(95:5) (v/v) as the eluant) to give 2.84 g (78%) of the desired product, mp 229-232 °C. Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.9; H, 7.1. The ^1H NMR spectrum was identical with that of (-)-**3**.[4] Recrystallization of this compound from ethyl acetate (in which it is very sparingly soluble) slowly afforded small platelets (mp 234 °C) of a monohydrate. Anal. Calcd for $C_{27}H_{30}O_6$, H_2O: C, 67.90; H, 6.96. Found: C, 67.8; H, 6.9.

Optical Resolution of (±)-3; Preparation and Separation of Diastereomers 26 and 27. Triphenol (±)-**3** (500 mg, 1.1 mmol, 3.3 mequiv) and (*R*)-(+)-2-phenoxypropionic acid[15] (810 mg, 4.9 mmol) were allowed to react in 5 mL of dimethylformamide in the presence of dicyclohexylcarbodiimide (1.03 g, 5 mmol) and 4-(dimethylamino)pyridine (60 mg, 0.2 mmol);[38] after the solution was stirred for 3 h at 20 °C under nitrogen, the precipitate (dicyclohexylurea) was removed by filtration and washed with 50 mL of dichloromethane. The filtrate was washed with 1 N HCl, water, and 5% aqueous $NaHCO_3$, dried over sodium sulfate, and evaporated to dryness. The solid residue (1.4 g) was taken up with 20 mL of ether and collected by suction filtration, affording 1 g (100%) of the 1:1 mixture of **26** and **27**. These diastereomers were separated over silica gel, using dichloromethane-ether (99:1) as the eluant; the 1:1 mixture was first chromatographed on a column (200 g of adsorbent), giving four partially resolved fractions which then were submitted to preparative TLC. In this way, 345 mg of **27** (first eluted) was obtained as a white amorphous powder having $[\alpha]^{25}_D$ +99° (*c* 0.5, $CHCl_3$), and 335 mg of **26** was isolated after crystallization from ether, $[\alpha]^{25}_D$ +37° (*c* 0.5, $CHCl_3$) (**26** very likely forms a crystalline complex with ether, as suggested from ^1H NMR). Both diastereomers were pure, as judged from TLC and from their 250-MHz ^1H NMR spectra: ^1H NMR (internal TMS in $CDCl_3$) δ (**27**) 1.33 (t, *J* = 6.9 Hz, C_2H_5O), 3.99 (q, *J* = 6.9 Hz, C_2H_5O), 1.78 (d, *J* = 6.8 Hz, CH_3CH), 4.79 (q, *J* = 6.8 Hz, CH_3CH), 3.53 and 4.67 (d, *J* = 13.8 Hz, H_e and H_a), 6.80 and 6.90 (s, aromatic H's of the cyclotriveratrylene cap), 6.99-7.02 and 7.26-7.32 (m, aromatic H's of the phenoxypropionate residue), (**26**) 1.26 (t), 3.77-4.00 (m), 1.77 (d), 4.95 (q), 3.49 and 4.65 (d), 6.72 and 6.80 (s), 6.95-7.02 and 7.27-7.33 (m).

Cleavage of Diastereomers 27 and 26 to (+)- and (-)-3. Diastereomer **27** (278 mg, 0.31 mmol) was added by portion to a stirred suspension of lithium aluminum hydride (150 mg) in 5 mL of tetrahydrofuran at -5 °C under nitrogen. The mixture was stirred for 15 min at this temperature and then 1 h at 20 °C. Hydrolysis was carried out at 0 °C (internal temperature) by adding successively several drops of ethyl acetate, ether (nonanhydrous), water, and finally 1 N sulfuric acid in order to dissolve precipitated alumina. Extraction with ether (100 mL) followed by evaporation to dryness under vacuum (*no heating*!) afforded a mixture of the desired triphenol and 2-phenoxypropanol, which was separated by chromatography over 40 g of silica gel (dichloromethane-ether (99:1)). The purest fractions on evaporation (20 °C) afforded a glass (130 mg, 93%), which on standing in the presence of ether became crystalline; 110 mg (79%) of pure (+)-**3** was thus collected: mp 250 °C; $[\alpha]^{25}_D$ +293° (*c* 0.34, $CHCl_3$). Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.5; H, 6.8.

In a similar way, cleavage of **26** afforded (-)-**3**, having $[\alpha]^{25}_D$ -293° (*c* 0.30, $CHCl_3$).

(38) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522-524.

Appendix

Spectra Calculations and Curve Plotting. The A and E components of each CD couplet were assigned wavenumbers $\tilde{\nu}_A = \tilde{\nu}_0 + {}^2/_3\Delta\tilde{\nu}$ and $\tilde{\nu}_E = \tilde{\nu}_0 - {}^1/_3\Delta\tilde{\nu}$, respectively, where $\tilde{\nu}_0$ is the wavenumber of the "monomer"; as discussed in the text, $\Delta\tilde{\nu}$, the exciton splitting, was considered to be 3 times the value calculated with the point-dipole approximation (eq II); i.e., $\Delta\tilde{\nu} = 3(3V/hc)$. Then, each component was given the corresponding rotatory strength from eq III, without configuration interaction, or from eq III + IV, with interaction, and, assuming that the CD spectrum is the sum of these *i* Gaussian bands, the theoretical spectrum was plotted by using function IX,[8] where $A = 4N(2\pi)^{5/2}/3hc10^3 \ln 10 = 18.8 \times 10^{37}$ cgsu.

$$\Delta\epsilon(\tilde{\nu}) = A\sum_i \left(\frac{R_i\tilde{\nu}_i}{\sigma_i}\right) \exp\left(\frac{-(\tilde{\nu} - \tilde{\nu}_i)^2}{2\sigma_i^2}\right) \qquad \text{(IX)}$$

The standard deviation of a band, $\sigma_i = \Gamma_i/2.354$, was considered to be a function of the wavenumber,[31] $\sigma_i = P(\tilde{\nu}_i)^{1/2}$, and the curve plotting function IX accordingly becomes (X).

$$\Delta\epsilon(\tilde{\nu}) = ((18.8 \times 10^{37})/P)\sum_i (R_i(\tilde{\nu}_i)^{1/2}) \exp\left(\frac{-(\tilde{\nu} - \tilde{\nu}_i)^2}{4P^2\tilde{\nu}_i}\right) \qquad \text{(X)}$$

Parameter *P* was usually taken to be 6.123, corresponding to $\Gamma = 2700$ cm^{-1} at 285 nm.

Stereoelectronic Effects in the Cationic Rearrangements of [4.3.2]Propellanes

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Abstract: The preparation and cationic rearrangement of some 15 [4.3.2]propellane derivatives are described. The resulting products are summarized in Tables I-III. The rearrangements were found to be under strict stereoelectronic control, wherein the central or peripheral σ-bond of the cyclobutane ring best aligned with the leaving group (π-system in the case of olefins) undergoes initial migration. Product assignments were based either on single-crystal X-ray analysis or chemical correlation with known compounds.

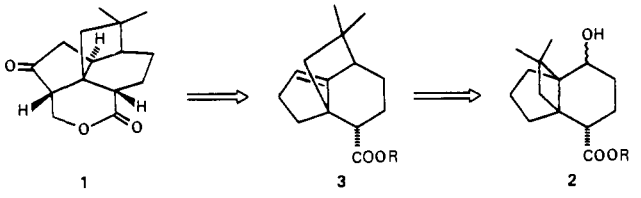
In 1978 Ranieri and Calton published the isolation and characterization of quadrone (**1**), a biologically active sesquiterpene with a unique carbon skeleton.[2,3] The years since this discovery have witnessed significant activity directed toward the synthesis of **1**; to date seven syntheses of *racemic* quadrone have been reported.[4a-g] Our own interest in the quadrone structure[5] led us

(1) Camille and Henry Dreyfus Teacher-Scholar, 1978-1983; National Institutes of Health (National Career Institute) Career Development Award, 1980-1985.

(2) Ranieri, R. L.; Calton, G. J. *Tetrahedron Lett.* **1978**, 499-502.
(3) Calton, G. J.; Ranieri, R. L.; Epenshade, M. A. *J. Antibiot.* **1978**, *31*, 38-42.

0002-7863/85/1507-1308$01.50/0

to consider a synthetic strategy wherein the key step would entail the acid-catalyzed rearrangement of hydroxypropellane **2** to olefin **3**, thereby generating the desired quadrone skeleton (i.e., eq 1).



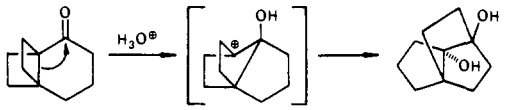
1 3 2 (1)

While carbonium ion mediated rearrangements of propellanes are well documented (vide infra), reactions initiated by alcohol and olefinic functionalities in the cyclohexane ring have been little explored. We report herein a full account of our work in this area, which demonstrates that, in general, such processes are under strict stereoelectronic control.[6]

Background

Acid-catalyzed rearrangements of [*m.n.*2]propellane derivatives ($m \geq 3$, $n \geq 3$) have been studied extensively over the years. Important contributions of Cargill,[7] Tobe,[8] Eaton,[9] and others have helped to clarify the course of these reactions. As depicted in Scheme I, products of the Cargill rearrangement are best explained by an initial 1,2-migration of the external bond of the cyclobutane ring.

Recently, however, several reports have appeared which indicate that central bond migration is possible. Eaton and co-workers[9] explored the acid-catalyzed rearrangement of the strained tricyclo[4.2.2]decane **4**. The product isolated, tricyclic diol **5**, derives

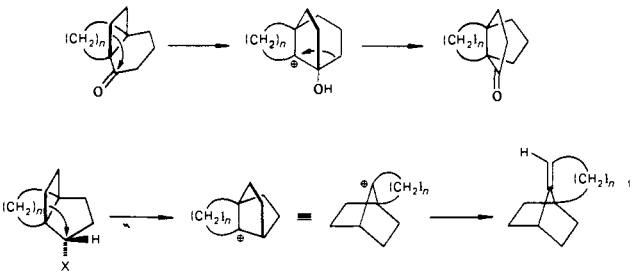


4 5

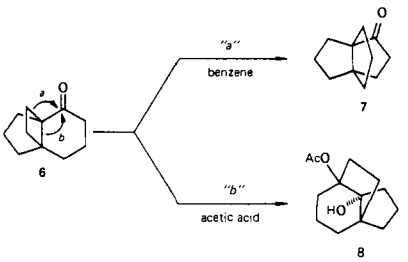
from central bond migration. Here the energetically expensive process of forming a bridgehead carbonium ion is offset by release of the strain energy of two cyclobutane rings.

Employing less strained propellanes, Tobe and co-workers[8] demonstrated that the course of the rearrangement can be profoundly affected by the reaction conditions. For example, treatment of **6** with *p*-toluenesulfonic acid in benzene gave the expected [3.3.3]propellane **7** (mechanism "a", Scheme II), whereas the same reaction carried out with acetic acid as solvent afforded **8**. While no explanation was given by the authors for the ease with which central bond migration occurs, it would seem reasonable to suggest a kinetic preference[10] for central bond migration in this case, followed by efficient capture of the carbonium ion by solvent.

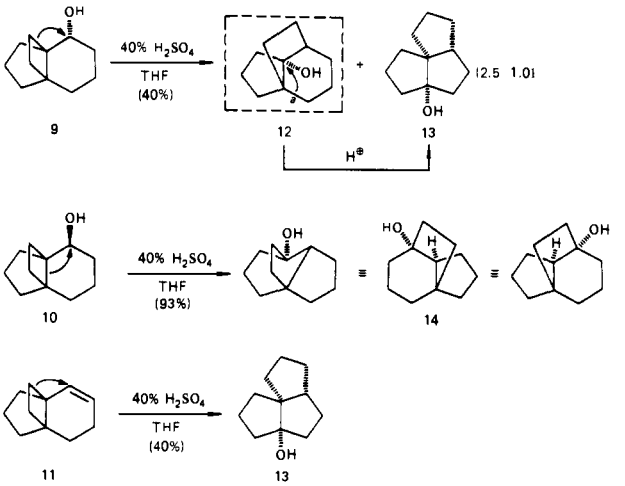
Scheme I



Scheme II



Scheme III



Rearrangement Studies and Discussion. At the outset we considered it prudent to examine the rearrangements of several simple propellane derivatives **9–11** before initiating the quadrone venture (see Scheme III). Toward this end, treatment of anti alcohol **9** with 40% sulfuric acid in THF led to a mixture of two compounds, identified as **12** and **13**. Compound **12**, the result of initial peripheral bond migration, was found to undergo further rearrangement to **13** via a secondary 1,2-shift (bond "a"), thereby affording the isocomene ring system. The syn propellane **10**, on the other hand, afforded a single product when similarly treated. To our surprise, **14**, which is isomeric with **12** and **13**, derived from *central* bond migration. Thus the isomeric alcohols **9** and **10** react via different pathways under the same reaction conditions. Probing further, when olefin **11** was subjected to the standard acid rearrangement conditions, only the secondary product **13** (i.e., initial peripheral bond migration) was isolated.

These data indicated that the rearrangements of model propellanes **9–11** are under stereoelectronic control, as is in evidence in the rearrangements of other polycyclic molecules. For example, the elegant studies of Schleyer and co-workers[11] on the rear-

(4) (a) Danishefsky, S.; Vaughan, K.; Gadwood, R. C.; Tsuzuki, K. J. *J. Am. Chem. Soc.* **1981**, *103*, 4136–4141; **1980**, *102*, 4262–4263. (b) Bornack, W. K.; Bhagwat, S. S.; Ponton, J.; Helquist, P. *J. Am. Chem. Soc.* **1981**, *103*, 4647–4648. (c) Burke, S. D.; Murtiashaw, C. W.; Saunders, J. O.; Dike, M. S. *J. Am. Chem. Soc.* **1982**, *104*, 872–874. (d) Takeda, K.; Shimono, Y.; Yoshii, E. *J. Am. Chem. Soc.* **1983**, *105*, 563–568. (e) Kende, A. S.; Roth, B.; Sanfilippo, P. J.; Blacklock, T. J. *J. Am. Chem. Soc.* **1982**, *104*, 5808–5810. (f) Schlessinger, R. H.; Wood, J. L.; Poss. A. J.; Nugent, R. A.; Parsons, W. H. *J. Org. Chem.* **1983**, *48*, 1146–1147. (g) Dewanckele, J. M.; Zutterman, F.; Vandewalle, M. *Tetrahedron*, **1983**, *39*, 3235–3244.

(5) Smith, A. B., III; Wexler, B. A.; Slade, J. *Tetrahedron Lett.* **1982**, 1631–1634.

(6) For a preliminary account of this work, see: Smith, A. B., III; Wexler, B. A. *Tetrahedron Lett.* **1984**, *22*, 2317–2320. For the now complete synthesis and assignment of absolute stereochemistry of quadrone, see: Smith, A. B., III; Konopelski, J. P. *J. Org. Chem.* **1984**, *49*, 4094.

(7) Cargill, R. L.; Jackson, T. E.; Pert, N. P.; Pond, D. M. *Acc. Chem. Res.* **1974**, *7*, 106–113 and references therein.

(8) (a) Tobe, Y.; Hayauchi, Y.; Sakai, Y.; Odaira, Y. *J. Org. Chem.* **1980**, *45*, 637–641. (b) Kakiuchi, K.; Hato, Y.; Tobe, Y.; Odaira, Y. *J. Chem. Soc., Chem. Commun.* **1982**, 6–7. (c) Kakiuchi, K.; Itoga, K.; Tsugara, T.; Hato, Y.; Tobe, Y.; Odaira, Y. *J. Org. Chem.* **1984**, *49*, 659–665. (d) Kakiuchi, K.; Nakao, T.; Takeda, M.; Tobe, Y.; Odaira, Y. *Tetrahedron Lett.* **1984**, *25*, 557–560.

(9) Eaton, P. E.; Jobe, P. G.; Nyi, K. *J. Am. Chem. Soc.* **1980**, *102*, 6636–6638.

(10) A kinetic preference for central bond migration is evidenced in a related bicyclo[4.2.0] system. See: Pirrung, M. C. *J. Am. Chem. Soc.* **1981**, *103*, 82–87; **1979**, *101*, 7130–7131.

Table I. *syn*-Propellanols and Rearrangement Products

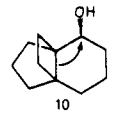
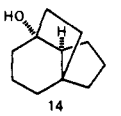
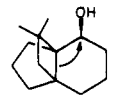
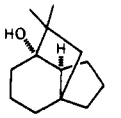
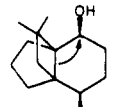
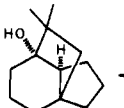
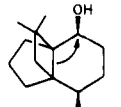
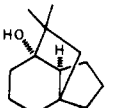
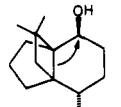
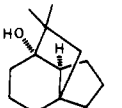
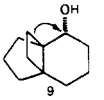
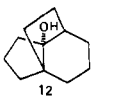
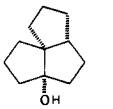
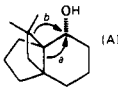
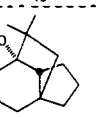
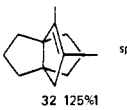
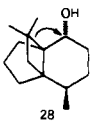
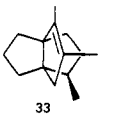
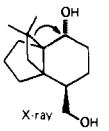
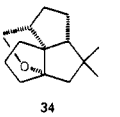
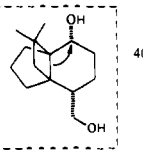
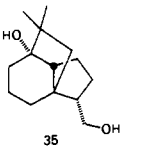
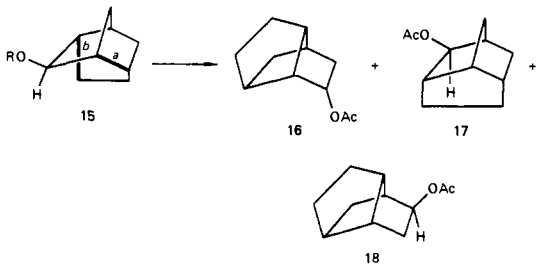
Substrate	Conditions and yield (percent)	Product	Method of structure assignment
 10	40% H_2SO_4/THF 30 min/60° C (93%)	 14	X-ray
 19	40% H_2SO_4/THF 18 hr/75° C (85%)	 23	X-ray
 20	40% H_2SO_4/THF 18 hr/75° C (86%)	 24	(1) MsCl/pyr (2) $LiEt_3BH$
 21	40% H_2SO_4/THF 18 hr/60° C (89%)	 25	X-ray
 X-ray 22	40% H_2SO_4/THF 18 hr/40° C (83%)	 26	X-ray

Table II. *Anti*-Propellanols and Rearrangement Products

Substrate	Conditions and yield (percent)	Product(s)	Method of structure assignment
 9	40% H_2SO_4/THF 3 days/room temp (40%)	 12	correlation with known compound
		 13	correlation with known compound
 27	(A) 40% H_2SO_4/THF 18 hr/60° C/88% (bond *a* migration)	 31	spectral comparison to 54
	(B) CH_3SO_3H/benzene 3 hr/60° C (bonds *a* and *b* migration)	31 +  32 (29%) (25%)	39 spectroscopic analysis and degradation
 28	40% H_2SO_4/THF 18 hr/60° C or CH_3SO_3H/benzene 18 hr/70° C/92%	 33	alternate synthesis
 X-ray 29	40% H_2SO_4/THF 18 hr/45° C (60%)	 34	X-ray of derivative
Quadrone substrate  30 X ray	40% H_2SO_4/THF 48 hr/40° C (83%)	 35	X ray

rangements of adamantane systems clearly demonstrate the importance of overlap of the vacant orbital and the σ-bond of the migrating group. Similarly, Nickon and Weglein[12] demonstrated the importance of bond alignment of the migrating and leaving groups in concerted Wagner–Meerwein rearrangements. In their example, polycyclic hydrocarbon **15**, when subjected to acetolysis



15 16 17 18

conditions, afforded acetate **16** (bond "a" migration, dihedral angle 166°) as the predominant product over the thermodynamically more stable products **17** and **18** (bond "b" migration, dihedral angle 152°).

A similar interpretation of our results seemed reasonable. The empty orbital of protonated olefin **11** would be expected to be well aligned with the peripheral bond of the cyclobutane ring. The syn alcohol **10**, which cannot attain a conformation with the secondary hydroxyl group antiperiplanar to the peripheral bond, undergoes central bond migration. On the other hand, anti alcohol **9** can assume both conformations (hydroxyl group antiperiplanar to either the central or the external bond), yet affords only the product of external bond migration. Following this argument, one is led to the conclusion that the *reactive conformation* of **9** (in a concerted rearrangement) is one in which the hydroxyl group is antiperiplanar to the external bond.[13]

In order to gain more insight into the demands of these systems, a series of tricyclic compounds were prepared that contain some or all of the structural features needed to implement a quadrone synthesis. These compounds, together with their rearrangement products, are illustrated in Tables I–III. Table I contains the propellanes that possess a syn alcohol as the carbocation initiating group; the propellanes in Table II are identical with those in Table I except for the configuration of the secondary hydroxyl group, which is anti; Table III contains the five unsaturated propellanes.

The results presented in Table I indicate that each propellanol affords a single rearranged product derived from central bond migration. Such results are consistent with the above mechanistic rationale. That is, regardless of the configuration of second substituents on the cyclohexane ring, the rearrangement products arise via backside attack of the migrating bond on the carbon bearing the equatorial secondary hydroxyl group.

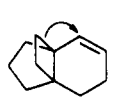
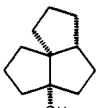
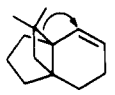
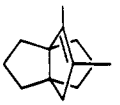
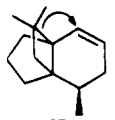
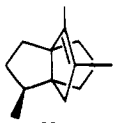
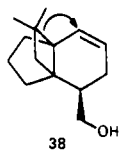
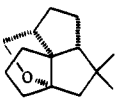
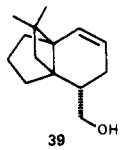
Similarly, the propellenes in Table III afford products derived solely from peripheral bond migration, again in accord with the suggested stereoelectronic control. However, in contrast to the carbonyl systems studied by Cargill,[7] a competition vis-à-vis secondary bond migrations is observed when the initiating group is an olefin. That is in the Cargill rearrangement, the results (as in Scheme I) are consistent with the driving force for secondary bond migration being re-formation of the ketone functionality, whereas with olefins no such driving force exists. Examination

(11) (a) Schleyer, P. v. R.; Lam, L. K. M.; Raber, D. J.; Fry, J. L.; McKervey, M. A.; Alford, J. R.; Cuddy, B. D.; Keizer, V. G.; Geluk, H. W.; Schlatmann, J. L. M. A. *J. Am. Chem. Soc.* **1970**, *92*, 5246–5247. (b) Majerski, Z.; Schleyer, P. v. R.; Wolf, A. P. *J. Am. Chem. Soc.* **1970**, *92*, 5731–5733.

(12) Nickon, A.; Weglein, R. C. *J. Am. Chem. Soc.* **1975**, *97*, 1271–1273.

(13) The information of a "free" carbonium ion is inconsistent with these results, since one would expect to see the same product(s) from the two isomeric alcohols under such conditions. Indeed this type of carbonium ion occurs frequently in the related bicyclo[4.2.0] system.[14-17]

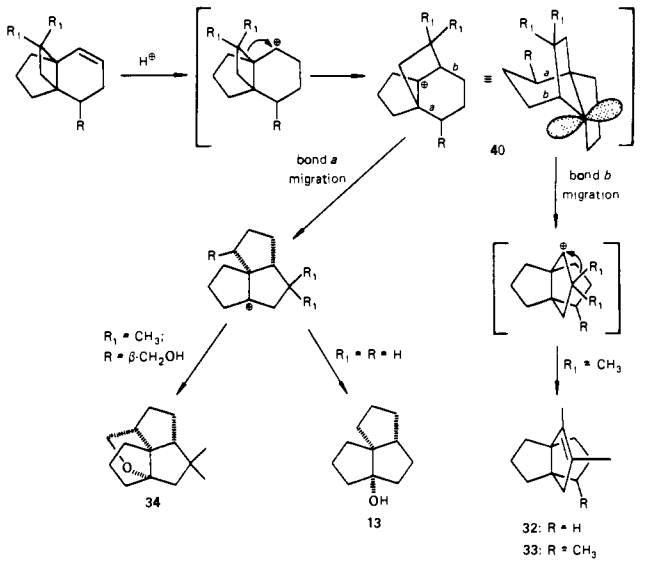
Table III. Olefins and Rearrangement Products

Substrate	*Condition and yield (percent)*	*Product*	*Method of structure assignment*
 11	40% H_2SO_4/THF 18 hr/40° C (40%)	 13	correlation with known compound
 36	CH_3SO_3H/benzene 3 hr/70° C/34%	 32	spectroscopic analysis and degradation
 37	60% H_2SO_4/THF 18 hr/90° C or CH_3SO_3H/benzene 18 hr/75° C/96%	 33	alternate synthesis
 38	40% H_2SO_4/THF 18 hr/60° C (85%)	 34	X-ray of derivative
 39	40% H_2SO_4/THF 18 hr/60° C	N. R.	

of molecular models of the intermediate carbocation (**40**) derived from peripheral bond migration indicates that the empty p orbital is in good alignment with two bonds of the original cyclohexane ring (Scheme IV). Bond "a" migration generates the isocomene skeleton, whereas bond "b" migration gives the [3.3.3]propellane skeleton. This secondary migration seems to be under very subtle control, since relatively minor changes in structure (**11** → **36**) or substitution pattern (**37** → **38**) result in a complete change in product formation.

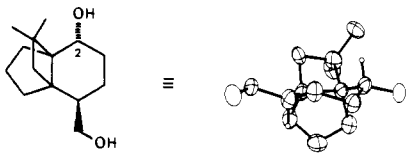
The *anti*-propellanols in Table II represent the most complicated set of rearrangement reactions. Examination of the products obtained indicates that both external and central bond migrations are manifest. Addition of the *gem*-dimethyl[18] substituents to **9** gives **27**, a compound that exhibits products derived from both

Scheme IV

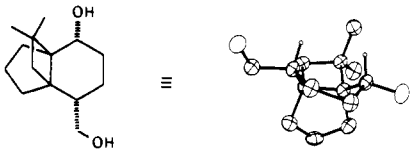


central (**31**) and external (**32**) bond shifts upon treatment with methanesulfonic acid in benzene. Use of more nucleophilic reaction conditions (aqueous sulfuric acid or formic acid) results in the isolation of only **31**. The formation of both **31** and **32** from a single reaction mixture is unique in this study[19] and indicates a delicate balance between the opposing pathways, while the exclusive formation of the product of central bond migration (i.e., **31**) under nucleophilic conditions is reminiscent of the results of Tobe[8b] involving ketone **6**. To our knowledge, the origin of this solvent effect is unknown.

More in line with our expectations were the results obtained from the rearrangements of **28** and **29**, both of which afforded a single product derived from peripheral bond shift. Indeed, compounds **33** and **34** were also obtained from the corresponding olefins **37** and **38** (Table III), indicating that similar forces are in effect in the anti alcohols and their unsaturated analogues. It therefore came as somewhat of a surprise when X-ray crystallographic analysis of **29** indicated that in the solid state **29** occupies



29

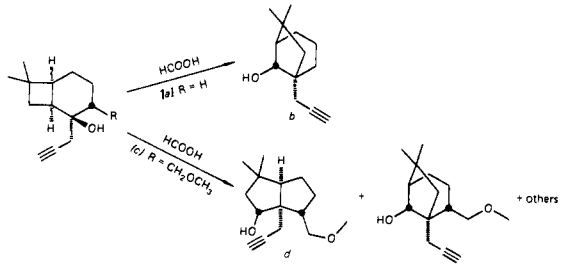


30

a half-chair conformation with both substituents equatorial! Our interpretation of the results to this point had rested on a concerted reaction mechanism with an antiperiplanar rearrangement of the migrating bond and leaving group. If such were the case, however, the conformation of **29** as displayed in the crystal structure (see ORTEP) would dictate central bond shift.

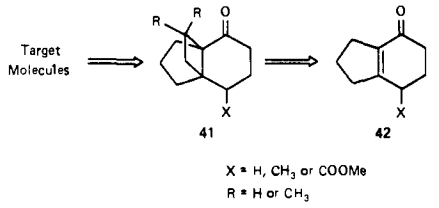
To resolve this issue we examined the possibility that the solution- and solid-state conformations of **29** differ. The ^1H NMR of **29** exhibits a doublet of doublets at δ 4.2 for the C-2 proton. The coupling constants of 11 and 5 Hz indicate an axial arrangement for this proton,[20] implying that the $CDCl_3$ solution

(14) Do Khac Manh Duc; Fetizon, M.; Flament, J. P. *Tetrahedron* **1975**, *31*, 1897–1902.
(15) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2869–2872.
(16) Do Khac Manh Duc; Fetizon, M.; Kone, M. *Tetrahedron* **1978**, *34*, 3513–3523.
(17) Hayanao, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Helv. Chim. Acta* **1981**, *64*, 1347–1364.
(18) Added substituents (for example, *gem*-dimethyl substituents[17] can cause a profound effect on the course of rearrangement reactions. In a recent synthesis of quadrone,[4d] the desired peripheral bond migration occurs exclusively in the model compound a → b. However, addition of the protected hydroxymethyl substituent (c) leads to appreciable amounts of the undesired central bond migration product d, resulting in drastically reduced yields of the desired material.



(19) This type of product mixture is not uncommon in the rearrangements of bicyclo[4.2.0]octane systems.[13-15]
(20) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: New York, 1969; p 288.

Scheme V



conformation of **29** is similar to that in the solid state.[21] Nevertheless, in light of the results given in Tables I–III we suggest that the *reactive* conformation of **29** is not the half chair occupied in the crystalline (or $CDCl_3$ solution) state, but rather one wherein the C-2 hydroxyl group is antiperiplanar to the peripheral cyclobutane bond.

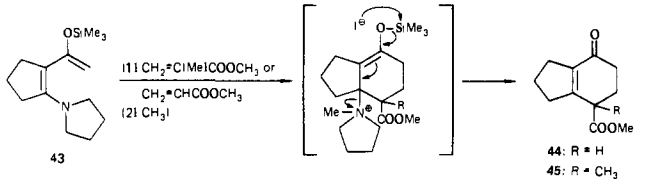
From the rearrangement reactions of **9**, **28**, and **29** we were confident that **30** would lead to the desired quadrone precursor, provided that secondary migrations could be suppressed. Much to our amazement, however, compound **35**, obtained from **30** in 83% yield, derived from *central* bond migration! Again we sought insight to this result through conformational analysis. The solid-state structure of **30**, depicted above, clearly shows that the cis-1,4-disubstituted cyclohexane ring occupies a boat conformation with both substituents pseudoequatorial. In this case the conformation of the molecule in the solid state corresponds to the theory of backside assistance of the migrating bond, leading to inversion at C-2, with concomitant generation of the energetically less favored *trans*-bicyclo[3.3.0]octane embodied in **35**.

Thus, with the possible exception of product **34** derived from diol **29**, it appears that the acid-catalyzed rearrangements of [4.3.2]propellan-2-ols undergo concerted rearrangements involving initial 1,2-alkyl shift of the best aligned cyclobutyl bond. In cases wherein initial peripheral bond migration pertains, facile secondary alkyl shifts occur, due to good bond alignment of a secondary migratory group with the empty orbital of the intermediate carbonium ion (**40**).

Preparative Experiments

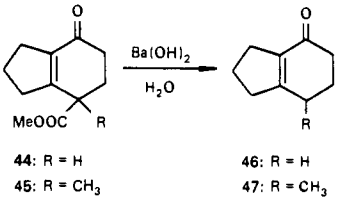
The [4.3.2]propellane derivatives employed in this study were prepared by using the methodology developed in connection with our recent modhephene synthesis.[22] Specifically, we envisioned the rearrangement termini (alcohol or olefin) of the target molecules to originate from the corresponding ketone **41**, which in turn could be obtained via [2 + 2]-photochemical cycloaddition of the requisite olefin (ethylene or isobutylene) to enone **42** (Scheme V).

In this regard we had observed in earlier work[22] that condensation of methyl acrylate (or methyl methacrylate) with azadiene **43**, followed by treatment with methyl iodide, afforded enone **44**

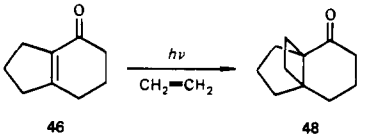


(or **45**) in good yield without concomitant formation of the isomeric α,β-unsaturated ester (in the case of **44**).[23]

Treatment of enones **44** and **45** with barium hydroxide in water at reflux achieved concomitant hydrolysis and decarboxylation to afford enones **46** and **47**, respectively, in high yield.[22]



Photochemical Cycloadditions: Construction of the Propellane Skeleton. Attention was next focused on the synthesis of the various [4.3.2]propellanones. The simplest of these, propellanone **48**, was formed in 86% yield by irradiation of a methylene chloride



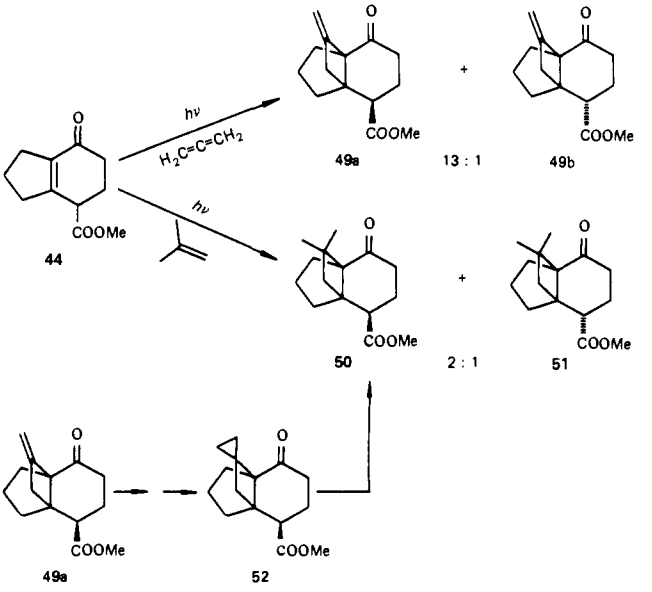
solution of **46** in the presence of ethylene at −78 °C for 17 h. In this case, there is no possibility for regio- or stereochemical ambiguity; only one cyclobutane can result.

Such is not the case for the photoaddition of isobutylene to enones **44**, **46**, and **47**; two possible problems were anticipated. First, there is the problem of regiocontrol of cyclobutane formation (i.e., head to head vs. head to tail). Second, in the case of **44** and **47**, there is the question of the stereochemical relationship of the ester (or methyl) substituent to the cyclobutyl ring.

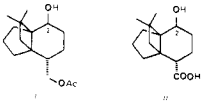
With regard to regioselectivity, the classic study of Corey[24] demonstrated that the regiochemistry of olefin additions is governed by a combination of electronic and steric factors. Allene, for example, was shown to give only head-to-head product, whereas isobutylene gave different products depending on the enone substitution pattern.

The stereochemical question has been addressed by Wiesner,[25] who developed a predictive rule based on the [2 + 2]-photo-

Scheme VI



(21) We also examined the structure of **22**, which should exist in a diequatorial conformation similar to **29**. Indeed, this is the case in the solid state, as evidenced by the X-ray analysis. Furthermore, while the ^1H NMR of **22** is difficult to interpret due to similar chemical shifts of the C-2 proton and the methylene protons of the hydroxymethyl moiety, the closely related analogues *i* and *ii* each exhibit a doublet of doublets in the NMR consistent with an equatorial conformation of the secondary hydroxyl group. Therefore, in the case of **22** the solid state and $CDCl_3$ solution structure and the reaction product are all consistent with the idea of stereoelectronic control of the rearrangement process.



(22) Smith, A. B., III; Jerris, P. J. *J. Org. Chem.* **1982**, *47*, 1845–1855.

(23) In contrast, hydrolysis of Diels–Alder adducts derived from *trans*-1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene requires aqueous acid which results in double bond isomerization in certain cases. See: Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996–7000.

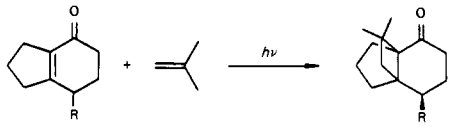
(24) Corey, E. J.; Bass, J. D.; LeMahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570–5583.

(25) (a) Wiesner, K. *Tetrahedron* **1975**, *31*, 1655–1658. (b) Marini-Bettolo, G.; Sahov, S. P.; Poulton, G. A.; Tsai, T. Y. R.; Wiesner, K. *Tetrahedron* **1980**, *36*, 719–721.

cycloaddition of allene to enones. The Wiesner mnemonic implies that since the β-carbon of the enone system in the excited state has increased electron density,[26] the position is pyramidalized prior to cycloaddition and as a result assumes the most stable conformation. It is this conformation that reacts with the allene to give the observed products.

Irradiation of a hexane solution of enone **44** and allene at −20 °C afforded, as expected, the head-to-head product **49** as a 13:1 mixture of ester isomers (Scheme VI). Single-crystal X-ray analysis confirmed the syn stereochemistry of the ester group in the major isomer (**49a**), consistent with the Wiesner hypothesis. When isobutylene was substituted for allene in the above reaction, adducts **50** and **51** were obtained as a 2:1 mixture. For preparative purposes pure **50** could be obtained by recrystallization. Furthermore, treatment of the reaction mixture with $NaOCH_3$/$HOCH_3$ gave a new mixture enriched in the anti isomer **51** (5:1), from which pure **51** could be obtained by crystallization. That the major isomer was the syn compound derived from the interconversion of **49a** to **50**. Toward this end, reduction of **49a** with sodium borohydride, followed by cyclopropanation and oxidation using the procedure of Swern,[27] afforded ketone **52**. Hydrogenolysis (which resulted in cyclopropane ring cleavage and ketone reduction) followed by oxidation gave **50**, identical with the sample isolated from the isobutylene photoreaction.[28]

Reaction of enone **46** with isobutylene under similar conditions afforded **53** as a single compound in 41% yield. In a like manner,

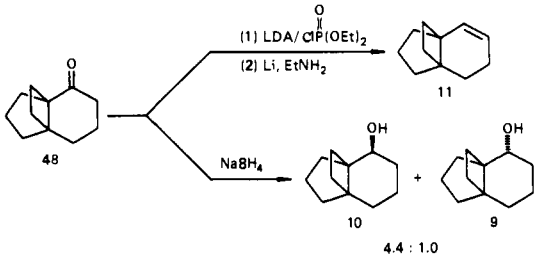


46: R = H
47: R = CH_3

53: R = H
54: R = CH_3

enone **47** gave a 10:1 mixture of isomeric propellanones (56%), the major isomer (**54**) having the syn relationship of the cyclobutane ring to the methyl substituent. Regio- and stereochemical assignments here were based on analogy with that observed for **44**, in conjunction with rigorous assignment of the subsequent rearrangement products. Thus, isobutylene is seen to add in a head-to-head fashion to the enones **44**, **46**, and **47**. Furthermore, the stereoselectivity is always in favor of the *syn* compound as predicted by the Wiesner model; the degree of the selectivity, however, varies considerably.

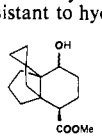
Preparation of the Rearrangement Substrates: An Exercise in Functional Group Manipulation. With propellanones **48**, **50**, **51**, **53**, and **54** in hand, we turned to the functional group manipulations required to generate the rearrangement substrates. Toward this end, ketone **48** was reduced with sodium borohydride in



(26) (a) Zimmerman, H. E.; Swenton, J. S. *J. Am. Chem. Soc.* **1964**, *86*, 1436–1437. (b) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486–4488.

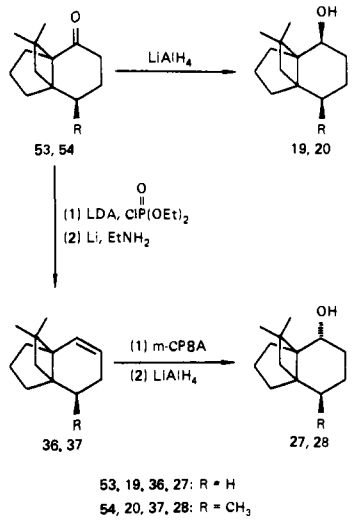
(27) (a) Sharma, A. K.; Ku, T.; Dawson, A. D.; Swern, D. *J. Org. Chem.* **1975**, *40*, 2758–2764. (b) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.

(28) It proved impossible to form cyclopropane **52** directly from **49a**. Likewise, alcohols *iii* proved resistant to hydrogenolysis.



iii

Scheme VII



53, **19**, **36**, **27**: R = H
54, **20**, **37**, **28**: R = CH_3

ethanol to give a mixture of diols **9** and **10**, which were separable by medium-pressure liquid chromatography. The major isomer was assigned structure **10** on the basis of the ^1H NMR resonance for the axial methine proton (δ 3.58), which appeared upfield by 0.5 ppm from the corresponding resonance in the minor isomer **9**,[29] and the expected approach of hydride reducing agents from the least hindered side of the molecule (i.e., anti to the cyclobutyl ring).[30] Olefin **11**, on the other hand, was prepared from ketone **48** via the Ireland protocol.[31] The basic conditions employed for both the preparation of the enol phosphate derivative and its reduction were anticipated to ensure that the propellane framework remained intact.

Reduction of ketones **53** and **54** with lithium aluminum hydride afforded alcohols **19** and **20**, respectively, with no trace of the isomeric anti alcohols (Scheme VII). Undoubtedly, the stereoselectivity of this reaction derives from the steric influence of the methyl substituent on the cyclobutane ring that blocks approach from the top face of the molecule.

Application of the Ireland procedure[31] to ketones **53** and **54** gave the corresponding olefins **36** and **37** in 88% and 85% yield, respectively. These olefins, in turn, were used in the synthesis of the anti alcohols **27** and **28**. Treatment of **36** and **37** with *m*-chloroperbenzoic acid at 0 °C in the presence of solid sodium bicarbonate gave, in each case, only the anti epoxide (again due to the steric influence of the cyclobutyl methyl group). Reduction with $LiAlH_4$ in THF at reflux afforded the anti alcohols **27** and **28**, respectively, free from the corresponding syn isomers.

The protocols developed for ketones **53** and **54** were also employed (with only minor modification) for the preparation of propellanes **21–22**, **29–30**, and **38–39** (see Experimental Section for details).

Structure Determination: A Testimony to X-ray Crystallography. Since the rearrangement products obtained in this study were architecturally complex, we felt that structure determination could not be achieved by spectroscopic analysis alone. Therefore, the majority of the structural proofs were based either on single-crystal X-ray analysis or chemical correlation with known compounds.[32]

In Table I, column 3 indicates that, except for **24**, all structures in this series were determined by X-ray analysis. The identity

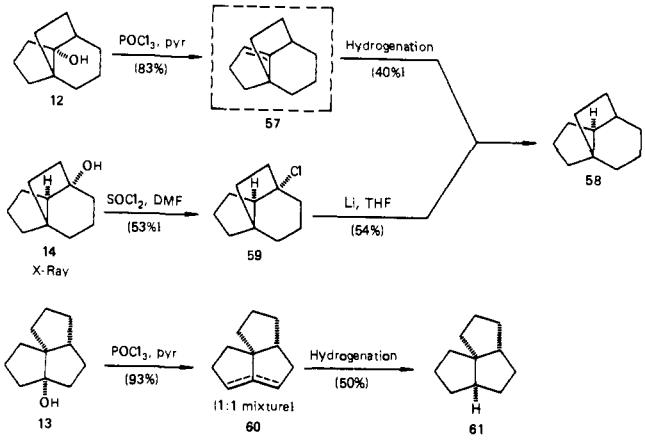
(29) See ref 20, p 239.

(30) Tobe, Y.; Doi, A.; Kimura, K.; Odaira, Y. *Bull. Chem. Soc. Jpn.*, **1979**, *52*, 639–640.

(31) (a) Ireland, R. E.; Pfister, G. *Tetrahedron Lett.* **1969**, 2145–2148. (b) Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098–5100.

(32) A full account of the X-ray crystallographic analysis of compounds **14**, **22**, **23**, **26**, **29**, **30**, **49a**, and **67** will be forthcoming; unpublished results of P. Carroll, Director, University of Pennsylvania, X-ray crystallographic faculty. For review purposes, cell parameters, atomic coordinates, and refined temperature factor expressions were provided.

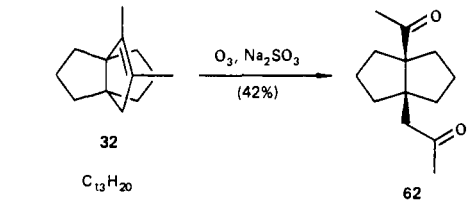
Scheme VIII



of **24** was established by chemical correlation with **25**. That is, treatment of **25** with methanesulfonyl chloride followed by reduction of the primary mesylate with lithium triethyl borohydride afforded **24**.

The structures of compounds **12** and **13** were also assigned by chemical transformation (Scheme VIII). Compound **12** was treated with phosphorus oxychloride in pyridine to give a single olefin assigned structure **57**.[33] Hydrogenation with palladium on carbon afforded undecane **58**. The latter was also obtained from **14** (the structure of which was determined by X-ray analysis) by treatment with thionyl chloride in dimethylformamide (to give the bridgehead chloride **59**) followed by reduction with lithium metal. Finally, alcohol **13**, having the isocomene ring system, was dehydrated with phosphorus oxychloride to afford a mixture of olefins (**60**) that was hydrogenated to the known undecane **61**.[34]

In Table II, propellane **32** was identified via a combination of spectroscopic and chemical methods. Specifically, the ^{13}C NMR spectrum of **32**, which contains resonances for two sp^2 carbons and two quaternary carbons, displayed a total of only ten resonances, even though high-resolution mass spectrometry clearly demonstrated the molecular formula to be $C_{13}H_{20}$. This simplification in the ^{13}C NMR stems from a symmetry plane that bisects the cyclopentene ring. Treatment of **32** with ozone followed by sodium sulfite workup affords a new compound (**62**) that



32

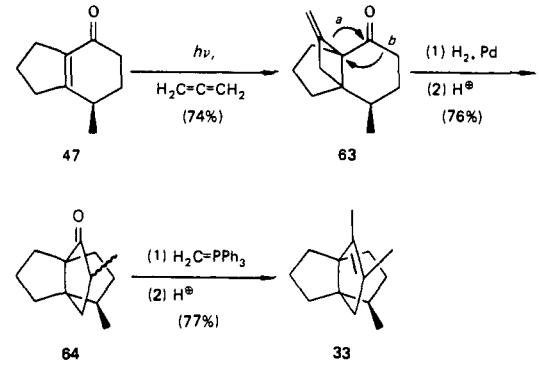
$C_{13}H_{20}$

10 singlets in ^{1}H-decoupled ^{13}C NMR

62

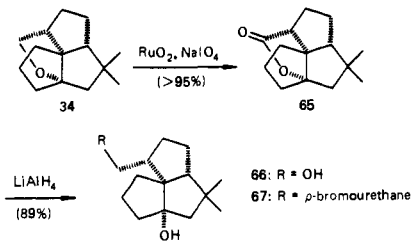
contains two methyl ketones, one of which is bonded to a quaternary carbon while the other is bonded to a methylene group that displays as a singlet (δ 2.75) in the ^{1}H NMR spectrum. Such data, in conjunction with a rigorous structure proof for **33** (vide infra), are compatible only with structure **32**.

Turning to propellane **33**, we relied on alternate synthesis. Toward this end, irradiation of enone **47** in the presence of allene led to a 7:1 mixture of tricyclic ketone **63** and its methyl epimer. Pure **63** was hydrogenated and then subjected to the acid-catalyzed Cargill rearrangement. As expected,[7] propellanone **64** was formed in 76% yield. Wittig olefination followed by isomerization of the double bond into the cyclopentane ring afforded **33**, identical in all respects with the product obtained from **28**.



47 63 64 33

Finally, tetracyclic ether **34**, the only product obtained in the rearrangement of both diol **29** and olefin **38**, was chemically modified to enable the preparation of a crystalline derivative. Toward this end, ruthenium tetraoxide mediated oxidation[35] afforded lactone **65** which, when reduced with $LiAlH_4$, was converted to diol **66**. Treatment of the latter with *p*-bromophenyl isocyante afforded the crystalline *p*-bromourethane **67**, which was shown via simple-crystal X-ray analysis to have the structure shown.



34 65

Experimental Section

Materials and Equipment. All solvents used were reagent grade and were distilled prior to use. The zinc copper couple was prepared from zinc powder and aqueous copper sulfate according to the procedure of Shank.[36] All VPC separations were achieved by using a Varian Aerograph Model 920 gas chromatograph fitted with one of the following columns: column A, 12.5% QF-96, 10 ft × $^1/_4$ in.; column B, 25% Carbowax 20M, 20 ft × $^1/_4$ in.; column C; 12.5% SE-10, 20 ft × $^1/_4$ in. The column support employed was Chromosorb W BW 60/30. The helium carrier gas flow was 60 mL/min, and the oven temperature was as stated in the text. The photolysis apparatus, as described by Cargill,[37] employed a 1000-W mercury lamp equipped with a G.E. ballast 35, 9627-6009 power source. Precoated silica gel plates (250 μm) with a fluorescent indicator, obtained from Merck, were used for both analytical thin-layer chromatography (TLC) and preparative thin-layer chromatography. Silica gel 60 (particle size 0.04–0.063 mm) obtained from Merck was employed for flash chromatography and medium-pressure liquid chromatography (MPLC). High-pressure liquid chromatography (HPLC) was performed on either a Waters Associates Prep LC/System 500 using silica gel columns or a Waters Associates analytical system using a 33 cm × 7 mm column packed with μPorasil. Melting points were obtained by using a Thomas-Hoover instrument and are uncorrected. Boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer. Proton NMR were obtained on either a Varian Model T-60A (60 MHz) or a Bruker WP-250 FT (250 MHz). Chemical shifts are reported in δ values in parts per million relative to tetramethylsilane (δ Me_4Si 0.0). Carbon NMR were obtained on the Bruker WP-250 FT (62.9 MHz) or on a Bruker WP-200SY (50.327 MHz). Chemical shifts are reported in δ values in parts per million relative to chloroform (δ $CHCl_3$ 77.0).

(33) Structure **57** is comparable to structure **3** (see eq 1), a synthetic intermediate in our proposed quadrone synthesis.

(34) Takaishi, N.; Inamoto, Y.; Tsuchihashi, K.; Yashima, K.; Aigami, K. *J. Org. Chem.* **1975**, *40*, 2929–2937.

(35) Smith, A. B.; Scarborough, R. M. *Synth. Commun.* **1980**, *10* 205–211.

(36) Shank, R. S.; Schecter, H. *J. Org. Chem.* **1959**, *24*, 1825–1826.

(37) Cargill, R. L.; Dalton, J. R.; Murton, G. H.; Caldwell, W. E. *Org. Synth.* **1984**, 118–124.

(38) The numbering system used for fused pentalenes in this paper follows that of the unfused pentalenes. Compound **13**, using systematic numbering, would be named (3a*S**,5a*R**,8a*R**)-1,2,3,3a,4,5,5a,6,7,8-dodecahydro-5a-hydroxycyclopenta[*c*]pentalene.

Rearrangement Reactions: General Procedure. Three sets of acid/solvent mixtures were employed in the present study: (A) 40% sulfuric acid in THF, (B) methanesulfonic acid in benzene, and (C) formic acid. The reactions were run as follows: a solution of the substrate in the appropriate solvent/acid mixture was allowed to react under the indicated conditions of time and temperature. After being cooled to room temperature, the reaction solution was diluted with ether and water, and the layers were separated. The organic layer was washed with water and brine and dried with magnesium sulfate. Removal of the solvent in vacuo afforded the crude product mixture.

(3a*S,4*S**,7a*S**)-3a-Hydroxy-4,7a-ethanoperhydroindene (12) and (3*R**,3a*R**,6a*S**)-3-Hydroxycyclopenta[*c*]perhydropentalene (13).**[38] A solution of alcohol **9** (970 mg, 5.84 mmol) in 10 mL of tetrahydrofuran and 6.0 mL of 40% sulfuric acid was stirred at room temperature for 3 days. Normal workup gave 993 mg of a gummy oil, which was a mixture of three compounds. Flash chromatography (25% ether, hexane (v/v)) gave 263 mg (27%) of **12** and 123 mg (12.6%) of **13** as well as 393 mg of recovered starting material. Increased reaction temperatures and reaction time resulted in isolation of products containing a higher ratio of alcohol **13**. At 60 °C for 2 h only **13** was isolated in good yields.

The alcohol **13** had the following spectral data: IR (CCl_4) 3600 (m), 3325–3525 (m), 2950 (br s), 2850 (s), 1445 (m), 1240 (m), 910 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.14–1.30 (m, 6 H), 1.30–2.04 (m, 12 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 89.792, 62.18, 52.21, 41.80, 41.15, 40.48, 35.27, 34.12, 30.01, 27.24, 23.48; mass spectrum, *m/e* 166.1351 (M^+, calcd for $C_{11}H_{18}O$, 166.1358).

The alcohol **12** had the following spectral data: IR (CCl_4) 3615 (m), 2975 (s), 2860 (s), 1450 (m), 1150 (m), 1005 (m), 910 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.14–1.68 (m, 12 H), 1.68–1.96 (m, 5 H), 2.10 (dd, J = 4, 3.5 Hz, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 86.88, 50.30, 41.39, 36.01, 33.60, 22.18, 31.30, 26.74, 24.71, 20.39, 17.69; mass spectrum, *m/e* 166.1354 (M^+, calcd for $C_{11}H_{18}O$, 166.1358).

Resubmitting purified alcohol **12** to the same acid conditions at 60 °C afforded alcohol **13** as the only observed product.

(3a*S,7a*R**)-4-Hydroxy-4,7a-ethanoperhydroindene (14).** A solution of alcohol **10** (46 mg, 0.28 mmol) in 3 mL of THF and 5 mL of 40% sulfuric acid was warmed to 60 °C for 30 min. Normal workup afforded 43 mg (93%) of **14** as a crystalline white solid: mp 74.5–75 °C; IR (CCl_4) 3600 (m), 3150–3525 (br m), 2840–2925 (br s), 1450 (m), 1320 (m), 1140 (m), 1060 (m), 910 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.14–2.0 (m, 18 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 81.50, 60.41, 52.74, 40.89, 37.18, 36.68, 34.65, 31.48, 25.07, 22.51, 21.30; mass spectrum, *m/e* 166.1351 (M^+, calcd for $C_{11}H_{18}O$, 166.1358).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.18; H, 10.95.

(3*R,3a*R**,6a*S**)-3-Hydroxycyclopenta[*c*]perhydropentalene (13).** Olefin **11** (11 mg, 0.07 mmol) in 0.3 mL of tetrahydrofuran and 0.5 mL of 40% sulfuric acid was warmed to 40 °C overnight. Standard workup followed by preparative vapor-phase chromatography (column C, 155 °C) afforded 4 mg of **13**, identical in all respects with the previously isolated material.

(3a*S,4*S**,7a*R**)-4-Hydroxy-9,9-dimethyl-4,7a-ethanoperhydroindene (23).** A solution of the alcohol **19** (53 mg, 0.27 mmol) in THF (6 mL) containing 40% H_2SO_4 (3 mL) was stirred at 75 °C for 18 h. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:10) as the eluting solvent to give 45 mg (85%) of pure **23** as a colorless oil: IR ($CHCl_3$) 3610, 2940, 2870, 1450, 1125, 1050 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.99 (s, 3 H), 1.08 (s, 3 H), 1.22–1.97 (m, 16 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 21.51, 24.12, 24.20, 25.95, 28.41, 38.26, 38.43, 39.91, 42.21, 49.98, 50.24, 62.62, 82.90; mass spectrum, *m/e* 194.1632 (M^+, calcd for $C_{13}H_{22}O$, 194.1671).

(1*R,3a*S**,4*S**,7a*R**)-4-Hydroxy-1,9,9-trimethyl-4,7a-ethanoperhydroindene (24).** A solution of the alcohol **20** (50 mg, 0.24 mmol) in THF (60 mL) containing 40% H_2SO_4 (3 mL) was stirred at 75 °C for 18 h. After workup, the crude product was purified by flash chromatography using ethyl acetate/hexane (1:10) as the eluting solvent to give 43 mg (86%) of pure **24** as a white solid: mp 55–58 °C; IR ($CHCl_3$) 3600, 2950, 2860, 1060 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.81 (d, J = 6.4 Hz, 3 H), 0.98 (s, 3 H), 1.05 (s, 3 H), 1.10–1.90 (m, 15 H); NMR (^{13}C, 50.327 MHz, $CDCl_3$) δ 12.93, 21.33, 23.78, 24.14, 28.11, 32.48, 37.10, 40.05, 41.62, 42.76, 42.95, 52.33, 62.90, 82.24; mass spectrum, *m/e* 208.1805 (M^+, calcd for $C_{14}H_{24}O$, 208.1827).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.87; H, 11.80.

(1*R,3a*S**,4*S**,7a*R**)-(Hydroxymethyl)-4-hydroxy-9,9-dimethyl-4,7a-ethanoperhydroindene (25).** A solution of cis diol **21** (210 mg, 0.94 mmol) in 12 mL of tetrahydrofuran containing 36 mL of 40% sulfuric acid was heated to 60 °C overnight. Normal workup, followed by removal of the solvent in vacuo, gave 200 mg of a mobile clear oil. Purification via MPLC afforded 192 mg (89%) of **25** as a white crystalline solid: mp 132–133 °C; IR (KBr) 3325–3440 (br s), 2840–2950 (br s), 1450 (m), 1360 (m), 1300 (m), 1110 (s), 1050 (m), 1030 (s), 1000 (m), 980 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.0 (s, 3 H), 1.18 (s, 3 H), 1.20–1.62 (m, 6 H), 1.62–2.06 (m, 10 H), 3.57 (dd, J = 7.1, 10.6 Hz, 1 H), 3.71 (dd, J = 5.9, 10.6 Hz, 1 H); mass spectrum, *m/e* 224.1770 (M^+, calcd for $C_{14}H_{24}O_2$, 224.1776).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.55; H, 10.68.

(1*S,3a*S**,4*S**,7a*R**)-1-(Hydroxymethyl)-4-hydroxy-9,9-dimethyl-4,7a-ethanoperhydroindene (26).** A solution of diol **22** (144 mg, 0.64 mmol) in 3 mL of tetrahydrofuran containing 9 mL of 40% sulfuric acid was warmed to 40 °C overnight. Standard workup afforded 140 mg of a white solid. Crystallization of the solid with ether afforded 120 mg (83%) of **26** as a white crystalline solid: mp 106–107 °C; IR ($CHCl_3$) 3605 (m), 3525–3260 (br w), 2950 (s), 2925 (s), 2870 (m), 1450 (m), 1380 (w), 1360 (w), 1110 (m), 1070 (m), 1055 (m), 1015 (m), 905 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.06 (s, 3 H), 1.26 (s, 3 H), 1.50–1.72 (m, 7 H), 1.78–2.18 (m, 9 H), 3.50 (dd, J = 8.5, 10.7 Hz, 1 H), 3.82 (dd, J = 5.5, 10.7 Hz, 1 H).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.09; H, 10.82.

(3a*R,4*S**,7a*R**)-4-Hydroxy-9,9-dimethyl-4,7a-ethanoperhydroindene (31).** (A) A solution of alcohol **27** (40 mg, 0.2 mmol) in 40% H_2SO_4 (6 mL) containing THF (2 mL) was stirred at 60 °C for 18 h. The crude reaction mixture obtained from normal workup was passed through a short column of silica gel. The solvent was distilled off carefully to give 34 mg (85%) of pure **31** as a colorless oil: IR ($CHCl_3$) 3600, 2940, 2860, 1450, 1070 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.95 (dd, J = 6.4, 14.0 Hz, 1 H), 1.05 (s, 3 H), 1.09 (s, 3 H), 1.14–1.74 (comp, 12 H), 2.00 (m, 2 H, 2.27 (dd, J = 8.1, 11.3 Hz, 1H); NMR (^{13}C, 62.7 MHz, $CDCl_3$) δ 18.34, 20.32, 22.54, 26.71, 29.08, 29.14, 29.91, 35.26, 46.75, 47.39, 49.22, 56.71, 77.83; mass spectrum, *m/e* 194.1647 (M^+, calcd for $C_{13}H_{22}O$, 194.1671).

(B) A solution of alcohol **27** (30 mg, 0.15 mmol) in formic acid (20 mL) was heated at 70 °C for 18 h. The resulting solution was diluted with pentane and water, and the layers were separated. Solid sodium carbonate was added to the organic layer. Filtration was followed by careful removal of the solvent by distillation. The crude product was purified by flash chromatography (heptane/ether 20:1–5:1) to give **31** (11 mg, 37%) and the formate ester of **31** (10 mg, 29%), which was hydrolyzed to **31** by treatment with 4 N sodium hydroxide (0.5 mL) in THF (2 mL) at room temperature for 4 h.

(3a*R,4*S**,7a*R**)-4-Hydroxy-9,9-dimethyl-4,7a-ethanoperhydroindene (31) and 3,3a,4,5,6,6a-Hexahydro-1,2-dimethyl-3a,6a-propanopentalene (32).** A solution of alcohol **27** (35 mg, 18 mmol) in 2 mL of benzene was treated with methanesulfonic acid (2 drops) and heated to 65 °C for 3 h. Standard workup, followed by removal of solvent by careful distillation, afforded 25 mg of crude material. Separation of the products by flash chromatography (pentane followed by hexane/ethyl acetate (18:1) afforded olefin **32** (8 mg, 25%) and alcohol **31** (10 mg, 29%), both as colorless oils. Alcohol **31** was identical with the sample previously isolated. Olefin **32** had the following spectral properties: IR ($CHCl_3$) 2930, 2850, 1440 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.52 (s, 6 H), 1.25–1.56 (comp, 12 H), 2.15 (br s, 2 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 11.15, 13.87, 25.89, 37.95, 41.74, 53.48, 57.62, 71.80, 128.62, 135.07; mass spectrum, *m/e* 176.1572 (M^+, calcd for $C_{13}H_{20}$, 176.1565).

Anal. Calcd for $C_{13}H_{20}$: C, 88.56; H, 11.44. Found: C, 88.36; H, 11.62.

(3a*S,4*S**,6a*S**)-3,3a,4,5,6,6a-Hexahydro-1,2,4-trimethyl-3a,6a-propanopentalene (33).** To a solution of the alcohol **28** (110 mg, 0.53 mmols) in benzene (5 mL) was added methanesulfonic acid (2 drops), and the mixture was stirred at 70 °C for 18 h. The product obtained from standard workup was purified by flash chromatography (pentane) to give 92 mg (92%) of the olefin **33** as a colorless oil: IR ($CHCl_3$) 2940, 2860, 1590, 1420 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.93 (d, J = 6.6 Hz, 3 H), 1.00–1.80 (comp, 12 H), 1.51 (s, 3 H), 1.54 (s, 3 H), 2.32 (br d, J = 15 Hz, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 10.72, 13.92, 14,48, 25.80, 34.36, 36.57, 38.80, 40.54, 43.68, 45.01, 60.65, 72.09, 128.64, 135.14; mass spectrum, *m/e* 190.1721 (M^+, calcd for $C_{14}H_{22}$, 190.1722).

Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.23; H, 11.56.

Treatment of olefin **37** (300 mg, 1.58 mmol) in benzene (10 mL) with methanesulfonic acid (5 drops) at 75 °C for 18 h gave, after workup, 290 mg (96%) of **33**, identical with the above material.

(1*S,3a*R**,4*S**,7a*R**)-1-(Hydroxymethyl)-4-hydroxy-9,9-dimethyl-4,7a-ethanoperhydroindene (35).** A solution of cis diol **30** (40 mg, 0.17 mmol) in 1 mL of tetrahydrofuran containing 2 mL of 40% sulfuric acid was warmed to 40 °C for 48 h. Standard workup gave 59 mg of a white oily solid. Crystallization with ether afforded 33 mg (83%) of a white crystalline solid (**35**): mp 170–170.5 °C; IR ($CHCl_3$) 3600 (w),

3125–3520 (br m), 2950 (br s), 2860 (m), 1450 (m), 1430 (m), 1375 (w), 1280 (m), 1055 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.1–1.26, 1.16, 1.20 (m, s, s, 8 H), 1.28–1.76 (m, 8 H), 1.76–1.96 (m, 4 H), 2.12–2.30 (m, 1 H), 2.44 (dd, J = 9, 8.5 Hz, 1 H), 3.59 (s, 1 H), 3.61 (s, 1 H); mass spectrum, m/e 224.1793 (M^+, calcd for $C_{14}H_{24}O_2$, 224.1777).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.94; H, 10.84.

3,3a,4,5,6,6a-Hexahydro-1,2-dimethyl-3a,6a-propanopentalene (32). To a solution of the olefin **36** (50 mg, 0.28 mmol) in benzene (2 mL) was added methanesulfonic acid (1 drop). The resulting solution was heated at 70 °C for 18 h. Normal workup, followed by removal of solvent by careful distillation, afforded the crude product, which was purified by VPC (column A) to give 17 mg (34%) of pure **32** as a colorless oil, identical with the sample previously prepared.

(2a*R,2b*S**,2c*S**,4a*R**)-3,3-Dimethyl-2a,2c-ethanoperhydropentaleno[3a,6a-*b*]perhydrofuran (34).** A solution of olefin **38** (65 mg, 0.32 mmol) in 6 mL of tetrahydrofuran and 4 mL of 40% sulfuric acid was warmed to 60 °C overnight. Standard workup gave 65 mg of mobile oil, which was purified by flash chromatography (25% ether, hexane (v/v)) to give 55 mg (85%) of ether **34** as a clear oil: IR (CCl_4) 2825–2960 (br s), 1400 (m), 1375 (w), 1350 (m), 1300 (w), 1275 (m), 1085 (m), 1070 (m), 1055 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.05 (s, 3 H), 1.11 (s, 3 H), 1.11 (s, 3 H), 1.55–1.98 (m, 12 H), 2.0–2.12 (m, 1 H), 2.21–2.38 (m, 1 H), 3.35 (dd, J = 9.6, 10 Hz, 1 H), 4.02 (dd, J = 8.3, 10 Hz, 1 H); mass spectrum, m/e 206.1696 (M^+, calcd for $C_{14}H_{22}O$, 206.1681).

Treatment of diol **29** (5 mg, 0.02 mmol) in tetrahydrofuran (1 mL) with 1 mL of 40% sulfuric acid at room temperature for 36 h afforded, after workup, 3 mg (60%) of **34**, identical with the above material.

Methyl 2,3,4,5,6,7-Hexahydro-7-oxo-1*H*-indene-4-carboxylate (44). Methyl acrylate (40 g, 158 mmol) was added to a solution of diene **43** (19.8 g, 78.8 mmol) in 100 mL of anhydrous benzene, and the solution was warmed to 50 °C for 24 h. The reaction mixture was cooled in a dry ice/acetone bath, and an excess of methyl iodide (55.9 g, 396 mmol) was introduced in one portion. The solution was warmed to 0 °C and washed quickly with cold 10% hydrochloric acid, followed by washing with water and drying over anhydrous magnesium sulfate. Concentration in vacuo gave a red oil, which was purified by flash chromatography (25% ether, hexane (v/v)) to afford 7.0 g (45%) of **44** as a colorless oil: IR (CCl_4) 2975–2840 (br s), 1725 (s), 1650 (s), 1435 (m), 1375 (m), 1330 (br s), 1200 (br s), 1100 (m), 1040 (m), 1000 (m), 955 (w) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.78–2.06 (m, 2 H), 2.16–2.44 (m, 3 H), 2.44–2.88 (m, 5 H), 3.40 (br s, 1 H), 3.74 (s, 3 H); mass spectrum, m/e 194.0946 (M^+, calcd for $C_{11}H_{14}O_3$, 194.0943).

Methyl 2,3,4,5,6,7-Hexahydro-4-methyl-7-oxo-1*H*-indene-4-carboxylate (45). A solution of diene **43** (1 g, 3.95 mmol) and methyl methacrylate (790 mg, 7.9 mmol) in toluene (5 mL) was heated to reflux for 36 h. Workup of the reaction as in the synthesis of enone **44** afforded a red oil, which was purified by flash chromatography (25% ether, hexane (v/v) to give 530 mg (63%) of **45** as a colorless oil: IR ($CHCl_3$) 3000–2800 (br s), 1745 (s), 1675 (s), 1450 (m), 1390 (m), 1260 (br), 1100 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.43 (s, 3 H), 1.94 (m, 2 H), 2.58 (m, 8 H), 3.73 (s, 3 H); mass spectrum, m/e 208.1099 (M^+, calcd for $C_{12}H_{16}O_3$, 208.1095).

(3a*S,7a*R**)-4-Oxo-3a,7a-ethanoperhydroindene (48).** A degassed solution of enone **46** (3.5 g, 25.7 mmol) in 2.3 L of methylene chloride was cooled to −78 °C and saturated with ethylene by bubbling the gas into the solution at a rate of 25 mL/min for 2 h. The solution was irradiated at −78 °C through a Pyrex filter for 17 h. The progress of the reaction was monitored by VPC column C, 140 °C. Removal of the solvent in vacuo afforded 4.2 g of a crude oil. Flash chromatography gave 3.63 g (86%) of tricyclic ketone **48**: IR ($CHCl_3$) 3075 (w), 2950–3045 (s), 2925 (m), 1690 (m), 1435 (m), 1240 (w), 1220 (m), 1160 (m), 920 (m), 890 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.34–1.64 (m, 2 H), 1.66–2.34 (m, 13 H), 2.44–2.64 (m, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 216.19, 54.89, 48.39, 40.54, 38.21, 34.71, 34.21, 26.83, 25.66, 24.16, 20.13; mass spectrum, m/e 164.1200 (M^+, calcd for $C_{11}H_{16}O$, 164.1199).

(3a*S,7a*S**)-Methyl 8-Methylene-7-oxo-3a,7a-ethanoperhydroindene-4-carboxylate (49a, 49b).** A degassed solution consisting of enone **44** (4.0 g, 20.6 mmol) and allene (3.2 g, 205 mmol) in 2 L of distilled hexane was cooled to −50 °C and irradiated for 10 h through a Pyrex filter. Removal of the solvent in vacuo afforded a white oil solid, which was crystallized from a 50% ether/hexane (v/v) solution to afford 3.8 g (80%) of a white crystalline solid (mp 79–83 °C, mixture of epimers). A second recrystallization from ether gave 3.5 g (74%) of the β-epimer **49a** (mp 98–99 °C) along with 275 mg (6%) of the minor α-epimer **49b** as a clear waxy oil. The ratio of **49a** to **49b** was 12.7:1.

The major epimer **49a** had the following spectral properties: IR ($CHCl_3$) 2950 (br m), 2855 (m), 1725 (s), 1695 (s), 1445 (m), 1365 (w), 1325 (m), 1325 (m), 1175 (m), 915 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.4–1.93 (m, 4 H), 1.96–2.53 (m, 7 H), 2.56–2.72 (m, 1 H), 2.86–3.0 (m, 1 H), 3.68 (s, 3 H), 4.87 (br s, 1 H), 4.93 (dd, J = 2.5, 1.5 Hz, 1 H); mass spectrum, m/e 234.1262 (M^+, calcd for $C_{14}H_{18}O_3$, 234.1256).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.82; H, 7.84.

The minor epimer **49b** had the following spectral data: IR ($CHCl_3$) 2950 (br s), 2875 (m), 1725 (s), 1695 (s), 1445 (w), 1375 (w), 1170 (br m), 910 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.48–2.08 (m, 8 H), 2.08–2.54 (m, 2 H), 2.56–2.76 (m, 2 H), 2.75–2.97 (m, 1 H), 3.66 (s, 3 H), 4.78–4.94 (m, 1 H), 5.05 (dd, J = 2.5, 1.5 Hz, 1 H); mass spectrum, m/e 234.1241 (M^+, calcd for $C_{14}H_{18}O_3$, 234.1256).

(3a*S,7a*S**)-Methyl 8,8-Dimethyl-7-oxo-3a,7a-ethanoperhydroindene-4-carboxylate (50, 51).** A degassed solution containing enone **44** (6.0 g, 30.9 mmol) in 1.75 L of distilled hexane was cooled to −20 °C. Isobutylene was bubbled into the solution at a rate of approximately 30 mL/min for 2 h. The reactants were irradiated through a Pyrex filter for 8 to 10 h. The reaction was monitored either by thin-layer chromatography (50% ether, hexane (v/v)) or by vapor-phase chromatography (VPC) (column A, 180 °C). Removal of the solvent in vacuo afforded 7.3 g of a pale yellow oil, which was purified by flash chromatography to give 5.7 g (74%) of a 2:1 mixture of epimers **50** and **51** as a clear oil that crystallized on standing. Recrystallization of the mixture from ether/hexane afford pure **50**: mp 52–53 °C; IR (CCl_4) 2950 (br s), 2870 (m), 1725 (s), 1695 (s), 1440 (m), 1360 (m), 1165 (br m), 900 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.03 (s, 3 H), 1.10 (s, 3 H), 1.44–1.73 (m, 5 H), 1.80–1.96 (m, 2 H), 1.98–2.24 (m, 4 H), 2.25–2.59 (m, 2 H), 3.75 (s, 3 H); NMR (^{13}C, 50.327 MHz, $CDCl_3$) δ 214.36, 173.67, 61.56, 51.24, 49.14, 44.88, 43.07, 40.09, 39.04, 34.29, 32.38, 27.78, 25.58, 25.00, 23.82; mass spectrum, m/e 250.1561 (M^+, calcd for $C_{15}H_{22}O_3$, 250.1569).

A solution of 415 mg of the above mixture of ester epimers in methanol was added to a stirred solution of 25 mL of methanol in which 100 mg of sodium had been dissolved. The resulting solution was allowed to stir at 50 °C under a blanket of argon for 3 days. The reaction mixture was allowed to cool, neutralized by the addition of 1 N HCl, and evaporated to dryness. The resulting oil was diluted with water and extracted with dichloromethane. The combined organic layers were washed with brine and dried ($MgSO_4$). Removal of the solvent in vacuo afforded 350 mg (84%) of a mixture of epimers **50** and **51** (ca. 1:5 **50** to **51** by NMR analysis) as a white solid. Recrystallization (2×) from ether/hexane afforded pure **51**: mp 48–50 °C; IR ($CHCl_3$) 2950 (br s), 2870 (m), 1725 (s), 1685 (s), 1440 (m), 1360 (m), 1165 (br m), 900 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.98 (s, 3 H), 1.10 (s, 3 H), 1.14–2.26 (m, 11 H), 2.52–2.66 (m, 1 H), 3.0 (dd, J = 3.6, 12.5 Hz, 1 H), 3.66 (s, 3 H); ^{13}C NMR (50.327 MHz, $CDCl_3$) δ 214.10, 173.89, 60.90, 51.20, 49.09, 45.39, 44.21, 39.87, 35.76, 33.52, 33.22, 29.59, 25.07, 23.93, 20.73; mass spectrum, m/e 250.1574 (M^+, calcd for $C_{15}H_{22}O_3$, 250.1569).

(3a*S,4*S*,7a*S**)-Methyl 8-Methylene-7-hydroxy-3a,7a-ethanoperhydroindene-4-carboxylate (49c).** To a stirring solution of ketone **49a** (623 mg, 2.71 mmol) in 10 mL of absolute ethanol cooled to 0 °C was added sodium borohydride (105 mg, 2.7 mmol). The solution was warmed to room temperature, stirred for 1 h, and then quenched with saturated aqueous ammonium chloride. The solution was diluted with ether and separated. The organic layer was washed once with saturated aqueous ammonium chloride, and the combined organic extracts were dried over anhydrous potassium carbonate. Removal of the solvent in vacuo afforded 616 mg (96%) of **49c** as an oil, which was a mixture of epimers: IR (CCl_4) 3275–3625 (br s), 2850–3060 (br s), 1720 (s), 1660 (m), 1440 (m), 1355 (m), 1040 (s), 895 (s) cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 1.16–3.16 (m, 15 H), 3.63 (s, 3 H), 4.66–5.1 (m, 2 H); mass spectrum, m/e 236.1440 (M^+, calcd for $C_{14}H_{20}O_3$, 236.1413).

Methyl Hexahydro-7′-hydroxyspiro[cyclopropane-1,8′-[3a,7a]ethanol-[1*H*]indene]-4′-carboxylate (49d). To a stirred solution of ZnCu couple (1.9 g, 295 mmol) in 3 mL of anhydrous ether was added freshly distilled diiodomethane (7.9 g, 29.5 mmol) in 2 mL of ether. The solution was warmed to reflux with vigorous stirring. After approximately 30 min the gray suspension began to turn black, at which time olefin **49c** (2.3 g, 9.82 mmol) in 1 mL of ether was introduced to the solution. The reaction was continued for 30 min at the reflux point and then was quickly cooled to 0 °C and carefully quenched with sodium sulfate decahydrate. The salts were removed by filtration and rinsed thoroughly with ether. The filtrate was washed with 10% hydrochloric acid and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave 7.1 g of a red oil. Flash chromatography (30% ether, hexane (v/v)) afforded 1.07 g (44%) of **49d** as a clear oil consisting of a mixture of epimers, which were not separated: IR ($CHCl_3$) 3600 (m), 3450–3560 (br m), 2860–3050 (br s), 1720 (s), 1445 (m), 1350 (m), 1300 (m), 1230 (br s), 1170 (s), 1140

(m), 1050 (w), 1020 (m), 945 (m), 720–700 (br s), 665 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.20–0.60 (m, 4 H), 1.10–2.64 (m, 14 H), 3.65 (s, 3 H), 3.68–3.88 (m, 1 H).

Methyl Hexahydro-7′-oxospiro[cyclopropane-1,8′-[3a,7a]ethano[1*H*]-indene]-4′-carboxylate (52). To a stirring solution of oxalyl chloride (15 mg, 1.26 mmol) in 5 mL of methylene chloride cooled to −60 °C was added dropwise dimethyl sulfoxide (295 mg, 3.78 mmol) in 3 mL of methylene chloride. After the mixture was stirred for 5 min at −60 °C, cyclopropyl alcohol **49d** (89 mg, 0.63 mmol) dissolved in 1 mL of methylene chloride was added. After this mixture was stirred for an additional 2 h at −60 °C, triethylamine (954 mg, 9.45 mmol) was added and the solution was warmed to room temperature. The reaction mixture was washed twice with brine and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo afforded 96 mg of a pale yellow oil. Preparative thin-layer chromatography (50% ether, hexane (v/v)) afforded 69 mg (78%) of ketone **52**: IR (CCl_4) 2995 (m), 2950 (s), 2900 (m), 2855 (m), 1725 (s), 1695 (s), 1425 (m), 1350 (m), 1305 (m), 1275 (m), 1235 (s), 1165 (br s), 915 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.32–0.58 (m, 4 H), 1.40–2.72 (m, 13 H), 3.68 (s, 3 H); mass spectrum, *m/e* 248.1405 (M^+, calcd for $C_{15}H_{20}O_3$, 248.1413).

(3a*S,4*S**,7a*S**)-Methyl 8,8-Dimethyl-7-oxo-3a,7a-ethanoperhydroindene-4-carboxylate (50).** To a Parr hydrogenator bottle containing platinum oxide (200 mg, 0.9 mmol) was added cyclopropane **52** (1.0 g, 4.03 mmol) in 40 mL of acetic acid. The apparatus was evacuated with a water aspirator and then pressurized to 3.5 atm with hydrogen. After the mixture was shaken for 24 h at room temperature, the pressure was released, and the reaction mixture was diluted with ether. The platinum was removed by filtering the solution through a pad of Celite. The filtrate was washed twice with water and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo afforded 446 mg (44%) of the hydrogenolysis product where concomitant reduction of the ketone had occurred. A solution of this alcohol (75 mg, 0.3 mmol) in 10 mL of methylene chloride was stirred with pyridinium chlorochromate (12.7 mg, 0.6 mmol) for 3 h. The solution was diluted with ether, and the chromate salts were removed by filtering the mixture through a pad of Celite. Removal of the solvent in vacuo afforded a gummy oil. Flash chromatography (25% ether, hexane (v/v)) gave 61 mg (81%) of ketone **50**, identical with the major isomer obtained from irradition of enone **44** with isobutylene.

(3a*S,7a*S**)-7-Oxo-8,8-dimethyl-3a,7a-ethanoperhydroindene (53).** A solution of the enone **46** (9.5 g, 0.07 mol) in hexane (2.5 L) was cooled to −50 °C and was saturated with isobutylene. The mixture was photolyzed for 8 h through a Pyrex filter at ca. −35 °C to −50 °C and then was allowed to warm to room temperature. The solvent was removed under reduced pressure, and the crude product was purified by preparative HPLC using ethyl acetate/hexane (1:10) as the eluting solvent to give 5.5 g (41%) of the desired ketone **53** as a colorless oil: IR ($CHCl_3$) 2945, 2850, 1675, 1450 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.99 (s, 3 H), 1.07 (s, 3 H), 1.20–1.91 (comp, 9 H), 2.04 (m, 1 H), 2.10 (m, 1 H), 2.19 (m, 1 H), 2.38 (m, 1 H), 2.47 (m, 1 H); mass spectrum, *m/e* 192.1540 (M^+, calcd for $C_{13}H_{20}O$, 192.1514).

(3a*S,4*S**,7a*S**)-7-Oxo-4,8,8-trimethyl-3a,7a-ethanoperhydroindene (54).** A solution of the enone **47** (6.2 g, 0.04 mol) in hexane (2.5 L) was cooled to −40 °C and saturated with isobutylene. The resulting solution was photolyzed for 8 h (Pyrex filter) at ca. −30 °C to −50 °C and was then allowed to warm to room temperature. The solvent was removed at reduced pressure, and the crude product was purified by preparative HPLC using ethyl acetate/hexane (1:9) as the eluting solvent to give 4.77 g (56%) of a 10:1 mixture of the desired ketone **54** and its isomer at C-4. A pure sample of **54** could be obtained via $LiAlH_4$ reduction of the ketone mixture to the corresponding alcohols followed by HPLC separation and oxidation of the requisite alcohol. Pure ketone **54** was isolated as a white solid: mp 59–60 °C; IR ($CHCl_3$) 2940, 2870, 1670, 1010, 900 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.90 (d, J = 6.6 Hz, 3 H), (s, 3 H), 1.07 (s, 3 H), 1.31–2.20 (comp, 11 H), 2.36 (dd, J = 2.2, 4.0 Hz, 1 H), 2.43 (dd, J = 2.2, 4.4 Hz, 1 H); mass spectrum, *m/e* 206.1682 (M^+, calcd for $C_{14}H_{22}O$, 206.1670).

(3a*S,7a*R**)-4-Hydroxy-3a,7a-ethanoperhydroindene (9, 10).** To a stirring solution of the ketone **48** (175 mg, 1.1 mmol) in 15 mL of absolute ethanol was added sodium borohydride (89 mg, 23.3 mmol) in one portion. After the mixture was stirred 1 h at room temperature the reaction was quenched with saturated ammonium chloride. The aqueous layer was separated and extracted twice with ether. The combined organics were washed once with brine and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave 179 mg of a clear oil as a mixture of epimers. MPLC (10% ethyl acetate, hexane (v/v)) gave 132 mg (69%) of the major epimer **10** and 35 mg (18%) of the minor compound **9**.

The major epimer **10** had the following spectral data: IR (CCl_4) 3605 (w), 3325–3525 (br m), 2920 (s) 2845 (m), 1445 (m), 1360 (w), 1250 (m), 1045 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.26–2.08 (m, 16 H), 2.09–2.24 (m, 1 H), 3.58 (dd, J = 5.5, 10.8 Hz, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 74.56, 49.00, 47.65, 40.06, 32.39, 28.71, 27.45, 24.89, 19.98, 19.42.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.18; H, 11.03.

The minor isomer **9** had the following spectral data: IR (CCl_4) 3625 (m), 3225–3525 (br m), 2950 (br s), 2875 (m), 1460 (m), 1275 (w), 1030 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.20–2.18 (m, 17 H), 4.04 (dd, J = 4.4, 9.9 Hz, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 74.79, 50.15, 47.00, 40.33, 31.95, 31.57, 28.68, 27.18, 26.63, 24.89, 18.80.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.48; H, 11.09.

(3a*S,7a*R**)-Diethyl 2,3,3a,6,7,7a-Hexahydro-3a,7a-ethanoinden-4-yl Phosphate.** A solution of lithium diisopropylamide (LDA) was generated by the addition of *n*-butyllithium (107 mg, 1.67 mmol) to diisopropylamine (1.69 mg, 1.67 mmol) in 5 mL of anhydrous tetrahydrofuran at 0 °C. The solution was cooled to −78 °C, and ketone **48** (250 mg, 1.52 mmol) in 3 mL of tetrahydrofuran was added dropwise. The enolate was allowed to form for 1 h and then trapped at −78 °C by the addition of diethyl chlorophosphate (289 mg, 1.67 mmol). The reaction was warmed to room temperature and quenched with saturated ammonium chloride. Ether was added, and the organic was separated from the aqueous layer and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo followed by flash chromatography (75% ether, hexane (v/v)) afforded 425 mg (93%) of the phosphate ester: IR (CCl_4) 2900–3025 (br s), 2860 (s), 1675 (m), 1450 (m), 1400 (w), 1370 (m), 1290 (s), 1030–1060 (br s), 980 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.44 (t, J = 7.0 Hz, 6 H), 1.58–2.40 (m, 14 H), 4.10 (dq, J = 7.0, 7.5 Hz, 4 H), 5.59 (dd, J = 1.75), 4.5 Hz, 1 H); mass spectrum, *m/e* 300.1525 (M^+, calcd for $C_{15}H_{25}O_4P$, 300.1573).

(3a*S,7a*R**)-2,3,3a,4,5,7a-Hexahydro-3a,7a-ethanoindene (11).** Lithium metal (82 mg, 11.6 mmol) was added to a stirred solution of (3a*S**,7a*R**)-diethyl 2,3,3a,6,7,7a-hexahydro-3a,7a-ethanoinden-4-yl phosphate (350 mg, 1.16 mmol) in 20 mL of methylamine and 2 mL of *tert*-butyl alcohol. The reaction was allowed to stir at the reflux point until all the blue color had discharged. The methylamine was allowed to evaporate, and the reaction mixture was diluted with ether. The solution was washed twice with saturated ammonium chloride and dried over anhydrous potassium carbonate. Careful removal of the solvent gave 110 mg of crude product. Flash chromatography afforded 27 mg (16%) of **11** as a volatile liquid: IR (CCl_4) 3075 (m), 2950 (s), 2875 (s), 1445 (m), 1235 (m), 1085 (br s), 910 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.22–1.54 (m, 4 H), 7.56–1.90 (m, 8 H), 1.90–2.24 (m, 2 H), 5.83 (ddd, J = 3.7, 5.1, 9.9 Hz, 1 H), 5.95 (d, J = 9.9 Hz, 1 H); mass spectrum, *m/e* 148.1228 (M^+, calcd for $C_{11}H_{16}$, 148.1252).

(3a*S,7*R**,7a*R**)-7-Hydroxy-8,8-dimethyl-3a,7a-ethanoperhydroindene (19).** To a solution of the ketone **53** (500 mg, 2.6 mmol) in ether (20 mL) was added slowly $LiAlH_4$ (297 mg, 78 mmol) at 0 °C. The mixture was allowed to stir at room temperature for 3 h and then the excess $LiAlH_4$ was decomposed by the sequential addition of H_2O (0.3 mL), 4 N NaOH (0.3 mL), and H_2O (1.0 mL). The solid was removed by suction filtration and was washed with ether (2 × 15 mL). The filtrate was dried ($MgSO_4$), and the solvent was removed under reduced pressure. The crude product was purified by preparative HPLC using ethyl acetate/hexane (1:10) as the eluting solvent to give 447 mg (88%) of the pure **19** as a white solid: mp 64–65 °C; IR ($CHCl_3$) 3610, 2940, 2860, 1440 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.99 (s, 3 H), 1.45 (s, 3 H), 1.13–1.90 (comp, 14 H), 2.35 (m, 1 H), 3.61 (dd, J = 6.7, 11.9 Hz, 1 H); mass spectrum, *m/e* 194.1726 (M^+, calcd for $C_{13}H_{22}O$, 194.1671).

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.29; H, 11.44.

(3a*R,7a*R**)-2,3,3a,4,5,7a-Hexahydro-8,8-dimethyl-3a,7a-ethanoindene (36).** A solution of the ketone **53** (1.0 g, 5.2 mmol) in THF (5 mL) was added slowly to a solution of LDA (7.81 mmol) [generated from diisopropylamine (7.81 mmol) and *n*-butyllithium (7.81 mmol) in THF (10 mL)] at −78 °C. The mixture was then stirred at −78 °C for 0.5 h and quenched with diethyl chlorophosphate (1.34 g, 7.81 mmol). The resulting solution was stirred at −78 °C for another hour and then was allowed to warm to room temperature. The reaction mixture was diluted with ether (15 mL), washed with saturated aqueous $NaHCO_3$ (10 mL) and saturated aqueous NaCl (5 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the crude phosphate was dissolved in ethylamine (40 mL), to which *tert*-butyl alcohol (4.4 g, 60 mmol) and lithium metal (426 mg, 61 mmol) were added. The mixture was allowed to reflux at room temperature for 3 h until no starting material was seen by TLC analysis. Sodium benzoate and NH_4Cl were added, and the solvent was allowed to evaporate. Saturated aqueous NaCl (20 mL) was then added, the resulting solution was extracted with ether (3 × 20 mL) and dried ($MgSO_4$), and the solvent was distilled off

carefully. The crude product was purified by flash column chromatography using pentane as the eluting solvent to give 744 mg (82%) of the olefin **36** as a colorless oil: IR ($CHCl_3$) 2925, 2840, 1440 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.93 (s, 3 H), 1.02 (s, 3 H), 0.90–1.93 (comp. 10 H), 1.98 (m, 1 H), 2.03 (m, 1 H), 5.74 (m, 2 H).

Anal. Calcd for $C_{13}H_{20}$: C, 88.56; H, 11.44. Found: C, 88.72; H, 11.62.

(3a*S,7*S**,7a*R**)-8,8-Dimethyl-7-hydroxy-3a,7a-ethanoperhydroindene (27).** To a solution of the olefin **36** (180 mg, 1.0 mmol) in CH_2Cl_2 (9 mL) were added $NaHCO_3$ (128 mg, 1.5 mmol) and *m*-chloroperbenzoic acid (258 mg, 1.5 mmol) at 0 °C. The mixture was stirred at 0 °C for 3 h and then washed with saturated aqueous $NaHCO_3$ (2 × 10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layer was dried ($MgSO_4$). The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography using ethyl acetate/hexane (1:20) as the eluting solvent to give 182 mg (93%) of pure anti epoxide as a colorless oil: IR ($CHCl_3$) 2940, 2870 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.91 (m, 1 H), 1.04 (s, 3 H), 1.09 (s, 3 H), 1.22–1.93 (comp, 9 H), 2.05 (m, 2 H), 3.02 (d, J = 4.3 Hz, 1 H), 3.32 (m, 1 H); mass spectrum, *m/e* 192.1532 (M^+, calcd for $C_{13}H_{20}O$, 192.1514). To a solution of the epoxide (187 mg, 0.97 mmol) in THF (15 mL) was added $LiAlH_4$ (555 mg, 14.6 mmol) at 0 °C. The mixture was heated to reflux for 60 h and then was allowed to cool to room temperature. The excess $LiAlH_4$ was decomposed by the sequential addition of H_2O (0.5 mL), 4 N NaOH (0.5 mL), and H_2O (1.5 mL). The solid was removed by suction filtration and was then washed with ether (3 × 20 mL). The filtrate was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography using ethyl acetate/hexane (1:20) as the eluting solvent to give 135 mg (72%) of the pure alcohol **27** as a white solid: mp 31–32 °C; IR ($CHCl_3$) 3590, 2940, 2850, 1440 cm^{-1}; NMR (250 MHz), $CDCl_3$) δ 0.91 (m, 1 H), 0.99 (s, 3 H), 1.24 (s, 3 H), 1.20, 1.90 (comp, 14 H), 4.34 (dd, J = 4.6, 12.4 Hz, 1 H); mass spectrum, *m/e* 194.1639 (M^+, calcd for $C_{13}H_{22}O$, 194.1671).

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.58; H, 11.61.

(3a*S,4*S**,7*R**,7a*S**)-7-Hydroxy-4,8,8-trimethyl-3a,7a-ethanoperhydroindene (20).** The reduction of ketone **54** with $LiAlH_4$ was accomplished in like manner to the transformation of **53** to **19**, and afforded **20** in 89% yield as a clear oil: IR ($CHCl_3$) 3600, 2940, 2860, 1050, 1000 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.74 (d, J = 6.6 Hz, 3 H), 1.04 (s, 3 H), 1.27 (s, 3 H), 1.07–1.87 (comp, 12 H), 2.11 (m, 1 H), 2.27 (m, 1 H), 3.79 (t, J = 9.2 Hz, 1 H); mass spectrum, *m/e* 208.1831 (M^+, calcd for $C_{14}H_{24}O$, 208.1827).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.56; H, 11.70.

(3a*S*,4*S,7a*S**)-2,3,3a,4,5,7a-Hexahydro-4,8,8-trimethyl-3a,7a-ethanoindene (37).** Formation of olefin **37** from ketone **54** via the Ireland protocol was accomplished as described for the converion of **53** and **36**. Enol phosphate: IR ($CHCl_3$) 2950, 2860, 1650, 1040, 980 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.8 (d, J = 6.6 Hz, 3 H), 0.97 (s, 3 H), 1.11 (s, 3 H), 1.21–2.19 (comp, 11 H), 1.34 (m, 6 H), 4.13 (m, 4 H), 5.60 (br d, J = 6.6 Hz, 1 H); mass spectrum, *m/e* 342.1967 (M^+, calcd for $C_{18}H_{31}O_4P$, 342.1960).

Compound **37** was obtained as a clear oil: IR ($CHCl_3$) 2950, 2860, 1650, 1040, 980 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.81 (d, J = 5.9 Hz, 3 H), 0.82 (s, 3 H), 1.08 (s, 3 H), 1.20–2.10 (comp, 11 H), 5.62 (dd, J = 2.9, 9.9 Hz, 1 H), 5.79 (m, 1 H).

Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.48; H, 11.61.

(3a*S,4*S**,7*S**,7a*S**)-7-Hydroxy-4,8,8-trimethyl-3a,7a-ethanoperhydroindene (28).** Transformation of olefin **37** to anti alcohol **28** followed from the procedure described for the formation of **27** from **36**. Epoxide: IR ($CHCl_3$) 2950, 2860 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.73 (d, J = 6.4 Hz, 3 H), 1.05 (s, 6 H), 0.91–1.82 (comp, 8 H), 1.89 (m, 1 H), 1.94 (m, 1 H), 1.99 (m, 1 H), 3.02 (d, J = 4.3 Hz, 1 H), 3.29 (t, J = 4.0 Hz, 1 H); mass spectrum, *m/e* 206.1710 (M^+, calcd for $C_{14}H_{22}O$, 206.1670).

Compound **28** was obtained as a colorless oil (58%) from **37**: IR 3600, 2940, 2860, 1075, 1040, 1005 cm^{-1}; NMR (250 MHz) δ 0.76 (d, J = 6.1 Hz, 3 H), 1.12 (s, 3 H), 1.14 (s, 3 H), 1.04–1.96 (comp, 14 H), 4.12 (dd, J = 3.7, 11 Hz, 1 H); mass spectrum, *m/e* 208.1800 (M^+, calcd for $C_{14}H_{24}O$, 208.1827).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.56; H, 11.46.

(3a*S,7*R**,7a*S**)-8,8-Dimethyl-7-hydroxy-4-(hydroxymethyl-3a,7a-ethanoperhydroindene (21, 22).** The tricyclic ketones **50** and **51** (250 mg, 1.0 mmol, mixture of isomers) dissolved in 10 mL of tetrahydrofuran were added dropwise to a stirred solution of lithium aluminum hydride in 15 mL of tetrahydrofuran cooled to 0 °C. After the mixture was stirred for 30 min the reaction was quenched with sodium sulfate decahydrate. Removal of the salts by filtration and concentration in vacuo gave 194 mg (87%) of a clear oil. Medium-pressure chromatography (50% ether, hexane (v/v)) afforded a 2:1 mixture of the two epimers **21** and **22**.

The major component (cis diol **21**) had the following spectral data: IR ($CHCl_3$) 3600 (m), 3300–3505 (br m), 2975 (m), 2925 (br s), 2855 (m), 1450 (m), 1425 (m), 1360 (m), 1025 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.82–1.12, 1.01 (m, s, 4 H), 1.13–1.66, 1.14 (m, s, 2 H), 1.66–2.40 (m, 8 H), 3.15 (dd, J = 9.0, 11.0 Hz, 1 H), 3.64 (dd, J = 5.0, 10.0 Hz, 1 H), 3.79 (dd, J = 10.0, 15.0 Hz, 1 H).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.09; H, 10.88.

The minor component (**22**, mp 136–137 °C) had the following spectral data: IR ($CHCl_3$) 3600 (m), 3500–3350 (br m), 2975 (m), 2925 (br s), 2850 (m), 1435 (m), 1305 (w), 1300 (w), 1025 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$), δ 0.82–1.14, 0.97 (m, s, 4 H), 1.28–1.48 (m, 5 H), 1.49–1.68, 1.59 (m, s, 5 H), 1.74–2.08 (m, 5 H), 2.10–2.24 (m, 1 H), 2.40–2.52 (m, 1 H), 3.44 (dd, J = 8.0, 8.5 Hz, 1 H), 3.62–3.78 (m, 2 H); mass spectrum, *m/e* 224.1749 (M^+, calcd for $C_{14}H_{24}O_2$, 224.1776).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.93; H, 10.75.

(3a*S,4*R**,7a*S**)-2,3,4,5-Tetrahydro-8,8-dimethyl-3a,7a-ethano-1*H*-indene-4-methanol (39).** Ketone **51** (780 mg, 3.12 mmol) was transformed into the corresponding enol phosphate derivative via the procedure described for the synthesis of olefin **37**. Flash chromatography afforded 1.02 g (85%) of the enol phosphate: NMR (250 MHz, $CDCl_3$) 80.96 (s, 3 H), 1.25 (s, 3 H), 1.30 (m, 6 H), 1.4a 2.40 (m, 10 H), 2.90 (m, 1 H), 3.62 (s, 3 H), 4.12 (m, 4 H), 5.45 (m, 1 H).

A solution of the enol phosphate (200 mg, 0.52 mmol) was subjected to dissolving metal reduction as described in the procedure for olefin **37**. The crude product (153 mg) was purified by preparative TLC using CH_2Cl_2 as the eluting solvent to afford 16 mg (15%) of olefin **39** as a clear oil: IR ($CHCl_3$) 3265 (m), 3200–3550 (br w), 2925 (s br), 2850 (m), 1445 (m), 1375 (m), 1250 (m), 1110 (s), 1010 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) 80.9 (s, 3 H), 1.06 (s, 3 H), 0.98–1.16 (m, 1 H), 1.17–1.46 (m, 3 H), 1.50–1.90 (ml 6 H), 2.0–2.19 (m, 2 H), 3.44 (dd, J = 10.6, 8.1 Hz, 1 H), 3.64 (dd, J = 10.6, 5.5 Hz, 1 H), 5.162–5.7 (m, 1 H), 5.76 (dd, J = 4.2, 10.0 Hz, 1 H); mass spectrum, *m/e* 206.1657 (M^+, calcd for $C_{14}H_{22}O$, 206.1664).

In like manner, ketone **50** was transformed into olefin **38**: IR ($CHCl_3$) 3620 (m), 3300–3525 (br m), 3000 (m), 2950 (br s), 2865 (m), 1450 (m), 1375 (m), 1370 (w), 1230 (br m), 1115 (m), 1020 (m), 915 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.90 (s, 3 H), 1.14 (s, 3 H), 1.24–1.54 (m, 4 H), 1.56–1.98 (m, 5 H), 2.00–2.18 (m, 1 H), 2.26 (dddd, J = 4.8, 6.8, 8.0, 8.1 Hz, 1 H), 3.42–3.58 (m, 2 H), 3.65 (dd, J = 4.8, 5.0 Hz, 1 H), 5.90 (dd, J = 2.9, 9.9 Hz, 1 H), 5.8–5.92 (m, 1 H); mass spectrum, *m/e* 206.1612 (M^+, calcd for $C_{14}H_{22}O$, 206.1664.

(3a*S,4*R**,7*S**,7a*S**)-8,8-Dimethyl-7-hydroxy-4-(hydroxymethyl)-3a,7a-ethanoperhydroindene (29).** A stirred solution of olefin **38** (325 mg, 1.57 mmol) in 25 mL of methylene chloride was cooled to 0 °C. Sodium bicarbonate (163 mg, 1.9 mmol) and *m*-chloroperbenzoic acid (341 mg, 1.94 mmol) were added sequentially in one portion. The reaction was monitored by TLC (50% ether, hexane (v/v)), and when approximately 75% of the starting material had reacted the reaction was quenched by the addition of saturated sodium bicarbonate. The reaction mixture was diluted with methylene chloride and separated. The organic layer was washed twice with saturated bicarbonate and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave 427 mg. Flash chromatography (50% ether, hexane (v/v), gradually increased to 100% ether) afforded 271 mg of isomerically pure epoxide: IR ($CHCl_3$) 3610 (m), 3300–3525 (br m), 2975 (s), 2950 (br m), 2860 (m), 1450 (w), 1420 (m), 1365 (w), 1305 (w), 1230 (br m), 1050 (m), 1015 (m), 980 (w), 855 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.14 (s, 3 H), 1.17 (s, 3 H), 1.23–1.56 (m, 2 H), 1.66–2.0 (m, 9 H), 2.42 (dddd, J = 3.6, 6.7, 9.9, 10 Hz, 1 H), 3.10 (d, J = 3.5 Hz, 1 H), 3.43 (d, J = 4 Hz, 1 H), 3.46 (d, J = 3.6 Hz, 1 H), 3.58–3.70 (m, 1 H); mass spectrum, *m/e* + 1 223.1685 (M^+, calcd for $C_{14}H_{22}$ +1, 223.1698).

To a stirred solution of the above epoxide (25 mg, 0.11 mmol) in 0.5 mL of tetrahydrofuran was added 1 mL of a stock solution of tetrahydrofuran saturated with lithium aluminum hydride. The reaction mixture was warmed to reflux overnight. After the reaction mixture cooled to 0 °C, solid sodium sulfate decahydrate was added. The salts were removed by filtration and washed thoroughly with ether. Removal of the solvent in vacuo afforded 20 mg of a yellow oil. Preparative thin-layer chromatography (75% ether, hexane (v/v)) afforded 14 mg (57%) of diol 29 as a white solid: mp 121–123 °C; IR ($CHCl_3$) 3605 (m), 3225–3525 (br w), 2990 (m), 2925 (br s), 2850 (m), 1445 (m), 1360 (w), 1215 (m), 1030 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.10–1.58, 1.28 (m, s, 11 H), 1.68–2.22 (m, 10 H), 3.53 (dd, J = 8.0, 10.0 Hz, 1 H), 3.70 (dd, J = 5.57, 10 Hz, 1 H), 4.23 (dd, J = 5.0, 11.0 Hz, 1 H).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.01; H, 10.79.

(3a*S,4*R**,5*S**,7*R**,7a*S**)-2,3,3a,6,7,7a-Hexahydro-7-(hydroxymethyl)-9,9-dimethyl-3a,7a-ethanooxirano[*e*]indene (56).** To a stirred solution of the epimerically pure olefin **39** (104 mg, 0.5 mmol) in 10 mL of methylene chloride were added sodium bicarbonate (50 mg, 0.59 mmol) and *m*-chloroperbenzoic acid (108 mg, 0.59 mmol). The reaction was stirred at room temperature for 2 to 3 h followed by quenching with saturated sodium bicarbonate. The layers were separated, and the organics were washed twice with saturated sodium bicarbonate and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave 127 mg of a clear oil. Flash chromatography (75% ether, hexane (v/v)) afforded 109 mg (an overall yield of 97%) of the desired anti epoxide **56** contaminated with approximately 5% of the isomeric syn epoxide **55**. The mixture was not readily separable by chromatography. IR ($CHCl_3$) 3605 (m), 3275–3540 (br m), 2945 (br s), 2875 (s), 1445 (m), 1375 (m), 1360 (m), 1250 (br m), 1095 (m), 1050 (s), 1030 (m), 1015 (m), 1000 (m), 850 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.93 (s, 3 H), 0.96–1.28, 1.19 (m, s, 5 H), 1.29–1.98 (m, 8 H), 2.0–2.32 (m, 1 H), 2.77, 2.90, 3.02 (d, J = 4 Hz, d, J = 4.0 Hz, dd, J = 3.3, 3.6 Hz, 2 H), 3.16–3.58 (m, 3 H); mass spectrum, m/e 222.1593 (M^+, calcd for $C_{14}H_{22}O_2$, 222.1620).

(3a*S,4*R**,7*S**,7a*S**)-4-(Hydroxymethyl)-7-hydroxy-8,8-dimethyl-3a,7a-ethanoperhydroindene (30).** To a stirred solution of the mixture of epoxides **55** and **56** (56 mg, 0.25 mmol) in 1 mL of anhydrous tetrahydrofuran was added 5 mL of a saturated stock solution of lithium aluminum hydride, and the solution was warmed to 38 °C for 48 h. The reaction was cooled to 0 °C and quenched cautiously with solid sodium sulfate decahydrate. The salts were removed by filtration and washed with ether. Removal of the solvent in vacuo gave 63 mg of a white solid. The mixture of cis diol **30** and trans diol **22** were readily separable by flash chromatography (50% ether, hexane (v/v)) yielding 3 mg of trans diol **22** identical with the previously prepared material. The cis diol **30** (53 mg, 95%) was isolated as a crystalline white solid: mp 156–157 °C; IR ($CHCl_3$) 3620 (m), 3150–3500 (br m), 2825–3000 (br s), 1700 (w), 1460 (m), 1450 (m), 1375 (m), 1350 (m), 1260 (m), 1030 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.08 (s, 3 H), 1.13 (br s, 1 H), 1.20–2.18, 1.36 (m, s, 17 H), 3.36 (dd, J = 8.1, 10.3 Hz, 1 H), 3.65 (dd, J = 5.1, 10.3 Hz, 1 H), 4.4 (dd, J = 4.4, 11.2 Hz, 1 H); mass spectrum, m/e 224.1761 (M^+, calcd for $C_{14}H_{24}O_2$, 224.1816).

(1*R,3a*S**,4*S**,7a*R**)-4-Hydroxy-1,9,9-trimethyl-4,7a-ethanoperhydroindene (24).** To a solution of diol **25** (30 mg, 0.14 mmol) in CH_2Cl_2 (2 mL) containing triethylamine (20 mg, 0.2 mmol) was added methanesulfonyl chloride (22 mg, 0.2 mmol) at 0 °C under nitrogen. The mixture was stirred at 0 °C for 2 h and then was diluted with CH_2Cl_2 (5 mL). The solution was washed with saturated aqueous NaCl (2 × 3 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. The crude mesylate was then dissolved in THF (2 mL), and lithium triethyl borohydride (1.20 mmol) was added. The mixture was heated at 70 °C for 8 h and then was cooled to 0 °C. Excess reducing agent was decomposed by the sequential additon of H_2O (0.5 mL), 4 N NaOH (0.4 mL), and 30% H_2O_2 (0.4 mL). The resulting mixture was heated to reflux for 1 h, allowed to cool to room temperature, and poured into saturated aqueous NaCl (2 mL). The solution was then extracted with pentane (3 × 10 mL) and dried ($MgSO_4$), and the solvent was removed by distillation. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:12) as the eluting solvent to give 7 mg (30%) of pure **24**, identical with the compound obtained previously.

(3a*S,7*S**)-2,3,4,5-Tetrahydro-3a,7-ethano-6*H*-indene (57).** A solution consisting of alcohol **12** (100 mg, 0.60 mmol) and phosphorus oxychloride (373 mg, 2.4 mmol) was stirred for 5 min at 0 °C. Pyridine (5 mL) was added, and the solution was stirred at room temperature overnight. After the reaction mixture cooled to 0 °C, 10% hydrochloric acid was cautiously added, followed by ether. The organic layer was separated, washed with 10% hydrochloric acid, and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo afforded 83 mg (83%) of olefin **57** as a volatile liquid: IR ($CHCl_3$) 3025 (w), 2980 (w), 2930 (s), 2850 (s), 1440 (m), 1090 (w), 1000 (w), 975 (w) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.30–1.44 (m, 1 H), 1.50–1.86 (m, 10 H), 1.88–2.06 (m, 1 H), 2.44–2.78 (m, 3 H), 5.00 (s, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 158.429, 109.378, 56.238, 39.359, 35.888, 35.712, 35.359, 34.742, 34.006, 31.124, 19.832; mass spectrum, m/e 148.1246 (M^+, calcd for $C_{11}H_{16}$, 148.1252).

(3a*S,4*R**,7a*R**)-4-Chloro-4,7a-ethanoperhydroindene (59).** The alcohol **14** (300 mg, 1.8 mmol) was added to a stirred solution of thionyl chloride (716 mg, 6.0 mmol) in 50 mL of dimethylformamide at room temperature. After the mixture was stirred for 3 h, the reaction mixture was treated with saturated ammonium chloride and diluted with ether, and the organic layer was separated and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave 410 mg of a yellow oil. Flash chromatography (hexane) afforded 293 mg (88%) of chloride **59** as a mobile oil: IR (CCl_4) 2950 (br s), 2865 (s), 1460 (m), 1445 (s), 1310 (m), 1240 (m), 1200 (m), 1110 (m), 965 (m), 885 (m), 865 (s), 735 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.04–1.26 (m, 4 H), 1.27–2.20 (m, 10 H), 2.22–2.50 (m, 3 H); mass spectrum, m/e 184.1012 (M^+, calcd for $C_{11}H_{17}Cl$, 184.1018).

(3a*S,4*S**,7a*S**)-4,7a-Ethanoperhydroindene (58).** To a suspension of lithium metal (25.4 mg, 3.6 mmol) in 50 mL of tetrahydrofuran cooled to 0 °C was added chloride **59** (134 mg, 0.72 mmol) in 2 mL of tetrahydrofuran. The reaction mixture was vigorously stirred for 16 h at room temperature followed by quenching with 1 mL of ethanol. Ether was added, and the mixture was washed twice with brine and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave 129 mg of a yellow oil. The crude product was filtered through a column of silica gel with hexane. Removal of the hexane in vacuo afforded 59 mg (54%) of **58** as a volatile liquid: IR (CCl_4) 2950 (s), 2920 (s), 2860 (m), 2845 (m), 1445 (m), 1075 (w), 1000 (w) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.32–1.98 (m, 16 H), 1.99–2.18 (m, 1 H), 2.31 (br d, J = 4.5 Hz, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 57.36, 51.65, 39.86, 38.86, 36.15, 33.71, 33.30, 28.10, 22.71, 19.69; mass spectrum, m/e 150.1379 (M^+, calcd for $C_{11}H_{18}$, 150.1400).

(4*S,7a*S**)-4,7a-Ethanoperhydroindene (58).** A solution consisting of olefin **57** (40 mg, 0.27 mmol) in 2 mL of absolute ethanol and a catalytic quantity of 10% platinum on carbon (30 mg) was stirred for 3 h under 1 atm of hydrogen. The solution was diluted with hexane and filtered through a pad of celite. Removal of the solvent in vacuo afforded 16 mg (40%) of **58** contaminated with the trans ring juncture isomer. The major compound was identical with hydrocarbon **58** obtained from chloride **59**.

1,2,3,3a,4,5,7,8-Octahydrocyclopenta[*c*]pentalene and 2,3,3a,4,7,8-Hexahydro-1*H*,6*H*-cyclopenta[*c*]pentalene (60). A solution of alcohol **13** (115 mg, 0.7 mmol) and phosphorus oxychloride (417 mg, 2.72 mmol) was stirred at 0 °C for 5 min. Pyridine was added, and the reaction was stirred overnight at room temperature. The reaction mixture was cooled to 0 °C and cautiously quenched with 10% hydrochloric acid. After the mixture was diluted with ether and separated, the organic layer was washed twice with 10% hydrochloric acid and dried over anhydrous potassium carbonate. Removal of the solvent in vacuo afforded 93 mg (90%) of a volatile liquid as a mixture of isomers of **60**, which were not separated: IR ($CHCl_3$) 3030 (w), 2875–3000 (br s), 2850 (s), 1450 (s), 2160 (m), 900 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.18–1.86 (m, 8 H), 1.87–2.10 (m, 3 H), 2.11–2.26 (m, 2 H), 2.45–2.96 (m, 1 H), 5.08, 5.25 (s, s, 1 H); mass spectrum, m/e 148.1214 (M^+, calcd for $C_{11}H_{16}$, 148.1252).

Decahydrocyclopenta[*c*]pentalene (61). A solution consisting of a mixture of olefins **60** (80 mg, 0.54 mmol) in 1 mL of ethanol and a catalytic quantity of 10% platinum on carbon (10 mg) was stirred for 5 h under 1 atm of hydrogen. The solution was diluted with pentane and filtered through a pad of Celite. Removal of the solvent in vacuo afforded 40 mg (50%) of a volatile liquid (**61**), whose ^{13}C NMR spectrum was identical with the known compound: NMR (250 MHz, $CDCl_3$) δ 1.18–1.44 (m, 4 H), 1.45–1.92 (m, 13 H), 1.93–2.06 (m, 1 H); NMR (^{13}C, 62.9 MHz, $CDCl_3$) δ 62.00 (62.0), 52.30 (52.4), 42.03 (42.1), 33.51 (33.6), 33.42 (33.5), 26.74 (26.8); mass spectrum, m/e 150.1427 (M^+, calcd for $C_{11}H_{18}$, 150.1408).

(3a*R,6a*S**)-3a-(2-Oxopropyl)-6a-(2-oxoethyl)perhydropentalene (62).** The crude reaction product from the methanesulfonic acid catalyzed rearrangement of olefin **36** (80 mg, 0.45 mmol) was dissolved in methanol (3 mL) and treated with ozone at −78 °C. A solution of sodium sulfite (200 mg, 1.59 mmol) in H_2O (10 mL) was added, and the resulting solution was allowed to stir at room temperature for 2 h. Methanol was removed at reduced pressure, and the aqueous layer was extracted with ether. The organic solution was dried ($MgSO_4$), and the solvent was removed by distillation at atmosphere pressure. The crude product was purified by HPLC using ethyl acetate/hexane (1:10) as eluting solvent to give 40 mg (42%) of the diketone **62** as a colorless oil: NMR (250 MHz, $CDCl_3$) δ 1.2–2.4 (comp, 12 H), 2.01 (s, 3 H), 2.16 (s, 3 H), 2.75 (s, 2 H).

(3a*S,4*S**,7a*S**)-7-Oxo-4-methyl-8-methylene-3a,7a-ethanoperhydroindene (63).** Through a solution of enone **42** (3.0 g, 0.02 mol) in hexane (800 mL) was bubbled allene (16.0 g, 0.4 mol) at −60 °C. The mixture was then photolyzed at −60 °C for 8 h through a Pyrex filter. The solvent was removed under reduced pressure, and the crude product was purified by prepartive HPLC using ethyl acetate/hexane (1:3) as the eluting solvent to give 2.8 g (74%) of a 7:1 mixture of the desired ketone **63** and its isomer at C-4. A pure sample of **63** could be obtained by $LiAlH_4$ reduction of the ketone mixture to the corresponding alcohols followed by HPLC separation and subsequent oxidation of the correct alcohol to the desired ketone **63**: IR ($CHCl_3$) 2950, 2880, 1690, 1400,

895 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.94 (d, J = 6.6 Hz, 3 H), 1.20–2.25 (comp, 11 H), 2.57 (ddd, J = 2.5, 5.0, 17.5 Hz, 1 H), 2.75 (br d, J = 17.5 Hz, 1 H), 4.88 (m, 2 H); mass spectrum, m/e 190.1362 (M^+, calcd for $C_{13}H_{18}O$, 190.1357).

(3a*S,4*S**,6a*R**)-2,4-Dimethyl-1-oxo-3a,6a-propanoperhydropentalene (64).** A solution of ketone **63** (300 mg, 1.58 mmol) in ether (15 mL) containing 10% Pt/C (90 mg) was stirred under H_2 (1 atm) at room temperature for 1 h. The catalyst was removed by suction filtration and washed with ether (2 × 20 mL). The solvent was distilled off carefully at 1 atm to give 280 mg (92%) of a colorless oil consisting of the two C-8 methyl isomers: IR 2940, 2870, 1670, 900 cm^{-1}; NMR (250 MHz) δ 0.88 (m, 6 H), 1.07–2.30 (comp, 12 H), 2.40 (ddd, J = 2.5, 4.3, 17.8 Hz, 1 H), 2.65 (dd, J = 5, 17.8 Hz, 1 H); mass spectrum, m/e 192.1513 (M^+, calcd for $C_{13}H_{20}O$, 192.1514).

To a solution of this ketone (280 mg, 1.49 mmol) in benzene (25 mL) was added *p*-toluenesulfonic acid (369 mg, 1.94 mmol). The mixture was heated to reflux for 18 h and then was allowed to cool to room temperature. The solution was diluted with ether (25 mL), washed with saturated aqueous NaCl (2 × 10 mL), and dried ($MgSO_4$). The solvent was distilled off carefully at 1 atm, and the crude product was purified by preparative HPLC using ethyl acetate/hexane (1:20) as the eluting solvent to give 232 mg (83%) of pure **64** as a colorless oil: IR ($CHCl_3$) 2940, 2860, 1720 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.97 (d, J = 6.6 Hz, 3 H), 1.03 (d, J = 6.7 Hz, 3 H), 1.06–1.93 (comp, 12 H), 2.23 (dd, J = 6.5, 12.8 Hz, 1 H), 2.61 (m, 1 H); mass spectrum, m/e 192.1511 (M^+, calcd for $C_{13}H_{20}O$, 192.1514).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.35; H, 10.48.

(3a*S,4*S**,6a*S**)-3,3a,4,5,6,6a-Hexahydro-1,2,4-trimethyl-3a,6a-propanopentalene (33).** To a flask containing methyltriphenylphosphonium bromide (2.31 g, 6.46 mmol) were added *tert*-amyl oxide (6.48 mmol) and benzene (0.5 mL) at 80 °C under nitrogen. The resulting yellow solution was stirred for 0.5 h at 85 °C, and a solution of ketone **64** (160 mg, 0.83 mmol) in benzene (0.5 mL) was added. The mixture was mixed for another 2 h at 85 °C, and then was allowed to cool to room temperature. The solution was diluted with ether (15 mL), washed with saturated aqueous NaCl (2 × 5 mL), and dried ($MgSO_4$). The solvent was distilled off carefully at 1 atm, and the crude product was purified by flash chromatography using pentane as eluting solvent to give 132 mg (84%) of the desired exocyclic olefin as a colorless oil: IR ($CHCl_3$) 2930, 2850, 1720, 1650, 1435, 880 cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.91 (d, J = 6.5 Hz, 3 H), 1.04 (d, J = 6.4 Hz, 3 H), 0.89–1.71 (comp, 12 H), 1.95 (dd, J = 6.4, 12.2 Hz, 1 H), 2.46 (m, 1 H), 4.57 (d, J = 2.5 Hz, 1 H), 4.73 (d, J = 2.5 Hz, 1 H); mass spectrum, m/e 190.1725 (M^+, calcd for $C_{14}H_{22}$, 190.1722).

To a solution of the olefin (120 mg, 0.63 mmol) in CH_2Cl_2 (3 mL) was added *p*-toluenesulfonic acid (50 mg, 0.25 mmol). The mixture was stirred at room temperature for 18 h and then was diluted with CH_2Cl_2 (10 mL). The resulting solution was washed with saturated aqueous NaCl (1 × 5 mL) and dried ($MgSO_4$), and the solvent was distilled off at 1 atm to give 110 mg (92%) of pure **33** as a colorless oil, identical with the compound obtained previously.

Hexahydro-9,9-dimethyl-1*H*-3a,8-ethano-5*H*-dicyclopenta[*b*,*c*]furan-5-one (65). To a solution of ether **34** (190 mg, 0.92 mmol) in 10 mL of carbon tetrachloride was added a solution of ruthenium dioxide (12 mg, 0.09 mmol) containing sodium periodate (586 mg, 2.8 mmol) dissolved in 10 mL of water. The reaction was stirred vigorously for 24 h. Carbon tetrachloride was added to the solution, and the layers were separated. Isopropyl alcohol (2 mL) was added to the organics, and the solution was dried over anhydrous potassium carbonate. Removal of the solvent in vacuo gave a dark oil, which was purified via flash chromatography (25% ether, hexane (v/v)) affording 202 mg (100%) of lactone **65**: IR (CCl_4) 2950 (br s), 2860 (m), 1750 (s), 1450 (w), 1320 (w), 1270 (m), 1190 (m), 970 (m), 910 (s) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 0.97 (s, 3 H), 1.14 (s, 3 H), 1.17–1.40 (m, 1 H), 1.58–1.96 (m, 10 H), 2.0–2.28 (m, 2 H), 2.56 (br d, J = 11.2 Hz, 1 H); mass spectrum, m/e 220.1464 (M^+, calcd for $C_{14}H_{20}O_2$, 220.1463).

(1*R,3a*R**,5a*S**,8a*S**)-Decahydro-5a-hydroxy-4,4-dimethylcyclopenta[*c*]pentalene-1-methanol (66).** To a stirred solution of lithium aluminum hydride (22 mg, 0.57 mmol) in 20 mL of tetrahydrofuran was added lactone **65** (64 mg, 0.28 mmol), and the solution was warmed to 65 °C for 1 h. The reaction was cooled to room temperature, and solid sodium sulfate decahydrate was added. The salts were removed by filtering them through a pad of Celite and washing with ether. Concentration of the filtrate in vacuo afforded 102 mg of a gummy solid. MPLC (20% ether acetate, hexane (v/v)) gave 57 mg (89%) of **66** as a white crystalline solid: mp 70–72 °C; IR ($CHCl_3$) 3600 (w), 3100–3500 (br m), 2950 (br s), 2860 (m), 1450 (m), 1445 (m), 1375 (w), 1360 (w), 1280 (m), 1260 (m), 1070 (m) cm^{-1}; NMR (250 MHz, $CDCl_3$) δ 1.0 (s, 3 H), 1.08 (s, 3 H), 1.44–2.01 (m, 15 H), 3.14–3.40 (br s, 1 H), 3.84–4.0 (m, 2 H); mass spectrum, 224.1770 (M^+, calcd for $C_{14}H_{24}O_2$, 224.1776).

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The Unusual Reactivity of Hydroxymethylene

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Abstract: Hydroxymethylene (**1**) has been produced by the reaction of arc generated carbon atoms with water, and several of its intermolecular reactions have been studied. Deuterium-labeled **1** reacts with formaldehyde to generate glycolaldehyde (**2**) which is labeled with deuterium on the aldehydic carbon. This result, along with those obtained from ab initio molecular orbital studies ([MP2/6-31G*]), indicates that **1** reacts with formaldehyde via a 5-center transition state involving nucleophilic attack of the carbene carbon on the aldehydic carbon with concurrent transfer of the hydroxyl hydrogen to the carbonyl oxygen. This mechanism is more favorable than C–H insertion. Studies of the reaction of **1** with **2** and acetaldehyde indicate that the 5-center mechanism predominates in these systems as well. Carbene **1** can also effect intermolecular hydrogenation of an alkene. Thus, generation of **1** in the presence of (*Z*)-2-butene results in the formation of small amounts of butane. The analogous process in which ethylene is hydrogenated by **1** to form ethane is calculated at the [MP2/6-31G*] level to proceed without barrier.

Hydroxymethylene (**1**) may be regarded as the parent of a series of carbenes in which the attachment of one or two oxygen atoms to the carbene carbon modifies the traditional electrophilicity of the carbene center. The existence of resonance structures such as **1b** may bring about ambiphilic or nucleophilic reactivity in such carbenes. Although there have been numerous theoretical studies

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