H*-heptalen-4-one (20)

p-Nitrobenzoyl chloride (33 mg, 0.18 mL) was added to lactol **19** (38 mg, 0.15 mmol) in dry pyridine (0.36 mL). After 5.5 h, saturated aqueous NH_4Cl and brine were added, and the mixture was extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give ester **20** (37 mg, 61%) as a white solid: R_f (hexanes/EtOAc 1:1) 0.58; mp 188–190 °C (EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.36 (s, 3H), 2.02 (m, 1H), 2.64 (m, 8H), 5.53 (d, *J*=6 Hz, 1H), 6.60 (m, 1H), 8.26 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.4, 30.0, 36.7, 38.9, 39.8, 47.2, 58.3, 80.0, 83.4, 86.3, 89.2, 99.7, 123.6, 131.1, 134.7, 150.8, 163.0, 208.1.

4.18. (1*S*,2*R*,4*S*,5*SR*)-6,6-Dimethyl-1,2-di-(2-hydroxyethyl)-7-oxabicyclo[3.2.1]octane-2,4-diol (21)

Ozone was bubbled through alcohol **6** (257 mg 1.15 mmol) in CH_2Cl_2 and MeOH (3:1, 4 mL) at −75 °C with stirring until the blue color persisted (30 min). The excess of ozone was removed by bubbling O_2 through the solution at −75 °C. After replacement of O_2 with an atmosphere of N_2, $NaBH_4$ (117 mg, 3.09 mmol) was added. After 3 h at −75 °C, the

mixture was allowed to warm to room temperature, quenched with H_2O, and saturated aqueous NH_4Cl and extracted with EtOAc. The separated organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, CH_2Cl_2/MeOH 95:5 to 9:1) to give tetraol **21** (138 mg, 46%) as a colorless oil: R_f (CH_2Cl_2/MeOH 95:5) 0.19; IR (film) 3336, 1658, 1464, 1429, 1385, 1140, 1077, 1018, 943, 884 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 1.27 (s, 3H), 1.30 (s, 3H), 1.76 (m, 4H), 1.90 (m, 1H), 2.16 (m, 3H), 2.80 (d, J=12 Hz, 1H), 3.75 (m, 4H), 4.08 (m, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 22.1, 28.4, 3.39, 36.3, 38.6, 38.9, 50.2, 57.7, 58.2, 66.7, 75.5, 81.8, 87.1; MS (CI) m/z 261 $(M+H)^+$, 278 $(M+NH_4)^+$; HRMS (CI) m/z calcd for $C_{13}H_{28}NO_5$: 278.1967; found: 278.1972. Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.83; H, 9.19.

4.19. (1*SR*,3*SR*,9*RS*)-3-Hydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodeca-4,6-dien-8-one (25)

Method A: ketone **8** (40 mg, 0.18 mmol) in CH_2Cl_2 (1 mL) was cooled to 0 °C and Br_2 (10 μL, 0.20 mmol) was added dropwise. The reaction was quenched, after 5 min, with saturated aqueous $Na_2S_2O_3$, extracted with CH_2Cl_2, and the organic extract was dried ($MgSO_4$). Rotary evaporation gave an adduct, possibly the dibromide **22**, which was used directly in the next step due to its instability. *N″-tert*-Butyl-*N*,*N*,*N′*,*N′*-tetramethylguanidine (46 μL, 0.39 mmol) was added dropwise to dibromide **22** (67.8 mg, 0.18 mmol) in CH_2Cl_2 (1 mL). After 4 h at room temperature, the mixture was diluted with H_2O, extracted with CH_2Cl_2, dried ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexanes/EtOAc 1:1) gave dienone **25** (25.5 mg, 65%) as a yellow oil. *Method B*: dibromide **22** (34 mg, 0.09 mmol) and DABCO (15 mg, 0.13 mmol) in MeCN (1.5 mL) were heated at reflux for 3 h when H_2O (5 mL) was added. Extraction with CH_2Cl_2, drying ($MgSO_4$), rotary evaporation, and chromatography (silica, hexanes/EtOAc 1:1) gave dienone **25** (5 mg, 26%). *Method C*: DBU (67 μL, 0.45 mmol) was added to dibromide **22** (86 mg, 0.20 mmol) in DMSO (0.5 mL) at 5–10 °C. After 2.5 h at room temperature, Et_2O was added and the mixture was washed with H_2O, dried ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexanes/EtOAc 1:1) gave dienone **25** (33.5 mg, 76%). *Method D*: H_2O_2 (0.22 mL) was added to selenide **28** (85.5 mg, 0.22 mmol) in THF (1 mL) at 0 °C. After 50 min at room temperature, the mixture was quenched with EtOAc, washed with saturated aqueous $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexanes/EtOAc 1:1) gave dienone **25** (20 mg, 41%). *Method E*: *p*-TsOH·H_2O (3 mg) and 2,2-dimethoxypropane (2.82 mL, 2.3 mmol) were added to diol **10** (58 mg, 0.23 mmol) in THF (2 mL) at room temperature. After 13 h, H_2O was added, the mixture was extracted with EtOAc, and the separated organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give dienone **25** (40 mg, 79%). *Method F*: $MeNO_2$ (10 μL, 0.18 mmol) and DBU (5 μL, 0.05 mmol) were added with stirring to enone **33** (13 mg, 0.05 mmol) in MeCN. After 13 h at 40 °C, the mixture was cooled to room temperature, diluted with H_2O, acidified with 1 M HCl, and extracted with Et_2O. The organic extract was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give dienone **25** (6 mg, 64%): R_f (hexanes/EtOAc 1:1) 0.34; IR (film) 3386, 1670, 1368, 1050, 890; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.35 (s, 3H), 1.91 (m, 1H), 2.26 (m, 3H), 2.87 (s, 1H), 4.73 (m, 1H), 5.74 (s, 1H), 6.18 (m, 1H), 6.35 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8, 29.6, 41.3, 42.9, 60.1, 65.2, 78.7, 81.7, 123.3, 125.3, 143.4, 155.9, 201.5; MS (CI) m/z 221 $(M+H)^+$, 238 $(M+NH_4)^+$; HRMS (CI) m/z calcd for $C_{13}H_{17}O_3$: 221.1178; found: 221.1181.

4.20. (1*SR*,3*RS*,9*RS*)-3-Hydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodeca-4,6-dien-8-one (26)

Diol **9** (162 mg, 0.63 mmol), MsCl (220 mg, 1.92 mmol), DMAP (117 mg, 0.96 mmol) in H_2O (14 mg, 0.77 mmol), and CH_2Cl_2 (2.5 mL) were stirred at room temperature for 13 h. The mixture was diluted with saturated aqueous $NaHCO_3$, extracted with CH_2Cl_2, washed with brine, dried, ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexanes/EtOAc 1:1) gave dienone **26** (86 mg, 62%) as a white solid: R_f (hexanes/EtOAc 1:1) 0.53; mp 118–120 °C (EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.38 (s, 3H), 2.26 (m, 4H), 2.89 (s, 1H), 4.32 (m, 1H), 5.78 (s, 1H), 6.30 (m, 1H), 6.50 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 30.1, 37.7, 43.2, 60.3, 62.8, 78.9, 83.8, 123.9, 126.7, 138.5, 155.6, 200.8; MS (CI) m/z 221 $(M+H)^+$, 238 $(M+NH_4)^+$.

4.21. (1*SR*,3*SR*,4*SR*,6*RS*,9*RS*)-6-Hydroxy-4-phenylselenenyl-3-trifluoroacetoxy-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodecan-8-one (27)

PhSeCl (172 mg, 0.89 mmol) in CH_2Cl_2 (1 mL) was added to CF_3CO_2Ag (198 mg, 0.89 mmol) in CH_2Cl_2 (4 mL) (Ar) giving an orange solution with a precipitate of AgCl. Ketone **8** (200 mg, 0.89 mmol) was added and, after 3 h, the mixture was filtered through Celite and the filtrate was rotary evaporated. Chromatography (silica, hexanes/EtOAc 7:3) gave trifluoroacetate **27** (277 mg, 63%) as a yellow oil: R_f (hexanes/EtOAc 1:1) 0.79; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.27 (s, 3H), 2.26 (m, 9H), 3.48 (m, 1H), 5.37 (m, 1H), 7.31 (m, 3H), 7.56 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 29.2, 35.3, 37.6, 40.6, 42.1, 51.7, 60.1, 74.6, 76.7, 82.8, 83.4, 115.1, 127.4, 128.2, 129.2, 135.3, 160.5, 208.3; MS (CI) m/z 510 $(M+NH_4)^+$. The crude product was used directly in the next step without further purification.

4.22. (1*SR*,3*SR*,4*SR*,6*RS*,9*RS*)-3,6-Dihydroxy-4-phenylselenenyl-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodecan-8-one (28)

$NaHCO_3$ (25 mg) in H_2O (1.5 mL) was added to trifluoroacetate **27** (277 mg, 0.56 mmol) in MeOH (4 mL). After 50 min at room temperature, H_2O (5 mL) was added and the mixture was extracted with CH_2Cl_2. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give selenide **28** (195 mg, 88%) as a yellow oil: R_f (hexanes/EtOAc 7:3) 0.39; IR (film) 3422, 1705, 1255, 1026, 896, 738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.25 (s, 3H), 2.25 (m, 9H), 3.26 (m, 1H), 3.83 (m, 1H), 7.29 (m, 3H), 7.59 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 29.2, 35.5, 39.5, 42.1, 48.1, 51.9, 60.3, 69.9, 75.2, 82.3, 84.0, 127.4,

128.1, 129.3, 135.2, 209.2; MS (CI) *m/z* 414 $(M+NH_4)^+$. Anal. Calcd for $C_{19}H_{24}O_4Se$: C, 57.72; H, 6.12. Found: C, 57.84; H, 6.00.

4.23. (1*SR*,3*RS*,4*RS*,5*SR*,9*RS*)-4,5-Epoxy-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodeca-6-en-8-one (30)

*m*CPBA (83 mg, 0.37 mmol) was added to dienone **26** (62.7 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After 13 h at room temperature, the mixture was diluted with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic extracts were washed with brine, dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give epoxide **30** (47 mg, 71%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.72; IR (film) 3493, 1679, 1073, 877 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.34 (s, 3H), 1.90 (m, 1H), 2.15 (m, 3H), 2.91 (s, 1H), 3.56 (m, 1H), 3.63 (m, 1H), 4.40 (s, 1H), 6.18 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 29.8, 32.7, 43.5, 51.4, 55.2, 60.4, 64.9, 78.6, 82.9, 130.9, 158.1, 199.4; MS (CI) *m/z* 237 $(M+H)^+$, 254 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{20}NO_4$: 254.1392; found: 254.1396.

4.24. (1*SR*,3*RS*,4*SR*,5*RS*,9*RS*)-4,5-Epoxy-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodeca-6-en-8-one (31)

Epoxide **31** (13 mg, 19%) was isolated as the minor diastereoisomer from the epoxidation of dienone **26** as a white solid: R_f (hexanes/EtOAc 1:1) 0.31; IR (film) 3417, 1676, 1034 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.37 (s, 3H), 2.16 (m, 4H), 2.94 (m, 1H), 3.65 (m, 1H), 3.75 (m, 1H), 4.13 (m, 1H), 6.10 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8, 29.9, 36.9, 46.6, 54.4, 59.0, 61.6, 65.5, 79.1, 80.5, 129.0, 160.9, 200.0; MS (CI) *m/z* 237 $(M+H)^+$, 254 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{20}NO_4$: 254.1392; found: 254.1392.

4.25. (1*SR*,3*RS*,4*RS*,5*SR*,6*RS*,7*SR*,9*RS*)-4,5,6,7-Diepoxy-10,10-dimethyl-11-oxapentacyclo[7.2.1.0^{1,6}]dodecan-8-one (32)

NaOH in H_2O (6 M, 0.6 mL) was added to epoxide **30** (28 mg, 0.10 mmol) in MeOH (0.6 mL), the mixture was cooled to 0 °C, and H_2O_2 (35%, 0.3 mL) was added with caution. Stirring was continued for 3 h and the mixture was quenched with saturated aqueous $NaHCO_3$, extracted with EtOAc, and the organic extract was dried ($MgSO_4$) and rotary evaporated to give diepoxide **32** (15 mg, 50%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.81; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.31 (s, 3H), 1.93 (m, 2H), 2.23 (m, 1H), 2.42 (m, 1H), 2.62 (m, 1H), 3.05 (m, 1H), 3.41 (m, 1H), 3.59 (m, 1H), 3.89 (m, 1H); MS (CI) *m/z* 253 $(M+H)^+$, 270 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{17}O_5$: 253.1076; found: 253.1078.

4.26. (1*SR*,3*SR*,4*RS*,5*SR*,6*RS*,7*SR*,9*RS*)-4,5,6,7-Diepoxy-10,10-dimethyl-11-oxapentacyclo[7.2.1.0^{1,6}]dodecan-8-one (34)

NaOH in H_2O (6 M, 0.6 mL) was added to enone **33** (57 mg, 0.20 mmol) in MeOH (0.6 mL). The mixture was cooled to 0 °C and H_2O_2 (35%, 0.3 mL) was added dropwise (Ar). After stirring for 3 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and the mixture was extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give diepoxide **34** (33 mg, 65%) as a white solid: R_f (hexanes/EtOAc 1:1) 0.75; mp 150–155 °C (EtOAc); IR (film) 3421, 1720, 1264, 1091, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.26 (s, 3H), 1.83 (dd, J_1=4.4 Hz, J_2=12.8 Hz, 1H), 1.98 (m, 2H), 2.21 (br s, 1H), 2.36 (m, 1H), 2.61 (m, 1H), 3.13 (d, J=4.0 Hz, 1H), 3.38 (m, 1H), 3.65 (m, 1H), 4.49 (t, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.8, 29.9, 32.1, 36.1, 53.8, 57.1, 58.1, 58.9, 59.8, 65.6, 81.4, 81.8, 201.7; MS (CI) *m/z* 270 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{13}H_{20}NO_5$: 270.1341; found: 270.1347.

4.27. (1*SR*,3*SR*,8*RS*,9*SR*)-8-Hydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodeca-4,6-dien-3-yl acetate (35)

$NaBH_4$ (22 mg, 0.60 mmol) was added in one portion to ketone **14** (77 mg, 0.30 mmol) in EtOH (1.5 mL) at 0 °C. After 1.5 h, the reaction was quenched with saturated aqueous NH_4Cl and brine, and the mixture was extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give alcohol **35** (39.5 mg, 52%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.58; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.44 (s, 3H), 1.83 (m, 2H), 2.07 (s, 3H), 2.18 (m, 2H), 2.35 (s, 1H), 4.77 (s, 1H), 5.51 (s, 1H), 5.56 (m, 1H), 5.99 (d_{AB}, J=9.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 26.9, 32.1, 37.8, 41.9, 50.1, 68.7, 74.3, 76.9, 83.9, 126.9, 127.2, 129.8, 138.1, 170.5; MS (CI) *m/z* 265 $(M+H)^+$, 282 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{15}H_{24}NO_4$: 282.1705; found: 282.1708.

4.28. (1*SR*,3*SR*,8*RS*,9*SR*)-8-(*tert*-Butyldimethylsilyloxy)-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodeca-4,6-dien-3-yl acetate (36)

Imidazole (26.5 mg, 0.39 mmol) and ^{t}BuMe$_2$SiCl (56.3 mg, 0.37 mmol) were added to alcohol **35** (39.5 mg, 0.15 mmol) in dry DMF (1.5 mL) at room temperature. After 13 h, H_2O (10 mL) was added and the suspension was extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 4:1) to give silyl ether **36** (20 mg, 35%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.93; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.09 (d, J=2.7 Hz, 6H), 0.91 (s, 9H), 1.23 (s, 3H), 1.39 (s, 3H), 1.74 (m, 2H), 2.07 (s, 3H), 2.19 (m, 2H), 4.72 (s, 1H), 5.39 (s, 1H), 5.59 (m, 1H), 5.87 (d_{AB}, J=8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.82, −4.66, 17.98, 21.26, 25.78, 27.22, 32.27, 37.88, 41.92, 50.89, 68.84, 74.20, 76.74, 84.22, 127.44, 128.30, 129.13, 137.11, 170.34.

4.29. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-6-Hydroxy-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (37)

Diol **9** (200 mg, 0.78 mmol) and I_2 (20 mg, 0.078 mmol) in Me_2CO (10 mL) were stirred for 13 h. Saturated aqueous

$Na_2S_2O_3$ was added and the mixture was extracted with Et_2O, washed with H_2O, dried ($MgSO_4$), and rotary evaporated. Chromatography (silica, hexanes/EtOAc 1:1) gave ketal **37** (163 mg, 71%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.69; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (s, 3H), 1.30 (s, 3H), 1.34 (s, 3H), 1.53 (s, 3H), 2.25 (m, 5H), 2.53 (m, 4H), 4.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 26.3, 28.7, 29.5, 33.3, 35.7, 37.2, 52.3, 60.2, 72.1, 72.5, 75.9, 82.7, 84.2, 108.2, 210.0; MS (CI) *m/z* 296 $(M+H)^+$, 314 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{16}H_{28}NO_5$: 314.1967; found: 314.1969.

4.30. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-6-Hydroxy-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (38)

Following the procedure for the preparation of **37**, protection of diol **10** (200 mg, 0.78 mmol) gave ketal **38** (150 mg, 65%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.73; IR (film) 3386, 1711, 1462, 1382, 1053, 1019 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.25 (s, 3H), 1.32 (s, 3H), 1.50 (s, 3H), 2.21 (m, 9H), 4.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 26.3, 28.8, 29.3, 33.7, 35.4, 35.6, 50.9, 59.9, 72.5, 72.7, 73.6, 82.7, 84.3, 108.7, 208.8; MS (CI) *m/z* 314 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{16}H_{28}NO_5$: 314.1967; found: 314.1969. Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.96; H, 8.05.

4.31. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3,4-(2,2-Propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodeca-6-en-8-one (33)

$SOCl_2$ (0.14 mL, 1.9 mmol) was added dropwise to ketal **38** (114 mg, 0.38 mmol) in dry pyridine (4 mL). After 2 h at room temperature, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The organic extract was washed with brine, dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give ketal **33** (63 mg, 60%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.65; IR (film) 3408, 1677, 1367, 1252, 1045, 885 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.31 (s, 3H), 1.35 (s, 3H), 1.36 (s, 3H), 2.18 (m, 3H), 2.50 (m, 3H), 2.90 (m, 1H), 4.53 (m, 2H), 5.83 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 25.8, 26.1, 29.9, 33.6, 34.6, 45.8, 62.0, 71.3, 72.8, 79.1, 79.3, 107.8, 126.7, 164.2, 201.3; MS (CI) *m/z* 279 $(M+H)^+$, 296 $(M+NH_4)^+$. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 70.25; H, 7.79.

4.32. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-3,4-(2,2-Propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodeca-6-en-8-one (39)

Following the procedure for the preparation of **33**, enone **39** (58%) was obtained from alcohol **37** as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.68; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.29 (s, 3H), 1.33 (s, 3H), 1.48 (s, 3H), 2.19 (m, 3H), 2.69 (m, 3H), 2.87 (s, 1H), 4.15 (m, 2H), 5.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.5, 25.7, 26.8, 29.9, 33.7, 36.1, 44.5, 61.4, 71.8, 72.5, 80.0, 83.9, 108.9, 126.1, 164.4, 200.9; MS (CI) *m/z* 279 $(M+H)^+$, 296 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{16}H_{23}O_4$: 279.1596; found: 279.1602.

4.33. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-6-Cyano-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (40)

Et_2AlCN in PhMe (1 M, 1.26 mL) was added dropwise to ketal **33** (117 mg, 0.42 mmol) in THF (1 mL). After 13 h at room temperature, saturated aqueous NH_4Cl was added and the suspension was extracted with CH_2Cl_2. The extract was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give nitrile **40** (113 mg, 88%) as a colorless oil: R_f (hexanes/EtOAc 2:3) 0.75; IR (film) 2287, 1721, 1370, 1220, 1084 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.27 (s, 3H), 1.33 (s, 3H), 1.53 (s, 3H), 2.22 (m, 8H), 2.90 (m, 1H), 4.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 24.4, 26.4, 28.0, 28.9, 33.9, 37.4, 38.2, 38.7, 59.1, 71.4, 72.4, 82.3, 83.8, 109.3, 122.8, 204.8; MS (CI) *m/z* 306 $(M+H)^+$, 323 $(M+NH_4)^+$. Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.95; H, 7.55; N, 4.57.

4.34. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-6-Cyano-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (41)

Reaction of **39** with Et_2AlCN as for the preparation of **40** gave nitrile **41** (121 mg, 94%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.87; IR (film) 2232, 1719, 1463, 1430, 1089, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.34 (s, 3H), 1.37 (s, 3H), 1.53 (s, 3H), 2.38 (m, 8H), 2.80 (m, 1H), 4.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 26.1, 28.6, 28.9, 34.4, 34.6, 38.4, 42.3, 46.5, 59.0, 71.5, 71.9, 79.6, 83.9, 108.9, 121.9, 204.7; MS (CI) *m/z* 306 $(M+H)^+$, 323 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{24}NO_4$: 306.1705; found: 306.1708.

4.35. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-6-Cyano-3,4-dihydroxy-8-(1,2-ethylenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecane (42)

Ketal **40** (194 mg, 0.64 mmol), PhH (6 mL), ethylene glycol (5 mL), and *p*-TsOH·H_2O (5 mg) were heated to reflux for 3 h (Dean–Stark apparatus). After cooling to room temperature, EtOAc was added and the mixture was washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 3:7) to give acetal **42** (65 mg, 33%) as a colorless oil: R_f (EtOAc) 0.58; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.37 (s, 3H), 2.01 (m, 7H), 2.70 (m, 2H), 4.14 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 30.9, 36.9, 37.5, 37.7, 38.2, 41.9, 51.7, 63.9, 65.1, 68.0, 68.2, 81.8, 82.9, 108.9, 123.9; MS (CI) *m/z* 310 $(M+H)^+$, 327 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{16}H_{27}N_2O_5$: 327.1920; found: 327.1917.

4.36. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-6-Cyano-3,4-dihydroxy-8-(1,2-ethylenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecane (43)

Reaction of nitrile **41** with ethylene glycol as for ketal **40** gave ketal **43** (59 mg, 30%) as a colorless oil: R_f (hexanes/EtOAc 3:7) 0.33; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 3H), 1.44 (s, 3H), 2.00 (m, 6H), 2.24 (m, 2H), 2.65 (m, 1H), 3.97 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 30.7, 35.6, 37.6, 38.1, 41.3, 42.1, 50.9, 63.9, 65.3, 67.8,

69.4, 81.3, 85.2, 108.1, 122.2; MS (CI) *m/z* 310 $(M+H)^+$, 327 $(M+NH_4)^+$.

4.37. (1*SR*,3*SR*,4*RS*,6*RS*,8*RS*,9*RS*)-6-Cyano-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-ol (44)

$NaBH_4$ (116 mg, 3.07 mmol) was added in one portion to ketone **40** (469 mg, 1.5 mmol) in EtOH (6 mL) at 0 °C. After 1 h, the solution was allowed to warm to room temperature, then saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The organic extracts were washed with brine, dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give alcohol **44** (317 mg, 69%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.43; IR (film) 3406, 2234, 1647, 1464, 1106, 1019, 898, 801 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.29 (s, 3H), 1.42 (s, 3H), 1.49 (s, 3H), 1.98 (m, 8H), 2.34 (m, 1H), 4.23 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 26.4, 28.1, 31.6, 33.6, 37.6, 37.8, 39.9, 40.5, 48.4, 69.8, 71.6, 72.4, 81.5, 84.9, 109.0, 123.6; MS (CI) *m/z* 308 $(M+H)^+$, 325 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{29}N_2O_4$: 325.2127; found: 325.2133.

4.38. (1*SR*,3*RS*,4*SR*,6*RS*,8*RS*,9*RS*)-6-Cyano-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-ol (45)

Reduction of ketone **41** as for **40** gave alcohol **45** (210 mg, 65%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.71; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (s, 3H), 1.33 (s, 3H), 1.46 (s, 3H), 1.51 (s, 3H), 2.12 (m, 9H), 4.18 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 26.2, 28.7, 31.7, 34.1, 34.8, 39.3, 39.9, 41.2, 48.3, 69.9, 71.7, 72.2, 78.9, 84.9, 108.7, 122.7; MS (CI) *m/z* 308 $(M+H)^+$, 325 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{26}NO_4$: 308.1862; found: 308.1869.

4.39. (1*SR*,3*SR*,4*RS*,6*RS*,8*RS*,9*RS*)-3,4-(2,2-Propylidenedioxy)-8-hydroxy-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-6-carboxaldehyde (46)

$LiAlH_4$ in THF (2 M, 0.14 mL) was added dropwise to alcohol **44** (55 mg, 0.18 mmol) in dry THF (1 mL). After 2 h, H_2O (40 μL) and aqueous NaOH (2 M; 20 μL) were added and the resulting mixture was stirred at room temperature for 1 h, filtered, and the solids were washed with EtOAc. The combined filtrates were rotary evaporated and chromatographed (silica, hexanes/EtOAc 3:7) to give aldehyde **46** (32 mg, 58%) as a colorless oil: R_f (EtOAc) 0.72; IR (film) 3423, 1721, 1462, 1368, 1160, 1021 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.31 (s, 3H), 1.40 (s, 3H), 1.50 (s, 3H), 2.05 (m, 9H), 3.87 (m, 1H), 4.32 (m, 2H), 9.65 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 26.6, 28.0, 32.1, 33.2, 36.1, 37.6, 38.8, 48.7, 52.5, 70.7, 72.2, 72.9, 81.2, 82.8, 108.9, 203.1; MS (CI) *m/z* 311 $(M+H)^+$, 328 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{27}O_3$: 311.1858; found: 311.1849.

4.40. (1*SR*,3*RS*,4*SR*,6*RS*,8*RS*,9*RS*)-3,4-(2,2-Propylidenedioxy)-8-hydroxy-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-6-carboxaldehyde (47)

Reduction of nitrile **45** as for **44** gave aldehyde **47** (115 mg, 54%) as a colorless oil: R_f (EtOAc) 0.81; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 3H), 1.34 (s, 3H), 1.51 (s, 3H), 1.56 (s, 3H), 2.16 (m, 9H), 3.87 (m, 1H), 4.23 (m, 2H), 9.60 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 26.2, 28.8, 32.1, 33.4, 35.3, 36.8, 38.8, 48.9, 56.6, 70.8, 71.5, 72.7, 78.5, 82.6, 108.2, 204.1; MS (CI) *m/z* 311 $(M+H)^+$, 328 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{27}O_3$: 311.1858; found: 311.1843.

4.41. (1*SR*,3*SR*,4*RS*,6*RS*,8*RS*,9*RS*)-6-Hydroxymethyl-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-ol (48)

Method A: $NaBH_4$ (7.3 mg, 0.19 mmol) was added in one portion to aldehyde **46** (30 mg, 0.09 mmol) in EtOH (0.5 mL) at 0 °C. After 1.5 h, the mixture was allowed to warm to room temperature, diluted with saturated aqueous NH_4Cl and brine, and extracted with EtOAc. The organic phase was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, EtOAc) to give alcohol **48** (17 mg, 60%) as a colorless oil. *Method B*: $LiAlH_4$ in THF (2 M, 0.38 mL) was added to aldehyde **46** in dry THF (1 mL). After 20 min, saturated aqueous Na_2SO_4 was added and the solvent was rotary evaporated. Chromatography (silica, EtOAc) gave alcohol **48** (26.5 mg, 71%) as a colorless oil: R_f (EtOAc) 0.37; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.34 (s, 3H), 1.49 (s, 6H), 1.59 (m, 1H), 1.94 (m, 8H), 2.37 (br s, 1H), 3.55 (q_{AB}, J=11.7 Hz, 2H), 4.22 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 26.3, 28.2, 32.0, 32.3, 37.5, 38.3, 40.1, 42.6, 49.3, 67.5, 70.8, 72.7, 73.2, 81.9, 83.3, 108.5; MS (CI) *m/z* 313 $(M+H)^+$, 330 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{29}O_5$: 313.2015; found: 313.2026.

4.42. (1*SR*,3*RS*,4*SR*,6*RS*,8*RS*,9*RS*)-6-Hydroxymethyl-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-ol (49)

Reduction of aldehyde **47** as for **46** gave alcohol **49** (145 mg, 75%) as a colorless oil (method A): R_f (hexanes/EtOAc 1:1) 0.54; IR (film) 3407, 1725, 1583, 1462, 1040 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.34 (s, 3H), 1.50 (s, 3H), 1.56 (s, 3H), 2.04 (m, 9H), 3.45 (q_{AB}, J=10.8 Hz, 2H), 3.70 (m, 1H), 4.03 (m, 1H), 4.22 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 26.3, 28.7, 32.2, 33.7, 35.5, 37.4, 37.9, 45.3, 49.2, 64.7, 70.8, 72.3, 72.7, 80.0, 81.7, 107.7; MS (CI) *m/z* 313 $(M+H)^+$, 330 $(M+NH_4)^+$; HRMS (CI) *m/z* calcd for $C_{17}H_{29}O_5$: 313.2015; found: 313.2019.

4.43. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-6-Hydroxymethyl-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (50)

Trichloroisocyanuric acid (42 mg, 0.18 mmol) in Me_2CO (0.5 mL) was added to diol **48** (126 mg, 0.4 mmol) in Me_2CO (0.2 mL) and pyridine (30 μL, 0.56 mmol). After 0.5 h, the mixture was rotary evaporated and chromatographed (silica, hexanes/EtOAc 3:7) to give ketone **50** (60 mg, 48%) as a colorless oil: R_f (EtOAc) 0.89; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 6H), 1.37 (s, 3H), 1.52 (s, 3H), 2.07 (m, 5H), 2.21 (m, 2H), 2.42 (m, 1H), 2.58 (m, 1H), 3.67 (q_{AB}, J=11.6 Hz, 2H), 4.27 (m, 1H), 4.40 (m, 1H,); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 26.3, 28.2, 29.5, 32.7, 36.5, 37.9, 43.8, 48.9, 60.3, 68.0, 72.4, 73.1, 81.6, 83.8, 108.7, 209.4.

4.44. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-6-Hydroxymethyl-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (51)

Oxidation of alcohol **49** as for **48** gave ketone **51** (65 mg, 52%) as a colorless oil: R_f (EtOAc) 0.72; IR (film) 3442, 1707, 1368, 1243, 1041, 860 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.29 (s, 3H), 1.32 (s, 3H), 1.53 (s, 3H), 2.16 (m, 6H), 2.42 (m, 2H), 2.51 (m, 1H), 3.47 (q_{AB}, J=11.2 Hz, 2H), 4.10 (m, 1H), 4.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.9, 26.3, 28.7, 29.7, 34.6, 34.9, 36.7, 46.7, 47.3, 60.3, 65.5, 71.8, 72.4, 80.8, 81.6, 107.9, 211.1; MS (CI) m/z 311 (M+H)$^+$, 328 (M+NH$_4$)$^+$; HRMS (CI) m/z calcd for $C_{17}H_{27}O_5$: 311.1858; found: 311.1848. Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.64; H, 8.34.

4.45. (1*SR*,3*RS*,4*SR*,6*RS*,9*RS*)-3-Acetoxy-6-acetoxymethyl-4-hydroxy-10,10-dimethyl-11-oxatricyclo[7.2.1.0^{1,6}]dodecan-8-one (53)

p-TsOH·H_2O (3 mg) was added to ketone **51** (60 mg, 0.19 mmol) in MeOH (2.5 mL) and the mixture was heated to reflux for 1.5 h, cooled to room temperature, and rotary evaporated to give diol **52**, which was used directly in the next step without purification. DMAP (3 mg) and Ac_2O (59 μL, 0.63 mmol) were added to the crude diol **52** in dry pyridine (1 mL). After 13 h at room temperature, the mixture was diluted with saturated aqueous $NaHCO_3$ and extracted with EtOAc (3×15 mL). The combined organic layers were dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give diester **53** (21 mg, 31% over two steps) as a white solid: R_f (hexanes/EtOAc 1:1) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 6H), 1.77 (m, 1H), 2.04 (m, 2H), 2.10 (s, 3H), 2.11 (s, 3H), 2.20 (m, 5H), 2.60 (m, 1H), 4.02 (q_{AB}, J=11.6 Hz, 2H), 4.10 (m, 1H), 4.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 21.3, 23.7, 29.3, 30.7, 36.3, 37.6, 45.4, 47.5, 59.3, 66.1, 67.6, 70.2, 83.2, 83.9, 170.5, 170.7, 207.5; MS (CI) m/z 355 (M+H)$^+$, 372 (M+NH$_4$)$^+$; HRMS (CI) m/z calcd for $C_{18}H_{27}O_7$: 355.1757; found: 355.1749.

4.46. (1*SR*,3*SR*,4*RS*,6*RS*,8*RS*,9*RS*)-6-Ethenyl-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-ol (54)

$KN(SiMe_3)_2$ in PhMe (0.5 M, 3.9 mL, 1.96 mmol) was added to Ph_3PCH_3Br (757 mg, 2.12 mmol) in dry THF (10 mL) (Ar) at room temperature. The suspension was stirred for 1 h, cooled to −78 °C, and aldehyde **46** (263 mg, 0.85 mmol) in dry THF (3 mL) was added dropwise. The mixture was allowed to warm to room temperature over 2 h, diluted with MeOH, and added to saturated aqueous potassium sodium tartrate and H_2O (1:1). The mixture was extracted with EtOAc and the extract was dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 3:7) to give alkene **54** (173 mg, 66%) as a colorless oil: R_f (EtOAc) 0.91; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.27 (s, 3H), 1.45 (s, 3H), 1.47 (s, 3H), 1.77 (m, 6H), 2.14 (m, 2H), 2.34 (m, 1H), 3.99 (m, 1H), 4.18 (m, 1H), 4.29 (m, 1H), 5.07 (m, 2H), 6.25 (dd, J_1=10.4 Hz, J_2=17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.2, 26.2, 28.7, 32.0, 37.2, 37.5, 38.1, 39.3, 45.1, 49.8, 70.5, 73.1, 73.3, 82.9, 84.0, 108.0, 112.8, 143.6; MS (CI) m/z 309 (M+H)$^+$; HRMS (CI) m/z calcd for $C_{18}H_{29}O_4$: 309.2066; found: 309.2053.

4.47. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-6-Ethenyl-3,4-(2,2-propylidenedioxy)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (55)

IBX (184 mg, 0.66 mmol) was added in one portion to alcohol **54** (135 mg, 0.44 mmol) in DMSO (3 mL). After 2.5 h, H_2O was added and the mixture was extracted with EtOAc and the separated organic phase was dried ($MgSO_4$) and rotary evaporated. Chromatography (silica, hexanes/EtOAc 3:7) gave ketone **55** (117 mg, 87%) as a colorless oil: R_f (EtOAc) 0.87; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 3H), 1.29 (s, 3H), 1.35 (s, 3H), 1.53 (s, 3H), 1.88 (m, 2H), 2.10 (m, 3H), 2.35 (m, 2H), 2.53 (m, 1H), 2.73 (m, 1H), 4.29 (m, 1H), 4.42 (m, 1H), 5.10 (m, 2H), 6.25 (dd, J_1=15.2 Hz, J_2=17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 26.2, 28.6, 29.4, 36.2, 36.9, 37.2, 46.8, 46.7, 60.8, 72.8, 73.2, 82.4, 84.4, 108.2, 115.4, 143.2, 209.8; MS (CI) m/z 307 (M+H)$^+$, 324 (M+NH$_4$)$^+$; HRMS (CI) m/z calcd for $C_{18}H_{27}O_4$: 307.1909; found: 307.1911.

4.48. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-6-Ethenyl-3,4-dihydroxy-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (56)

p-TsOH (5 mg) was added to ketone **55** (117 mg, 0.38 mmol) in MeOH (4 mL) and the mixture was heated to reflux for 1.5 h, rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give diol **56** (70 mg, 69%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.34; IR (film) 3386, 1584, 1462, 1441, 1117, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 6H), 1.72 (dd, J_1=12.8 Hz, J_2=4.4 Hz, 1H), 1.85 (dq, J_1=3.2 Hz, J_2=18.4 Hz, 2H), 2.09 (m, 2H), 2.28 (m, 2H), 2.50 (m, 1H), 2.67 (m, 1H), 4.03 (m, 1H), 4.13 (m, 1H), 5.06 (m, 2H), 6.46 (dd, J_1=11.2 Hz, J_2=17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 29.3, 36.4, 37.0, 40.2, 47.1, 48.2, 60.9, 68.8, 68.8, 81.7, 84.7, 114.3, 143.9, 210.2; MS (CI) m/z 284 (M+NH$_4$)$^+$.

4.49. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3,4-Diacetoxy-6-ethenyl-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (57)

Ac_2O (62 μL, 0.66 mmol) and DMAP (3 mg) were added to diol **56** (70 mg, 0.26 mmol) in dry pyridine (1.5 mL). After 13 h at room temperature, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 7:3) to give diester **57** (103 mg, 100%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.85; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 6H), 1.84 (m, 2H), 2.00 (s, 3H), 2.03 (s, 3H), 2.03 (m, 1H), 2.12 (m, 1H), 2.29 (m, 3H), 2.51 (m, 1H), 2.66 (m, 1H), 5.06 (m, 2H), 5.27 (m, 1H), 5.32 (m, 1H), 6.24 (dd, J_1=11.2 Hz, J_2=17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 21.0, 23.4, 29.1, 33.7, 36.9, 38.3, 46.9, 47.9, 60.8, 68.5, 69.41, 81.9, 83.9, 114.7, 142.4, 170.0, 170.1, 208.9; MS (CI) m/z 368 (M+NH$_4$)$^+$; HRMS (CI) m/z calcd for $C_{19}H_{30}NO_6$: 368.2073; found: 368.2072.

4.50. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3,4-Diacetoxy-6-(1,2-dihydroxyethyl)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (58)

N-Methylmorpholine-*N*-oxide (52 mg, 0.44 mmol) and OsO_4 in ^{t}BuOH (2.5 wt %, 0.72 mL) were added to alkene **57** (103 mg, 0.29 mmol) in Me_2CO and H_2O (4:1, 10 mL). The resultant mixture was stirred for 6 days at room temperature then saturated aqueous Na_2SO_3 was added and the suspension was stirred vigorously for 0.5 h. The aqueous phase was extracted with EtOAc (3×15 mL) and the combined organic layers were dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 3:7 to EtOAc) to give diol **58** (39.5 mg, 36%) as a colorless oil: R_f (EtOAc) 0.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.29 (s, 3H), 1.82 (m, 2H), 1.99 (s, 3H), 2.15 (s, 3H), 2.15 (m, 1H), 2.32 (m, 2H), 2.51 (m, 3H), 3.16 (m, 1H), 3.50 (m, 2H), 3.72 (m, 1H), 5.30 (m, 1H), 5.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 21.2, 23.7, 29.0, 32.1, 35.4, 36.5, 45.0, 50.5, 60.5, 64.5, 67.9, 69.3, 75.4, 81.0, 84.4, 168.8, 170.1, 209.1; MS (CI) *m*/*z* 402 $(M+NH_4)^+$.

4.51. (1*SR*,3*SR*,4*RS*,6*RS*,9*RS*)-3,4-Diacetoxy-6-(1,2-diacetoxyethyl)-10,10-dimethyl-11-oxatetracyclo[7.2.1.0^{1,6}]dodecan-8-one (59)

Ac_2O (24 μL, 0.25 mmol) and DMAP (3 mg) were added to diol **58** (39 mg, 0.1 mmol) in dry pyridine (1 mL). After 13 h at room temperature, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The combined organic phases were dried ($MgSO_4$), rotary evaporated, and chromatographed (silica, hexanes/EtOAc 1:1) to give tetra-ester **59** (35 mg, 75%) as a colorless oil: R_f (hexanes/EtOAc 1:1) 0.68; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.27 (s, 3H), 1.78 (m, 2H), 1.96 (s, 3H), 2.02 (s, 3H), 2.09 (s, 3H), 2.11 (s, 3H), 2.25 (m, 5H), 2.63 (m, 2H), 4.14 (m, 1H), 4.45 (m, 1H), 5.30 (m, 1H), 5.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 20.9, 21.1, 21.2, 23.5, 29.1, 34.4, 35.5, 35.7, 44.9, 49.1, 60.4, 63.8, 66.8, 69.3, 73.1, 80.9, 83.6, 169.9, 170.2, 170.4, 170.7, 207.8; MS (CI) *m*/*z* 486 $(M+NH_4)^+$; HRMS (CI) *m*/*z* calcd for $C_{23}H_{36}NO_{10}$: 486.2339; found: 486.2355.

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Supplementary data

Full crystal structure data for X-ray analyses of alcohol **4**, fluoride **7**, the 4-nitrobenzoate ester from diol **6**, diacetate **13**, 4-nitrobenzoate ester **20**, dienone **26**, epoxide **31**, and diepoxide **34** are available free of charge via the internet. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.02.021.

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