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Synthesis of CDE and BCDE Molecular Fragments of the Limonoids Havanensin and Azadiradione

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Received August 9, 2002

A new approach to the synthesis of CDE and BCDE molecular fragments of the limonoids havanensin and azadiradione has been achieved from cyclocitral and drimenal in seven steps in overall yields of 20 and 9%, respectively.

Introduction

Limonoid insect antifeedants are examples of natural weapons included within the arsenal of pest control compounds expected to furnish promising results in future crop protection.[1] In some cases, model compounds based on the CDE or BCDE rings of bioactive limonoids show a similar archetype activity.[2] In recent years we have been developing a program for the synthesis of model compounds of azadiradione and related compounds that contain only part of their skeleton and functionality and that are amenable for testing structure−activity relationships.[3]

The new strategies for synthesis developed by us aim to be both efficient and versatile. In the present work, they rely on two key steps: electrocyclization, which constructs the D ring, and a Michael-type reaction based on the conjugate addition of an organozinc reagent, which introduces the E ring. The method has been applied to the synthesis of CDE and BCDE model compounds related to havanensin and azadiradione, as depicted in Scheme 1.

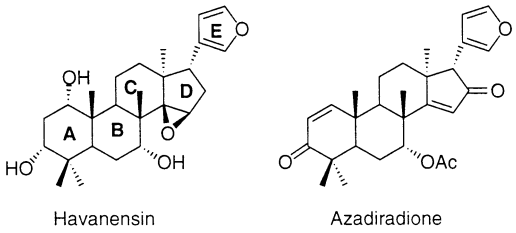

FIGURE 1.

Results and Discussion

Starting from β-cyclocitral,[3c] we obtained dienone **2a**, required for the electrocyclization reaction[4] through Grignard addition of vinylmagnesium bromide followed by allylic oxidation (Scheme 2).[5]

We first attempted to induce the electrocyclization of dienone **2a** with a mixture of 10^{-2} M $HClO_4$ /1 M Ac_2O in AcOEt, previously introduced by us for the cyclization of similar dienones.[6] This, however, was unsuccessful; after 16 h at room temperature, compound **2a** was recovered unaltered. This result was unexpected, since under those conditions the phenyl derivative **2b** was transformed into the cyclization product **3b** in five minutes with 54% yield[6] (Scheme 3).

We have shown that variations in the concentration of perchloric acid and/or acetic anhydride cause important changes in the cyclization rate.[6] This prompted us to explore the cyclization of dienone **2a** with perchloric acid/acetic anhydride, taking the time and component concentrations as variables. The results are shown in Table 1.

As mentioned above, while a concentration of 10^{-1} M $HClO_4$ promoted the cyclization of **2a**, 10^{-2} M $HClO_4$ did

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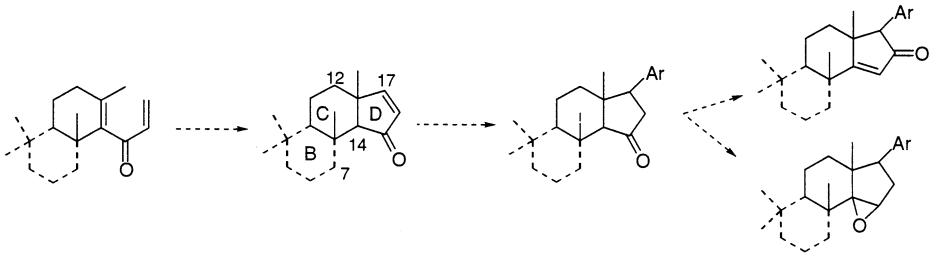
(5) All compounds synthesized were racemic, although only one enantiomer is depicted.

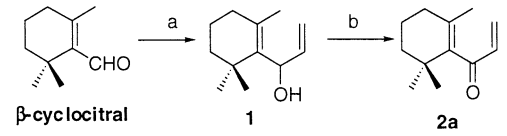
(6) Fernández-Mateos, A.; Martín de la Nava, E. M.; Rubio González, R. *Tetrahedron* **2001**, *57*, 1049−1057

10.1021/jo0205311 CCC: $25.00
Published on Web 04/01/2003

SCHEME 1

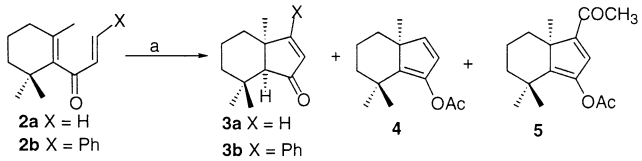


SCHEME 2[a]



[a] Reaction conditions: (a) $BrMgCH{=}CH_2$, THF. (b) MnO_2, pentane.

SCHEME 3[a]



[a] Reaction conditions: (a) $HClO_4$, AcO_2, AcOEt.

TABLE 1. Electrocyclization Reaction of Dienone 2a

promoter acid	T[a]	time	**3a**:**4**:**5**	yield[a]
10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	5 min	4:2:1	73%
10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	10 min	5:2:2	86%
10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	20 min	2:1:2	90%
10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	40 min	3:1:4	89%
10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	1 h, 30 min	5:1:7	87%
10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	12 h	−:−:1	70%
10^{-1} M $HClO_4$−0.5 M Ac_2O	25 °C	1 h	1:−:−	75%
H_3PO_4−HCOOH	70 °C	30 min	1:−:−	70%

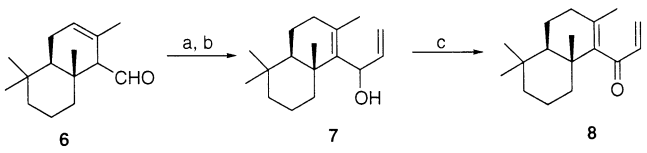
[a] Combined yields.

not. Several aspects shown in the table are remarkable. Besides the two expected cyclization products **3a** and **4**, a third product, **5**, was obtained. The proportion of **5** increased with time, and it was the only product detected after 12 h of reaction. This compound must arise through a Friedel−Crafts reaction of enol acetate **4**. As expected, upon lowering the concentration of acetic anhydride, the Friedel−Crafts compound **5** was not produced. To compare these results with those obtained under classic conditions,[4] we subjected the dienone **2a** to treatment with a mixture of H_3PO_4/HCOOH at 70 °C; this afforded the bicyclic enone **3a** in 30 min with 70% yield.

The above approach would gain further relevance if it could be successfully applied to the synthesis to tricyclic analogues of the BCD type such as **9**. The dienone precursor **8** was obtained from the readily available drimenal **6**[7] in three simple steps, in high overall yield (58%), as depicted in Scheme 4.

The mixture of $HClO_4/OAc_2$ (entry 1, Table 2) promoted the electrocyclization of **8** to give two products in equal

SCHEME 4[a]



[a] Reaction conditions: (a) KOH, MeOH. (b) $BrMgCH{=}CH_2$, THF. (c) MnO_2, pentane.

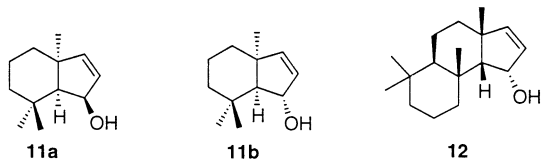


FIGURE 2.

TABLE 2. Electrocyclization Reaction of Dienone 8

	promoter acid	T[a]	time	**9a**	**9b**	**9c**	**10**	yield
1	10^{-1} M $HClO_4$−1 M Ac_2O	25 °C	20 min	1		1		70%
2	10^{-1} M $HClO_4$−0.5 M Ac_2O	50 °C	2 h	1	1			72%
3	H_3PO_4−HCO_2H	90 °C	6 h	2			3	63%

amounts, which were identified as **9a** and **9c**. The reactivity of enones **9a** and **9b** is striking: whereas **9a** does not undergo further transformation, **9b** is rapidly further acetylated and acylated in the reaction mixture. By lowering the concentration of acetic anhydride (entry 2), the transformation of **9b** does not occur. The reaction of dienone **8** with H_3PO_4/HCO_2H (entry 3) also afforded two products: **9a** and **10**. The latter must arise from a carbocationic intermediate of **9b** through methyl migration followed by proton elimination. From the data shown in Tables 1 and 2, it is clear that fine-tuning of the perchloric acid/acetic anhydride mixture concentration could afford nonacylated or acylated cyclization products. The acylated products could be valuable intermediates in the synthesis of limonoids.

Addition of the E ring (E = phenyl) to the enones **3a**, **9a**, and **9b** was attempted by means of the Heck reaction under reducing conditions,[8] $Pd(OAc)_2$, PPh_3, PhI, Et_3N, HCO_2H, DMF, 80 °C, or $Pd(PPh_3)_4$ PhI, Et_3N, 80 °C. Although several already described conditions were tested, no addition products were obtained. Two experiments were performed with 2-cyclohexenone under the above conditions, and the expected 3-phenylcyclohexanone was obtained, although in low yield.

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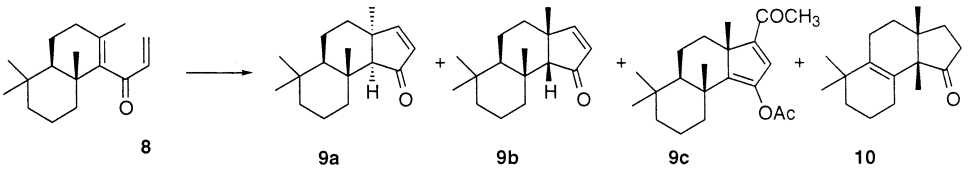
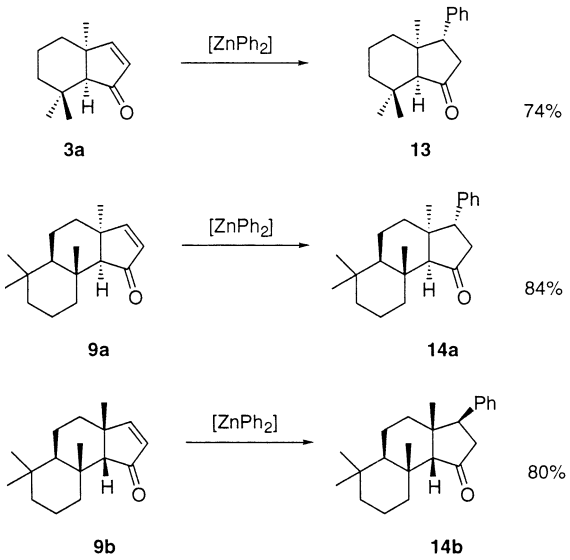
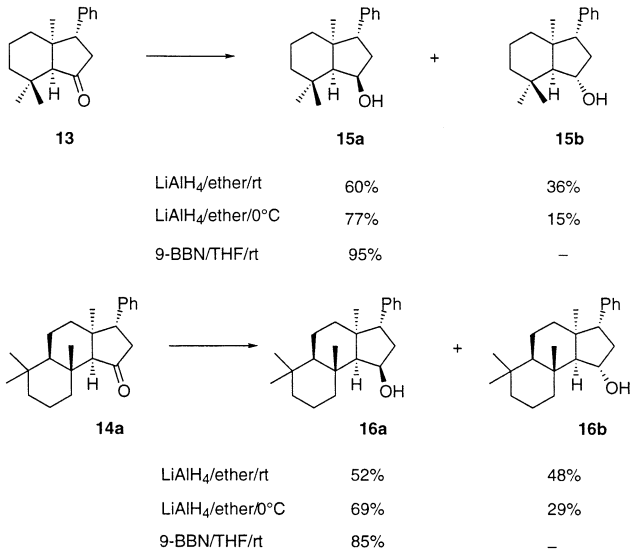
SCHEME 5



SCHEME 6



SCHEME 7



Recently, Heck coupling of aryl halides or benzoic anhydrides with alkenes has been performed in excellent yields at room-temperature ionic liquids.[9] These types of liquids provide a medium that dissolves the palladium catalyst and allows the product to be easily separated. However, the use of *N*-hexylpyridinium chloride as a solvent in the Heck reaction with enones **3a**, **9a**, and **9b** failed. The Heck reaction of iodobenzene with the allylic alcohols **11a**, **11b**, and **12**, obtained by reduction of the corresponding enones with 9-BBN or $LiAlH_4$, also failed.[10] The reagents most commonly used for 1,4-addition to enones are organocuprates. However, these compounds are frequently unstable at room temperature and are very sensitive to steric hindrance. We believed that enones **3a**, **9a**, and **9b** are very sterically hindered and, hence, an alternative would be organozinc compounds.[11] This type of compound has not been used very often, although in our hands it was very successful. We followed the procedure of J.L. Luche et al.[11b] in which the reagent is first prepared by mixing iodobenzene, zinc bromide, and lithium in ether under ultrasound (40 kHz) in an ice bath for 1 h. To the black suspension formed was added a mixture of the enone and nickel acetylacetonate at room temperature. As seen in Scheme 6, all conjugated additions to enones **3a**, **9a**, and **9b** with the organozinc compounds afforded good yields in an absolutely stereoselective manner. The relative configurations of the new stereocenter were assigned by X-ray (**13**) or NOE experiments (**14a** and **14b**).[12]

In all additions, the entering phenyl group adds from the less hindered *exo*-side of the enone, and the resulting products maintain a cis relationship between the angular methyl group and the entering phenyl group,[12] which is the type of relative configuration found in naturally occurring limonoids of the havanensin group such as azadiradione or havanensin.[1]

Elaboration of the cyclopentene D ring of the bicyclic phenyl ketone **13** and tricyclic phenyl ketone **14a** to the corresponding CDE and BCDE models of havanensin, azadiradione, and related compounds was straightforward. Reduction of the bicyclic ketone **13** with lithium aluminum hydride afforded a mixture of diastereoisomeric alcohols **15a** and **15b** in different ratios at different temperatures. With 9-BBN as the reducing agent, only isomer **15a**, resulting from *exo*-attack of the hydride, was obtained in 95% yield. Similar results were obtained in the reduction of the homologue tricyclic ketone **14a** (Scheme 7).

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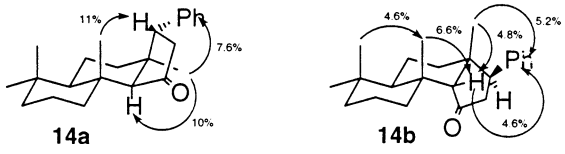
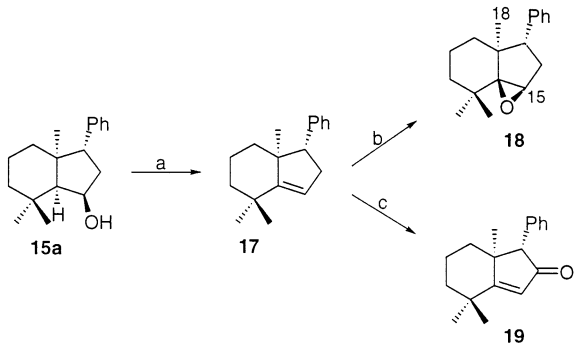
(11) (a) Greene, A. E.; Lansard, J. P.; Luche, J. L.; Petrier, C. *J. Org. Chem.* **1984**, *49*, 931−932. (b) Greene, A. E.; Lansard, J. P.; Luche, J. L.; Petrier, C. *J. Org. Chem.* **1983**, *48*, 3837−3839.

(12) (a) Crystallographic data for structures **13** and **22** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication nos. CCDC 189604 and 189605, respectively. (b) The stereochemistry for compounds **14a** and **14b** was determined by NOE experiments:



SCHEME 8[a]



[a] Reaction conditions: (a) $SOCl_2$/pyr, CH_2Cl_2, 0°C. (b) *m*-CPBA, CH_2Cl_2. (c) CrO_3·DMP, CH_2Cl_2.

Subsequent dehydration of alcohol **15a** with thionyl chloride in pyridine afforded only the desired olefin **17** in 86% yield (Scheme 8). The reaction of alkene **17** with *m*-chloroperoxybenzoic acid furnished the expected CDE molecular fragment of havanensin **18**, in excellent yield (93%). The β-configuration assigned to the oxyranic oxygen of **18** was based on the upfield shift of the ^{13}C NMR signal (γ-effect) for the homoallylic carbon bearing an axial hydrogen cis to the oxygenated function (49.1 ppm), compared with the unsaturated precursor **17** (60.5 ppm)[13] and the NOE correlation between H-15 (geminal with oxygen) and H-18 (the angular methyl group).[14,15] The transformation of alkene **17** to the corresponding CDE fragment of azadiradione **19** was accomplished with CrO_3-3,5-dimethylpyrazole in 72% yield.

Similar results were obtained in the transformation of the tricyclic alcohol **16a** in the BCDE molecular fragment of havanensin **21** and azadiradione **22**, (Scheme 9). The epoxidation of alkene **20** was exocyclic, as demonstrated by the absence of the γ-effect in the ^{13}C NMR spectra. The chemical shift of C-17 is 61.4 ppm for the alkene **20** and 63.7 ppm for the epoxide **21**. The NOE correlation (3%) between H-15 (geminal with oxygen) and H-30 (the angular methyl group bonded to C-8) in epoxide **21** corroborates the α assignment for the oxyranic oxygen.[15] The structure of enone **22**, preparated by allylic oxidation of **20**, was assigned by X-ray analysis.[12]

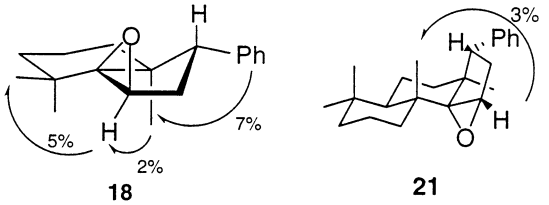
Conclusion

A new synthetic approach to the CDE and BCDE fragments of limonoids havanensin and azadiradione was achieved from cyclocitral and drimenal in seven steps in overall yield of 20 and 9%, respectively. The required D ring was formed by electrocyclization induced by perchloric acid. Installation of the E ring involved a conjugate addition of diphenylzinc to an enone catalyzed by Ni(II). The versatility of the method allows it to be applied to the synthesis of more complicated limonoids with an oxygenated function in carbon C-7 and C-12 positions.

(13) Fernández-Mateos, A.; de la Fuente Blanco, J. A. *J. Org. Chem.* **1990**, *55*, 1349−1354.

(14) Limonoid numbering.

(15) Stereochemistry for compounds **18** and **21** was determined by NOE experiments:



Experimental Section

General Methods. When required, all solvents and reagents were purified by standard techniques. Reactions were monitored by TLC on 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 silica gel 60 (0.040−0.063 mm). ^1H and ^{13}C NMR spectra were recorded at 200/400 and 50/75 MHz, respectively.

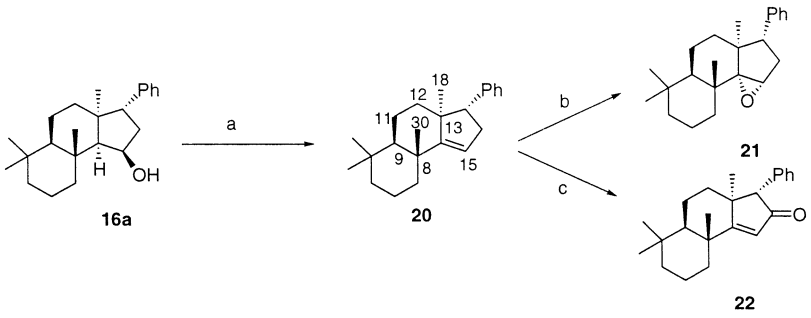
1-(2,6,6-Trimethyl-cyclohex-1-enyl)-prop-2-en-1-ol 1. To a stirred solution of β-cyclocitral (4.90 g, 32.2 mmol) in THF (92 mL) at room temperature under argon was added a 1 M solution of $BrMgCH{=}CH_2$ in THF (32 mL). The reaction mixture was stirred for 5 m. Then, saturated aqueous NH_4Cl was added and the heterogeneous mixture was stirred for 5 m. 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 **1** (5.68 g, 31.6 mmol, 100%) as a yellow oil. IR, ν: 3418, 2928 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.90−1.70 (5H, m), 0.97 (3H, s), 1.12 (3H, s), 1.74 (3H, s), 1.94 (2H, m), 4.81 (1H, dt, $J_t = 2.1$, $J_d = 4.4$ Hz), 5.10 (1H, dt, $J_t = 1.9$, $J_d = 11$ Hz), 5.24 (1H, dt, $J_t = 1.9$, $J_d = 17$ Hz), 6.06 (1H, ddd, $J_1 = 4.4$, $J_2 = 11$, $J_3 = 17$ Hz). ^{13}C NMR $CDCl_3$, δ: 19.3, 20.9, 28.0, 28.4, 33.8, 34.8, 39.7, 71.1, 113.4, 132.9, 138.8, 140.6. MS EI, *m*/*z* (relative intensity): 180 (M^+, 4), 165 (7), 162 (14), 147 (38), 123 (32), 119 (54), 105 (81), 91 (100), 77 (48), 55 (69). HRMS (EI): 180.1529 (M^+, $C_{12}H_{20}O$); calcd, 180.1514.

1-(2,6,6-Trimethyl-cyclohex-1-enyl)-propenone 2a. To a stirred solution of **1** (5.60 g, 31.1 mmol) in pentane (112 mL) was added MnO_2 (39.2 g, 450 mmol). The reaction mixture was stirred under argon at room temperature for 12 h. The resulting mixture was filtered. Removal of the solvent afforded **2a** (4.14 g, 23.3 mmol, 75%) as a yellow oil. IR, ν: 2932, 1657 cm^{-1}. ^1H NMR $CDCl_3$, δ: 1.03 (6H, s), 1.45 (2H, m), 1.51 (3H, s), 1.70 (2H, m), 2.00 (2H, d, $J = 6.4$ Hz), 5.97 (1H, dd, $J_1 = 1.8$, $J_2 = 10$ Hz), 6.12 (1H, dd, $J_1 = 1.8$, $J_2 = 17$ Hz), 6.38 (1H, dd, $J_1 = 10$, $J_2 = 17$ Hz). ^{13}C NMR $CDCl_3$, δ: 18.9, 21.2, 28.7 (2C), 31.2, 33.4, 38.8, 130.0, 131.1, 138.9, 139.7, 202.0. MS EI, *m*/*z* (relative intensity): 178 (M^+, 15), 163 (45), 123 (34), 107 (27), 91 (30), 81 (61). HRMS (EI): 178.1365 (M^+, $C_{12}H_{18}O$); calcd, 178.1358.

Reaction of 2a with 10^{-1}M $HClO_4$/1 M Acetic Anhydride. To **2a** (3.50 g, 19.7 mmol) was added a solution of 10^{-1} M $HClO_4$/1 M Ac_2O in AcOEt (350 mL). The reaction mixture was stirred under argon at room temperature for 20 min. Then, saturated $NaHCO_3$ was added to quench the reaction. The organic layer was separated, and the aqueous phase was extracted with AcOEt. The combined organic extracts were washed with Na_2CO_3 (5%) and brine. Removal of the solvent afforded a crude residue, which was purified by flash chromatography. Eluting with hexane/Et_2O (97/3) furnished 3a,7,7-trimethyl-4,5,6,7-tetrahydro-3a*H*-inden-1-yl acetate **4** (779 mg, 3.54 mmol, 18%) as a yellow oil. IR, ν: 2928, 1759 cm^{-1}. ^1H NMR $CDCl_3$, δ: 1.00−2.00 (6H, m), 1.14 (3H, s), 1.18 (3H, s), 1.25 (3H, s), 2.16 (3H, s), 6.07 (1H, d, $J = 5.5$ Hz), 6.17 (1H, d, $J = 5.5$ Hz). ^{13}C NMR $CDCl_3$, δ: 19.3, 20.9, 21.1, 25.1, 30.6, 35.2, 35.5, 42.9, 51.7, 125.8, 139.7, 141.3, 144.9, 169.0. MS EI, *m*/*z* (relative intensity): 220 (M^+, 9), 178 (33), 163 (100), 135 (21), 109 (46), 91 (42), 77 (27), 55 (24), 43 (95). HRMS (EI): 220.1501 (M^+, $C_{14}H_{20}O_2$); calcd, 220.1463.

Eluting with hexane/Et_2O (95/5) furnished (3aSR,7aSR)-3a,7,7-trimethyl-3a,4,5,6,7,7a-hexahydroinden-1-one **3a** (1.30 g, 7.29 mmol, 37%) as a yellow oil. IR, ν: 2949, 2870, 1703 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.89 (3H, s), 1.15 (6H, s), 1.20−1.70

SCHEME 9[a]



[a] Reaction conditions: (a) $SOCl_2$/pyr, CH_2Cl_2, 0 °C. (b) *m*-CPBA, CH_2Cl_2. (c) CrO_3·DMP, CH_2Cl_2.

(6H, m), 1.75 (1H, s), 5.93 (1H, d, J = 5.6 Hz), 7.33 (1H, d, J = 5.6 Hz). ^{13}C NMR $CDCl_3$, δ: 17.3, 24.9, 28.9, 31.6, 32.7, 33.7, 35.9, 44.5, 61.8, 131.5, 172.0, 211.1. MS EI, *m*/*z* (relative intensity): 178 (M^+, 10), 163 (42), 145 (5), 135 (10), 121 (14), 109 (58), 96 (100), 79 (51), 55 (63), 44 (54). HRMS (EI): 178.1361 (M^+, $C_{18}H_{18}O$); calcd, 178.1358.

Eluting with hexane/Et_2O (90/10) furnished 3-acetyl-3a,7,7-trimethyl-4,5,6,7-tetrahydro-3a*H*-inden-1-yl acetate **5** (1.81 g, 6.89 mmol, 35%) as a yellow solid, mp 55−57 °C. IR Nujol, ν: 2930, 1751, 1657 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.90−1.80 (6H, m), 1.21 (3H, s), 1.27 (3H, s), 1.34 (3H, s), 2.21 (3H, s), 2.29 (3H, s), 7.02 (1H, s). ^{13}C NMR $CDCl_3$, δ: 18.8, 20.9 (2C), 25.5, 26.8, 30.7, 35.1, 35.8, 43.5, 52.5, 138.9, 140.8, 151.7, 152.6, 168.9, 191.9. MS EI, *m*/*z* (relative intensity): 262 (M^+, 2), 220 (12), 177 (11), 151 (26), 91 (10), 77 (7), 43 (100). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.55; H, 8.15.

1-(2,5,5,8a-Tetramethyl-3,4,4a,5,6,7,8,8a-octahydro-naphthalen-1-yl)-prop-2-en-1-ol 7. To a stirred solution of **6** (4.50 g, 20.4 mmol) in MeOH (9 mL) at room temperature under argon was added KOH (2.28 g, 40.8 mmol) in MeOH (6 mL). The reaction mixture was stirred for 15 min. Then, the reaction mixture was concentrated in vacuo to afford a residue, which was dissolved with water and extracted with diethyl ether. The organic layers were washed with brine, dried, and filtered. The solvent was evaporated to afforded β-drimenal **6a** (3.81 g, 17.3 mmol, 85%), as a yellow solid, mp 43−45 °C. IR, ν: 2926, 2866, 1674 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.70−1.80 (8H, m); 0.82 (3H, s), 0.85 (3H, s), 1.14 (3H, s), 1.99 (3H, s), 2.22 (2H, dd, J_1 = 4.2, J_2 = 8.4), 2.51 (1H, ddt, J_{d1} = 1.6, J_t = 3.4, J_{d2} = 13 Hz), 10.0 (1H, s). ^{13}C NMR $CDCl_3$, δ: 18.3, 18.9, 19.1, 20.2, 21.6, 33.3, 33.4, 36.3, 36.5, 37.6, 41.7, 51.6, 143.8, 152.8, 192.4. MS EI, *m*/*z* (relative intensity): 220 (M^+, 38), 205 (29), 191 (75), 95 (100), 55 (75).

To a stirred solution of β-drimenal **6a** (3.10 g, 14.1 mmol) in THF (41 mL) at room temperature under argon was added a 1 M solution of $BrMgCH{=}CH_2$ in THF (14 mL). The reaction mixture was stirred for 5 min. Then, saturated NH_4Cl was added, and the mixture was stirred for 10 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 **7** (3.40 g, 13.7 mmol, 97%) as a yellow oil. IR, ν: 3347, 2942 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.80 (3H, s), 0.80−1.80 (9H, m), 0.85 (3H, s), 0.92 (3H, s), 1.65 (3H, s), 2.00 (3H, m), 4.81 (1H, dt, J_t = 2.0, J_d = 4.3 Hz), 5.01 (1H, dt, J_t = 2.0, J_d = 10 Hz), 5.14 (1H, dt, J_t = 2.0, J_d = 17 Hz), 6.01 (1H, ddd, J_1 = 4.3, J_2 = 10, J_3 = 17 Hz). ^{13}C NMR $CDCl_3$, δ: 18.8, 19.0, 20.1, 20.9, 21.5, 33.2 (2C), 34.8, 36.6, 38.9, 41.1, 52.2, 69.8, 112.6, 132.2, 141.8, 142.1. MS EI, *m*/*z* (relative intensity): 248 (M^+, 4), 233 (4), 230 (11), 215 (14), 191 (35), 121 (54) 91 (59), 55 (100). HRMS (EI): 248.2138 (M^+, $C_{17}H_{28}O$); calcd, 248.2140.

1-(2,5,5,8a-Tetramethyl-3,4,4a,5,6,7,8,8a-octahydro-naphthalen-1-yl)-propenone 8. To a stirred solution of **7** (3.30 g, 13.3 mmol) in pentane was added MnO_2 (23.1 g, 265 mmol). The reaction mixture was stirred under argon at room temperature for 12 h. The mixture was filtered. Removal of the solvent afforded **8** (2.32 g, 9.44 mmol, 71%) as a colorless oil. IR, ν: 2942, 2868, 1651 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.80−1.80 (8H, m), 0.83 (3H, s), 0.89 (3H, s), 1.17 (3H, s), 1.46 (3H, s), 2.10 (3H, m), 5.95 (1H, dd, J_1 = 1.9, J_2 = 10 Hz), 6.07 (1H, dd, J_1 = 1.9, J_2 = 17 Hz), 6.34 (1H, dd, J_1 = 10, J_2 = 17 Hz). ^{13}C NMR $CDCl_3$, δ: 18.6 (2C), 20.7, 20.8, 21.4, 32.0, 33.1 (2C), 37.3, 37.4, 41.7, 50.5, 129.9, 130.4, 139.1, 142.9, 202.1. MS EI, *m*/*z* (relative intensity): 246 (M^+, 75), 231 (38), 191 (100), 109 (79). HRMS (EI): 246.1997 (M^+, $C_{17}H_{26}O_2$); calcd, 246.1984.

Reaction of 8 with 10^{-1} M $HClO_4$/0.5 M Acetic Anhydride. To **8** (2.20 g, 8.94 mmol) was added a solution of 10^{-1} M $HClO_4$/0.5 M Ac_2O in AcOEt (220 mL). The reaction mixture was stirred under argon at 50 °C for 2 h. The mixture was cooled to room temperature, and then an aqueous solution of saturated $NaHCO_3$ was added. The organic layer was separated, and the aqueous phase was extracted with AcOEt. The combined organic extracts were washed with Na_2CO_3 (5%) and brine. Removal of the solvent afforded a crude residue, which was purified by flash chromatography. Eluting with hexane/AcOEt (98/2) furnished 3a,6,6,9a-tetramethyl-3a,4,5,5a,6,7,8,9,-9a,9b-decahydrocyclopenta[a]naphthalen-1-one **9b** (857 mg, 3.48 mmol, 39%) as a colorless solid, mp 79−81 °C. IR, ν: 2947, 2868, 1697 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.75 (3H, s), 0.84 (3H, s), 1.00−1.70 (10H, m), 1.15 (3H, s), 1.24 (3H, s), 1.75 (1H, s), 2.40 (1H, m), 5.92 (1H, d, J = 5.7 Hz), 7.29 (1H, d, J = 5.7 Hz). ^{13}C NMR $CDCl_3$, δ: 18.1, 19.2, 21.4, 24.4, 28.6, 32.5, 33.8, 34.8, 35.8, 39.3, 41.9, 45.7, 45.9, 66.6, 131.6, 172.5, 211.0. MS EI, *m*/*z* (relative intensity): 246 (M^+, 46), 231 (35), 109 (56), 96 (100). Anal. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.91; H, 10.76.

Eluting with hexane/ether (95/5) furnished 3a,6,6,9a-tetramethyl-3a,4,5,5a,6,7,8,9,9a,9b-decahydrocyclopenta[a]naphthalene-1-one **9a** (726 mg, 2.95 mmol, 33%) as a colorless solid, mp (*t*-BuOMe/Hexane) 60−65 °C. IR, ν: 2947, 2868, 1697 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.81 (3H, s), 0.85 (3H, s), 0.89 (3H, s), 1.10−1.60 (10H, m), 1.17 (3H, s), 1.66 (1H, s), 2.43 (1H, m), 5.96 (1H, d, J = 5.6 Hz), 7.37 (1H, d, J = 5.6 Hz). ^{13}C NMR $CDCl_3$, δ: 17.1, 18.3 (2C), 21.1, 28.0, 29.8, 32.8, 33.7, 38.3, 42.3, 43.2, 44.3, 47.8, 67.1, 131.8, 173.0, 211.6. MS EI, *m*/*z* (relative intensity): 246 (M^+, 48), 231 (38), 109 (53), 96 (100). Anal. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 90.01; H, 10.22.

Reaction of 8 with H_3PO_4/HCOOH. Ketone **8** (50 mg, 0.20 mmol) was dissolved in 85% phosphoric acid (0.1 mL) and 90% formic acid (0.1 mL). The mixture was stirred at 90 °C for 4 h under argon. After cooling, the reaction mixture was diluted with Et_2O and water. The organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with aqueous solution of NaOH (2%) and brine. Removal of the solvent afforded a crude residue, which was purified by flash chromatography. Eluting with hexane/AcOEt (98/2) furnished 3a,6,6,9b-tetramethyl-2,3,-3a,4,5,6,7,8,9,9b-decahydrocyclopenta[a]naphthalen-1-one **10** (19 mg, 77 μmol, 38%) as a colorless oil. IR, ν: 2938, 2868, 1738 cm^{-1}. ^{1}H NMR $CDCl_3$, δ: 0.70−2.10 (12H, m), 0.84 (3H, s), 0.96 (3H, s), 0.97 (6H, s), 2.25 (2H, m). ^{13}C NMR $CDCl_3$, δ:

16.1, 19.6, 21.4, 23.5, 26.6, 28.2 (2C), 28.8, 29.8, 33.8, 34.4, 39.6, 40.1, 56.6, 126.7, 136.7, 220.8. MS EI, *m/z* (relative intensity): 246 (M^+, 100), 231 (20), 190 (51), 175 (65), 119 (30), 77 (37). HRMS (EI): 246.1990 (M^+, $C_{17}H_{26}O_2$); calcd, 246.1984.

Eluting with hexane/AcOEt (98/2) furnished 3a,6,6,9a-tetramethyl-3a,4,5,5a,6,7,8,9,9a,9b-decahydrocyclopenta[a]naphthalen-1-one **9a** (12 mg, 4 μmol, 25%).

Reaction of 3a with 9-BBN. To a solution of **3a** (600 mg, 3.37 mmol) in THF (6 mL) was slowly added 9-BBN (411 mg, 6.74 mmol). The reaction mixture was stirred under argon at room temperature for 15 min, and then MeOH was slowly added, stirring for 1 h. Removal of the solvent afforded a crude product, which was purified by flash chromatography. Eluting with hexane/Et_2O (95/5) furnished 3a,7,7-trimethyl-3a,4,5,6,7,-7a-tetrahydro-1*H*-inden-1-ol **11b** (320 mg, 1.78 mmol, 53%) as a colorless oil. IR, ν: 3447, 2940, 2864 cm^{-1}. ^1H NMR $CDCl_3$, δ: 1.07 (3H, s), 1.15−1.30 (2H, m), 1.17 (3H, s), 1.22 (3H, s), 1.29 (1H, d, J = 5.5 Hz), 1.45−1.90 (5H, m), 4.61 (1H, dd, J_1 = 2.7, J_2 = 5.5 Hz), 5.81 (1H, dd, J_1 = 2.7, J_2 = 5.7 Hz), 5.92 (1H, d, J = 5.7 Hz). ^{13}C NMR $CDCl_3$, δ: 19.5, 26.3, 28.8, 31.1, 32.6, 37.5, 39.0, 45.2, 57.8, 79.4, 129.4, 150.7. MS EI, *m/z* (relative intensity): 180 (M^+, 5), 165 (10), 162 (23), 147 (100), 91 (94), 55 (84). HRMS (EI): 180.1522 (M^+, $C_{12}H_{20}O$); calcd, 180.1514. Eluting with hexane/Et_2O (93/7) furnished 3a,7,7-trimethyl-3a,4,5,6,7,7a-tetrahydro-1*H*-inden-1-ol **11a** (279 mg, 1.55 mmol, 46%) as a white solid, mp 58−60 °C. IR $CHCl_3$, ν: 3285, 2926, 2868 cm^{-1}. ^1H NMR, $CDCl_3$, δ: 0.80−1.00 (2H, m), 1.03 (3H, s), 1.07 (3H, s), 1.19 (3H, s), 1.20−1.40 (2H, m), 1.33 (1H, d, J = 7.7 Hz), 1.40−1.60 (2H, m), 1.75 (1H, m), 4.64 (1H, d, J = 7.7 Hz), 5.53 (1H, d, J = 5.7 Hz), 5.64 (1H, d, J = 5.7 Hz). ^{13}C NMR $CDCl_3$, δ: 18.0, 27.7, 30.1, 31.6 (2C), 36.4, 37.1, 46.0, 65.1, 79.4, 130.2, 145.4. MS EI, *m/z* (relative intensity): 180 (M^+, 3), 165 (10), 162 (21), 147 (100), 91 (81), 55 (61). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.66; H, 11.05.

3a,6,6,9a-Tetramethyl-3a,4,5,5a,6,7,8,9,9a,9b-decahydro-1*H*-cyclopenta[a]naphthalen-1-ol 12. To a solution of ketone **9b** (75 mg, 0.30 mmol) in dry ethyl ether (2.7 mL) cooled to 0 °C was added $LiAlH_4$ (75 mg, 0.30 mmol). The reaction mixture was vigorously stirred under argon for 30 min, after which the reaction was quenched with $Na_2SO_4 \cdot 10H_2O$. The resulting mixture was filtered, and then the filtrate was evaporated under reduced pressure to afford a white solid identified as **12** (76 mg, 0.30 mmol, 100%), mp (*t*-BuOMe/hexane) 115−117 °C. IR Nujol, ν: 3320, 2928, 2868 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.80−1.80 (13, m), 0.83 (3H, s), 0.87 (3H, s), 1.11 (3H, s), 1.28 (3H, s), 4.80 (1H, d, J = 7.8 Hz), 5.49 (1H, d, J = 5.7 Hz), 5.64 (1H, d, J = 5.7 Hz) ppm. ^{13}C NMR $CDCl_3$, δ: 18.0, 18.3, 22.0, 23.8, 28.0, 33.0, 33.5, 36.2, 39.6, 40.0, 42.3, 46.1, 49.7, 71.2, 78.7, 129.4, 145.7 ppm. MS EI, *m/z* (relative intensity): 248 (M^+, 10), 233 (7), 215 (9), 191 (8), 152 (25), 97 (100), 69 (23). Anal. Calcd for $C_{17}H_{28}O$: C, 82.20; H, 11.36. Found: C, 82.54; H, 11.13.

3a,7,7-Trimethyl-3-phenyloctahydroinden-1-one 13. Bromobenzene (1.17 mL, 11.2 mmol), zinc bromide (1.26 g, 5.6 mmol), and Li (157 mg, 22.4 mmol) in anhydrous diethyl ether (55 mL) under an argon atmosphere were sonicated in a 250 mL Erlenmeyer flask equipped with a magnetic stirring bar. The mixture turned black almost immediately, and the lithium was totally consumed within 60 min. Sonication was then discontinued, and a mixture of enone **3** (200 mg, 1.2 mmol) and nickel acetylacetonate (14 mg, 56 mmol) in diethyl ether (5.5 mL) was then added and the resulting mixture magnetically stirred for 3 h at room temperature. Then, an aqueous solution of saturated NH_4Cl was added and the heterogeneous mixture stirred for 5 min. The organic layer was separated, and the aqueous phase was extracted with ether. The combined organic extracts were washed with brine. Removal of the solvent afforded a crude residue, which was purified by flash chromatography. Eluting with hexane/Et_2O (96/4) gave the phenyl ketone **13** (212 mg, 0.83 mmol, 74%) as a colorless solid, mp (*t*BuOMe/hexane) 95−97 °C. IR, ν: 2924, 2868, 1730, 775, 735, 702 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.67 (3H, s), 0.90−1.90 (6H, m), 1.05 (3H, s), 1.10 (3H, s), 1.84 (1H, s), 2.52 (1H, dd, J_1 = 9.4, J_2 = 20 Hz), 2.76 (1H, dd, J_1 = 11, J_2 = 20 Hz), 3.66 (1H, dd, J_1 = 9.4, J_2 = 11 Hz), 7.15−7.40 (5H, m). ^{13}C NMR $CDCl_3$, δ: 17.9, 24.0, 26.8, 29.6, 32.8, 33.0, 40.3, 42.0, 42.6, 45.3, 65.7, 126.6, 127.8 (2C), 129.0 (2C), 138.5, 220.1. MS EI, *m/z* (relative intensity): 256 (M^+, 30), 109 (100), 91 (13), 77 (19). HRMS (EI): 256.1795 (M^+, $C_{18}H_{24}O$); calcd, 256.1827. Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.50; H, 9.11.

3-Phenyl-3a,6,6,9a-tetramethyldodecahydrocyclopenta-[a]naphthalen-1-one 14a. Bromobenzene (1.49 mL, 14.2 mmol), zinc bromide (1.60 g, 7.1 mmol), and Li (199 mg, 28.4 mmol) in anhydrous diethyl ether (70 mL) under an argon atmosphere were sonicated in a 250 mL Erlenmeyer flask equipped with a magnetic stirring bar. The mixture turned black almost immediately, and the lithium was totally consumed within 60 min. Sonication was then discontinued, and a mixture of enone **9a** (350 mg, 1.42 mmol) and nickel acetylacetonate (18 mg, 71 μmol) in diethyl ether (7 mL) was then added and the resulting mixture magnetically stirred for 2 h at room temperature. Then, an aqueous solution of saturated NH_4Cl was added and the heterogeneous mixture was stirred for 5 min. The organic layer was separated and the aqueous phase extracted with ether. The combined organic extracts were washed with brine. Removal of the solvent afforded a crude residue, which was purified by flash chromatography. Eluting with hexane/Et_2O (98/2) furnished **14a** (3.87 g, 1.20 mmol, 84%) as a colorless solid, mp (*t*BuOMe/hexane) 118−120 °C. IR, ν: 2926, 2882, 1732, 731, 702 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.68 (3H, s), 0.88 (1H, m), 0.90 (3H, s), 0.92 (3H, s), 1.09 (3H, s), 1.10−1.30 (3H, m), 1.40−1.65 (5H, m), 1.78 (1H, s), 1.90 (1H, dt, J_t = 3.2, J_d = 14 Hz), 2.10 (1H, dd, J_1 = 1.7, J_2 = 13 Hz), 2.48 (1H, dd, J_1 = 9.1, J_2 = 20 Hz), 2.74 (1H, ddd, J_1 = 1.6, J_2 = 11, J_3 = 20 Hz), 3.68 (1H, dd, J_1 = 9.1, J_2 = 11 Hz), 7.15−7.35 (5H, m). ^{13}C NMR $CDCl_3$, δ: 17.0, 18.1 (2C), 22.0, 27.3, 33.3, 33.5, 34.6, 37.5, 41.4, 41.7, 42.5, 42.9, 46.1, 53.8, 71.7, 126.7, 127.9 (2C), 129.2 (2C), 138.4, 220.7. MS EI, *m/z* (relative intensity): 324 (M^+, 44), 309 (5), 173 (95), 123 (32), 104 (100). HRMS (EI): 324.2487 (M^+, $C_{23}H_{32}O$); calcd, 324.2453. Anal. Calcd for $C_{23}H_{32}O$: C, 85.13; H, 9.94. Found: C, 85.23; H, 10.13.

3-Phenyl-3a,6,6,9a-tetramethyldodecahydrocyclopenta-[a]naphthalen-1-one 14b. Bromobenzene (0.43 mL, 4.1 mmol), zinc bromide (450 mg, 2 mmol), and Li (57 mg, 8.2 mmol) in anhydrous diethyl ether (4 mL) under an argon atmosphere were sonicated in a 250 mL Erlenmeyer flask equipped with a magnetic stirring bar. The mixture turned black almost immediately, and the lithium was totally consumed within 60 min. Sonication was then discontinued, and a mixture of enone **9b** (100 mg, 0.41 mmol) and nickel acetylacetonate (5 mg, 0.02 μmol) in diethyl ether (4 mL) was then added and the resulting mixture magnetically stirred for 2 h at room temperature. Then, an aqueous solution of saturated NH_4Cl was added, and the heterogeneous mixture was stirred for 5 min. The organic layer was separated and the aqueous phase extracted with ether. The combined organic extracts were washed with brine. Removal of the solvent afforded a crude residue, which was purified by flash chromatography. Eluting with hexane/Et_2O (80/20) furnished **14b** (107 mg, 0.33 mmol, 80%) as a white solid, mp 132−134 °C. IR, ν: 2922, 2870, 1726, 756, 702 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.80 (3H, s), 0.86 (3H, s), 0.92 (3H, s), 1.01 (3H, s), 1.07 (1H, m), 1.15−1.75 (9H, m), 1.94 (1H, s), 2.48 (1H, d, J = 19 Hz), 2.81 (1H, d, J = 10 Hz), 2.90 (1H, m), 2.95 (1H, dd, J_1 = 10, J_2 = 19 Hz), 7.05−7.15 (2H, m), 7.20−7.35 (3H, m). ^{13}C NMR $CDCl_3$, δ: 18.1, 19.6, 21.6, 23.2, 26.8, 32.9, 33.2, 34.5, 38.0, 39.2, 42.0, 44.7, 45.2, 49.6, 50.0, 64.1, 126.4, 128.1 (2C), 128.4 (2C), 143.6, 220.2. MS EI, *m/z* (relative intensity): 324 (M^+, 3), 230 (14), 153 (43), 89 (55), 77 (100). HRMS (EI): 324.2429 (M^+, $C_{23}H_{32}O$); calcd, 324.2453. Anal. Calcd for $C_{23}H_{32}O$: C, 85.13; H, 9.94. Found: C, 85.54; H, 9.87.

Reaction of 13 with $LiAlH_4$. Lithium aluminum hydride (4 mg, 0.098 mmol) was added to a solution of **13** (50 mg, 0.19 mmol) in dry diethyl ether (2 mL) cooled to 0 °C. The mixture was vigorously stirred under argon for 15 min, after which the reaction was quenched with $Na_2SO_4 \cdot 10H_2O$. The resulting mixture was filtered, and the filtrate was concentrated under reduced pressure to afford a crude residue, which was purified by flash chromatography. Eluting with hexane/AcOEt (93/7) furnished 3a,7,7-trimethyl-3-phenyloctahydroinden-1-ol **15a** (39 mg, 0.15 mmol, 77%) as a colorless oil. IR, ν: 3482, 2938, 1454 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.61 (3H, s), 1.04 (3H, s), 1.20 (3H, s), 1.20−2.20 (9H, m), 3.35 (1H, dd, $J_1 = 7.7$, $J_2 = 12.0$ Hz), 4.51 (1H, t, $J = 3.7$ Hz), 7.12−7.33 (5H, m). ^{13}C NMR $CDCl_3$, δ: 19.3, 27.2, 30.6, 31.7, 32.2, 37.6, 39.9, 41.2, 42.0, 56.5, 59.7, 75.8, 125.8, 127.7 (2C), 128.7 (2C), 143.0. MS EI, *m*/*z* (relative intensity): 258 (M^+, 10), 134 (100), 109 (78), 92 (93), 69 (33). HRMS (EI): 258.1954 (M^+, $C_{18}H_{26}O$); calcd, 258.1984. Eluting with hexane/AcOEt (96/4) furnished 3a,7,7-trimethyl-3-phenyloctahydroinden-1-ol **15b** (7.5 mg, 29 μmol, 15%) as a colorless oil. IR, ν: 3418, 2928, 1495, 1456 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.72 (3H, s), 1.00 (3H, s), 1.06 (3H, s), 1.20−2.00 (9H, m), 2.70 (1H, m), 4.45 (1H, m), 7.17−7.33 (5H, m). ^{13}C NMR $CDCl_3$, δ: 18.7, 26.0, 29.6, 29.8, 31.8, 35.7, 35.9, 39.5, 45.4, 55.9, 61.9, 75.1, 125.7, 127.6 (2C), 129.1 (2C), 144.2. MS EI, *m*/*z* (relative intensity): 258 (M^+, 13), 134 (69), 124 (100), 109 (72), 92 (71), 69 (40). HRMS (EI): 258.1986 (M^+, $C_{18}H_{26}O$); calcd, 258.1984.

Reaction of 13 with 9-BBN. To a solution of **13** (25 mg, 0.098 mmol) in THF (0.5 mL) was slowly added 9-BBN (23.9 mg, 0.196 mmol). The reaction mixture was stirred under argon at room temperature for 20 min, and then MeOH was slowly added, stirring for 1 h. Removal of the solvent afforded a crude product, which was purified by flash chromatography. Eluting with hexane/AcOEt (96/4) furnished 3a,7,7-trimethyl-3-phenyloctahydroinden-1-ol **15a** (24 mg, 93 μmol, 95%).

Reaction of 14a with $LiAlH_4$. Lithium aluminum hydride (5 mg, 0.1 mmol) was added to a solution of **14a** (80 mg, 0.25 mmol) in dry diethyl ether (2.7 mL) cooled to 0 °C. The mixture was vigorously stirred under argon for 30 min, after which the reaction was quenched with $Na_2SO_4 \cdot 10H_2O$. The resulting mixture was filtered, and the filtrate was concentrated under reduced pressure to afford a crude residue, which was purified by flash chromatography. Eluting with hexane/AcOEt (96/4) furnished 3-phenyl-3a,6,6,9a-tetramethyldodecahydrocyclopenta-[a]naphthalen-1-ol **16a** (55 mg, 0.17 mmol, 69%) as a colorless oil. IR, ν: 3428, 2932, 2872, 1458, 733, 708 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.63 (3H, s), 0.88 (3H, s), 0.92 (1H, m), 0.95 (3H, s), 1.00−1.80 (10H, m), 1.36 (3H, s), 1.50 (1H, d, $J = 7.0$ Hz), 2.02 (1H, m), 2.25 (1H, m), 2.50 (1H, ddd, $J_1 = 8.5$, $J_2 = 10$, $J_3 = 14$ Hz), 3.43 (1H, t, $J = 10$ Hz), 4.90 (1H, ddd, $J_1 = 5.3$, $J_2 = 7.0$, $J_3 = 8.5$ Hz), 7.15−7.35 (5H, m). ^{13}C NMR $CDCl_3$, δ: 17.8, 18.4, 18.5, 21.9, 28.0, 33.4, 33.6, 34.9, 38.0, 39.0, 42.1, 43.3, 45.0, 50.2, 53.0, 65.6, 74.8, 126.0, 127.6 (2C), 129.0 (2C), 141.0. MS EI, *m*/*z* (relative intensity): 326 (M^+, 35), 308 (29), 293 (21), 221 (87), 192 (71), 69 (96), 55 (100). HRMS (EI): 326.2589 (M^+, $C_{23}H_{34}O$); calcd, 326.2610.

Eluting with hexane/AcOEt (96/4) furnished 3-phenyl-3a,6,6,9a-tetramethyldodecahydrocyclopenta[a]naphthalen-1-ol **16b** (23 mg, 0.07 mmol, 29%) as a colorless oil. IR, ν: 3339, 2932, 2870, 1458, 733, 700 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.74 (3H, s), 0.80−1.70 (12H, m), 0.84 (3H, s), 0.92 (3H, s), 1.01 (3H, s), 2.20 (2H, m), 2.81 (1H, dd, $J_1 = 7.5$, $J_2 = 12$ Hz), 4.31 (1H, dt, $J_d = 5.3$, $J_t = 7.4$ Hz), 7.10−7.40 (5H, m). ^{13}C NMR $CDCl_3$, δ: 17.4, 18.4 (2C), 21.3, 27.6, 32.8, 33.4, 33.7, 36.7, 38.5, 42.2, 42.6, 43.4, 50.1, 53.6, 70.4, 73.2, 126.1, 127.6 (2C), 128.6 (2C), 140.3. MS EI, *m*/*z* (relative intensity): 326 (M^+, 25), 308 (13), 293 (9), 222 (24), 194 (43), 134 (65), 69 (100), 55 (69). HRMS (EI): 326.2637 (M^+, $C_{23}H_{34}O$); calcd, 326.2610.

Reaction of 14a with 9-BBN. To a solution of **14a** (200 mg, 0.62 mmol) in THF (1.5 mL) was slowly added 9-BBN (151 mg, 1.24 mmol). The reaction mixture was stirred under argon at room temperature for 20 min, and then MeOH was slowly added, stirring for 1 h. Removal of the solvent afforded a crude product, which was purified by flash chromatography. Eluting with hexane/AcOEt (96/4) furnished 3-phenyl-3a,6,6,9a-tetramethyldodecahydrocyclopenta[a]naphthalen-1-ol **16a** (172 mg, 0.53 mmol, 85%).

4,4,7a-Trimethyl-1-phenyl-2,4,5,6,7,7a-hexahydro-1*H*-indene 17. To a solution of **15a** (20 mg, 0.078 mmol) in CH_2Cl_2 (0.2 mL) at 0 °C under argon were gradually added pyridine (0.1 mL, 0.03 mmol) and a solution of $SOCl_2$ (0.012 mL, 0.16 mmol) in CH_2Cl_2 (0.12 mL). The reaction mixture was stirred at room temperature 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 **17** (16 mg, 0.066 mmol, 86%) as a colorless oil. IR, ν: 2924, 1460 cm^{-1}. ^1H NMR $CDCl_3$ δ: 0.69 (3H, s), 1.10 (3H, s), 1.15 (3H, s), 1.20−1.85 (6H, m), 2.34 (1H, m), 2.69 (1H, m), 3.08 (1H, dd, $J_1 = 7.5$, $J_2 = 11.4$ Hz), 5.50 (1H, br s), 7.19−7.29 (5H, m). ^{13}C NMR $CDCl_3$, δ: 19.2, 19.9, 28.6, 31.1, 33.0, 34.1, 40.7, 40.8, 48.1, 60.5, 118.8, 126.0, 127.7 (2C), 128.7 (2C), 141.3, 157.4. MS EI, *m*/*z* (relative intensity): 240 (M^+, 30), 225 (31), 169 (17), 105 (28), 91 (100). HRMS (EI): 240.1857 (M^+, $C_{18}H_{24}$); calcd, 240.1878

3a,7,7-Trimethyl-3-phenyloctahydro-1-oxacyclopropa-[c]indene 18. To a stirred solution of **17** (8 mg, 0.033 mmol) in CH_2Cl_2 (0.3 mL) was added *m*-CPBA (5.7 mg, 0.033 mmol). The reaction mixture was stirred under argon at room temperature for 20 min. Then, Na_2SO_3 (5%) was added and the resulting heterogeneous mixture was vigorously stirred. 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. Eluting with hexane/Et_2O (99/1) furnished **18** (8 mg, 31 μmol, 93%) as a white solid, mp 74−77 °C. IR $CHCl_3$, ν: 2980, 2890, 1495 cm^{-1}. ^1H NMR $CDCl_3$, δ: 0.65 (3H, s), 0.85 (3H, s), 1.17 (3H, s), 1.40−2.15 (8H, m), 2.86 (1H, dd, $J_1 = 7.9$, $J_2 = 11.3$ Hz), 3.58 (1H, s), 7.07−7.29 (5H, m). ^{13}C NMR $CDCl_3$, δ: 17.5, 19.1, 25.6, 27.7, 29.4, 33.7, 34.2, 38.2, 43.0, 49.1, 57.5, 73.3, 126.0, 127.8 (2C), 129.1 (2C), 139.8. MS EI, *m*/*z* (relative intensity): 256 (M^+, 34), 223 (11), 123 (93), 117 (100), 81 (41). Anal. Calcd for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.29; H, 9.58.

4,4,7a-Trimethyl-1-phenyl-1,4,5,6,7,7a-hexahydroinden-2-one 19. To a stirred suspension of CrO_3 (60 mg, 0.4 mmol) in CH_2Cl_2 (1.1 mL) at −25 °C was added 3,5-dimethylpyrazole (38.4 mg, 0.4 mmol); after 1 h, a solution of **17** (8 mg, 0.033 mmol) in CH_2Cl_2 (0.1 mL) was added. The mixture was stirred at −10 °C for 20 min; then, the mixture was warmed to 0 °C, and a solution of 5 M NaOH was added. The resulting heterogeneous mixture was stirred for 1 h, after which it was diluted with CH_2Cl_2. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with 0.5 M HCl, H_2O, and brine. Removal of the solvent afforded a crude product, which was purified by flash chromatography. Eluting with hexane/Et_2O (9/1) furnished **19** (6 mg, 0.023 mmol, 72%) as a colorless solid, mp (*t*-BuOMe/hexane) 79−81 °C. IR, ν: 2930, 2868, 1699, 1599,1456 cm^{-1}. ^1H NMR $CDCl_3$ δ: 0.88 (3H, s), 1.25 (3H, s), 1.27 (3H, s), 1.30−2.05 (6H, m), 3.55 (1H, s), 6.02 (1H, s), 7.07−7.32 (5H, m). ^{13}C NMR $CDCl_3$, δ: 18.6, 24.9, 27.2, 31.2, 36.1, 39.7, 40.8, 48.8, 68.7, 125.7, 126.9, 128.2 (2C), 130.2 (2C), 136.2, 191.9, 207.1. MS EI, *m*/*z* (relative intensity): 254 (M^+, 100), 239 (70), 185 (37), 115 (38), 91 (66), 77 (39), 55 (33). HRMS (EI) 254.1685 (M^+, $C_{18}H_{22}O$); calcd, 254.1670. Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 85.10; H, 8.61.

3a,6,6,9a-Tetramethyl-3-phenyl-3,3a,4,5,5a,6,7,8,9,9a-decahydro-2*H*-cyclopenta[a]naphthalene 20. To a solution of **16a** (172 mg, 0.53 mmol) in CH_2Cl_2 (6.4 mL) at 0 °C under argon were gradually added pyridine (0.17 mL, 2.12 mmol) and a solution of $SOCl_2$ (78 μL, 1.1 mmol) in CH_2Cl_2 (0.8 mL). The reaction mixture as stirred at 0 °C for 3 h 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 **20** (117 mg, 0.38 mmol, 72%) as a colorless oil. IR, *ν*: 2932, 2868, 760, 733, 700 cm^{-1}. ^1H NMR $CDCl_3$, *δ*: 0.73 (3H, s), 0.83 (3H, s), 0.90−1.80 (10H, m), 0.92 (3H, s), 1.12 (3H, s), 1.95 (1H, m), 2.27 (1H, ddd, J_1 = 3.5, J_2 = 6.8, J_3 = 15 Hz), 2.79 (1H, ddd, J_1 = 1.5, J_2 = 11, J_3 = 15 Hz), 3.02 (1H, dd, J_1 = 6.8, J_2 = 11 Hz), 5.43 (1H, dd, J_1 = 1.5, J_2 = 3.5 Hz), 7.20−7.40 (5H, m). ^{13}C NMR $CDCl_3$, *δ*: 17.7, 19.3, 20.5, 21.4, 26.2, 32.2, 33.2, 33.3, 33.4, 37.6, 40.0, 42.5, 44.4, 47.7, 61.4, 117.2, 126.0, 127.7 (2C), 128.8 (2C), 141.2, 164.7. MS EI, *m*/*z* (relative intensity): 308 (M^+, 49), 293 (53), 205 (31), 170 (47), 91 (100), 69 (41). MSHR (EI): 308.2527 (M^+, $C_{23}H_{32}$); calcd, 308.2504.

2a,5,5,8a-Tetramethyl-2-phenyldodecahydro-9-oxacyclopropa[1,5]cyclopenta[1,2-a]naphthalene 21. To a stirred solution of **20** (40 mg, 0.13 mmol) in CH_2Cl_2 (0.8 mL) was added *m*-CPBA (24 mg, 0.14 mmol). The reaction mixture was stirred under argon at room temperature for 2 h. Then $Na_2S_2O_3$ (5%) was added, and the resulting heterogeneous mixture was vigorously stirred. 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. Eluting with hexane/Et_2O (99/1) furnished **21** (29 mg, 90 *μ*mol, 70%) as a colorless oil. IR $CHCl_3$, *ν*: 2940, 2870, 2454, 758, 702 cm^{-1}. ^1H NMR $CDCl_3$, *δ*: 0.60 (3H, s), 0.80−1.80 (11H, m), 0.83 (3H, s), 0.93 (3H, s), 1.19 (3H, s), 2.11 (2H, dd, J_1 = 2.0, J_2 = 10 Hz), 3.27 (1H, t, J = 10 Hz), 3.36 (1H, t, J = 2.0 Hz), 7.10−7.35 (5H, m). ^{13}C NMR $CDCl_3$, *δ*: 17.8, 17.9, 18.5, 21.4, 22.7, 32.3, 32.8, 32.9, 33.8 (2C), 36.2, 42.0, 44.3, 44.5, 61.1, 63.7, 81.3, 126.3, 127.7 (2C), 128.5 (2C), 139.8. MS EI, *m*/*z* (relative intensity): 324 (M^+, 25), 309 (40), 191 (100), 117 (95), 91 (55), 69 (42). HRMS (EI): 324.2434 (M^+, $C_{23}H_{32}O$); calcd, 324.2453.

3a,6,6,9a-Tetramethyl-3-phenyl-3,3a,4,5,5a,6,7,8,9,9a-decahydrocyclopenta[a]naphthalen-2-one 22. To a stirred suspension of CrO_3 (192 mg, 1.92 mmol) in CH_2Cl_2 (3.3 mL) at −25 °C was added DMP (184 mg, 1.92 mmol); after 1 h, a solution of **20** (50 mg, 0.16 mmol) in CH_2Cl_2 (0.3 mL) was added. The mixture was stirred at −10 °C for 30 min; then, the mixture was warmed to 0 °C, and a solution of 5 M NaOH was added. The resulting heterogeneous mixture was stirred for 1 h, after which it was diluted with CH_2Cl_2. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were washed with 0.5 M HCl, H_2O, and brine. Removal of the solvent afforded a crude product, which was purified by flash chromatography. Eluting with hexane/Et_2O (9/1) furnished **22** (36 mg, 0.11 mmol, 69%) as a colorless solid, mp (*t*-BuOMe/hexane) 147−150 °C. IR, *ν*: 2922, 2866, 1696, 752, 708 cm^{-1}. ^1H NMR $CDCl_3$, *δ*: 0.88 (3H, s), 0.94 (3H, s), 0.97 (3H, s), 1.20−2.10 (11H, m), 1.24 (3H, s), 3.54 (1H, s), 5.98 (1H, s), 7.10−7.40 (5H, m) ppm. ^{13}C NMR $CDCl_3$, *δ*: 17.0, 18.8, 21.2, 25.2, 26.8, 30.2, 33.0, 33.6, 38.3, 39.7, 41.9, 43.8, 49.1, 69.6, 123.6, 126.9, 128.1 (2C), 130.3 (2C), 135.7, 197.9, 206.9 ppm. MS EI, *m*/*z* (relative intensity): 322 (M^+, 100), 307 (31), 184 (72), 91 (41), 77(39). HRMS (EI) 322.2325 (M^+, $C_{23}H_{30}O$); calcd, 322.2297. Anal. Calcd for $C_{23}H_{30}O$: C, 85.66; H, 9.38. Found: C, 85.82; H, 9.19.

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 and the Junta de Castilla y León for the fellowship to L.M.B.

Supporting Information Available: ^1H and ^{13}C spectra for compounds **1**, **2a**, **3a**, **4**, **5**, **7**, **8**, **9a**, **11a**,**b**, **12**, **13**, **14a**,**b**, **15a**,**b**, **16a**,**b**, and **17**−**22**; H−C correlations for compounds **9a**,**b**, **14a**,**b**, and **18**−**22**; and X-ray crystallographic data for compounds **13** and **22**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0205311