Synthesis of Active Antifeedant CDE Fragments of 11-Ketoepoxyazadiradione Based on an Electrocyclization Reaction Catalyzed by Perchloric Acid

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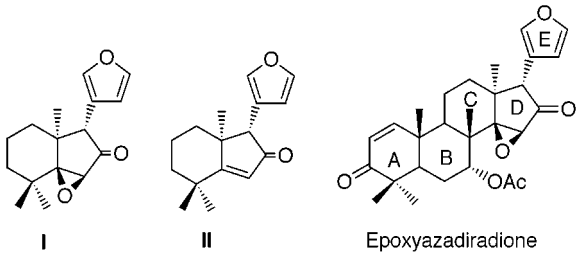
Received July 23, 1998

A synthetic route to mimics of the insect antifeedant epoxyazadiradione containing the CDE molecular fragment with an oxygenated function on ring C has been developed. The key step is based on a 2,6-diene-1,5-dione electrocyclization reaction catalyzed by perchloric acid. The rearrangement of the epoxy alcohol epimers **12** and **19** induced by acids deserves special mention. Several of the compounds obtained show significant antifeedant activity against *Spodoptera frugiperda*.

Introduction

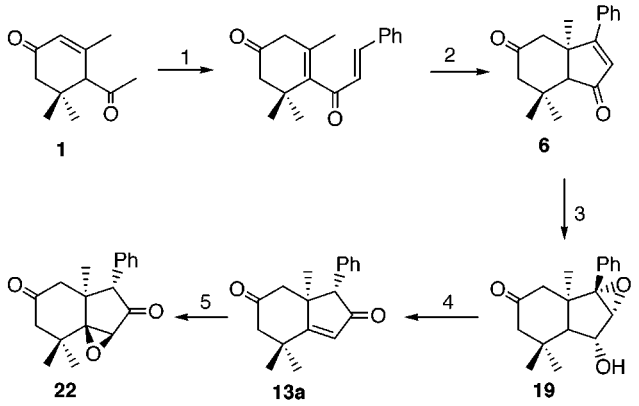
The epoxy ketone **I**, a structural fragment of the naturally occurring limonoid epoxyazadiradione, has been shown to be a potent antifeedant at low concentrations and also to have anti-AIDS properties.[1] Over the past few years, studies have been carried out in our laboratories on the synthesis of azadiradione fragments and analogues with a view to finding simple compounds that display biological activity related to that shown by epoxy ketone **I**.[2] To increase the water solubility and



I II Epoxyazadiradione

lower the volatility of compounds related to epoxy ketone **I**, it would be of interest to introduce oxygenated functions in the structure of limonoids. A further modification, replacement of the furan by a phenyl ring, has been introduced to simplify chemical manipulation, owing to the extreme sensitivity of the former to many reagents. All these changes are directed to SAR studies.

Scheme 1



Results and Discussion

The strategy we have developed for the synthesis of model compounds is depicted in Scheme 1. The key step in the synthesis is cationic electrocyclization, which is shown idealized in the second general step.

The starting material **1** was obtained from mesityl oxide and acetylacetone[3] by a Robinson-type annelation catalyzed by boron trifluoride etherate in 50% yield (Scheme 2). Conversion of the diketone **1** into the key intermediate **4** was achieved in a three-step sequence. Thus, selective reduction of the diketone **1** with $NaBH_4$·$CeCl_3$ at −40 °C furnished the hydroxy ketone **2**, which on subsequent aldolic condensation with benzaldehyde[4] followed by Jones oxidation of the intermediate hydroxy ketone **3** gave the diketone **4** in 81% overall yield from **1**. The first step in this sequence was done to avoid double condensation with benzaldehyde. It is noteworthy that the reduction is chemoselective for the conjugated carbonyl, which shows the high neopentylic character of the carbonyl side chain.

With the diketone **4** in hand, the stage was set for a study of the cationic electrocyclization key step.[5] The

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(3) Rubinstein, M. *J. Org. Chem.* **1962**, *27*, 3886.

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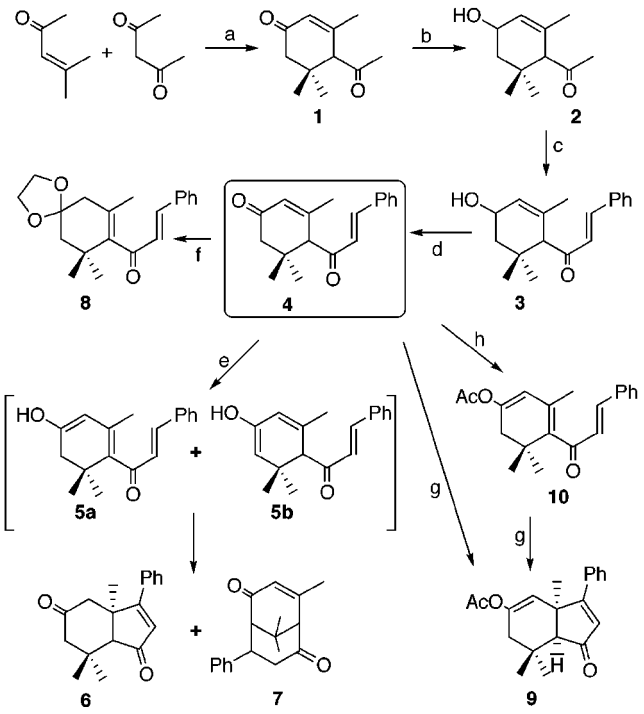
10.1021/jo981456q CCC: $15.00
Published on Web 11/20/1998

Scheme 2



(a) $BF_3.Et_2O$, 5°C; (b) $NaBH_4$, $CeCl_3.7H_2O$, MeOH, -40°C; (c) PhCHO, NaOH, EtOH, -20°C; (d) Jones, CH_3COCH_3, 0°C; (e) H_3PO_4-H_2SO_4, 100°C; (f) $(CH_2OH)_2$, TsOH, benzene, reflux; (g) $HClO_4$ 10^{-2} M, Ac_2O, AcOEt, r.t.; (h) i) NaH, N,N′-dimethylpropyleneurea, THF, 20°C; ii) Ac_2O.

diketone **4** is not purely a Nazarov substrate, although its enolic tautomer **5a** has the necessary requisites to afford the electrocyclization. However, the enolization of **4** would give two enolic forms, **5a** and **5b**, which could follow different reactivity pathways. To our knowledge, this type of compound, a dienedione that is not fully conjugated, has never been studied as an electrocyclization substrate. Accordingly, if indeed the reaction occurs, its behavior and kinetics are not known. We aimed at finding a general method for the electrocyclization of this type of compound.

The first treatment was carried out directly on diketone **4** with a mixture of phosphoric and sulfuric acids at ratios from 1:1 to 9:1. The reaction does not occur below 100 °C and needs 16 h for completion. The reaction afforded a 3:1 mixture of two bicyclic products, **6** and **7**, in 80% yield.[6] As expected, the major product **6** (60%) comes from electrocyclization of the fully conjugated ketoenol **5a**; formally, this reaction resembles an intramolecular Michael addition of a benzylvinyl anion to the cyclohexenone on **4**. On the other hand, the isomeric minor product **7** (20%) results from a true intramolecular Michael addition of the not-fully conjugated ketoenol **5b**. To avoid formation of the Michael addition product and with the aim of accelerating the Nazarov cyclization, we prepared compound **8**. Unfortunately, treatment of compound **8** with the mixture of phosphoric and sulfuric acids at room temperature afforded only the dienedione **4**. Cleavage of the ketal is faster than the electrocyclization reaction.

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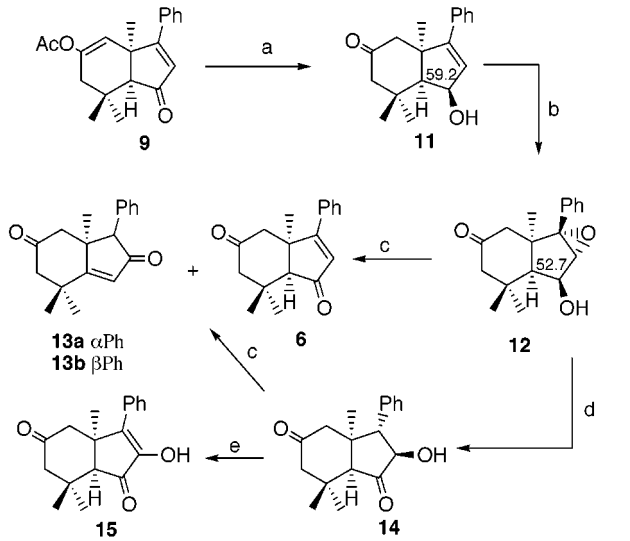
(6) All compounds synthesized are racemic modifications, although only one enantiomer is depicted.

Scheme 3



(a) $NaBH_4$, $CeCl_3.7H_2O$, MeOH, 0°C; (b) m-CPBA, CH_2Cl_2, r.t.; (c) TsOH, toluene, reflux; (d) BF_3 Et_2O, CH_2Cl_2, r.t.; (e) TsOH, Toluene, O_2, reflux

The conditions used for the cyclization of diketone **4** are too drastic for application to the furyl analogue, which prompted us to look for a more general and milder procedure. To avoid high temperatures and long reaction times, we decided to introduce a stronger acid than that usually employed in Nazarov cyclization, such as perchloric acid. This very strong protonic acid has never been used in this type of reaction. We found that a dilute solution of perchloric acid in a mixture of acetic anhydride and ethyl acetate, used to obtain enol acetates from ketones,[7] promotes the Nazarov cyclization of the diketone **4** at room temperature. The reaction of the diketone **4** with a 10^{-3} M solution of perchloric acid was very slow: after 24 h, less than 10% of conversion had occurred. Besides the starting material, we obtained a mixture of ketoester **9** and diketone **7**. After 24 h, the 10^{-2} M solution of perchloric acid afforded a 65:35 mixture of ketoester **9** and diketone **7** in 85% yield at room temperature. It is interesting that the enol acetate **10** is not found among the reaction products. This was interpreted by assuming it to be a transient intermediate, and this hypothesis later proved to be correct.

The enol acetate **10** was obtained in 87% yield by treatment of diketone **4** with sodium hydride in THF and *N*,*N*′-dimethylpropyleneurea at room temperature, followed by acetic anhydride.[8] The reaction of enol acetate **10** with a 10^{-2} M perchloric acid solution was instantaneous, giving the ketoester **9** quantitatively. This cyclization procedure is sufficiently mild to be applied to a large family of enol acetate analogues by changing the nature of the phenyl substituent.

The third step in the synthesis (Scheme 3) was achieved from ketoester **9** by reduction with sodium borohydride to give the hydroxy ketone **11**, followed by epoxidation with *m*-chloroperoxybenzoic acid to afford **12**. Both reactions were absolutely stereoselective, with the reagent attacking from the exocyclic face. The proposed structure and stereochemistry of compound **11** were assigned with the aid of NOE studies.[9] The α configu-

(7) Edwards, B. E., Rao, P. N. *J. Org. Chem.* **1966**, *31*, 324.

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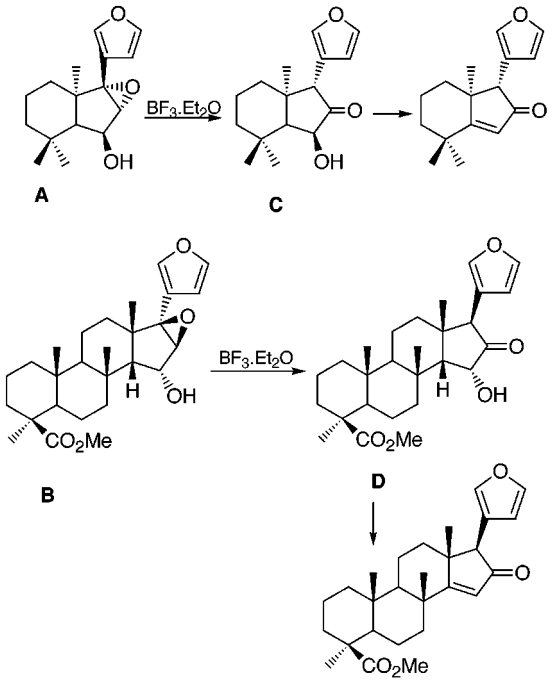


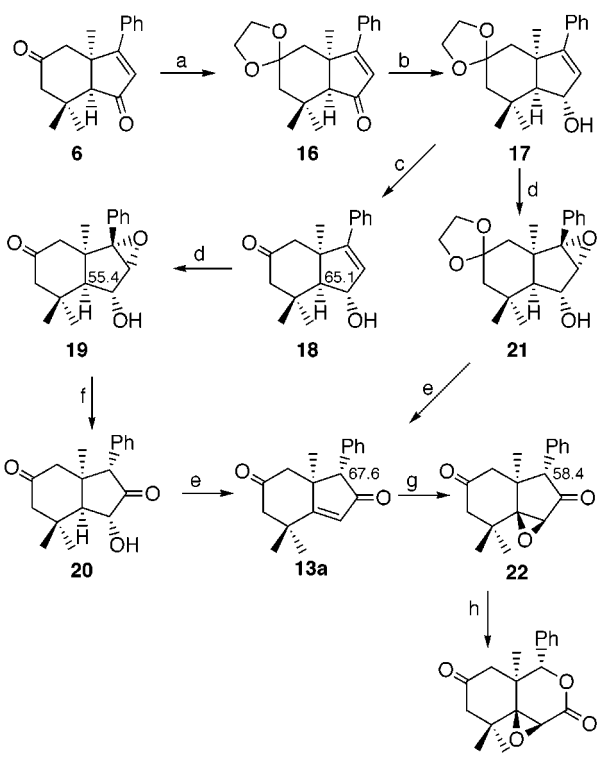
Figure 1.

ration assigned to the oxyranic oxygen in epoxide **12** is consistent with the upfield shift in the ^{13}C NMR signal for the homoallylic carbon bearing an axial proton cis to the oxygenated function (52.7 ppm for epoxide **12**) as compared with the unsaturated precursor **11** (59.2 ppm).[1a]

Rearrangement of epoxy alcohol **12** to the enone, the fourth step of the synthesis (Scheme 1), was carried out as described in a previous work[10] in two ways: directly, by treatment with TsOH, or in two steps with $BF_3 \cdot Et_2O$ and then TsOH. Treatment of epoxy alcohol **12** with TsOH in toluene under reflux afforded a mixture of diketone **6** (70%) and an epimeric mixture of the desired ketones **13a** and **13b** (14%). This contrasts with our previous findings for the deoxoanalogue **A**[2c] and the pentacyclic related epoxy alcohol **B**,[10] in which the orientation of the hydroxyl group is trans with respect to the angular methyl group and the oxyranic oxygen is arranged exactly as in **12**. The same contrast in reactivity occurred in the reaction with BF_3; whereas **12** afforded exclusively the hydroxy ketone **14** with the hydroxyl group in the α position with respect to the phenyl ring, the two epoxy ketones **A** and **B** gave the hydroxy ketones **C** and **D**, respectively, with the hydroxyl group in the β position with respect to the furyl ring (Figure 1). Another interesting feature of the rearrangement of **12** was the need to rigorously exclude oxygen from the reaction. When the solution was not degassed previously, the only product obtained was the triketone **15**.

Although no reasons were found to explain the different behaviors of **12**, **A**, and **B**, we decided to explore the rearrangement of an isomer of **12** with the opposite configuration of the hydroxylic carbon. To solve this, an alternative route was envisaged. Fortunately, it was found that after reduction of the monoketal **16**, further

Scheme 4



(a) $(CH_2OH)_2$,TsOH, benzene; (b) $LiAlH_4$, ether, 0°C; (c) PPTS, acetone, H_2O, r.t.; (d) m-CPBA, CH_2Cl_2, 20°C; (e)TsOH, toluene, reflux; (f)BF_3 .Et_2O, CH_2Cl_2, 20°C; (g) H_2O_2, NaOH, MeOH, 0°C; (h) H_2O_2, NaOH, MeOH, 20°C.

deprotection afforded the hydroxy ketone **18**, which is an epimer[11] of the unsaturated alcohol **11** (Scheme 4). The endoselective reduction of **16** must be governed by coordination of the reagent to the acetal oxygen. Epoxidation of the hydroxy ketone **18** with *m*-chloroperoxybenzoic acid is stereoselective and proceeds exclusively from the exocyclic face.[1a] Treatment of the epoxyalcohol **19** with boron trifluoride etherate in methylene dichloride at room temperature afforded the hydroxy ketone **20** as a single isomer.[12] It is relevant at this stage to comment on the remarkable stereoselectivity of the rearrangement of the epoxy alcohol epimers **12** and **19**, which could be atributed to the influence of the carbonyl group on the cyclohexane ring.

Dehydration of the hydroxy ketone **20** was achieved by treatment with TsOH in degassed toluene under reflux. The reaction furnished a 2:1 epimeric mixture in 80% yield of the unsaturated diketones **13a** and **13b**, respectively, which were separated by chromatography. When the single isomer **13b** was treated separately with TsOH, equilibration took place to afford a 2:1 epimeric mixture of **13a** and **13b**, respectively. The major isomer **13a** was identified as a CDE structural fragment of 11-ketoazadiradione. The assignment is based on the displacement of the methyl angular signal, shielded by the vicinal phenyl group in the ^1H NMR spectrum.[13]

An alternative and shorter route to **13a** was achieved from the hydroxy ketal **17** in two steps: epoxidation with

(9) The stereochemistry was assigned according to differential NOE experiments. Irradiation of H_1 resulted in an NOE enhancement of 24% at H_{7a}, indicating a cis orientation of H_1 and H_{7a}.

(10) Fernández-Mateos, A.; López Barba, A.; Martín de la Nava, E.; Pascual Coca, G.; Peréz Alonso, J. J.; Ramos Silvo, A. I.; Rubio González, R. *Tetrahedron* **1997**, *53*, 14131.

(11) The stereochemistry was assigned according to diffential NOE experiments. Irradiation of H_1 resulted in a NOE enhancements of 9% and 7% at equatorial methyl group at C-7 and H_6 axial, respectively.

(12) The ^1H and ^{13}C spectra of compounds **11**−**13a**,**b** and **18**, **19**, **22**, and **23** were assigned with the aid of $^1H-^{13}C$ correlation experiments and were found to be in complete agreement with the proposed structures and stereochemistries.

Table 1. Effects of Synthesized Compounds 4, 6, 7, 9, 13a, 13b, 15, and 22; I (±), I (+), and I (−); Unsaturated Ketone II, Azadiradione, and Epoxyazadiradione on the Feeding Behaviour of Larvae of *Spodoptera littoralis* and *Spodoptera frugiperda*

	antifeedant index at 100 ppm[a]		
compound	*Spodoptera littoralis*	compound	*Spodoptera frugiperda*
azadiradione	1	**4** (±)	10
epoxyazadiradione	22	**6** (±)	16
I (±)	28	**7** (±)	45[b]
I (+)	55[b]	**9** (±)	5
I (−)	32	**13a** (±)	4
II (±)	16	**13b** (±)	16
		15 (±)	35[b]
		22 (±)	23

[a] Antifeedant index = $[(C - T)/(C + T)]\%$. [b] Significant activity $p < 0.05$ (Wilcoxon matched pairs test, $n = 10$).

m-chloroperoxybenzoic acid to give the epoxide **21** and subsequent treatment with TsOH in degassed toluene under reflux. This afforded a 2:1 epimeric mixture of the unsaturated diketones **13a** and **13b** in 76% overall yield.

The final step of the synthesis (Scheme 1) consisted of the epoxidation of the diketone **13a**, which was carried out with basic hydrogen peroxide in methanol in 76% yield. A β configuration was assigned to the oxyranic oxygen of **22**, with the assumption of the usual endocyclic attack in this type of compound and on the basis of the upfield shift of the ^{13}C NMR signal for the homoallylic carbon bearing an axial hydrogen cis to the oxygenated function. When the reaction time was prolonged to 30 min at room temperature, a selective Baeyer−Villiger reaction took place to afford the CDE gedunin fragment **23** as the sole product in 73% yield.

Biological Results

Efforts to develop safe, selective, and less persistent pest control agents have attracted increasing attention during the past decade. With this aim, we have designed simple structural mimics of azadiradione and epoxyazadiradione to investigate the resulting effects on biological activity. Larvae of the African leafworm *Spodoptera frugiperda* were used to assess the antifeedant activity of our molecular fragments.[14] Unexpectedly, the most active compound was **7**, a bicyclic [3.3.1] system with a different skeleton of the [4.3.0] system searched (Table 1). This fact makes compound **7** a new prototype in the search for new insect antifeedants.

Experimental Section

General Methods. Commercial reagents were used as received. Dichloromethane was distilled under nitrogen from calcium hydride. Diethyl ether, benzene, and toluene were distilled from sodium. Hexane, acetone, and ethyl acetate were distilled before use. Melting points were determined on a hot-stage apparatus and are not corrected. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 200 and 50 MHz, respectively. IR spectra were obtained as thin films. Mass spectra were obtained on a VG-TS 250 instrument. All reactions were carried out under an argon atmosphere. Reactions were monitored by TLC. Flash column chromatographies were carried out using silica gel 60 (0.040−0.063 mm, Merck). Organic extracts were washed with saturated NaCl solution dried over Na_2SO_4 and concentrated under reduced presure with the aid of a rotary evaporator.

Solution of 10^{-3} M $HClO_4$.[6] To 50 mL of absolute ethyl acetate was added 0.05 mL of 72% perchloric acid (0.575 mmol). Then, 5 mL of this solution was added to 30 mL of absolute ethyl acetate and 4.8 mL (51 mmol) of acetic anhydride, and the solution was made up to 50 mL with ethyl acetate to give a reagent 1 M in acetic anhydride and 10^{-3} M in perchloric acid.

Solution of 10^{-2} M $HClO_4$. To 40 mL of absolute ethyl acetate was added 0.05 mL (0.58 mmol) of 72% perchloric acid and 4.8 mL (51 mmol) of acetic anhydride, and the solution was made up to 50 mL with absolute ethyl acetate.

4-Acetyl-3,5,5-trimethyl-cyclohex-2-enone (1). An Er-

Table 2. Assignments Based on Heteronuclear Multiple Bond Correlation

	11		**12**		**18**		**19**	
	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H
1	76.0	4.87	73.2	4.59	76.9	4.89	73.6	4.42
2	128.3	5.60	63.4	3.50	129.3	5.77	64.5	3.70
3	159.5		74.0		154.6		72.9	
3a	36.8		47.5		51.2		48.1	
4	53.5	2.71, 2.89	49.2	2.95, 1.75	49.3	2.5	47.8	2.36, 1.84
5	213.4		213.1		211.7		210.2	
6	52.2	2.00, 3.17	52.4	3.08, 1.88	50.8	2.15, 2.39	50.7	2.05, 2.42
7	51.7		36.7		34.9		36.2	
7a	59.2	1.81	52.7	1.65	65.1	1.94	55.4	1.55
Me (C-3)	26.1	1.18	21.9	1.17	30.5	1.36	22.5	1.26
Me(C-7)α	32.0	1.13	31.9	1.03	30.5	1.21	30.9	1.09
Me (C-7)β	28.8	1.36	29.6	1.25	28.0	1.16	30.1	1.20

Table 3. Assignments Based on Heteronuclear Multiple Bond Correlation

	13a		**13b**		**22**			**23**	
	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H		^{13}C	^1H
1	126.9	6.23	127.8	6.27	58.4	3.70	1	82.7	5.79
2	205.5		207.4		207.4		3	166.9	
3	67.6	3.71	66.2	3.57	58.3	4.09	4	53.2	3.85
3a	50.1		50.3		46.1		4a	68.2	
4	51.6	2.67	49.3	1.82, 1.99	49.8	2.35, 3.01	5	38.4	
5	207.7		208.7		206.9		6	52.8	2.34, 2.67
6	52.7	2.49, 2.55	53.0	2.36, 2.48	54.5	2.46, 2.73	7	206.4	
7	37.9		38.1		37.2		8	47.9	1.92, 2.69
7a	187.4		189.5		72.9		8a	42.9	
Me (C-3a)	26.2	0.89	30.2	1.52	21.7	0.82	Me (C-8a)	16.8	1.09
Me (C-7)α	31.9	1.37	31.8	1.37	27.4	1.31	Me (C-5)α	27.9	1.28
Me (C-7)β	29.7	1.35	29.0	1.37	27.3	1.04	Me (C-5)β	26.0	1.02

lenmeyer flask was surrounded by ice, and mesityl oxide (15 g, 0.15 mol), acetylacetone (15 g, 0.15 mol), and boron trifluoride etherate solution (43 g, 0.3 mol) were added and mixed. The resulting solution was allowed to stand on ice with intermittent shaking for 1 h and then was transferred to a refrigerator (0−5 °C) for 5 days. The reaction mixture was poured over cracked ice and carefully neutralized with sodium carbonate. The organic layer was separated, and the water layer was extracted twice with diethyl ether. The combined organic layers were dried and filtered. The solvent was removed, and the residue was purified by flash chromatography using hexane−diethyl ether (7:3) as eluent to yield the diketone **1** as a colorless oil (8.1 g, 50%): IR 1713, 1699, 1636 cm^{-1}; ^1H NMR δ 0.99 (s, 6H), 1.61 (s, 3H), 1.92 (d, 1H, J = = 17 Hz), 2.25 (s, 3H), 2.55 (d, 1H, J = = 17 Hz), 3.18 (s, 1H), 5.88 (s, 1H); ^{13}C NMR δ 206.6, 198.4, 155.1, 127.2, 64.8, 46.5, 36.3, 33.4, 28.8, 27.2, 23.7; MS *m*/*z* (relative intensity) 180 (2, M^+), 138 (36), 123 (100), 96 (11), 79 (18), 67 (13).

1-(4-Hydroxy-2,6,6-trimethyl-cyclohex-2-enyl)-ethanone (2). To a mixture of diketone **1** (7.5 g, 42 mmol) and $CeCl_3 \cdot 7H_2O$ (3.1 g, 8.4 mmol, 20%) in methanol (100 mL) at −40 °C was added $NaBH_4$ (800 mg, 21 mmol) in small amounts. The mixture was stirred for 20 min. Then, the solvent was distilled under reduced pressure, and the residue was treated with water and extracted with diethyl ether. The extracts were then washed with brine and dried. The solvent was evaporated under reduced presure to afford a solid identified as hydroxy ketone **2** as a colorless oil (7.2 g, 95%): IR 3410, 1699, 1670 cm^{-1}; ^1H NMR δ 0.91 (s, 3H), 0.92 (s, 3H), 1.59 (s, 3H), 1.60 (d, 2H, J = = 7 Hz), 2.20 (s, 3H), 2.74 (s, 1H), 4.15 (m, 1H), 5.64 (br s, 1H); ^{13}C NMR δ 210.7, 131.9, 127.8, 65.2, 64.0, 40.1, 34.1, 31.7, 28.0, 27.9, 22.5; MS *m*/*z* (relative intensity) 182 (1, M^+), 125 (28), 122 (21), 107 (100), 91 (24), 69 (13).

***E*-1-(4-Hydroxy-2,6,6-trimethyl-cyclohex-2-enyl)-3-phenyl-pro-2-en-1-one (3).** To a solution of the hydroxy ketone **2** (7 g, 38.5 mmol) and benzaldehyde (4.1 g, 38.5 mmol) in ethanol (47 mL) at −20 °C was gradually added NaOH (3.1 g, 77 mmol) in H_2O (10 mL). The reaction was stirred vigorously for 2 h at −20 °C. The 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, and the residue was purified by flash chromatography using hexane−diethyl ether (7:3) as the eluting solvent to give a product identified as the hydroxy ketone **3** as a colorless oil (9.3 g, 90%): IR 3408, 1667, 1599 cm^{-1}; ^1H NMR δ 0.93 (s, 3H), 1.02 (s, 3H), 1.63 (br s, 3H), 1.68 (d, 2H, J = 8 Hz), 3.03 (s, 1H), 4.25 (m, 1H), 5.73 (br s, 1H), 6.95 (d, 1H, J = 16 Hz), 7.3−7.6 (m, 5H), 7.60 (d, 1H, J = 16 Hz); ^{13}C NMR δ 201.4, 143.1, 134.6, 132.9, 130.6, 128.9 (2), 128.6 (2), 128.3, 126.1, 65.9, 62.3, 41.0, 35.1, 28.7, 28.4, 23.1.

***E*-3,5,5-Trimethyl-4-(3-phenyl-acryloyl)-cyclohex-2-enone (4).** To a stirred and ice-cooled solution of hydroxy ketone **3** (9 g, 33.3 mmol) in acetone (125 mL) was added Jones reagent dropwise until the red color in solution became permanent after 15 min. Then, isopropyl alcohol was added. The solvent was evaporated under reduced presure to afford a residue, which was dissolved in water and extracted with diethyl ether. The extracts were washed with brine, dried, and evaporated to afford a solid product identified as diketone **4** (8.5 g, 95%): mp 116−118 °C; IR 1678, 1657, 1601, 1574 cm^{-1}; ^1H NMR δ 1.06 (s, 3H), 1.14 (s, 3H), 1.91 (s, 3H), 2.10 (d, 1H, J = 17 Hz), 2.74 (d, 1H, J = 17 Hz), 3.48 (s, 1H), 6.06 (s, 1H), 6.88 (d, 1H, J = 16 Hz), 7.4−7.6 (m, 5H), 7.67 (d, 1H, J = 16 Hz); ^{13}C NMR δ 197.9, 197.2, 155.6, 143.5, 133.5, 130.3, 128.3 (2), 128.0 (2), 126.7, 126.1, 61.4, 46.5, 36.1, 28.3, 26.7, 23.2; Ms *m*/*z* (relative intensity) 268 (1, M^+), 184 (1), 131 (100), 103 (31), 91 (3), 77 (31). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.66; H, 7.72.

Cyclization of Diketone 4 with Phosphoric and Sulfuric Acids. Diketone **4** (4 g, 15 mmol) was dissolved in a mixture of 85% phosphoric acid (14 mL) and sulfuric acid (14 mL), and the mixture was heated at 100 °C for 16 h under a nitrogen atmosphere. After being allowed to cool, the reaction mixture was treated with water and extracted with diethyl ether. The organic layer was washed with NaOH (2%) and brine, dried, and evaporated. The residue was chromatographed using hexane−diethyl ether (8:2) as eluent. The first fraction (2.46 g, 60%), which was a crystalline product, was identified as (3a*R**,7a*S**)-3a,7,7-trimethyl-3-phenyl-3a,6,7,7a-tetrahydro-4*H*-indene-1,5-dione (**6**): mp 120−121 °C; IR 1697, 1684 cm^{-1}; ^1H NMR δ 1.01 (s, 3H), 1.40 (s, 3H), 1.44 (s, 3H), 2.28 (s, 2H), 2.30 (s, 1H), 2.68 (d, 1H, J = 17 Hz), 2.81 (d, 1H, J = 17 Hz), 6.25 (s, 1H), 7.42 (s, 5H); ^{13}C NMR δ 209.4, 206.9, 181.1, 134.0, 130.3, 129.9, 128.8 (2), 127.7 (2), 63.4, 52.2, 47.3, 47.0, 34.2, 31.3, 30.3, 24.1; MS *m*/*z* (relative intensity) 268 (31, M^+), 225 (33), 184 (68), 171 (32), 152 (17), 141 (29), 128 (22), 91 (22), 77 (26). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.43; H, 7.63.

The second fraction (0.8 g, 20%), which was an amorphous solid, was identified as (1*S**,5*R**,8*R**)-4,9,9-trimethyl-8-phenyl-bicyclo[3.3.1]non-3-ene-2,6-dione (**7**): IR 2971, 1717, 1670 cm^{-1}; ^1H NMR δ 1.01 (s, 3H), 1.20 (s, 3H), 1.98 (s, 3H), 2.48 (m, 1H), 2.81 (s, 1H), 3.14 (d, 1H, J = 13 Hz), 3.22 (d, 1H, J = 13 Hz), 3.65 (m, 1H), 6.11 (s, 1H), 7.0−7.5 (m, 5H); ^{13}C NMR δ 207.8, 198.6, 157.4, 139.6, 129.0, 128.5 (2), 127.6 (2), 127.2, 66.2, 59.5, 41.1, 40.8, 37.5, 26.2, 26.0, 23.4; MS *m*/*z* (relative intensity) 268 (14, M^+), 211 (33), 185 (11), 137 (38), 131 (100), 91 (67), 77 (95).

***E*-1,1-(Ethylenedioxy)-3,5,5-trimethyl-4-(3-phenyl-acryloyl)-cyclohex-2-enone (8).** The diketone **4** (100 mg, 0.37 mmol), ethylene glycol (91 mg, 1.48 mmol), a catalytic amount of *p*-TsOH, and anhydrous benzene (1 mL) were heated at reflux under argon for 12 h with a Dean and Stark apparatus. Saturated sodium bicarbonate was added, and the mixture was extracted with diethyl ether. The combined ethereal layers were washed with aqueous $NaHCO_3$ (10%) and brine, dried, filtered, and evaporated in vacuo to give a clear oil. Purification by flash chromatography (hexane−diethyl ether, 8:2) gave the ketal **8** as a crystalline product (87 mg, 75%): mp 90−91 °C; IR 1626, 1096 cm^{-1}; ^1H NMR δ 1.16 (s, 6H), 1.60 (s, 3H), 1.74 (s, 2H), 2.34 (s, 2H), 4.00 (s, 4H), 6.77 (d, 1H, J = 16 Hz), 7.4−7.6 (m, 5H), 7.47 (d, 1H, J = 16 Hz).

Cyclization of Diketone 4 with $HClO_4$. Diketone **4** (3 g, 11.2 mmol) was dissolved in 300 mL of the 10^{-2} M $HClO_4$ reagent, and the solution was allowed to stand under argon for 18 h at room temperature. The solution was washed with saturated sodium bicarbonate solution and extracted with ethyl acetate. The combined organic layers were washed with sodium carbonate solution and brine, dried, and evaporated. The remaining residue was flash chromatographed (hexane−diethyl ether, 75:25) to yield acetic acid (3a*R**,7a*S**)-3a,7,7-trimethyl-1-oxo-3-phenyl-3a,6,7,7a-tetrahydro-1*H*-inden-5-yl ester **9** as a crystalline product (1.9 g, 55%): mp 93 °C; IR 1753, 1694 cm^{-1}; ^1H NMR δ 0.94 (s, 3H), 1.27 (s, 3H), 1.47 (s, 3H), 1.83 (d, 1H, J = 16 Hz), 2.10 (s, 3H), 2.20 (s, 1H), 2.35 (dd, 1H, J = 16 and 2 Hz), 5.54 (d, 1H, J = 2 Hz), 6.04 (s, 1H), 7.42 (s, 5H); ^{13}C NMR δ 208.0, 179.4, 168.8, 147.6, 134.5, 129.4, 129.2, 128.6 (2), 127.8 (2), 114.9, 63.7, 48.6, 41.7, 35.3, 31.4, 28.6, 23.9, 20.9; MS *m*/*z* (relative intensity) 310 (9, M^+), 268 (28), 253 (100), 184 (56), 131 (14), 123 (11), 77 (15). Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.58; H, 7.23. The second fraction was identified as diketone **7** (0.9 g, 30%).

Acetic acid 3,5,5-trimethyl-4-(3-phenyl-acryloyl)-cyclohexa-1,3-dienyl ester (10). A solution of diketone **4** (300 mg, 1.12 mmol) in dry THF (1.7 mL) was added to a degreased suspension of sodium hydride (67 mg of 60% dispersion in mineral oil, 1.7 mmol) in dry THF (3.5 mL). *N*,*N*′-dimethylpropyleneurea (3.5 mL) was added, and the reaction mixture was stirred for 45 min under argon at room temperature. Acetic anhydride (230 mg, 2.24 mmol) in THF (1.7 mL) was added, and the mixture was stirred for an additional 30 min, diluted with water, and extracted with diethyl ether. The ether extracts were combined, washed with saturated brine, dried, filtered, and concentrated to yield a yellow oil identified

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(14) Blaney, W. M.; Simmonds, M. S. J.; Ley, S. V.; Anderson, J. C.; Toogood, P. L. *Entomol. Exp. Appl.* **1990**, *55*, 149.

as enol acetate **10** (295 mg, 87%): IR 2961, 1755, 1634, 1206 cm^{-1}; ^1H NMR δ 1.16 (s, 6H), 1.71 (s, 3H), 2.16 (s, 3H), 2.34 (s, 2H), 5.64 (s, 1H), 6.79 (d, 1H, $J = 16$ Hz), 7.3−7.6 (m, 5H), 7.49 (d, 1H, $J = 16$ Hz); ^{13}C NMR δ 200.2, 168.8, 150.1, 145.5, 137.2, 134.5, 130.6, 128.9 (3), 128.3 (3), 114.0, 42.2, 37.2, 26.5 (2), 21.1, 19.8; MS *m*/*z* (relative intensity) 310 (4, M^+), 268 (15), 137 (18), 131 (100), 91 (12), 77 (29).

Cyclization of Enol Acetate 10 with $HClO_4$. Enol acetate **10** (250 mg, 0.81 mmol) was dissolved in 25 mL of the 10^{-2} M $HClO_4$ reagent, and the solution was allowed to stand under argon for 5 min at room temperature. The solution was washed with saturated sodium bicarbonate solution and extracted with ethyl acetate. The combined organic layers were washed with sodium carbonate solution and brine, dried, and evaporated. The remaining white solid crystals were identified as enol acetate **9** (250 mg, 100%).

(1*R,3a*R**,7a*S**)-1-Hydroxy-3a,7,7-trimethyl-3-phenyl-1,3a,4,6,7-hexahydro-inden-5-one (11).** To a mixture of enol acetate **9** (1.0 g, 3.20 mmol) and $CeCl_3 \cdot 7H_2O$ (1.2 g, 3.20 mmol) in methanol (40 mL) at 0 °C was added $NaBH_4$ (486 mg, 12.8 mmol). The mixture was stirred for 1 h. Then, the solvent was distilled under reduced presure, and the residue was treated with saturated NaCl (100 mL) and diethyl ether (50 mL) and stirred for 4 h at room temperature. The organic layer was separated, and the aqueous phase was washed with brine and dried. The solvent was evaporated under reduced presure to afford a crystalline solid identified as hydroxy ketone **11** (700 mg, 83%): mp 110−112 °C; IR 3482, 1699 cm^{-1}; ^1H NMR δ 1.13 (s, 3H), 1.18 (s, 3H), 1.36 (s, 3H), 1.81 (d, 1H, $J = 5$ Hz), 2.00 (d, 1H, $J = 12$ Hz), 2.71 (d, 1H, $J = 12$ Hz), 2.89 (d, 1H, $J = 12$ Hz), 3.17 (d, 1H, $J = 12$ Hz), 4.87 (dd, 1H, $J = 5$ and 3 Hz), 5.60 (d, 1H, $J = 3$ Hz), 7.2−7.4 (m, 5H); ^{13}C NMR δ 213.3, 159.5, 136.3, 128.3 (3), 127.7, 127.4 (2), 76.0, 59.2, 53.5, 52.2, 51.7, 36.8, 32.0, 28.8, 26.1; MS *m*/*z* (relative intensity) 270 (5, M^+), 185 (31), 172 (93), 115 (42), 91 (61), 77 (80), 55 (100). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.85; H, 8.08.

(1*S,2*R**,3*S**,3a*R**,7a*S**)-2,3-Epoxy-1-hydroxy-3a,7,7-trimethyl-3-phenyl-perhydro-inden-5-one (12).** A solution of *m*-chloroperoxybenzoic acid (638 mg, 3.7 mmol) in dry CH_2Cl_2 (7 mL) was added dropwise under argon at room temperature to a solution of hydroxy ketone **11** (500 mg, 1.85 mmol) in dry CH_2Cl_2 (7 mL), and the resulting mixture was stirred at this temperature for an additional 40 min. A solution of Na_2SO_3 (10%) was added, and the resulting heterogeneous mixture was stirred. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined extracts were washed with $NaHCO_3$ (5%), water and brine, dried, and filtered. Removal of the solvent afforded the epoxy compound **12** as a crystalline solid (402 mg, 76%): mp 128−130 °C; IR 3434, 1699 cm^{-1}; ^1H NMR δ 1.03 (s, 3H), 1.17 (s, 3H), 1.25 (s, 3H), 1.65 (d, 1H, $J = 5$ Hz), 1.75 (d, 1H, $J = 12$ Hz), 1.88 (d, 1H, $J = 12$ Hz), 2.95 (d, 1H, $J = 12$ Hz), 3.08 (d, 1H, $J = 12$ Hz), 3.50 (s, 1H), 4.59 (d, 1H, $J = 5$ Hz), 7.3−7.4 (m, 5H); ^{13}C NMR δ 213.1, 133.6, 129.0 (2), 128.3, 127.8 (2), 74.0, 73.2, 63.4, 52.7, 52.4, 49.2, 47.5, 36.7, 31.9, 29.6, 21.9. Anal. Calcd for $C_{18}H_{22}O_2$: C, 75.49; H, 7.74. Found: C, 75.68; H, 7.91.

Rearrangement of Epoxide Alcohol 12 with TsOH. To a solution of epoxide alcohol **12** (210 mg, 0.73 mmol) in degassed toluene (3 mL) was added a catalytic amount of TsOH, and the mixture was heated at reflux under argon for 30 min. Then, a saturated solution of $NaHCO_3$ was added, and the mixture was extracted with diethyl ether. The extracts were washed with H_2O and brine and dried. The solvent was evaporated under reduced pressure to afford a crude oil. Purification by flash chromatography (hexane−diethyl ether, 7:3) gave the diketone **6** (137 mg, 70%).

The second fraction (9 mg, 5%), which was a colorless oil, was identified as (3*S**,3a*S**)-3a,7,7-trimethyl-3-phenyl-3a,4,6,7-tetrahydro-3*H*-indene-2,5-dione **13b**: IR 1717, 1699 cm^{-1}; ^1H NMR δ 1.37 (s, 6H), 1.52 (s, 3H), 1.82 (d, 1H, $J = 16$ Hz), 1.99 (d, 1H, $J = 16$ Hz), 2.36 (d, 1H, $J = 16$ Hz), 2.48 (d, 1H, $J = 16$ Hz), 3.57 (s, 1H), 6.27 (s, 1H), 6.9−7.5 (m, 5H); ^{13}C NMR δ 208.7, 207.4, 189.5, 137.0, 128.9 (2), 128.6 (2), 127.8, 127.6, 66.2, 53.0, 50.3, 49.3, 38.1, 31.8, 30.2, 29.0; MS *m*/*z* (relative intensity) 268 (8, M^+), 253 (20), 184 (100), 115 (47), 105 (22), 91 (72), 89 (31), 77 (53).

The third compound (18 mg, 9%) was an oily product identified as (3*R**,3a*S**)-3a,7,7-trimethyl-3-phenyl-3a,4,6,7-tetrahydro-3*H*-indene-2,5-dione **13a**: IR 1705, 1607 cm^{-1}; ^1H NMR δ 0.89 (s, 3H), 1.35 (s, 3H), 1.37 (s, 3H), 2.49 (d, 1H, $J = 12$ Hz), 2.55 (d, 1H, $J = 12$ Hz), 2.67 (s, 2H), 3.71 (s, 1H), 6.23 (s, 1H), 7.0−7.5 (m, 5H); ^{13}C NMR δ 207.7, 205.5, 187.4, 134.8, 130.0 (2), 128.5 (2), 127.5, 126.9, 67.6, 52.7, 51.6, 50.1, 37.9, 31.9, 29.7, 26.2; MS *m*/*z* (relative intensity) 268 (13, M^+), 184 (28), 141 (24), 115 (56), 105 (35), 91 (83), 77 (90), 51 (100).

(2*R,3*S**,3a*S**,7a*S**)-2-Hydroxy-3a,7,7-trimethyl-3-phenyl-perhydroindene-1,5-dione (14).** To a solution of the epoxide **12** (97 mg, 0.34 mmol) in dry CH_2Cl_2 (1.6 mL) was added a solution of 0.5 M boron trifluoride−diethyl ether in CH_2Cl_2 (0.05 mL) at room temperature, and the reaction mixture was stirred for 10 min. Then, it was diluted with diethyl ether, and water was added. The layers were separated, and the organic phase was washed with $NaHCO_3$ (5%) and brine and then dried. Evaporation of the solvent afforded the hydroxy ketone **14** as a crystalline solid (92 mg, 95%): mp 159 °C; IR 3488, 1738, 1699 cm^{-1}; ^1H NMR δ 0.94 (s, 3H), 1.15 (s, 3H), 1.39 (s, 3H), 2.20 (d, 1H, $J = 18$ Hz), 2.28 (d, 1H, $J = 18$ Hz), 2.34 (d, 1H, $J = 17$ Hz), 2.35 (s, 1H), 2.73 (d, 1H, $J = 17$ Hz), 3.05 (d, 1H, $J = 13$ Hz), 4.72 (d, 1H, $J = 13$ Hz), 7.2−7.4 (m, 5H); ^{13}C NMR δ 214.7, 209.7, 135.3, 128.5 (2), 128.4 (2), 127.7, 75.2, 60.2, 58.9, 53.1, 49.9, 39.7, 35.4, 31.7, 28.5, 24.1; MS *m*/*z* (relative intensity) 286 (3, M^+), 129 (16), 115 (30), 91 (100), 77 (49). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74. Found: C, 75.35; H, 7.61.

Rearrangemet of Hydroxy Ketone 14 with TsOH. To a solution of hydroxy diketone **14** (90 mg, 0.31 mmol) in degassed toluene (1 mL) was added a catalytic amount of TsOH, and the mixture was heated at reflux under argon for 30 min. Then, a saturated solution of $NaHCO_3$ was added, and the mixture extracted with diethyl ether. The extracts were washed with H_2O and brine and dried. The solvent was evaporated under reduced pressure to afford a crude oil. Purification by flash chromatography (hexane−diethyl ether, 7:3) gave the diketones **6** (61 mg, 73%), **13b** (4 mg, 4%), and **13a** (7 mg, 9%).

(3a*R,7a*S**)-2-Hydroxy-3a,7,7-trimethyl-3-phenyl-3a,6,7,-7a-tetrahydro-4*H*-indene-1,5-dione (15).** To a solution of hydroxy diketone **14** (30 mg, 0.1 mmol) in toluene (1 mL) was added a catalytic amount of TsOH, and the mixture was heated at reflux for 30 min. Then, a saturated solution of $NaHCO_3$ was added, and the mixture extracted with diethyl ether. The extracts were washed with H_2O and brine and dried. The solvent was evaporated under reduced pressure to afford a crude oil. Purification by flash chromatography (hexane−diethyl ether, 75:25) gave the triketone **15** as a crystaline solid (28 mg, 93%): mp 88 °C (dec); IR 3310, 2924, 1700, 1682, 1630 cm^{-1}; ^1H NMR δ 1.01 (s, 3H), 1.41 (s, 3H), 1.43 (s, 1H), 2.31 (s, 2H), 2.35 (s, 1H), 2.77 (s, 2H), 7.3−7.6 (m, 5H); ^{13}C NMR δ 210.0, 201.8, 147.8, 147.1, 132.1, 128.9 (2), 128.6 (2), 127.7, 60.0, 51.8, 47.8, 42.6, 34.2, 31.5, 30.3, 23.8; MS *m*/*z* (relative intensity) 284 (31, M^+), 186 (100), 158 (13), 115 (20), 83 (57), 77 (17). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.21; H, 6.88.

(3a*R,7a*S**)-5,5-(Ethylenedioxy)-3a,7,7-trimethyl-3-phenyl-3a,6,7,7a-tetrahydro-4*H*-indene-1,5-dione (16).** The diketone **6** (2 g, 7.5 mmol), ethylene glycol (0.93 g, 15 mmol), and a catalytic amount of TsOH were heated to 80 °C in anhydrous benzene (25 mL) under argon for 12 h with a Dean and Stark apparatus. Saturated sodium bicarbonate was added, and the mixture was extracted with diethyl ether. The combined ethereal layers were washed with aqueous $NaHCO_3$ (10%) and brine, dried, filtered, and evaporated in vacuo to give a clear oil. Purification by flash chromatography (hexane−diethyl ether, 8:2) gave the compound **16** (2.1 g, 90%): IR 1694, 1593 cm^{-1}; ^1H NMR δ 0.86 (s, 3H), 1.17 (s, 3H), 1.29 (s, 3H), 1.56 (d, 1H, $J = 16$ Hz), 1.65 (d, 1H, $J = 16$ Hz), 1.90 (d, 1H, $J = 13$ Hz), 1.94 (s, 1H), 2.02 (d, 1H, $J = 13$ Hz), 3.6−3.8 (m, 4H), 5.97 (s, 1H), 7.2−7.4 (m, 5H); ^{13}C NMR δ 208.0,

182.3, 134.9, 130.0, 129.3, 128.4 (2), 127.7 (2), 109.1, 63.7, 63.6, 63.4, 48.4, 46.9, 41.0, 33.7, 32.5, 28.9, 23.9; MS *m*/*z* (relative intensity) 312 (3, M^+), 165 (15), 152 (16), 127 (100), 113 (53), 102 (32), 91 (32), 77 (43).

(1*S,3a*R**,7a*S**)-5,5-(Ethylenedioxy)-1-hydroxy-3a,7,7-trimethyl-3-phenyl-1,3a,4,6,7-hexahydroinden-5-one (17).** Lithium aluminum hydride (116 mg, 3.05 mmol) was added portionwise to a solution of the ketal **16** (1.9 g, 6.10 mmol) in dry diethyl ether (32 mL) cooled to 0 °C. The mixture was vigorously stirred for 10 min, after which it was quenched with $Na_2SO_4 \cdot 10H_2O$. The resulting mixture was filtered, and the filtrate was concentrated in vacuo to give the alcohol **17** as a crystalline product (1.9 g, 100%): mp 70−71 °C; IR 3430 cm^{-1}; ^1H NMR δ 1.16 (s, 3H), 1.25 (s, 3H), 1.35 (s, 3H), 1.6−2.1 (m, 5H), 3.8−4.1 (m, 4H), 4.76 (dd, 1H, J = 7 and 2 Hz), 5.65 (d, 1H, J = 2 Hz), 7.2−7.4 (m, 5H); ^{13}C NMR δ 155.2, 136.7, 129.4, 127.7 (2), 127.6 (2), 126.6, 109.2, 76.3, 64.9, 64.2, 62.6, 49.5, 43.9, 43.3, 32.9, 30.8, 30.6, 26.9. Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.57; H, 8.15.

(1*S,3a*R**,7a*S**)-1-Hydroxy-3a,7,7-trimethyl-3-phenyl-1,3a,4,6,7-hexahydro-inden-5-one (18).** A catalytic amount of pyridinium *p*-toluenesulfonate was added to a stirred solution of ketal **17** (1.5 g, 5.4 mmol) in acetone (21 mL) and water (0.7 mL). The reaction mixture was stirred at room temperature for 48 h under an argon atmosphere. The solvent was evaporated under reduced pressure, and the resulting residue was dissolved in diethyl ether. The organic layer was successively washed with 10% aqueous $NaHCO_3$ solution and water and then dried and evaporated to give a crude colorless oil, which was flash chromatographed using hexane−diethyl ether (9:1) as eluent to yield **18** as a colorless oil (1.14 g, 89%): IR 3430, 1072 cm^{-1}; ^1H NMR δ 1.16 (s, 3H), 1.21 (s, 3H), 1.36 (s, 3H), 1.94 (d, 1H, J = 5 Hz), 2.15 (d, 1H, J = 16 Hz), 2.39 (d, 1H, J = 16 Hz), 2.50 (m, 2H), 4.89 (dd, 1H, J = 2 and 5 Hz), 5.77 (d, 1H, J = 2 Hz), 7.2−7.4 (m, 5H); ^{13}C NMR δ 211.7, 154.6, 135.7, 129.3, 128.2 (2), 127.9 (2), 127.7, 76.9, 65.1, 51.2, 50.8, 49.3, 34.9, 30.5 (2), 28.0.

(1*R,2*R**,3*S**,3a*R**,7a*S**)-2,3-Epoxy-1-hydroxy-3a,7,7-trimethyl-3-phenyl-1,3a,4,6,7-hexahydro-inden-5-one (19).** A solution of *m*-chloroperoxybenzoic acid (1.28 g, 7.4 mmol) in dry CH_2Cl_2 (6 mL) was added dropwise under N_2 at room temperature to a solution of hydroxy ketone **18** (1 g, 3.71 mmol) in dry CH_2Cl_2 (7 mL), and the resulting mixture was stirred at this temperature for an additional 30 min. A solution of Na_2SO_3 (10%) was added, and the resulting heterogeneous mixture was stirred. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined extracts were washed with $NaHCO_3$ (5%), water, and brine, dried, and filtered. Removal of the solvent afforded the epoxide compound **19** as a crystalline solid (1 g, 95%): mp 160 °C; IR 3466, 1696, 1045 cm^{-1}; ^1H NMR δ 1.09 (s, 3H), 1.20 (s, 3H), 1.26 (s, 3H), 1.55 (d, 1H, J = 8 Hz), 1.84 (d, 1H, J = 13 Hz), 2.05 (d, 1H, J = 13 Hz), 2.36 (d, 1H, J = 14 Hz), 2.42 (d, 1H, J = 14 Hz), 3.70 (s, 1H), 4.42 (m, 1H), 7.32 (m, 5H); ^{13}C NMR δ 210.2, 132.8, 128.9 (2), 125.5, 128.0 (2), 73.6, 72.9, 64.5, 55.4, 50.7, 48.1, 47.8, 36.2, 30.9, 30.1, 22.5; MS *m*/*z* (relative intensity) 271 (2, $M^+ - Me$), 202 (12), 171 (16), 123 (28), 115 (22), 105 (100), 91 (28), 77 (71). Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74. Found: C, 75.67; H, 7.87.

(1*R,3*S**,3a*R**,7a*S**)-1-Hydroxy-3a,7,7-trimethyl-3-phenyl-hexahydro-indene-2,5-dione (20).** To a solution of the epoxide **19** (200 mg, 0.70 mmol) in dry CH_2Cl_2 (8 mL) was added boron trifluoride−diethyl ether (0.05 mL) at room temperature, and the reaction mixture was stirred for 5 min. Then, it was diluted with diethyl ether, and water was added. The layers were separated, and the organic phase was washed with $NaHCO_3$ (5%) and brine and then dried. Evaporation of the solvent afforded the hydroxy ketone **20** as a colorless oil (184 mg, 92%): IR 3453, 1748, 1709 cm^{-1}; ^1H NMR δ 1.24 (s, 3H), 1.29 (s, 3H), 1.33 (s, 3H), 1.51 (d, 1H, J = 10 Hz), 1.9−3.0 (m, 4H), 3.51 (s, 1H), 4.34 (d, 1H, J = 10 Hz), 6.9−7.4 (m, 5H); ^{13}C NMR δ 213.7, 209.6, 133.2, 130.2 (2), 128.1 (2), 127.4, 74.4, 62.0, 56.5, 50.7, 49.7, 30.6, 28.5, 28.1; MS *m*/*z* (relative intensity) 269 (2, $M^+ - OH$), 253 (8), 169 (34), 153 (28), 115 (39), 105 (84), 91 (45), 77 (100).

3a,7,7-Trimethyl-3-phenyl-3a,4,6,7-tetrahydro-3*H*-indene-2,5-dione (13). To a solution of hydroxy ketone **20** (160 mg, 0.56 mmol) in degassed toluene (3 mL) was added a catalytic amount of TsOH, and the mixture was heated at reflux for 30 min. Then, a saturated solution of $NaHCO_3$ was added, and the mixture was extracted with diethyl ether. The extracts were washed with H_2O and brine and then dried. The solvent was evaporated under reduced pressure to afford a crude oil. Purification by flash chromatography (hexane−diethyl ether,7:3) gave the minor diketone **13b** (40 mg, 27%) and the major diketone **13a** (80 mg, 53%).

Epimerization of Diketone 13b. Diketone **13b** (20 mg, 0.07 mmol) dissolved in toluene (0.5 mL) was refluxed in the presence of *p*-toluenesulfonic acid and under N_2 for 30 min. Then, a saturated solution of $NaHCO_3$ was added, and the mixture was extracted with diethyl ether. The extracts were washed with H_2O and brine and dried. The solvent was evaporated under reduced pressure to afford a crude oil. Purification by flash chromatography (hexane−diethyl ether, 7:3) gave the diketone **13b** (6 mg, 30%) and the diketone **13a** (12 mg, 60%).

(1*S,2*R**,3*S**,3a*R**,7a*S**)-5,5-(Ethylenedioxy)-2,3-epoxy-1-hydroxy-3a,7,7-trimethyl-3-phenyl-1,3a,4,6,7-hexahydro-inden-5-one (21).** A solution of *m*-chloroperoxybenzoic acid (260 mg, 1.5 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise under argon at room temperature to a solution of hydroxy ketal **17** (320 mg, 1 mmol) in dry CH_2Cl_2 (4 mL), and the resulting mixture was stirred at this temperature for an additional 30 min. A solution of Na_2SO_3 (10%) was added, and the resulting heterogeneous mixture was stirred. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined extracts were washed with $NaHCO_3$ (5%), water and brine, dried, and filtered. Removal of the solvent afforded the epoxide compound **21** as a crystalline solid (320 mg, 95%): mp 97−99 °C; IR 3381, 1074 cm^{-1}; ^1H NMR δ 1.10 (s, 3H), 1.19 (s, 3H), 1.35 (s, 3H), 1.1−1.6 (m, 5H), 3.60 (d, 1H, J = 1 Hz), 3.7−4.0 (m, 4H), 4.18 (m, 1H), 7.3−7.4 (m, 5H); ^{13}C NMR δ 134.2, 129.4 (2), 128.1, 127.8 (2), 109.3, 73.6, 73.5, 64.8, 64.3, 63.0, 54.8, 45.4, 43.6, 40.6, 32.7, 31.5, 30.7, 21.6; MS *m*/*z* (relative intensity) 330 (3, M^+), 167 (27), 127 (100), 109 (8), 105 (54), 77 (65). Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.77; H, 7.79.

Rearrangement of Epoxide Alcohol 21 with TsOH. To a solution of epoxide alcohol **21** (300 mg, 0.91 mmol) in degassed toluene (4 mL) was added a catalytic amount of TsOH, and the mixture was heated at reflux under argon for 30 min. Then, a saturated solution of $NaHCO_3$ was added, and the mixture was extracted with diethyl ether. The extracts were washed with H_2O and brine and dried. The solvent was evaporated under reduced pressure to afford a crude oil. Purification by flash chromatography (hexane−diethyl ether, 7:3) gave the diketones **13a** (130 mg, 53%) and **13b** (65 mg, 27%).

(1*S,3*S**,3a*S**,7a*S**)-1,7a-Epoxy-3a,7,7-trimethyl-3-phenyl-3a,4,6,7-tetrahydro-3*H*-indene-2,5-dione (22).** To a stirred solution of diketone **13a** (22 mg, 0.08 mmol) in methanol (0.2 mL) maintained under argon at 0 °C were added H_2O_2 (0.1 mL, 30%) and NaOH (0.2 mL, 6 N, 1.2 mmol). The resulting solution was stirred for 40 min at this temperature and then poured into a solution of $NaHCO_3$ (10%). The aqueous solution was extracted with diethyl ether, dried, and filtered. Removal of the solvent afforded the epoxide compound **22** as a crystalline solid (18 mg, 76%): mp 113−114 °C; IR 1755, 1713 cm^{-1}; ^1H NMR δ 0.82 (s, 3H), 1.04 (s, 3H), 1.31 (s, 3H), 2.35 (dd, 1H, J = 13 and 2 Hz), 2.46 (dd, 1H, J = 14 and 2 Hz), 2.73 (d, 1H, J = 14 Hz), 3.01 (d, 1H, J = 13 Hz), 3.70 (s, 1H), 4.09 (s, 1H), 7.0−7.4 (m, 5H); ^{13}C NMR δ 207.4, 206.9, 132.1, 130.6 (2), 128.3 (2), 127.9, 72.9, 58.4, 58.3, 54.5, 49.7, 46.1, 37.2, 27.4, 27.3, 21.7; MS *m*/*z* (relative intensity) 284 (3, M^+), 186 (18), 129 (21), 118 (100), 115 (36), 109 (21), 91 (66), 77 (42), 69 (60). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.21; H, 7.20.

(1*S,4*S**,4a*S**,8a*S**)-4,4a-Epoxy-5,5,8a-trimethyl-1-phenyl-octahydro-2-benzopyrane-3,7-dione (23).** To a stirred solution of diketone **13a** (11 mg, 0.04 mmol) in methanol (0.1

mL) maintained under argon at 20 °C was added H_2O_2 (0.05 mL, 30%) and NaOH (0.1 mL, 6 N, 0.6 mmol). The resulting solution was stirred for 1 h at this temperature and then poured into a solution of $NaHCO_3$ (10%). The aqueous solution was extracted with diethyl ether, dried, and filtered. Removal of the solvent afforded the lactone **23** as a crystalline solid (9 mg, 73%): mp 140 °C; IR 1742, 1713 cm^{-1}; ^1H NMR δ 1.02 (s, 3H), 1.09 (s, 3H), 1.28 (s, 3H), 1.92 (dd, 1H, J = 13 and 2 Hz), 2.34 (dd, 1H, J = 13 and 2 Hz), 2.67 (d, 1H, J = 13 Hz), 2.69 (d, 1H, J = 13 Hz), 3.85 (s, 1H), 5.79 (s, 1H), 7.0−7.4 (m, 5H); ^{13}C NMR δ 206.4, 166.9, 133.4, 128.8, 128.0 (2), 127.9 (2), 82.7, 68.2, 53.2, 52.8, 47.9, 42.9, 38.4, 27.9, 26.0, 16.8; MS m/z (relative intensity) 300 (2, M^+), 165 (12), 123 (22), 115 (18), 105 (83), 91 (48), 77 (100). Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.83; H, 6.55.

Acknowledgment. Financial support for this work from the Ministerio de Educación y Ciencia of Spain PB 95-0943 and the Junta de Castilla y León SA 45/97 is gratefully acknowledged. We also thank the Junta de Castilla y León for the fellowship to A.I.R.S. and the Ministerio de Educación y Ciencia for the fellowship to E.M.N. The experiments with *Spodoptera littoralis* and *Spodoptera frugiperda* were covered by MAFF license no. PHF 1020/806/113. We would like to thank P. Green and M. Cullum for technical assistance in culturing the insects.

Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra and assignments based on heteronuclear multiple bond correlation of compounds **7**, **11-13a**,**b**, **18**, **19**, **22**, and **23** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO981456Q