

by higher iron concentration, in accord with the observations of Brady and Pettit who studied the reactions of diazomethane over metal surfaces (Fischer-Tropsch catalysts).<sup>6</sup> The diazomethane reaction with atomic and diatomic iron will be discussed in detail in a future publication.

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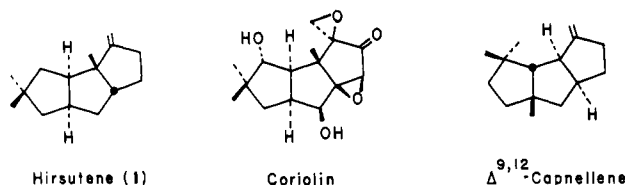
## Tandem Radical Approach to Linear Condensed Cyclopentanoids. Total Synthesis of (±)-Hirsutene

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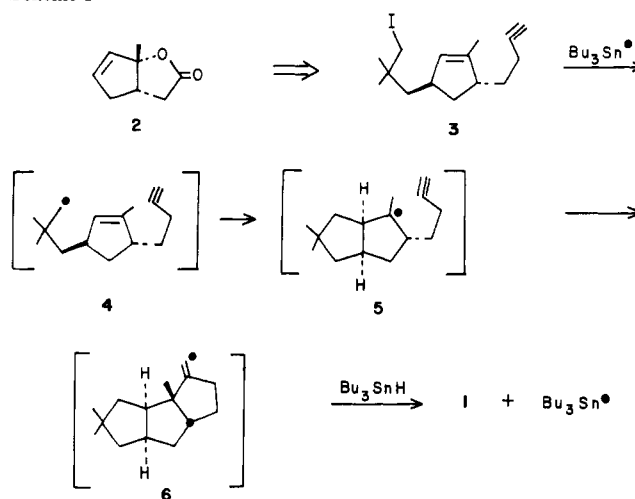
Hirsutene (1),<sup>2a</sup> the parent member of the hirsutane family,



has proven to be an important target for illustration of synthetic strategies directed toward linear condensed cyclopentanoids.<sup>2</sup> Frequently, new annulation procedures have been devised to sequentially construct each ring in the tricyclic system.<sup>3,4</sup> A tandem construction of rings can present an inherently more efficient approach to linear condensed cyclopentanoids provided that the stereochemistry can be controlled, that the cyclization precursors are readily available, and that the approach is sufficiently general to permit construction of the more functionalized coriolins and the isomerically related capnellenes.<sup>3a,b</sup> We now report a total synthesis of (±)-hirsutene via a tandem radical cyclization which realizes the first two of these goals.

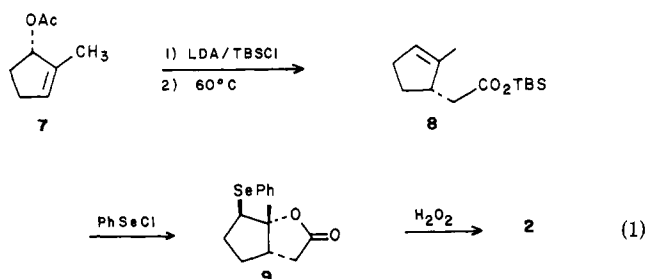
Synthesis of condensed cyclohexanoid systems by cation-initiated polyolefinic cyclizations has proven extremely fruitful.<sup>5</sup> We

Scheme I



felt that a related approach to condensed cyclopentanoids might be devised employing radical-initiated polyolefinic cyclizations.<sup>6,7</sup> In view of the extensive studies on the cyclization of hex-5-enyl radicals,<sup>6</sup> it is quite surprising that this reaction has received almost no use in condensed cyclopentanoid synthesis. The tandem radical approach to hirsutene is outlined in Scheme I. Treatment of iodide 3 with tri-*n*-butyltin hydride should generate transient radical 4. In turn, 4 should suffer two successive hex-5-enyl-like radical cyclizations ( $4 \rightarrow 5 \rightarrow 6$ ) and finally a hydrogen atom abstraction. This would produce hirsutene (1) from 3 in a single step via the standard radical chain mechanism. Of concern is the second cyclization ( $5 \rightarrow 6$ ) which involves conversion of a 3° radical to a significantly less stable vinyl radical.<sup>8</sup> It was envisioned that 3 would be readily available from simple vinyl lactone 2 by  $\text{S}_{\text{N}}2'$ -anti addition and subsequent chain elongation. Note that since both hexenyl radical cyclizations must proceed in a *cis* fashion,<sup>3a</sup> the  $\text{S}_{\text{N}}2'$ -anti opening of 2 effectively ensures the *cis*-anti-*cis* stereochemistry present in hirsutene.

Equation 1 illustrates the facile synthesis of vinyl lactone 2.



2-Methylcyclopentenone<sup>9a</sup> was reduced ( $\text{NaBH}_4$ ,  $\text{CeCl}_3$ )<sup>9b</sup> and

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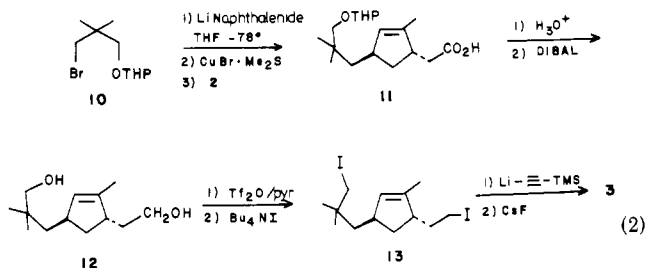
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acetylated to produce 7. Standard Ireland ester enolate Claisen rearrangement<sup>10</sup> of 7 gave crude silyl ester 8, which was directly subjected to phenyl selenolactonization<sup>11</sup> to yield 9. Routine oxidation and elimination produced vinyl lactone 2<sup>17</sup> in 62% overall yield from 7.

Vinyl lactone 2 was readily converted to iodide 3 as illustrated in eq 2. After much experimentation, it was found that the



organolithium reagent derived from 10 could be generated by reductive lithiation with 2.0 equiv of lithium naphthalene (THF, -78 °C).<sup>12</sup> Sequential addition of CuBr·Me<sub>2</sub>S, followed by 2, produced 11 as the sole acidic product after acid-base extraction. Although yields were variable, 50–75% of 11 could be isolated under the best conditions. The assignment of anti stereochemistry to 11 was based on model studies<sup>13</sup> and confirmed by ultimate conversion to hirsutene. Crude 11 was directly subjected to acid hydrolysis and reduction to produce diol 12<sup>17</sup> in 52–64% yield after purification by chromatography or distillation. Diol 12 was then converted to the diiodide 13 via the intermediate ditriflate (64%).<sup>14</sup> Treatment of 13 with 1 equiv of lithium trimethylsilylacetylide (THF, 0 °C),<sup>15</sup> followed by desilylation, produced the cyclization precursor 3<sup>17</sup> in 78% yield. As expected, the neopentyl iodide was unaffected.

The stage was now set for the key cyclization reaction. In the event, treatment of 3 with tri-*n*-butyltin hydride (C<sub>6</sub>H<sub>6</sub>, 0.02 M, catalytic AIBN, reflux 1 h) provided a single major non-tin-containing product in ~80% yield as evidenced by GC and <sup>1</sup>H NMR. Purification by medium-pressure liquid chromatography on silica gel with 100% hexanes provided hirsutene in 53% yield. Our synthetic sample was identical in all respects with a sample kindly provided by Professor P. Magnus. Ozonolysis of 1 also gave the well-known norketone.<sup>16</sup>

This short synthesis of hirsutene from the readily available vinyl lactone 2 demonstrates the potential of the tandem hexenyl radical cyclization approach to linear condensed cyclopentanoids. A series of model studies that confirm the generality of the tandem radical cyclization will be reported in a forthcoming paper<sup>13</sup> and extension to the synthesis of more complex hirsutanoids and related capnellenes is under active investigation.

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**Supplementary Material Available:** Spectra and analytical data for 2, 3, 9, 12, and 13 (2 pages). Ordering information is given on any current masthead page.

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(17) Spectra and analytical data for new compounds are included in the supplementary material.

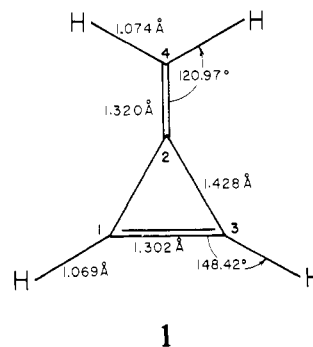
## Ab Initio Study of the Infrared Spectrum of Methylenecyclopropene

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Methylenecyclopropene (**1**) has recently been synthesized by Billups<sup>1</sup> and Staley<sup>2</sup> independently and found to be a highly reactive molecule that can only be observed at low temperature. Its synthesis was confirmed primarily by NMR and IR spectroscopy. Because of the unusual nature of **1** we have undertaken



an ab initio study of its IR spectrum for comparison with the experimental spectrum reported by Billups.<sup>1</sup> It has been shown that such studies can be useful both in confirming the structures<sup>3-7</sup> of unstable species and in making assignments of their IR bands.<sup>8</sup>

Pople's 6-31G\* basis set, which has been found to give reliable predictions of the IR spectra of cyclobutadiene<sup>6</sup> and ethylene oxide,<sup>8</sup> was used to give the fully optimized structure **1** of methylenecyclopropene with an energy of -153.669 777 au and a dipole moment of 2.3384 D. The structure was optimized with the assumption of C<sub>s</sub> geometry with atoms 2 and 4 in the single reflection plane. The fact that the force constant matrix of this structure has only positive eigenvalues shows the structure is still optimum if the symmetry assumption is removed.<sup>12</sup> The best previous calculation of **1** was by Johnson and Schmidt<sup>11</sup> who used an MC-SCF wave function. Their single-point calculation was done at the optimized MNDO geometry, and they obtained an energy of -153.605 53 au and a dipole moment of 1.33 D. While this latter value is considerably lower than ours, as they noted the actual MC-SCF dipole moment might be somewhat different since their calculation was not done at the optimized MC-SCF geometry.

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