A Stereoselective Synthesis of (±)-C-Secolimonoid BCDE Model Compounds Related to the Insect Antifeedant Ohchinolide

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Received April 30, 2001

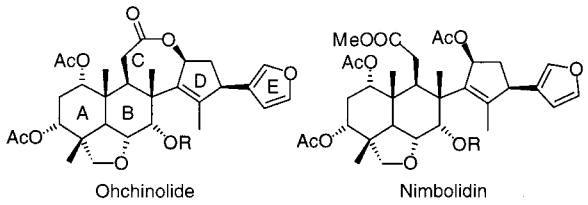
A short and stereoselective synthesis of a (±)-BCDE C-secolimonid model insect antifeedant related to ohchinolide and nimbolidin was accomplished in 13 (30% overall yield) and 15 (30% overall yield) steps, respectively, from ethyl drimanate. The key steps are the torquoselective electrocyclization of the divinyl ketone **6**, induced by perchloric acid, and the stereoselective rearrangement of the hydroxy lactone **12**, inspired in a biosynthetic proposal. An alternative route, which provides access to (±)-BCDE ohchinolide and nimbolidin isomers, is also described.

Introduction

The limonoids are a large family of complex tetranortriterpenoids that exhibit a wide range of biological activities.[1] Among the great diversity of limonoids, the C-seco group, which is considered the most bioactive, deserves special attention. Despite the considerable interest in the insect antifeedant, insecticidal, antimalarial, and anticancer properties of some members of the C-secolimonid group, the biogenesis and synthesis of these compounds has remained almost unexplored.[2] The total synthesis of limonoids for medicinal or agricultural applications will probably not be economically feasible, and hence, extensive synthetic studies directed to related model compounds have been conduced to find simple analogues that display similar biological activities.[3]

We now report the first synthesis of BCDE model compounds related to ohchinolide and nimbolidin, two representative C-secolimonoids with high insect antifeedant activity,[4] by a simple route that is sufficiently versatile to provide access to limonoids of all types by tuning the structure and functional groups of the starting materials.

The most relevant features of our strategy were inspired by the sequence of a hypothetical biogenetic route, which would allow the transformation of a 14,15-



en-12-oxo intermediate into ohchinolide by oxygen insertion between C12 and C13 carbons, a reaction that seems to be general in the potential biosynthesis of all secolimonoids, and further allylic rearrangement involving cleavage of the O−C13 bond and recyclization, forming the O−C15 bond (Scheme 1).

Results and Discussion

Our synthetic approach to the BCDE model compounds related to ohchinolide and nimbolidin involves 13 and 15 steps and allows the preparation of multigram quantities in high overall yield. The key steps are the construction of the D ring by an electrocyclic reaction (B), Baeyer−Villiger oxidation (D), and finally, stereoselective allylic rearrangement (E); see Scheme 2.

The ethyl drimanate ester **1** was selected as a convenient starting material.[5] It allowed ready access to the dienedione **6**, which will be the precursor of the BCDE model compound with the right skeleton and adequate funcionalization.

The bicyclic dienedione **6** was obtained by a high-yield procedure developed at our laboratory for the synthesis of a simpler analogue.[6] The transformation of ethyl drimanate ester **1** into the drimanal **2** was carried out in two steps: first, reduction with lithium aluminum hydride, and second Swern oxidation[7] of the intermediate

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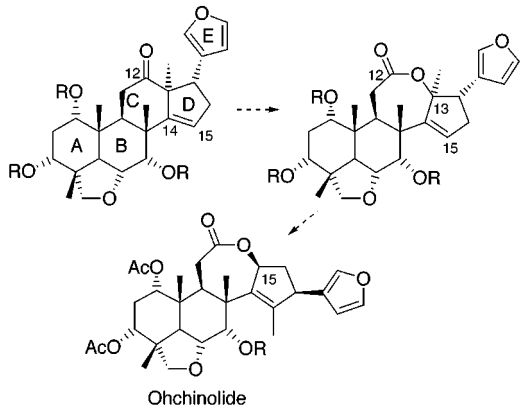
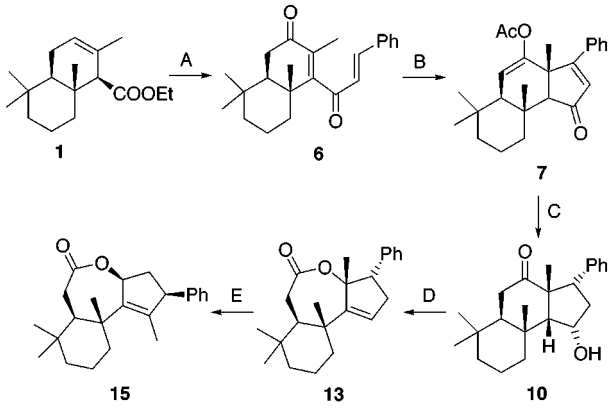
(7) (a) Takai, K.; Heathcock, C. H. *J. Org. Chem.* **1985**, *50*, 3247. (b) Tidwell, T. T. *Synthesis* **1990**, 857.

10.1021/jo010449q CCC: $20.00
Published on Web 10/13/2001

Scheme 1



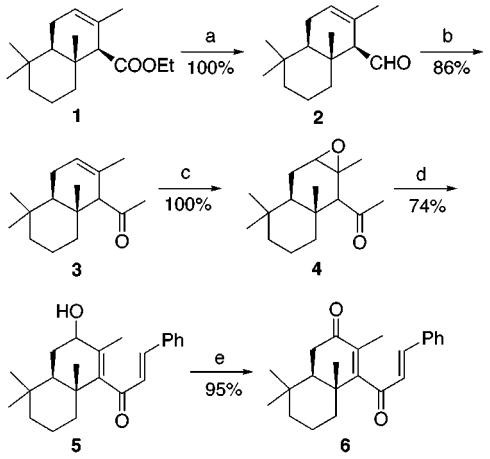
Scheme 2



alcohol. The methyl ketone **3** was obtained from drimanal **2** after treatment with methyllithium and further oxidation with pyridinium chlorochromate.[8] Epoxidation of the unsaturated ketone **3** with *m*-chloroperoxybenzoic acid gave the epoxy ketone **4**, which, after treatment with an ethanolic sodium hydroxide solution and benzaldehyde,[9] afforded the hydroxy divinyl ketone **5**. Finally, oxidation with pyridinium chlorochromate produced the divinyl diketone **6** (Scheme 3).[10]

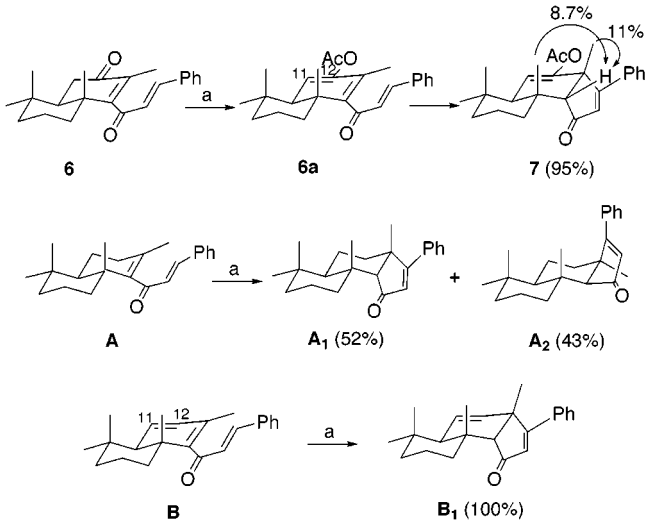
Cationic electrocyclization of the divinyl diketone **6** was performed following a procedure developed by our group consisting of treatment with a 10^{-2} M solution of perchloric acid in a mixture of acetic anhydride and ethyl acetate. The reaction required 2 h at room temperature to be completed and afforded only one product in 95% yield. On the basis of its spectroscopic data, H−C correlations, and NOE experiments, the structure of the ketoacetate **7** was assigned (Scheme 4). The absolute torquoselectivity of the Nazarov reaction achieved with the divinyl diketone **6** is remarkable and contrasts with the poor torquoselectivity attained for similar compounds such as **A**, which afforded nearly equal amounts of torquoisomers **A1** and **A2**. A similar result was found by us with a tricyclic trienone related to **A**.[11] However, with the trienone **B** the torquoselectivity was, as seen before for **6**, again absolutely clockwise. The factor responsible for the selectivity found in these systems, **6** and **B**, must

Scheme 3[a]



[a] Key: (a) (i) $LiAlH_4$, THF, 70 °C, (ii) $(ClCO)_2$, DMSO, Et_3N, CH_2Cl_2, −60 °C; (b) (i) MeLi, Et_2O, −10 °C, (ii) PCC, CH_2Cl_2; (c) *m*-CPBA, CH_2Cl_2; (d) PhCHO, NaOH, EtOH; (e) PCC, CH_2Cl_2.

Scheme 4[a]



[a] Key: (a) $HClO_4$, 10^{-2}, Ac_2O 1 M, AcOEt.

be the C11−C12[12] double bond, which is present in **6a** (enolacetylation must occur prior to cyclization) and **B**, whereas it is absent in **A**.

For the transformation of the ketoacetate **7** into the unsaturated lactone **13**, the plan depicted in Scheme 5 was approached. The chemo- and stereoselective catalytic hydrogenation of **7** was carried out, taking advantage of the electron density differences of the double bonds, to afford the ketoacetate **8** in nearly quantitative yield. Also stereoselective was the reduction of the **8** keto group, which was carried out with sodium borohydride to give the hydroxy ester **9** exclusively. In both reduction reactions, the hydrogen attacks from the more accessible convex face. Suprisingly, subsequent saponification of the acetate afforded an inseparable 2:1 mixture of the desired hydroxy ketone **10** and the hemiketal **11**. Fortunately, treatment of the mixture with *m*-chloroperoxybenzoic acid furnished only one compound: the hydroxy lactone **12**.

While the relative configuration of the carbinolic carbon C-15 in **12** is irrelevant in our route to the

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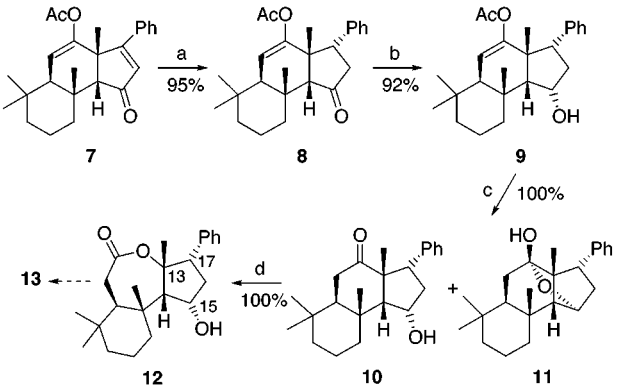
(9) Wattanasin, S.; Murphy, W. S. *Synthesis* **1980**, 647.
(10) All compounds synthesized are racemic, although only one enantiomer is depicted.
(11) Fernández Mateos, A.; López Barba, A.; Martín de la Nava, E. M.; Pascual Coca, G.; Ramos Silvo A. I.; Rubio González, R. *Tetrahedron* **1997**, *53*, 14131.

(12) Limonoid numbering.

Scheme 5[a]



[a] Key: (a) (i) H_2, 1 atm, Pd/C; (b) $NaBH_4$, MeOH, 0 °C; (c) KOH (aq), EtOH; (d) *m*-CPBA, CH_2Cl_2.

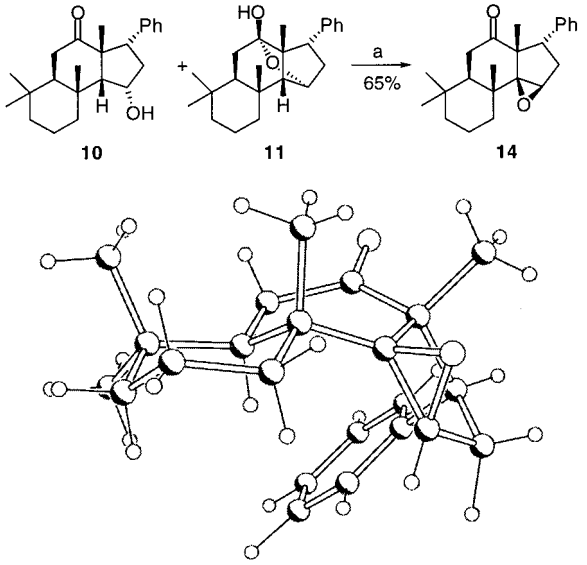
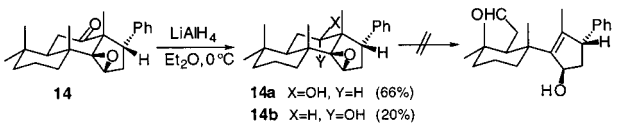


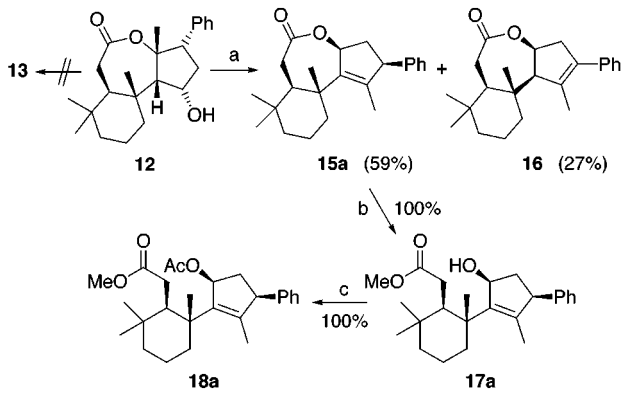
Figure 1. Obtention and X-ray structure of **14**. Key: (a) $SOCl_2$, pyridine, CH_2Cl_2, 0 °C; (b) *m*-CPBA, CH_2Cl_2.

ohchinolide model compound, the relative configuration of C-13 and C-17, or in other words the cis/trans relationship of methyl and phenyl groups, is very important, as will be seen later. Although structures **9**, **10,** and **12** were initially assigned on the basis of their spectroscopic data, they were confirmed by X-ray diffraction analysis of the epoxy ketone **14**,[13] obtained by dehydration of the mixture of **10** and **11**, followed by epoxidation (Figure 1). The X-ray structure of **14** clearly shows the trans-relationship of the methyl and phenyl groups, and also the β orientation of the oxyranic oxygen. Consequently, it can be stated that in all reactions around the cyclopentane region the attack occurs at the more accessible convex face.

(13) An attempt to chemically imitate the cleavage of the C ring, inspired by a biosynthetic proposal based on a Grob fragmentation (see ref 1a), was carried out with epoxy alcohols **14a** and **14b** obtained by reduction of the epoxy ketone **14**. Several bases were essayed to force the fragmentation, but without success, despite the right anti periplanar alignment of the potential breaking bonds in both epoxy alcohols.



Scheme 6[a]



[a] Key: (a) $SOCl_2$, pyridine, CH_2Cl_2, 0 °C; (b) MeONa, MeOH; (c) Ac_2O, pyridine, DMAP.

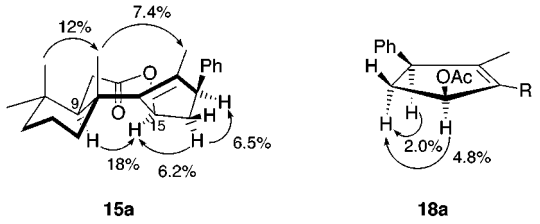


Figure 2. NOE experiments for compounds **15a** and **18a**.

Returning to the synthetic sequence, we faced the dehydration of the hydroxy lactone **12**, which must afford the unsaturated lactone **13**. Instead, treatment of **12** with thionyl chloride in pyridine[14] furnished the target BCDE ohchinolide model compound **15a**, together with the positional double-bond isomer **16**. This absolutely stereoselective and quite amazing result could be explained in terms of the orbital proximity through the space of the oxygen lactone and the carbocation formed after dissociation of the chlorosulfite intermediate. The BCDE nimbolidin model compound **18a** was obtained, in nearly quantitative yield, from ohchinolide model **15a** by transesterification to give **17a** and further acetylation (Scheme 6).

The structures of **15a** and **18a** were assigned on the basis of their spectroscopic data, H−C correlations, and NOE experiments (Figure 2), which were consistent with this D-ring structural type. Of relevance is the nOe (18%) between H-9 and H-15 in lactone **15a**, which is also observed in natural ohchinolide type compounds.[15]

Advantageously in our case, from a 13β unnatural intermediate such as **12**, the allylic rearrangement is concerted and gives only the right ohchinolide model isomer **15a**, in which the substituents of the cyclopentene at C-15 and C-17 keep a cis relationship (Scheme 7).

Another less stereoselective route to BCDE ohchinolide and nimbolidin models, which however permits the obtention of the C15−C17 trans diastereomers **15b** and **18b**,[16] was carried out starting from the hydroxy lactone **12** (Scheme 8). The oxidation of **12** with PCC gave the expected oxolactone **19**, which was treated with DBU in toluene to provide, through an α−β elimination and further esterification with diazomethane, the unsatur-

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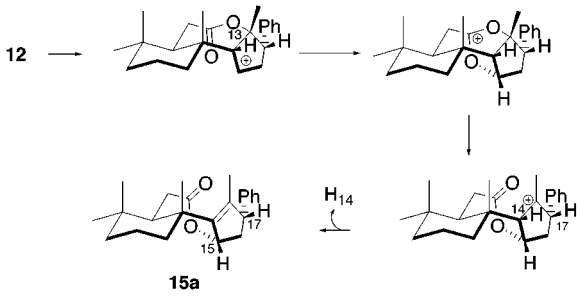
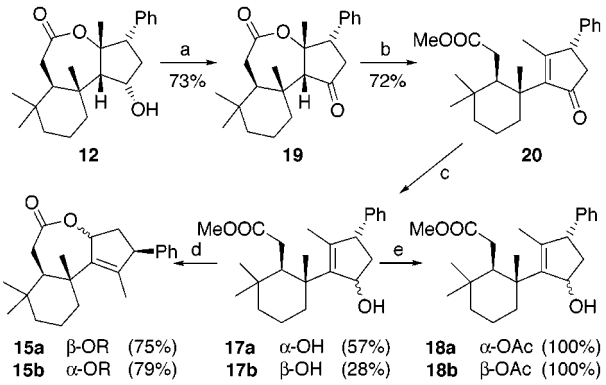
(15) Rajab, M. S.; Bentley, M. D. *J. Nat. Prod.* **1988**, *51*, 168.
(16) The trans diastereoisomers are very important compounds in the SAR insect antifeedant studies.

Scheme 7



Scheme 8[a]



[a] Key: (a) PCC, CH_2Cl_2; (b) (i) DBU, toluene, 80 °C, (ii) CH_2N_2, Et_2O; (c) BH_3·SMe_2, THF, 0 °C; (d) (i) KOH (aq) 5 M, EtOH, (ii) HCl (aq) 1 M, pH = 5, (iii) $(pyS)_2$, PPh_3, xilene; (e) Ac_2O, pyridine, DMAP.

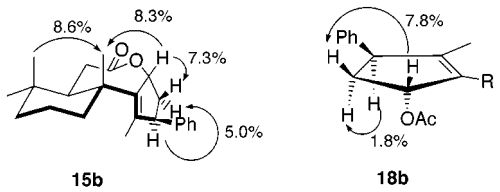


Figure 3. NOE experiments for compounds **15b** and **18b**.

ated oxoester **20**. Reduction with diborane methyl sulfide complex[17] afforded a diastereomeric 2:1 mixture of **17a** and **17b**, respectively. The hydroxy esters **17a** and **17b** were independently transformed into their corresponding BCDE ohchinolide models **15a** and **15b**, respectively, by hydrolysis and further Corey−Nicolaou lactonization[18] and to their corresponding BCDE nimbolidin models **18a** and **18b** by acetylation.

The major isomers **15a** and **18a** were identical to those obtained by the biomimetic sequence described above, and the structure of the minor C-15−C17 trans isomers **15b** and **18b** was determined by their spectroscopic data, H−C correlations, and NOE experiments (Figure 3).

The (±)-BCDE ohchinolide model compound **15a** shows potent insect antifeedant activity against *Spodoptera littoralis* larvae.[19]

Experimental Section

General Methods. All solvents and reagents were purified, when required, by standard techniques.[20] Reactions were monitored by TLC on Merck silica 60 F_{254}. Organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure with the aid of a rotary evaporator. Column chromatography was performed on Merck silica gel 60 (0.040−0.063 mm). ^1H and ^{13}C NMR spectra were recorded at 200/400 and 50/75 MHz, respectively.

(1*RS*,4*RS*,8a*RS*)-2,5,5,8a-Tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalene-1-carbaldehyde (2). $LiAlH_4$ (1.08 g, 28.4 mmol) was added portionwise to a solution of **1** (5.00 g, 18.9 mmol) in THF (88 mL). The mixture was refluxed under argon for 2 h with vigorous stirring. Then, the reaction mixture was cooled to 0 °C and quenched with Na_2SO_4·$10H_2O$ (1 h stirring). The resulting slurry was filtered and the filtrate concentrated providing the alcohol, which was suitable for using without further purification.

To a solution of $(COCl)_2$ (1.82 mL) in CH_2Cl_2 (68 mL) under argon at −60 °C was added dropwise a solution of DMSO (2.95 mL) in CH_2Cl_2 (11 mL). The mixture was stirred for 5 min, and then a solution of the crude alcohol in CH_2Cl_2/DMSO (20/7 mL) was added dropwise. The reaction mixture was stirred for 20 min, and Et_3N (13.8 mL) was added, allowing stirring for 10 min. Next, the mixture was warmed to room temperature and H_2O was added. The organic layer was separated and the aqueous phase extracted with CH_2Cl_2. The combined organic extracts were washed with H_2O, $NaHCO_3$ (5%), and brine. Removal of the solvent afforded a crude oil, which was purified by flash chromatography. Hexane/Et_2O (95/5) furnished **2** (4.16 g, 18.9 mmol, 100% overall) as a colorless oil: IR ν 2922, 1723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70−2.10 (9H, m), 0.85 (3H, s), 0.90 (3H, s), 1.05 (3H, s), 1.59 (3H, s), 2.60 (1H, m), 5.58 (1H, m), 9.59 (1H, d, J = 5.1 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 15.6, 18.2, 21.5, 22.0, 23.6, 32.9, 33.2, 36.9, 40.3, 42.0, 49.1, 67.5, 125.3, 127.8, 205.9 ppm; MS EI *m*/*z* (relative intensity) 220 (M^+, 38), 205 (6), 191 (21), 109 (100); HRMS EI 220.1793 (M^+, $C_{15}H_{20}O$) calcd 220.1827.

(1*RS*,4a*RS*,8a*RS*)-1-(2,5,5,8a-Tetramethyl-1,4,4a,5,6,7,8,-8a-octahydronaphthalen-1-yl)ethanone (3). To a stirred solution of **2** (4.00 g, 18.2 mmol) in Et_2O (85 mL) at −10 °C under argon was added a 1.6 M solution of MeLi in Et_2O (11.4 mL). The reaction mixture was stirred at −10 °C for 10 min and then warmed to 0 °C, and saturated NH_4Cl was added. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine. Removal of the solvent afforded an epimeric mixture of alcohols (7/1) as an orange oil, which was used without further purification.

To a stirred suspension of PCC (5.90 g, 27.3 mmol) and silica (5.90 g) in CH_2Cl_2 (150 mL) was added dropwise a solution of the epimeric alcohols in CH_2Cl_2 (40 mL). The reaction mixture was vigorously stirred at room temperature under argon for 45 min. The resulting dark brown slurry was filtered through a short column of silica and eluted with CH_2Cl_2. Removal of the solvent afforded **3** (3.66 g, 15.6 mmol, 86% overall) as a colorless oil: IR ν 2926, 1709 cm^{-1};^1H NMR ($CDCl_3$) δ 0.80−2.00 (9H, m), 0.87 (3H, s), 0.90 (3H, s), 0. 91 (3H, s), 1.52 (3H, br s), 2.17 (3H, s), 3.15 (1H, m), 5.55 (1H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 14.7, 18.6, 21.3, 21.9, 23.7, 32.9, 33.3, 34.1, 36.8, 41.0, 42.1, 49.6, 68.6, 124.5, 130.1, 210.7 ppm; MS EI *m*/*z* (relative intensity) 234 (M^+, 3), 220 (30), 205 (69), 149 (100).

(1a*SR*,2a*RS*,6a*RS*,7*SR*,7a*RS*)-1-(3,3,6a,7a-Tetramethyldecahydro-1-oxacyclopropa[*b*]naphthalen-7-yl)ethanone (4). To a stirred solution of **3** (3.50 g, 14.9 mmol) in CH_2Cl_2 (94 mL) was added *m*-CPBA (2.83 g, 16.4 mmol). The reaction mixture was stirred under argon at room temperature for 30 min. Then, Na_2SO_3 (5%) was added, and the resulting heterogeneous mixture was vigorously stirred for 15 min. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with $NaHCO_3$ (10%) and brine. Removal of the solvent afforded **4** (3.74 g, 14.9 mmol, 100%) as a colorless oil: IR ν 2930, 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70−2.20 (9H, m), 0.78

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(19) Essays of insect antifeedant activity will be published in due course.

(20) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Butterworth-Heimemann: Oxford, 1996.

(3H, s), 0.81 (3H, s), 0.94 (3H, s), 1.14 (3H, s), 2.17 (3H, s), 2.70 (1H, s), 2.92 (1H, s) ppm; ^{13}C NMR ($CDCl_3$) δ 14.4, 18.2, 22.0, 22.7, 22.8, 32.8 (2C), 36.3, 36.7, 39.4, 41.9, 45.1, 57.0, 60.0, 66.5, 210.0 ppm; MS EI *m/z* (relative intensity) 250 (M^+, 3), 235 (4), 232 (6), 217 (8), 109 (100).

(*E*)-(3*SR*,4a*RS*,8a*RS*)-1-(3-Hydroxy-2,5,5,8a-tetramethyl-3,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)-3-phenylpropenone (5). To a stirred solution of **4** (3.50 g, 14.0 mmol) in EtOH (61 mL) were added gradually benzaldehyde (1.42 mL, 14.0 mmol) and NaOH (1.12 g, 28.0 mmol). The reaction mixture was stirred at room temperature under argon for 24 h and then concentrated to afford a residue, which was dissolved in H_2O and extracted with Et_2O. The combined organic extracts were washed with brine. Removal of the solvent afforded an orange crude, which was purified by flash chromatography. Hexane/AcOEt (90/10) furnished **5** (3.50 g, 10.3 mmol, 74%) as a colorless solid: mp (*t*-BuOMe/hexane) 173−175 °C; IR ν 3412, 2926, 1605, 762 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80−0.90 (8H, m), 0.84 (3H, s), 0.92 (3H, s), 1.18 (3H, s), 1.68 (3H, s), 2.55 (1H, m), 4.04 (1H, t, J = 3.0 Hz), 6.74 (1H, d, J = 16 Hz), 7.47 (1H, d, J = 16 Hz), 7.30−7.60 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 18.4, 18.7, 19.3, 21.6, 29.1, 32.7, 33.0, 37.3, 38.7, 41.7, 45.3, 69.1, 128.5 (2C), 128.7, 128.9 (3C), 130.5, 134.8, 145.4, 147.3, 200.9 ppm; MS EI *m/z* (relative intensity) 338 (M^+, 5), 323 (5), 320 (7), 119 (100), 77 (28). Anal. Calcd for $C_{23}H_{30}O_2$: C 81.61, H 8.93. Found: C 81.77, H 9.11.

(*E*)-(4a*RS*,8a*RS*)-3,4a,8,8-Tetramethyl-4-(3-phenylacryloyl)-4a,5,6,7,8,8a-hexahydro-1*H*-naphthalen-2-one (6). The same procedure used above to obtain **3** through oxidation with PCC was applied to **5** (3.30 g, 9.75 mmol) yielding, after 45 min of reaction, **6** (3.12 g, 9.26 mmol, 95%) as a colorless solid: mp (*t*-BuOMe/hexane) 129−131 °C; IR ν 2942, 1674, 1626, 764, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80−1.70 (6H, m), 0.90 (3H, s), 0.92 (3H, s), 1.36 (3H, s), 1.64 (3H, s), 1.89 (1H, dd, J_1 = 5.1 Hz, J_2 = 13 Hz), 2.46 (1H, dd, J_1 = 13 Hz, J_2 = 18 Hz), 2.59 (1H, dd, J_1 = 5.1 Hz, J_2 = 18 Hz), 6.75 (1H, d, J = 16 Hz), 7.36 (1H, d, J = 16 Hz), 7.30−7.60 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 12.7, 18.3, 19.1, 21.2, 32.5, 33.2, 35.4, 36.3, 39.6, 41.0, 50.7, 127.2, 128.6 (2C), 128.8, 129.1 (2C), 131.1, 134.1, 146.5, 164.0, 197.7, 200.0 ppm; MS EI *m/z* (relative intensity) 336 (M^+, 11), 321 (3), 131 (100), 77 (21). Anal. Calcd for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39. Found: C, 81.98; H, 8.51.

Acetic Acid (3a*SR*,5a*RS*,9a*RS*,9b*RS*)-3a,6,6,9a-Tetramethyl-1-oxo-3-phenyl-3a,5a,6,7,8,9,9a,9b-octahydro-1*H*-cyclopenta[*a*]naphthalen-4-yl Ester (7). Compound **6** (3.00 g, 8.92 mmol) was dissolved in a mixture of $HClO_4$ (10^{-2} M)/Ac_2O (1 M)/AcOEt (300 mL). The solution was allowed to stand at room temperature for 2 h. Saturated $NaHCO_3$ was added to quench the reaction. The organic layer was separated and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with Na_2CO_3 (5%) and brine. Removal of the solvent afforded a crude solid, which was purified by flash chromatography. Hexane/Et_2O (85/15) furnished **7** (3.21 g, 8.47 mmol, 95%) as a colorless solid: mp (*t*-BuOMe/hexane) 73−75 °C; IR ν 2926, 1763, 1694, 733, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (6H, s), 1.20 (3H, s), 1.20−1.80 (5H, m), 1.50 (3H, s), 1.63 (3H, s), 1.87 (1H, d, J = 2.4 Hz), 2.10 (1H, s), 2.59 (1H, dt, J_d = 4.9 Hz, J_t = 14 Hz), 5.44 (1H, d, J = 2.4 Hz), 5.96 (1H, s), 7.25−7.45 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 17.9, 20.5, 22.0, 22.1, 22.6, 32.7, 33.0, 33.4, 40.6, 41.6, 47.7, 52.5, 67.5, 117.6, 127.6 (2C), 127.8 (2C), 128.6, 132.4, 136.1, 146.8, 168.8, 178.6, 207.4 ppm; MS EI *m/z* (relative intensity) 378 (M^+, 6), 335 (87), 172 (100), 77 (15), 55 (36). Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.17; H, 8.08.

Acetic Acid (3*SR*,3a*RS*,5a*RS*,9a*RS*,9b*RS*)-3a,6,6,9a-Tetramethyl-1-oxo-3-phenyl-2,3,3a,5a,6,7,8,9,9a,9b-decahydro-1*H*-cyclopenta[*a*]naphthalen-4-yl Ester (8). To a solution of **7** (3.10 g, 8.19 mmol) in AcOEt (25 mL) was added 10% Pd/C (490 mg). The mixture was vigorously stirred at room temperature under H_2 atmosphere for 10 h. After removal of the catalyst by filtration, the filtrate was concentrated to yield **8** (2.96 g, 7.78 mmol, 95%) as a colorless oil: IR ν 2926, 1757, 1734, 733, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80−2.50 (6H, m), 0.83 (3H, s), 0.89 (3H, s), 1.17 (3H, s), 1.39 (6H, s), 1.80 (1H, d, J = 2.0 Hz), 2.85−3.10 (3H, m), 2.95 (1H, m), 5.60 (1H, d, J = 2.0 Hz), 7.20−7.40 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 18.0, 20.3, 21.6, 22.2, 24.1, 32.6, 33.3, 33.6, 39.5, 40.7, 44.7, 49.0, 49.9, 52.9, 68.5, 119.0, 126.9, 127.7 (2C), 128.5 (2C), 137.8, 147.3, 168.8, 216.2 ppm; MS EI *m/z* (relative intensity) 380 (M^+, 9), 338 (9), 323 (3), 320 (9), 305 (6), 281 (36), 206 (100), 77 (31), 55 (63); HRMS EI 380.2364 (M^+, $C_{25}H_{32}O_3$), calcd 380.2351.

Acetic Acid (1*RS*,3*SR*,3a*RS*,5a*RS*,9a*RS*,9b*RS*)-1-Hydroxy-3a,6,6,9a-tetramethyl-3-phenyl-2,3,3a,5a,6,7,8,9,9a,-9b-decahydro-1*H*-cyclopenta[*a*]naphthalen-4-yl Ester (9). To a solution of **8** (2.80 g, 7.36 mmol) in MeOH (187 mL) at 0 °C was added $NaBH_4$ (1.40 g, 36.8 mmol). The reaction mixture was stirred at 0 °C under argon for 2 h and, after the addition of acetone, concentrated. The residue was treated with brine and Et_2O, stirring for 30 min. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine. Removal of the solvent afforded **9** (2.59 g, 6.77 mmol, 92%) as a colorless oil: IR ν 3503, 2926, 1744, 733, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84 (3H, s), 0.94 (3H, s), 1.15 (3H, s), 1.31 (3H, s), 1.41 (3H, s), 1.80−2.00 (7H, m), 1.84 (1H, d, J = 9.1 Hz), 2.16 (2H, dd, J_1 = 7.7 Hz, J_2 = 8.7 Hz), 2.50 (1H, dt, J_d = 4.0 Hz, J_t = 12 Hz), 2.73 (1H, t, J = 8.7 Hz), 2.94 (1H, d, J = 2.0 Hz), 4.58 (1H, m), 5.53 (1H, d, J = 2.0 Hz), 7.10−7.40 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 18.5, 20.5, 22.0, 24.8, 26.2, 33.1 (2C), 33.4, 38.7, 40.7, 40.9, 46.8, 51.6, 54.2, 61.6, 74.7, 119.6, 126.1, 126.1, 127.4 (2C), 129.0 (2C), 141.1, 147.2, 169.3 ppm; MS EI *m/z* (relative intensity) 382 (M^+, 3), 364 (5), 341 (8), 322 (24), 135 (100), 91 (78), 77 (35), 55 (97).

Treatment of 9 with KOH (aq)/EtOH. To a solution of **9** (2.40 g, 6.27 mmol) in EtOH (18 mL) was added a 5 M aqueous solution of KOH (2.5 mL). The mixture was stirred at room temperature for 1 h and then concentrated under reduced pressure. To the residue were added H_2O and Et_2O. The organic layer was separated and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine. Removal of the solvent afforded a 2/1 inseparable mixture of **10** and **11** (2.14 g, 6.27 mmol, 100%) as a white solid.

(1*SR*,3*SR*,3a*RS*,5a*RS*,9a*RS*,9b*RS*)-1-Hydroxy-3a,6,6,9a-tetramethyl-3-phenyldodecahydrocyclopenta[*a*]-naphthalen-4-one 10: ^{1}H NMR ($CDCl_3$) δ 0.84 (6H, s), 1.00−1.90 (6H, m), 1.14 (3H, s), 1.47 (3H, s), 1.68 (1H, d, J = 6.5 Hz), 2.00−2.60 (5H, m), 2.78 (1H, dd, J_1 = 5.8 Hz, J_2 = 13 Hz), 2.84 (1H, t, J = 9.0 Hz), 4.65 (1H, m), 7.20−7.45 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 18.7, 21.3, 24.0, 29.7, 32.8, 33.6, 35.4, 38.2, 38.7, 41.3, 41.5, 46.6, 55.6, 59.1, 66.1, 74.8, 126.3, 127.6 (2C), 129.8 (2C), 140.9, 216.0 ppm.

Hemiketal 11: ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, s), 0.88 (3H, s), 1.08 (3H, s), 1.31 (3H, s), 3.11 (1H, dd, J_1 = 4.9 Hz, J_2 = 11 Hz), 4.43 (1H, br s), 7.20−7.60 (5H, m) ppm.

(1*SR*,3*SR*,3a*RS*,6a*RS*,10a*RS*,10b*SR*)-1-Hydroxy-3a,7,7,-10a-tetramethyl-3-phenyldodecahydro-4-oxabenz[*e*]azulen-5-one (12). To a stirred solution of the inseparable mixture **10**/**11** (1.50 g, 4.41 mmol) in CH_2Cl_2 (33 mL) were added $NaHCO_3$ (37 mg, 0.44 mmol) and *m*-CPBA (840 mg, 4.87 mmol). The reaction mixture was stirred under argon at room temperature for 3 days. Then, Na_2SO_3 (5%) was added, and the resulting heterogeneous mixture was vigorously stirred for 1 h. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with Na_2CO_3 (5%) and brine. Removal of the solvent afforded **12** (1.57 g, 4.41 mmol, 100%) as a white solid: mp (CH_2Cl_2/hexane) 210−212 °C; IR ν 3576, 2926, 1717, 768, 708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80−2.00 (9H, m), 0.90 (3H, s), 1.05 (3H, s), 1.23 (3H, s), 1.34 (3H, s), 2.20−2.90 (4H, m), 3.02 (1H, dd, J_1 = 11 Hz, J_2 = 17 Hz), 5.10 (1H, ddd, J_1 = 2.4 Hz, J_2 = 5.5 Hz, J_3 = 7.7 Hz), 7.20−7.50 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 18.2 (2C), 21.8, 26.0, 33.1, 35.2, 35.7, 35.8, 39.8, 41.8, 44.9, 49.1, 56.1, 66.2, 80.1, 81.0, 127.2, 128.2 (2C), 129.8 (2C), 137.7, 174.7 ppm; MS EI *m/z* (relative intensity) 356 (M^+, 7), 341 (5), 338 (2), 207 (100), 91 (34), 55 (26); HRMS EI 356.2342 (M^+, $C_{23}H_{32}O_3$), calcd 356.2351. Anal. Calcd. for $C_{23}H_{32}O_3$: C, 77.49; H 9.05. Found: C, 77.33; H, 8.97.

(2*SR*,2a*RS*,4a*RS*,8a*RS*,8b*SR*)-2a,5,5,8a-Tetramethyl-2-phenyldecahydro-9-oxacyclopropa[1,5]cyclopenta[1,2-*a*]-naphthalen-3-one (14). To a solution of the inseparable mixture **10**/**11** (500 mg, 1.47 mmol) in CH_2Cl_2 (20 mL) at 0 °C under argon was added gradually pyridine (470 μL, 5.88 mmol) and a solution of $SOCl_2$ (210 μL, 2.94 mmol) in CH_2Cl_2 (2.2 mL). The reaction mixture was stirred at 0 °C for 30 min and then poured into ice−water. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with Na_2CO_3 (5%) and brine. Removal of the solvent afforded the unsaturated ketone, which was used without further purification.

The same procedure used above to obtain **4** from **3** was applied to the unsaturated ketone yielding, after 3 h of reaction, **14** (323 mg, 0.95 mmol, 65% overall) as a white solid: mp (*t*-BuOMe/hexane) 152−154 °C; IR ν 2934, 1699, 733, 702 cm cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.72 (3H, s), 0.82 (3H, s), 0.90−1.70 (7H, m), 1.16 (3H, s), 1.48 (3H, s), 1.71 (1H, dd, J_1 = 5.0 Hz, J_2 = 17 Hz), 2.15 (1H, ddd, J_1 = 2.4 Hz, J_2 = 7.1 Hz, J_3 = 14 Hz), 2.25 (1H, dd, J_1 = 7.1 Hz, J_2 = 14 Hz), 2.31 (1H, dd, J_1 = 13 Hz, J_2 = 17 Hz), 2.98 (1H, t, J = 7.1 Hz), 3.95 (1H, d, J = 2.4 Hz), 7.15−7.30 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 17.4, 17.7, 21.1, 21.9, 32.1, 32.3, 33.4, 33.8, 36.3, 37.7, 42.0, 47.6, 56.2, 59.5, 63.9, 77.5, 126.6, 127.7 (2C), 129.3 (2C), 140.0, 212.7 ppm; MS EI *m*/*z* (relative intensity) 338 (M^+, 50), 186 (31), 117 (100), 91 (43); HRMS EI 338.2233 (M^+, $C_{23}H_{30}O_2$), calcd 338.2246. Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.52; H, 8.85.

Crystal data: $C_{23}H_{30}O_2$; M_r = 338.47; orthorhombic; space group *Pna*2 (1); unit cell dimensions a = 23.342(5) Å, b = 11.211(2) Å; c = 7.209(1) Å, α = 90°, β = 90°, γ = 90°; volume 1886.4(1) Å^3; Z = 4, D_x = 1.192 g cm^{-3}; absorption coefficient 0.074 mm^{-1}; crystal size 0.42 × 0.16 × 0.16 mm; θ range for data collection 2.74−25.35°; limiting indices $-28 \le h \le 28$, $-13 \le k \le 13$, $-8 \le l \le 8$; R = 0.0576; Rw = 0.1323.

Reaction of 12 with $SOCl_2$/Pyridine. To a solution of **12** (200 mg, 0.56 mmol) in CH_2Cl_2 (7.8 mL) at 0 °C under argon was added gradually pyridine (180 μL, 2.24 mmol) and a solution of $SOCl_2$ (82 μL, 1.1 mmol) in CH_2Cl_2 (0.6 mL). The reaction mixture was stirred at 0 °C for 15 min and then poured into ice−water. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with Na_2CO_3 (5%) and brine. Removal of the solvent afforded a crude product, which was purified by flash chromatography. 85/15 hexane/Et_2O furnished (2*SR*,3a*SR*,6a*RS*,10a*RS*)-1,7,7,10a-tetramethyl-2-phenyl-2,3,3a,6,6a,7,8,9,10,10a-decahydro-4-oxabenz[*e*]azulen-5-one **15a** (112 mg, 0.33 mmol, 59%) as a white solid: mp (*t*-BuOMe/hexane) 183−185 °C; IR ν 2930, 1709, 760, 702 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.62 (3H, s), 0.69 (3H, s), 0.85−1.05 (2H, m), 1.12 (3H, s), 1.16 (2H, m), 1.30 (1H, m), 1.35 (3H, s), 1.67 (1H, dd, J_1 = 8.1 Hz, J_2 = 10 Hz), 1.90 (2H, m), 2.16 (1H, ddd, J_1 = 7.4 Hz, J_2 = 9.3 Hz, J_3 = 15 Hz), 2.75 (1H, dd, J_1 = 8.1 Hz, J_2 = 17 Hz), 2.77 (1H, dd, J_1 = 10 Hz, J_2 = 17 Hz), 3.26 (1H, d, J = 9.3 Hz), 5.10 (1H, d, J = 7.4 Hz), 7.02 (1H, m), 7.16 (2H, m), 7.34 (2H, m) ppm; ^{13}C NMR (C_6D_6) δ 15.7, 18.9, 20.5, 21.1, 32.9, 34.6, 36.3, 37.5, 39.1 (2C), 41.9, 48.4, 57.6, 83.9, 126.9, 128.5 (2C), 129.0 (2C), 142.1, 144.4, 145.3, 172.0 ppm; MS EI *m*/*z* (relative intensity) 338 (M^+, 10), 279 (8), 264 (42); HRMS EI 338.2207 (M^+, $C_{23}H_{30}O_2$), calcd 338.2246. Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.69; H, 9.01.

Hexane/Et_2O (80/20) furnished (3a*SR*,6a*RS*,10a*RS*,10b*RS*)-1,7,7,10a-tetramethyl-2-phenyl-3,3a,6,6a,7,8,9,10,10a,10b-decahydro-4-oxabenz[*e*]azulen-5-one **16** (51 mg, 0.15 mmol, 27%) as a white solid: mp (*t*-BuOMe/hexane) 183−185 °C; IR ν 2922, 1717, 764, 704 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.70 (3H, s), 0.70−1.60 (6H, m), 0.97 (3H, s), 1.18 (3H, s), 1.77 (3H, br s), 2.05 (2H, m), 2.30−2.80 (4H, m), 4.28 (1H, t, J = 4.8 Hz), 7.10−7.40 (5H, m) ppm; ^{13}C NMR (C_6D_6) δ 16.6, 17.3, 18.0, 20.9, 32.1, 34.5, 35.7, 38.3, 41.4, 42.4, 43.6, 48.8, 68.2, 78.2, 126.7, 128.1 (2C), 128.3 (2C), 133.2, 137.0 (2C), 173.5 ppm; MS EI *m*/*z* (relative intensity) 338 (M^+, 8), 157 (100), 91 (93), 69 (77). Anal. Calcd. for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.73; H, 8.84.

(1*RS*,2*RS*,3′*SR*,5′*SR*)-[2-(5′-Hydroxy-2′-methyl-3′-phenylcyclopent-1′-enyl)-2,6,6-trimethylcyclohexyl]acetic Acid Methyl Ester (17a). To a solution of **15a** (90 mg, 0.27 mmol) in MeOH (7.4 mL) was added a 5.5 M solution of MeONa in MeOH (230 μL). The reaction mixture was stirred at room temperature under argon for 10 min and then poured into a saturated solution of NH_4Cl. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine. Removal of the solvent afforded **17a** (100 mg, 0.27 mmol, 100%) as a colorless oil: IR ν 3488, 2951, 1721, 762, 702 cm^{-1};^{1}H NMR (C_6D_6) δ 0.80−1.80 (6H, m), 0.86 (3H, s), 0.92 (3H, s), 1.29 (3H, s), 1.73 (3H, s), 2.35 (2H, d, J = 5.2 Hz), 2.40 (1H, m), 2.60 (2H, ddd, J_1 = 7.3, J_2 = 9.2, J_3 = 14 Hz), 2.87 (1H, t, J = 5.2 Hz), 3.30 (1H, m), 3.39 (3H, s), 4.87 (1H, m), 7.10−7.30 (5H, m) ppm.

(1*RS*,2*RS*,3′*SR*,5′*SR*)-[2-(5′-Acetoxy-2′-methyl-3′-phenylcyclopent-1′-enyl)-2,6,6-trimethylcyclohexyl]acetic Acid Methyl Ester (18a). To a solution of **17a** (90 mg, 0.24 mmol) in pyridine (137 μL, 1.70 mmol) were added Ac_2O (137 μL, 1.46 mmol) and DMAP (3 mg, 0.02 mmol). The reaction mixture was stirred at room temperature under argon for 45 min and then diluted with Et_2O and poured into ice−water. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with $NaHCO_3$ (5%) and brine. Removal of the solvent afforded **18a** (99 mg, 0.24 mmol, 100%) as a colorless solid: mp (*t*-BuOMe/hexane) 124−126 °C; IR ν 2922, 2866, 1726, 762, 708 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.85 (3H, s), 0.95 (3H, s), 1.18 (3H, s), 1.30−1.50 (3H, m), 1.60 (1H, m), 1.75 (3H, s), 1.82 (1H, d, J = 16 Hz), 1.92 (3H, s), 2.04 (1H, dt, J_d = 3.6 Hz, J_t = 13 Hz), 2.18 (1H, dd, J_1 = 5.8 Hz, J_2 = 15 Hz), 2.27 (1H, dd, J_1 = 5.8, J_2 = 15 Hz), 2.60 (1H, ddd, J_1 = 7.1 Hz, J_2 = 9.2 Hz, J_3 = 16 Hz), 2.71 (1H, t, J = 5.2 Hz), 3.37 (3H, s), 3.41 (1H, d, J = 9.2 Hz), 6.02 (1H, d, J = 7.1 Hz), 7.10−7.35 (5H, m) ppm; ^{13}C NMR (C_6D_6) δ 16.7, 18.6, 19.1, 20.9, 22.1, 33.0, 33.5, 34.3, 38.6, 39.2, 40.6, 41.6, 47.3, 50.7, 57.1, 82.9, 126.3, 128.1 (2C), 128.5 (2C), 141.8, 144.3, 145.2, 169.4, 174.2 ppm; MS FAB *m*/*z* (relative intensity) 353 ($M^+ + 1 - 60$, 100), 321 (6), 223 (15), 197 (72), 91 (67), 69 (75). Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80. Found: C, 75.83; H, 8.85.

(3*RS*,3a*RS*,6a*RS*,10a*RS*,10b*RS*)-3a,7,7,10a-Tetramethyl-3-phenyldecahydro-4-oxabenz[*e*]azulene-1,5-dione (19). The same procedure used above to obtain **3** through oxidation with PCC was applied to **12** (1.00 g, 2.81 mmol) yielding, after 2 days, **19** (727 mg, 2.05 mmol, 73%) as a white solid: mp (CH_2Cl_2/hexane) 173−175 °C; IR ν 2924, 1732, 1699, 766, 689 cm^{-1};^{1}H NMR ($CDCl_3$) δ 0.70−1.70 (6H, m), 0.77 (3H, s), 0.96 (3H, s), 1.25 (3H, s), 1.58 (3H, s), 1.97 (1H, dd, J_1 = 2.6 Hz, J_2 = 9.4 Hz), 2.38 (1H, s), 2.60 (3H, m), 2.95 (1H, m), 3.17 (1H, t, J = 9.0 Hz), 7.20−7.50 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 17.8, 21.2, 22.5, 23.5, 32.7, 34.1, 34.6, 34.7, 39.9, 41.1, 42.0, 43.5, 52.7, 71.2, 88.2, 127.7, 128.2 (2C), 130.5 (2C), 136.3, 173.5, 210.6 ppm; MS EI *m*/*z* (relative intensity) 354 (M^+, 2), 206 (19), 104 (75), 84 (100), 69 (100); HRMS EI 354.2220 (M^+, $C_{23}H_{30}O_3$) calcd 354.2195. Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 78.01; H, 8.58.

(1*SR*,6*RS*,3′*SR*)-[2,2,6-Trimethyl-6-(2′-methyl-5′-oxo-3′-phenylcyclopent-1′-enyl)cyclohexyl]acetic Acid Methyl Ester (20). To a solution of **19** (650 mg, 1.83 mmol) in toluene (14 mL) was added DBU (1.38 mL, 9.18 mmol). The reaction mixture was stirred at 80 °C under argon for 10 min. Then, Et_2O and HCl (2 M) were added. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine and concentrated to afford a pale yellow oil, which was dissolved in Et_2O (2.5 mL). To the solution was added dropwise a solution of CH_2N_2 in Et_2O until the release of nitrogen stopped. Removal of the solvent afforded **20** (430 mg, 1.17 mmol, 72%) as a white solid: mp (*t*-BuOMe/hexane) 93−95 °C; IR ν 2940, 1734, 1699, 764, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.83 (3H, s), 0.93 (3H, s), 1.20−1.80 (5H, m), 1.30 (3H, s), 2.00 (3H, s), 2.00−2.40 (3H, m), 2.54 (1H, dt, J_d = 3.8 Hz, J_t = 13 Hz), 2.70−2.90 (3H, m), 3.60 (1H, m), 3.61 (3H, s), 7.00−7.30 (5H, m) ppm; ^{13}C NMR ($CDCl_3$) δ 18.2, 19.1, 21.4, 22.5, 33.1, 33.4, 34.4, 35.1,

41.1, 42.5, 45.4 (2C), 50.1, 51.5, 126.9, 127.5 (2C); 128.9 (2C), 142.9, 145.5, 171.9, 175.2, 208.5 ppm; MS EI *m*/*z* (relative intensity) 368 (M^+, 15), 353 (5), 308 (11), 295 (44), 91 (95), 55 (100); HRMS EI 368.2306 (M^+, $C_{24}H_{32}O_3$), calcd 368.2351. Anal. Calcd for $C_{24}H_{32}O_3$: C, 78.22; H, 8.75. Found: C, 78.12; H, 8.69.

Reaction of 20 with BH_3·SMe_2. To a solution of **20** (430 mg, 1.17 mmol) in THF (3 mL) at 0 °C under argon was added a 2 M solution of BH_3·SMe_2 in THF (1.2 mL). The reaction mixture was stirred at 0 °C for 5 h 30 min, and then MeOH (1.8 mL) was slowly added with stirring for 1 h. Removal of the solvent afforded a crude product, which was purified by flash chromatography. Hexane/Et_2O (85/15) furnished **17a** (247 mg, 0.67 mmol, 57%).

Hexane/Et_2O (80/20) furnished **17b** (70 mg, 0.19 mmol, 28%) as a colorless oil: IR ν 3447, 2926, 1734, 752, 702 cm^{-1}; ^1H NMR (C_6D_6) δ 0.88 (3H, s), 0.99 (3H, s), 1.20−1.90 (6H, m), 1.41 (3H, s), 1.72 (3H, s), 1.90−2.40 (4H, m), 2.60 (1H, dd, J_1 = 4.8 Hz, J_2 = 5.2 Hz), 2.76 (1H, dd, J_1 = 5.2 Hz, J_2 = 15 Hz), 3.36 (3H, s), 3.84 (1H, t, J = 7.5 Hz), 4.95 (1H, m), 7.00−7.30 (5H, m) ppm.

(2*SR*,3a*RS*,6a*RS*,10a*RS*)-1,7,7,10a-Tetramethyl-2-phenyl-2,3,3a,6,6a,7,8,9,10,10a-decahydro-4-oxabenz[*e*]azulen-5-one (15b). To a solution of **17b** (70 mg, 0.19 mmol) in EtOH (0.5 mL) was added a 5 M aqueous solution of KOH (87 μL). The mixture was stirred at room temperature for 15 min and then concentrated under reduced pressure. To the residue were added H_2O and Et_2O. The organic layer was separated, to the aqueous phase was added HCl (2 M, pH 5), and then the mixture was extracted with Et_2O. The combined organic extracts were washed with brine. Removal of the solvent afforded the crude hydroxy acid, which was suitable for using without further purification.

To a solution of the crude hydroxy acid in deoxygenated xilene (2.3 mL) were added $(pyS)_2$ (63 mg, 0.29 mmol) and PPh_3 (75 mg, 0.29 mmol). The reaction mixture was stirred at room temperature under argon for 24 h, and then the precipitate was filtered. Removal of the solvent afforded a crude product, which was purified by flash chromatography. 85/15 hexane/Et_2O furnished **15b** (51 mg, 0.15 mmol, 79%) as a white solid: mp (*t*-BuOMe/hexane) 147−150 °C; IR ν 2924, 1728, 768, 702 cm^{-1}; ^1H NMR (C_6D_6) 0.65 (3H, s), 0.95 (3H, s), 0.96 (3H, s), 1.01 (1H, m), 1.20−1.85 (7H, m), 1.47 (3H, s), 2.35 (1H, dd, J_1 = 11 Hz, J_2 = 14 Hz), 2.48 (1H, d, J = 14 Hz), 2.50 (1H, d, J = 14 Hz), 3.88 (1H, t, J = 7.3 Hz), 4.80 (1H, d, J = 6.1 Hz), 6.95 (2H, m), 7.15 (1H, m), 7.20 (2H, m) ppm; ^{13}C NMR (C_6D_6) δ 15.7, 18.5, 20.4, 21.1, 32.4, 33.1, 34.8, 38.5, 41.3, 41.7, 41.9, 49.2, 55.6, 83.0, 126.6, 128.2 (2C), 128.6 (2C), 139.1, 143.5, 144.4, 174.2 ppm; MS EI *m*/*z* (relative intensity) 338 (M^+, 100), 323 (6), 264 (17); HRMS EI 338.2229 (M^+, $C_{23}H_{30}O_2$), calcd 338.2246. Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.50; H, 8.85.

(1*RS*,2*RS*,3′*SR*,5′*RS*)-[2-(5′-Acetoxy-2′-methyl-3′-phenylcyclopent-1′-enyl)-2,6,6-trimethylcyclohexyl]acetic Acid Methyl Ester (18b). The same procedure used above to obtain **18a** from **17a** was applied to **17b** (40 g, 0.11 mmol) yielding, after 45 min of reaction, **18b** (44 mg, 0.11 mmol, 100%) as a colorless oil: IR 2951, 1738, 1732, 766, 702 cm^{-1}; ^1H NMR (C_6D_6) δ 0.92 (3H, s), 0.96 (3H, s), 1.15 (3H, s), 1.20−1.90 (5H, m), 1.83 (3H, s), 1.86 (3H, s), 2.15 (1H, m), 2.30 (1H, m), 2.45 (1H, dd, J_1 = 7.3 Hz, J_2 = 17 Hz), 2.75 (2H, m), 2.80 (1H, m), 3.43 (3H, s), 3.89 (1H, t, J = 7.5 Hz), 6.24 (1H, d, J = 6.1 Hz), 6.95−7.25 (5H, m) ppm; ^{13}C NMR (C_6D_6) δ 16.3, 18.8, 20.8, 22.5 (2C), 32.6, 33.0, 34.6, 38.2, 41.3 (2C), 42.0, 46.3, 40.8, 56.3, 81.1, 126.4, 127.7 (2C), 128.6 (2C), 142.5, 144.8, 145.1, 169.5, 174.6 ppm.

Acknowledgment. Financial support for this work from the Ministerio de Educación y Ciencia of Spain PB 98-0251 and the Junta de Castilla y León SA 24/00B is gratefully acknowledged. We also thank the Ministerio de Educación y Ciencia for the fellowship to E.M.M.N.

Supporting Information Available: ^1H and ^{13}C spectra for compounds **2**−**9**, **12**, **14**, **15a**,**b**, **16**, **18a**,**b**, **19**, and **20**. H−C correlations and NOE for compounds **7**, **15a**,**b**, and **18a**,**b**. Tables of crystal data, bond lengths and angles, atomic coordinates, and anisotropic thermal parameters for compound **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO010449Q