Generation of [5.5.n] Tricyclic Ring Systems by Radical-Promoted Inter- and Intramolecular [3 + 2] Cycloadditions

Michael E. Jung* and Heather L. Rayle
Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90024

Received April 4, 1997

A new method for the synthesis of [5.5.n] tricyclic ring systems via radical fragmentation and double cyclization is described. The general process (Scheme 1) involves addition of an alkylthio radical to an alkenylcyclopropane 1 to generate the cyclopentylcarbinyl radical which opens to the homoallylic radical; this radical then adds to an alkene or alkyne radical trap to give a new alkyl radical which then adds back to the thiocarbonyl system to generate, after loss of the alkylthio radical, the bi- or tricyclic product, 2, thus making the process analogous to a [3 + 2] cycloaddition. Thus addition of the butylthio radical (generated by photolysis of dibutyl disulfide) to the bicyclo[3.1.0]hex-2-en-6-ylcarboxylate 3 in the presence of an alkene or alkyne—either an acyclic radical trap, e.g., ethyl vinyl ether, isopropenyl acetate, methyl acrylate, or methyl propiolate, or a cyclic one, e.g., cyclopentenone, dihydrofuran, cyclopentenyl acetate, or cyclopentene—affords the desired bi- or tricyclic products 9–16 in yields of 54–88%. One can also use 6-vinylbicyclo[3.1.0]hexan-2-one 4 as the alkenylcyclopropane unit. Trapping of the radical generated by addition of butylthio radical to 4 with ethyl vinyl ether or cyclopentene affords the bi- and tricyclic products 17 and 18 in 66–68% yields. The products are formed as diastereomeric mixtures in all cases. This cyclization process can also be carried out in an intramolecular fashion, e.g., isomerization of the ketones 25 and 27 or the esters 28–30 with butylthio radical to give the tricyclic products 31–35 and 41–43. The use of dimethyl-substituted alkenes gives reasonably good diastereoselectivity favoring the cis-syn-cis isomer over the cis-anti-cis isomer, e.g., 7.5:1 for 33 over 34 and 4.2:1 for 41 over 42. The structures of the diastereomeric products were proven by comparison of the NMR spectra of the saturated analogues, which are known for the unsubstituted series and differ in their symmetry properties for the dimethyl-substituted case. These results indicate that the cyclization of a stabilized 5-hexenyl radical, e.g., 45 in Scheme 8, is reversible and leads to the most stable final product.

Introduction

Both the basic understanding and the synthetic utilization of radical processes have increased dramatically in the last twenty years or so. One of the most powerful methods in today’s synthetic arsenal is radical cyclization and/or radical rearrangement—cyclization. A large number of natural products have been prepared using these radical cyclization methods. The initiation of radical cyclizations by fragmentation of a strained ring system beginning with the addition of a sulfur-centered radical to an alkene is a valuable method in organic synthesis. Alkylthiyl radicals can be conveniently generated by photolysis of alkyl disulfides. Normally in the absence of a reducing agent, e.g., any hydride source, longer radical lifetimes are achieved. This methodology has also been applied most recently to the synthesis of cyclopentanes through radical reactions of vinylcyclopropanes. To date, the sulfur radical-promoted cyclization of vinylcyclopropanes with alkenes has been designed to produce a single cyclopentane ring. We report herein the application of this methodology to the facile high-yielding preparation of [5.5.n] tricyclic ring systems 2 by designing the alkenylcyclopropane precursor as part of a 6-substituted bicyclo[3.1.0]hex-2-ene system of type 1 and by trapping the radical intermediate with cyclic alkenes to give a new alkyl radical which then cyclizes onto the original ring system and terminates with loss of the alkylthio radical, an approach that permits the rapid construction of fused-ring compounds of type 2 (Scheme 1).

Results and Discussion

We reasoned that the alkenylcyclopropane starting materials should contain an activating substituent in

---

order to increase the ring-opening rate of the cyclopropylcarbinyl radical by stabilizing the resulting butenyl radical. Two known compounds of type 1 were identified which fulfilled this requirement: the ester 3 and the ketone 4.

The bicyclo[3.1.0]hexenyl ester 3 was prepared in good yield in three steps from 2,5-bicyclo[2.2.1]heptadiene (5) (norbornadiene). The diene was treated with 1 equiv of m-CPBA; the initially formed epoxide opened and rearranged under the mildly acidic conditions to give endo-substituted aldehyde 6. This endo aldehyde readily undergoes reversible Cope rearrangement to 2-oxa-bicyclo[3.2.1]-3,6-octadiene, and a mixture of the two compounds was clearly visible in the NMR spectrum. To prevent this rearrangement, the crude endo aldehyde 6 was treated with sodium methoxide in refluxing methanol for 24 h to convert it to the exo isomer 7 in 80% yield. Normally it is preferable to go directly from norbornadiene (5) to the exo aldehyde 7 without isolation of 6 in 72% isolated yield. This isomer is sterically incapable of performing the Cope rearrangement. The aldehyde 7 was treated with silver oxide to give the acid 8 which was then esterified to give the ester 3. While we utilized the racemic compound in our studies, the optically active ester 3 may be obtained through chiral resolution of acid 8.

The cyclopropyl ketone 4 was prepared by the reaction of the sulfur ylide (made from tert-butyllithium and allylphenylbenzenesulfonium tetrafluoroborate) with cyclopentenone. Only the exo isomer of the desired product is obtained in low yield.

![Diagram of the reaction](image)

For our first test of the sulfur radical-promoted cyclization, a degassed benzene solution containing the cyclopropyl ester 3, an alkene or alkyne trapping agent, and catalytic n-butyl disulfide was photolyzed using a medium-pressure mercury lamp. Table 1 shows the results of the reaction with various simple alkenes traps. The desired cyclization product was obtained in high yield with most alkenes and with the single alkyne studied. In most cases, a mixture of four diastereomers was obtained. Compound 12, generated from trapping of methyl propiolate, was obtained as a 1:1 mixture of two diastereomers. The tricyclic products that resulted from trapping with cyclic alkenes were obtained as four diastereomers, two with cis-syn-cis and two with cis-anti-cis ring junctions (Table 2). On the basis of Beckwith’s studies of tin-mediated radical cyclizations yielding (5,5) and (5,6) ring systems, we expected the cis ring fusions.

![Diagram of the reaction](image)

<table>
<thead>
<tr>
<th>Table 1. Cyclization Products from Alkylthiyl Radical-Promoted Ring Opening and Trapping with Simple Alkenes</th>
</tr>
</thead>
<tbody>
<tr>
<td>alkene substituents (Y, Z)</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>OEt, H</td>
</tr>
<tr>
<td>OCOCH₃, CH₃</td>
</tr>
<tr>
<td>CO₂CH₃, H</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Cyclization Products from Alkylthiyl Radical-Promoted Ring Opening and Trapping with Cyclic Alkenes</th>
</tr>
</thead>
<tbody>
<tr>
<td>alkene substituents (X, Y)</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>H, C=O</td>
</tr>
<tr>
<td>H, O</td>
</tr>
<tr>
<td>OCOCH₃, CH₂</td>
</tr>
<tr>
<td>H, CH₂</td>
</tr>
</tbody>
</table>

* Based on recovered 3.

Many of the reactions were complete within 48 h, although up to 2 weeks of photolysis was required when less reactive alkenes were used as radical traps. However, with the two cyclic alkenes, 1-(acetyloxy)cyclopentene and cyclopentene, the reaction was incomplete even after 2 weeks. The yields reported are based on recovered starting material.

The cyclization of the cyclopropyl ketone 4 was performed with ethyl vinyl ether and cyclopentene. Both alkenes were trapped successfully, although the reaction with cyclopentene was only 40% complete after 2 weeks.
of photolysis. Products 17 and 18 were obtained as mixtures of four diastereomers.

The structure and stereochemistry of the products was proven by transformation of the cyclopentene adduct 16 to the known triquinanes 12 and 22 (Scheme 2). The ester 16, obtained as a mixture of four diastereomers, was reduced to the corresponding alcohol with DIBAL and then oxidized to the aldehyde 19 with PCC in 72% yield for the two steps. The aldehyde 19 was then decarbonylated with Wilkinson’s catalyst, tris(triphenylphosphine)rhodium(1) chloride, to provide the two alkenes 20 and 21 in 67% yield. After catalytic hydrogenation over Pd on carbon, a 52:48 mixture of the cis-syn-cis (22) and cis-anti-cis (23) triquinanes was obtained. These two products were distinguished by comparison with the published 13C NMR spectra.

Nearly equal amounts of the two cis-fused adducts were obtained, indicating that the intermolecular trapping of the radical generated from ring opening of 3 with alkenes occurs with little or no stereocontrol. However, the subsequent cyclization occurs with good stereospecificity (caused by the preference for a cis ring fusion), generating 16 as two pairs of cis-fused triquinanes in nearly equal amounts (Scheme 3).

We next studied the ring opening and trapping of a nonstabilized alkylcyclopropane substrate. A solution of 3,7,7-trimethylbicyclo[4.1.0]hept-2-ene (2-carene), n-butyldisulfide, and ethyl vinyl ether was photolyzed for 4 days. Only unreacted starting material was recovered. As predicted, the rate of cyclopropylcarbinyl ring opening is significantly reduced by the inability to form an acyclic radical stabilized with an electron-withdrawing group. The rate of phenylthio-substituted cyclopropylcarbinyl radical reversion to alkylthio radical and vinylcyclopropane has been estimated to be on the order of 10^8 s^-1, comparable to the ring-opening rate of a dimethyl substituted cyclopropylcarbinyl radical. Addition of a stabilizing substituent such as an ester or phenyl group to a cyclopropylcarbinyl radical increases its ring-opening rate by a factor of 800–3000. The presence of a stabilizing substituent is essential to induce the cyclopropylcarbinyl radical to open at a reasonable rate to allow intermolecular trapping of the acyclic radical intermediate.

While the tandem radical fragmentation–cyclization was successful, the lack of stereoselectivity was disappointing. We therefore turned to intramolecular tandem radical reactions hoping that the stereoselectivity of the reactions might be improved by tethering the alkylcyclopropane system to the alkene trap. We therefore prepared several keto- and ester-substituted cyclopropyl alkenes as substrates. The two keto-substituted cyclopropanes 25 and 27 were prepared by a two-step route involving initially the Grignard addition of the organometallic reagent prepared from magnesium and 4-bromo-1-butene and 5-bromo-2-methyl-2-pentene to the aldehyde 7 to give the alcohols 24 and 26 in 85% and 70% yields respectively (Scheme 4). The intermediate alcohols were then oxidized with PCC to afford the ketones 25 and 27 in yields of 86% and 81%, respectively.

The three cyclopropyl esters 28–30 were also prepared by esterification of the acid 8 with allyl alcohol, 2-methyl-3-buten-2-ol, and 3-methyl-2-buten-1-ol (Scheme 5).

Each substrate was treated with catalytic n-butyl disulfide and photolyzed. Both keto-substituted cyclo-

propanes cyclized upon photolysis, and some stereo-selectivity was observed in these reactions. Ketone 25 afforded the cyclization product as two diastereomers, 31 and 32. The major isomer was proven to be the cis-anti-cis compound 31 (see below). The effect of varying the

solvent and the disulfide catalyst utilized in the cyclization of 25 was also studied (Table 3). The reaction was run under the same conditions in degassed DMSO and benzene. The cyclization proceeded over three times more slowly in DMSO. However, the diastereomeric ratio was improved; the cis-anti-cis product 31 comprised 82% of the product from the cyclization in DMSO, compared to the 65% obtained in benzene. This is an intriguing result, since radical reactions typically are not subject to solvent effects. However, the long reaction times required to complete the cyclization discouraged us from pursuing this observed solvent effect further.

Cyclization of the keto substrate 27, in which the keto-substituted cyclopropane was tethered to a trisubstituted alkene, afforded the desired adduct (81%) as a mixture of three isomers 33–35. The stereoselectivity of this reaction was even higher than that in the reaction of 25. The cis-anti-cis isomer 33 was preferentially formed as 82% of the product mixture. The second isomer (11%) was identified as the cis-syn-cis isomer 34, while the minor product (7%) was tentatively identified as 35.

The stereochemistry of the major isomers in both keto-substituted adducts was determined by conversion of the products to the corresponding unsubstituted triquinanes (Scheme 6). The mixture of diastereomeric ketones 31 and 32 was deoxygenated by conversion to the tosylhydrazones and treatment with catecholborane to afford a mixture of the alkenes 36 and 37. The alkene mixture was hydrogenated to give the known triquinanes 23 and 22 in a 2:2:1 ratio favoring the cis-anti-cis isomer 23. The two isomers were distinguished by comparison with the reported $^{13}$C NMR spectra. The dimethyl-substituted adduct containing isomers 33 and 34 was similarly deoxygenated, giving the alkenes 38 and 39 in a 12:1 ratio. The structure of the third isomer was unassignable, as it was a minor component of the product mixture. The alkene mixture was hydrogenated, producing the nearly pure cis-anti-cis compound 40 (Scheme 7). While the dimethyl-substituted triquinane was not known in the literature, the two diastereomers could be distinguished from the $^{13}$C NMR spectrum. The cis-anti-cis compound has a C$_2$ axis of symmetry, so both methyl groups are equivalent and seven peaks are expected. The cis-syn-cis isomer has a plane of symmetry cutting through the two methyl groups and thus these groups are not equivalent and eight peaks are expected. The $^{13}$C NMR spectrum of 40 contained only seven peaks, confirming our assignment.

The photolysis of the ester-activated alkenylcyclopropanes produced mixed results. The substrates tethered to terminal alkenes 28 and 29 failed to cyclize after 2 weeks of photolysis. The compound bearing a trisubstituted alkene as the radical trap, 30, cyclized within 60 h to give a mixture of three isomers (41–43). The stereoechemical assignments were based on those determined for cyclization of the keto-substituted analog. The major isomer, the cis-anti-cis compound 41, comprised 72% of the product. The cis-syn-cis isomer 42 was obtained as 17% of the product. The identification of the minor compound 43 (11%) is tentative.

Table 3. Solvent Effect on Diastereomeric Ratio and Reaction Time for the Cyclization of 25

<table>
<thead>
<tr>
<th>solvent</th>
<th>reaction time</th>
<th>product ratio (31:32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene</td>
<td>7–12 days</td>
<td>65:35</td>
</tr>
<tr>
<td>DMSO</td>
<td>6 weeks</td>
<td>82:18</td>
</tr>
</tbody>
</table>

and 32 was deoxygenated by conversion to the tosylhydrazones and treatment with catecholborane to afford a mixture of the alkenes 36 and 37. The alkene mixture was hydrogenated to give the known triquinanes 23 and 22 in a 2:2:1 ratio favoring the cis-anti-cis isomer 23. The two isomers were distinguished by comparison with the reported $^{13}$C NMR spectra. The dimethyl-substituted adduct containing isomers 33 and 34 was similarly deoxygenated, giving the alkenes 38 and 39 in a 12:1 ratio. The structure of the third isomer was unassignable, as it was a minor component of the product mixture. The alkene mixture was hydrogenated, producing the nearly pure cis-anti-cis compound 40 (Scheme 7). While the dimethyl-substituted triquinane was not known in the literature, the two diastereomers could be distinguished from the $^{13}$C NMR spectrum. The cis-anti-cis compound has a C$_2$ axis of symmetry, so both methyl groups are equivalent and seven peaks are expected. The cis-syn-cis isomer has a plane of symmetry cutting through the two methyl groups and thus these groups are not equivalent and eight peaks are expected. The $^{13}$C NMR spectrum of 40 contained only seven peaks, confirming our assignment.

The photolysis of the ester-activated alkenylcyclopropanes produced mixed results. The substrates tethered to terminal alkenes 28 and 29 failed to cyclize after 2 weeks of photolysis. The compound bearing a trisubstituted alkene as the radical trap, 30, cyclized within 60 h to give a mixture of three isomers (41–43). The stereoechemical assignments were based on those determined for cyclization of the keto-substituted analog. The major isomer, the cis-anti-cis compound 41, comprised 72% of the product. The cis-syn-cis isomer 42 was obtained as 17% of the product. The identification of the minor compound 43 (11%) is tentative.
The appearance of a minor third product from intramolecular trapping with trisubstituted alkenes was unexpected. We assumed that the minor product was derived either from 6-endo cyclization or from trans ring fusion. Calculations of the relative energies of the possible products revealed that the 6-endo cyclization adduct is 1.5 kcal/mol more stable than the most stable trans-fused product.\(^\text{16}\) Cyclization of an unsubstituted 5-hexenyl radical is kinetically controlled and gives a 98:2 ratio of methylcyclopentane and cyclohexane.\(^\text{17}\) However, a literature survey revealed that the cyclization of keto- and ester-stabilized 5-hexenyl radicals frequently affords significant amounts of the 6-endo cyclization product.\(^\text{18}\) Therefore, we tentatively assigned the structures 35 and 43, derived from 6-endo cyclization, to the minor products.

While we observed minor amounts of the 6-endo cyclization product from the reaction of 27 and 30, only 5-endo cyclization products were observed from the trapping of a keto-stabilized radical intermediate with a terminal alkene. A reasonable explanation is that the terminal methyl groups stabilize the intermediate radical obtained from the initial 5-exo cyclization, increasing its lifetime and, therefore, the reversibility of the cyclization. This reversibility leads to the formation of minor amounts of 6-endo cyclization product.

The preference for cis-anti-cis stereochemistry in our intramolecular tandem cyclizations is set by the first 5-exo cyclization. This stereocontrol could be due to either of two factors: stereochemical induction during alkene trapping by the stereocenter on the cyclopentene ring or the achievement of the most energetically favorable stereochemistry through a reversible cyclization of the keto-stabilized 5-hexenyl radical. Our results clearly show that no stereocontrol is achieved during intramolecular trapping of similar keto- and ester-stabilized bicyclo[3.1.0]hexenes. Therefore, steric induction cannot explain our results. Because cyclization of the keto- or ester-stabilized 5-hexenyl radical is reversible, the most energetically favorable stereoisomer is preferentially formed. The five potential radical intermediates 46–50 generated by addition of the butylthio radical to the substrates 25 and 27 are shown (Scheme 8). Intermediates 46 and 47 lead to the two potential cis-fused products, while 48 and 49 lead to the less energetically favorable trans-fused isomers. The reversibility of the 5-exo cyclization permits intermediates 48 and 49 to revert to 45. So while these two intermediates are probably formed, the trans-fused products are not observed. Instead, the lowest-energy intermediate, 46, is preferentially formed. This intermediate undergoes a second cyclization in which the stereochemistry is controlled by the preference for cis ring fusion; therefore, 31 and 33 are the major products obtained. The cyclization of 47 is slower than that of 46, because products 32 and 34 are higher in energy than 31 and 33. Because 47 has a longer lifetime than 46, it is more likely to revert to 45. This is the source of the observed cis-anti-cis selectivity. In the cyclization of 27, intermediate 50, corresponding to the product of a 6-endo cyclization, usually reverts to 45 but occasionally cyclizes to give 35.

Stereoselectivity in radical reactions is an area of current interest.\(^\text{19}\) While there are many examples of stereocontrol in radical reactions caused by steric and conformational factors, very little has been reported concerning stereoselectivity through reversible radical cyclization. Our results, therefore, represent a relatively unrecognized method for achieving stereoselective radical cyclizations.

**Experimental Section**

\(^3\)H and \(^13\)C NMR were recorded on Bruker AM-360 and AMX-400 spectrometers. Infrared spectra were recorded on a Nicolet 510 infrared spectrophotometer as a liquid film (neat). High-resolution mass spectra (MS) were recorded on a VG Analytical Autospec double-focusing instrument. All mass spectra are electron impact unless otherwise noted. Gas chromatographic analyses were performed using a Hewlett-Packard 5790A Series chromatograph equipped with an SE-30 crosslinked methyl silicone gum column (12 m × 0.2 mm film thickness).

---

\(^{(16)}\) MM2 minimizations were performed using PC Model, version KS 2.95, on a VAX datastation (Houk Computational Installation Organet Cluster, UCLA).


The following solvents and reagents were distilled from the indicated agent under dry nitrogen: tetrahydrofuran, diethyl ether, and benzene from sodium benzenophenone ketyl; hexane, dichloromethane, and chloroform from calcium hydride. Dimethyl sulfoxide was distilled from calcium hydride under reduced pressure and dried over 4 Å molecular sieves. All reactions were performed under an inert atmosphere of argon.

(±)-15x-Bicyclo[3.1.0]hex-2-ene-6-carboxaldehyde (7). 10 mCPBA (68.7%, 21.81 g, 86.82 mmol) was added in portions over 1 h to a 0 °C solution of 2.5-bicyclo[2.2.1]heptadiene (5) (norbornadiene, 8.00 g, 86.82 mmol) in 300 mL of dichloromethane. The resulting mixture was stirred for 2 h and filtered. The precipitated acid was washed thoroughly with dichloromethane, and the organic layer was evaporated to afford 6.8 g (72%) of the aldehyde 7 as a yellow oil. When the oil was purified by Kugelrohr distillation: bp 163–165 °C; 1H NMR (CDCl3) δ 2.93 (J = 2.0, 6.5 Hz, 1H), 5.93 (dd, J = 2.0, 5.5 Hz, 1H), 5.57 (dd, J = 2.6, 5.5 Hz, 1H), 1.27 (dd, J = 6.7, 19.0 Hz, 1H), 2.35 (m, 1H), 1.23 (dd, J = 2.6, 2.7 Hz, 1H); 13C NMR (CDCl3) δ 201.3, 132.5, 131.7, 41.1, 36.9, 36.1, 27.7.

(±)-15x-Bicyclo[3.1.0]hex-2-ene-6-carboxylic Acid (8). 10 The aldehyde 7 (4.00 g, 36.99 mmol) was dissolved in 4 mL of dry methanol and 25 mL of 2,2-dimethoxypropane. The cyclopropyl ester was obtained as a pale yellow oil: 1H NMR (CDCl3) 3 2.13 (m, 4H), 0.94 (dd, J = 2.1, 19.0 Hz, 1H), 2.35 (m, 1H), 1.23 (dd, J = 2.6, 2.7 Hz, 1H) as a pale yellow oil: 1H NMR (CDCl3) 3 174.1, 133.8, 129.6, 52.8, 52.3, 52.2, 48.8, 48.4, 42.7, 37.6, 25.5, 22.5 (IR neat) 1732 (s), 1175 (s), 1123 (bs) cm⁻¹; CI HRMS m/z calcd for C12H16O3 224.1048, found 224.1048.

Methyl 3-(Acetoxy)-1,2,3,3a,6a-hexahydro-2-methylpentalen-1-carboxylate (10). The cyclopropyl ester 3 (0.10 g, 0.72 mmol), isopropenyl acetate (1.09 g, 10.86 mmol), and n-butyl disulfide (0.019 g, 0.11 mmol) were combined in 2.5 mL of degassed benzene. After 2 days of photolysis, the product was purified as usual to provide 0.075 g (54%) of 11 as a colorless oil. The product was obtained as a colorless oil: 1H NMR (CDCl3) δ 2.56–5.40 (m, 2 H), 3.21–4.23 (m, 2 H), 2.28 (m, 1H), 0.94 (dd, J = 2.2, 2.7 Hz, 1H); 13C NMR (CDCl3) δ 176.9, 174.9, 130.4, 129.8, 129.7, 117.5, 63.9, 36.9, 35.9, 27.8. CI HRMS m/z calcd for C11H17O3 219.1263 (MH⁺), found 219.1264 (MH⁺).
consisting of three partially separable diastereomers in a ratio of 2.0:1.9:1.2:1.0:1H NMR (CDCl$_3$) diastereomer 1 (37%), δ 174.2, 129.5, 129.0, 86.8, 68.0, 55.0, 54.8, 51.7, 49.8, 44.8, 37.9, 39.1, 39.6, 34.1, 29.5, 29.4, 29.3; diastereomer 2 (17%), δ 173.6, 131.0, 130.5, 85.3, 70.6, 54.2, 51.3, 47.3, 46.7, 43.3, 38.0, 29.5, diastereomer 4 (30%), δ 175.6, 132.2, 129.2, 85.7, 84.8, 58.5, 52.7, 47.8, 46.2, 41.8, 37.6, 29.3; IR (neat) 1736 (s), 1175 (vs), 1063 (m); HRMS m/z calculated for C$_2$H$_2$O$_2$: 208.1100, found 208.1101.

Methyl 2,3,3a,4,4a,5,5a,6a,7,7a-Octahydropentalen-1(2b),6(1b)-furan-4-carboxylate (14). | The cyclopropyl ester 3 (0.075 g, 0.54 mmol), 2,3-di-O-difluorophenyl (0.31 g, 4.34 mmol), and n-butyl disulfide (0.064 g, 0.36 mmol) were combined in 1.5 mL of degassed benzene and photolyzed for 7 days. Purification afforded 0.094 g (83% of 14) as four partially separable diastereomers in a ratio of 2.0:1.7:1:0.1.1H NMR (CDCl$_3$) diastereomer 1 (36%) δ 221.1, 174.5, 134.6, 129.4, 57.7, 55.3, 54.8, 52.4, 54.7, 43.3, 40.0, 38.5, 24.1; diastereomer 2 (34%), δ 221.8, 172.4, 135.3, 130.9, 60.2, 57.7, 53.7, 53.2, 45.6, 24.6, 38.1, 36.1, 23.2; diastereomer 3 (31%) δ 221.6, 173.9, 132.4, 131.3, 57.7, 57.6, 52.4, 52.2, 47.1, 43.4, 41.3, 39.5, 25.1; IR (neat) 1732 (bs), 1169 (vs) cm$^{-1}$; HRMS m/z calculated for C$_2$H$_2$O$_2$: 220.1100, found 220.1100.

Methyl 2,3a,4,4a,5,5a,6a,7,7a-Octahydropentalen-1(2b),6(1b)-furan-4-carboxylate (14) (15). | The cyclopropyl ester 3 (0.080 g, 0.58 mmol), 1-acetoxy)cyclopentenone (0.075 g, 0.5 mmol), and n-butyl disulfide (0.023 g, 0.13 mmol) were combined in 2 mL of degassed benzene. After 2 weeks of photolysis, the reaction was worked up as described in section 1.1. Generation of 6.0 g (0.50 g, 19% based on unreacted starting material) as a colorless oil consisting of three inseparable diastereomers in a ratio of 1.9:1.6:1.0:1H NMR (CDCl$_3$) diastereomer 1 (85%) δ 48.0, 43.9, 37.3, 28.8, 26.0, 22.8; diastereomer 2 (22%), δ 176.0, 175.0, 150.3, 131.0, 99.3, 61.8, 56.7, 52.6, 46.8, 40.9, 33.4, 34.9, 28.5, 25.8, 22.5; IR (neat) 1736 (s), 1190 (vs) cm$^{-1}$; HRMS m/z calculated for C$_2$H$_2$O$_2$: 220.1100, found 220.1100.

Methyl 2,3a,4,4a,5,5a,6a,7,7a-Octahydropentalen-1(2b)-carboxaldehyde (19). | A solution of the ester 16 (0.60 g, 2.91 mmol) in 10 mL of ether was added to DI(BAL) (9.47 mL of a 1 M solution in hexane, 9.47 mmol) in 20 mL of ether. The reaction mixture was stirred for 2 h and quenched with 1 M NaOH solution. The layered organic phase was extracted with water, and evaporated. The residual oil (0.48 g, 2.69 mmol) was dissolved in 40 mL of dichloromethane. PCC (0.70 g, 3.26 mmol) and Celite (0.75 g) were added, and the mixture was stirred at room temperature for 3 h. Ether was added, and the reaction mixture was filtered through a pad of Florisil. The resulting solution was concentrated to afford the aldehyde (0.37 g, 72%) as a colorless oil. The product was a mixture of four diastereomers in a ratio of 1.3:1.2:1.0:1H NMR (CDCl$_3$) diastereomer 1 δ 179.5, 137.9, 137.7, 126.5, 51.6 (major), 115.5, 61.4, 51.2, 50.0, 45.2, 44.4, 35.2, 29.4, 27.3, 25.0, 21.3; diastereomer 2 (16%), δ 219.6, 136.1, 126.7, 57.2, 51.2, 44.3, 39.8, 34.6, 33.6, 31.4, 29.5, 25.0, 21.9; diastereomer 3 (33%), δ 213.1, 140.4, 114.2, 66.5, 53.5, 53.4, 42.8, 31.8, 30.8, 25.1, 25.0, 24.3, 21.9; diastereomer 4 (20%), δ 219.7, 136.1, 126.7, 57.2, 56.5, 44.3, 39.6, 32.7, 33.6, 30.3, 29.6, 28.0, 24.6; IR (neat) 1734 (s), 1154 (w) cm$^{-1}$; HRMS m/z calculated for C$_2$H$_2$O: 190.1385, found 190.1357.

Following the general procedure, 28 the acid (0.75 g, 6.04 mmol) and 1,1-carboxyldimiazole (0.98 g, 6.04 mmol) were mixed in DMF in 8 mL of THF and heated to 65 °C. Allylic alcohol (0.70 g, 12.08 mmol) and DCI (0.92 g, 5.04 mmol) were added, and the reaction was stirred at 50 °C for 20 h. The ester (28) (0.80 g, 80%) was isolated as a colorless oil: 1H NMR (CDCl 3 ) δ 5.92 (m, 1 H), 5.55 (m, 1 H), 5.06 (t, J = 7.2 Hz, 1 H), 2.71–2.20 (m, 8 H), 1.66 (s, 3 H), 1.60 (s, 3 H), 1.26 (dd, J = 2.5, 2.7 Hz, 1 H); 13C NMR (CDCl 3 ) δ 170.3, 132.2, 131.9, 130.4, 65.0, 36.1, 34.5, 30.1, 26.2, IR (neat) 1725 (s), 1170 (s) cm −1 ; HRMS m/z calc for C 13 H 20 O 192.1514, found 192.1506.

**General Procedure for Preparation of Esters 28–30.** The acid 8, 1,1-carboxyldimiazole, and DMF were combined and heated for 1 h. The allylic alcohol and DBU were added, and the reaction mixture was chromatographed to afford the ester. The reaction mixture was stirred until the esterification was complete. The reaction mixture was chromatographed (10% ether in pentane) to give the desired ester.

### 4-Hydroxy-4-pentenyl-1,5-cyclo[3.1.0]hex-2-ene (24)

Following the general procedure, 32 the acid (8) (0.75 g, 6.04 mmol) and 1,1-carboxyldimiazole (0.98 g, 6.04 mmol) were mixed in DMF and heated to 65 °C. Allylic alcohol (0.70 g, 12.08 mmol) and DBU (0.92 g, 5.04 mmol) were added, and the reaction was stirred at 50 °C for 20 h. The ester (28) (0.80 g, 80%) was isolated as a colorless oil: 1H NMR (CDCl 3 ) δ 5.92 (m, 1 H), 5.91 (tdd, J = 5.7, 10.4, 17.2 Hz, 1 H), 5.54 (m, 1 H), 5.31 (dd, J = 1.4, 17.2 Hz, 1 H), 5.24 (dd, J = 1.4, 10.4 Hz, 1 H), 4.56 (d, J = 5.7 Hz, 2 H), 2.71–2.20 (m, 4 H), 1.01 (dd, J = 2.6, 2.7 Hz, 1 H); 13C NMR (CDCl 3 ) δ 173.0, 132.2, 131.9, 130.4, 65.0, 36.1, 34.5, 30.1, 26.2, IR (neat) 1725 (s), 1180 (s), 1178 (s) cm −1 ; HRMS m/z calc for C 13 H 20 O 192.1514, found 192.1506.

### 1,1-Dimethyl-2-propenyl 1,5-cyclo[3.1.0]hex-2-ene-6-carboxylate (29)

The acid (8) (0.80 g, 6.44 mmol) and 1,1-carboxyldimiazole (1.04 g, 6.44 mmol) were combined in 7 mL of DMF and warmed to 65 °C for 1 h. 2-Methyl-3-buten-2-ol (2.2 g, 25.76 mmol) and DBU (0.98 g, 6.44 mmol) were added, and the reaction was stirred at 65 °C for 20 h. The ester (29) (0.77 g, 62%) was obtained as a colorless oil: 1H NMR (CDCl 3 ) δ 6.06 (dd, J = 10.9, 17.5 Hz, 1 H), 5.91–5.52 (m, 2 H), 5.15 (d, J = 17.5 Hz, 1 H), 5.05 (d, J = 10.9 Hz, 1 H), 2.70–2.12 (m, 4 H), 1.50 (s, 6 H), 0.915 (dd, J = 2.6, 2.7 Hz, 1 H); 13C NMR (CDCl 3 ) δ 172.2, 142.6, 132.0, 130.2, 112.3, 80.4, 36.0, 34.1, 31.1, 26.4 (2C), 25; IR (neat) 1725 (s), 1175 (bs), 1125 (bs) cm −1 ; HRMS m/z calc for C 15 H 22 O 2 294.1683, found 294.1682.

### 1,1-Dimethyl-2-propenyl 1,5-cyclo[3.1.0]hex-2-ene-6-carboxylate (30)

The acid (8) (0.25 g, 2.01 mmol) and 1,1-carboxyldimiazole (0.33 g, 2.01 mmol) were combined in 5 mL of DMF and warmed to 65 °C for 1 h. 2-Methyl-3-buten-2-ol (0.35 g, 4.02 mmol) and DBU (0.31 g, 2.01 mmol) were added, and the reaction was stirred at 50 °C for 20 h. The ester (30) (0.31 g, 80%) was obtained as a colorless oil: 1H NMR (CDCl 3 ) δ 5.91 (m, 1 H), 5.53 (m, 1 H), 5.34 (t, J = 7.2 Hz, 1 H), 2.70–2.12 (m, 4 H), 1.50 (s, 6 H), 0.915 (dd, J = 2.6, 2.7 Hz, 1 H); 13C NMR (CDCl 3 ) δ 172.2, 142.6, 132.0, 130.2, 112.3, 80.4, 36.0, 34.1, 31.1, 26.4 (2C), 25; IR (neat) 1725 (s), 1175 (bs), 1125 (bs) cm −1 ; HRMS m/z calc for C 15 H 22 O 2 294.1683, found 294.1682.
The ketones 33–35 (0.060 g, 0.32 mmol) and p-toluenesulfon fluoride (0.070 g, 0.38 mmol) were combined in 3 mL of THF. The resulting solution was refluxed for 3 h and cooled. The solvent was evaporated, and 3 mL of chloroform was added. The solution was cooled to 0 °C, and catecholborane (0.038 g, 0.032 mmol) was added. After 1 h of stirring, sodium acetate trihydrate (0.13 g) was added, and the reaction was refluxed for 1 h. The mixture was filtered, and the resulting solution was washed with MgSO4. The mixture of cis and trans was chromatographed with pentane eluent to provide the alkenes as a colorless oil; the cis-anti-cis isomer 38 comprised 88% of the mixture, while cis-syn-cis isomer 39 was 8%. The alkene derived from deoxygenation of the minor tricyclic product 35 was present as only 4% of the mixture, and its NMR spectrum could not be assigned. cis-NMR (CDCl3) δ 5.62 (t, 2 H), 2.92 (b, J = 11.4, 6.9 Hz, 1 H), 2.52 (dd, J = 1.8, 8.9, 16.5 Hz, 1 H), 2.36 (m, 1 H), 2.18–1.38 (m, 10 H), 1.16 (s, 0.12 H), 1.07 (s, 0.12 H), 0.943 (s, 0.24 H), 0.918 (s, 0.24 H), 0.853 (s, 2.64 H); 13C NMR (CDCl3) δ 131.4, 129.7, 63.2, 59.5, 52.4, 49.3, 43.0, 40.5 (2C), 32.7, 27.6, 27.0, 26.4; compound 39 (8%), δ 131.4, 129.6, 53.5, 52.7, 51.2, 48.1, 46.1, 42.1, 40.1, 34.0, 29.6, 27.4, 25.0; HRMS m/z calcd for C13H20 176.1566, found 176.1571.

(-7,7-Dimethyl-2,3,3a,3b,4,6a,6b,7a-octahydro-3(1H)-cyclopenta[a]pentalene (33), 7,7-Dimethyl-2,3,3a,3b,4,6a,6b,7a-octahydro-3(1H)-cyclopenta[a]pentalene (34), and 11,11-Dimethyl-1,2,6a,7,7b-tricyclo[5.3.1.02,6]undec-3-en-8-one (35). The cyclopropyl ketone 27 (0.20 g, 1.05 mmol) and n-butyl disulfide (0.11 g, 0.63 mmol) were combined in 4 mL of degassed benzene and photolyzed for 10 days. Chromatography afforded the adduct (0.16 g, 81%) as a colorless oil. The product consisted of three inseparable isomers; the two major products were the cis-isomers 35 (82%) and cis-syn-cis (11%) isomers. The third isomer (7%) was tentatively assigned structure 36, corresponding to a 6-exo cyclization product. cis-NMR (CDCl3) δ 3.75–5.44 (m, 2 H), 3.09–1.54 (m, 10 H), 1.11 (s, 0.33 H), 1.08 (s, 0.21 H), 0.994 (s, 0.33 H), 0.944 (s, 2.46 H), 0.761 (t, 2.46 H), 0.712 (s, 0.22 H). cis-NMR (CDCl3) δ 0.222.9, 130.7, 130.5, 63.8, 62.0, 51.9, 43.8, 42.3, 41.3, 37.6, 25.5, 24.5, 20.3; compound 34 (11%), δ 214.4, 129.9, 129.5, 64.2, 59.4, 54.5, 42.1, 40.5, 37.2, 35.5, 29.1, 20.1, 18.6; compound 35 (7%), δ 222.6, 132.3, 129.3, 68.9, 63.7, 54.7, 43.7, 42.7, 37.6, 34.9, 32.4, 24.1, 20.9; IR (neat) 1736 (s), 1171 (m); HRMS m/z calcd for C13H20O 190.1358, found 190.1357.

(-7,7-Dimethyl-2,3,3a,3b,4,6a,6b,7a-octahydro-3(1H)-cyclopenta[a]pentalene (40). The alkenes 36 and 39 (0.018 g, 0.098 mmol) and cobalt chloride hexahydrate (0.007 g, 0.04 mmol) were combined in 4 mL of THF. After photolysis, the resulting solution was dried with MgSO4 and concentrated. The residual oil was chromatographed with pentane eluent to provide the alkenes as a colorless liquid. The isomers comprised only 5% of the mixture; cis-NMR (CDCl3) δ 2.14–1.43 (m, 16 H), 0.92 (s, 6 H); 13C NMR (CDCl3) δ 57.5, 51.8, 42.4, 33.0, 27.0 (2C), 26.9; HRMS m/z calcd for C12H20 176.1722, found 176.1721.

(-7,7-Dimethyl-1,3a,3b,4,6a,6b,7a-octahydrofuran-1,2,6a,7,7b-tricyclo[5.3.1.02,6]undec-3-en-8-one (43). The cyclopropyl ester 30 (0.25 g, 1.30 mmol) and n-butyl disulfide (0.048 g, 0.26 mmol) were combined in 4 mL of degassed benzene and photolyzed for 2 days. After chromatography, the adduct (0.18 g, 70%) was isolated as a colorless oil which was an inseparable mixture of three isomers. The cis-anti-cis-triquinane 41 comprised 72% of the mixture, and the cis-syn-cis isomer 42 comprised 17%. The third product was tentatively identified as 43, the product of 6-exo cyclization (11%); cis-NMR (CDCl3) δ 5.77–5.60 (m, 2 H), 4.13 (m, 2 H), 3.16–2.36 (m, 6 H), 1.11 (s, 0.35 H), 1.08 (s, 0.35 H), 1.06 (s, 4.4 H), 1.01 (s, 0.5 H), 0.90 (s, 0.5 H); 13C NMR (CDCl3) δ 42 (72%), δ 173.8, 130.9, 130.2, 68.0, 63.7, 53.2, 50.6, 42.2, 41.6, 35.2, 34.1, 24.3; compound 42 (17%), δ 178.8, 132.0, 131.0, 69.4, 67.1, 53.3, 47.7, 43.4, 42.1, 31.9, 23.1, 20.4; compound 43 (11%), δ 181.0, 131.5, 130.1, 69.6, 65.0, 52.3, 49.5, 43.4, 39.7, 35.2, 25.0, 23.9; IR (neat) 1767 (s), 1177 (m), 1157 (s), 1109 (w) cm−1; HRMS m/z calcd for C13H20O 192.1151, found 192.1148.

Acknowledgment. We thank the National Institutes of Health (GM31349 and GM41592) and the Agricultural Research Division of American Cyanamid Company for generous financial support. H.L.R. thanks the National Science Foundation for fellowship support.

Supporting Information Available. 1H and 13C NMR spectra of 9–21 and 24–43 (50 pages). This material is contained in libraries on microfiche, immediately follows this document in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.