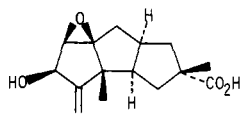
Intramolecular Diyl Trapping. Total Synthesis of *dl*-Hirsutene

R. Daniel Little*[1] and George W. Muller

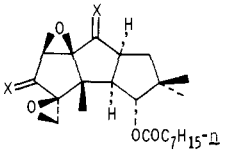
Contribution from the Department of Chemistry, University of California, Santa Barbara, California 93106. *Received October 10, 1980*

Abstract: A total synthesis of the mold metabolite *dl*-hirsutene (**4**) has been achieved. The key step of the sequence utilizes a regiospecific and highly stereoselective intramolecular diyl trapping reaction to construct the requisite linearly fused tricyclopentanoid ring system (see **12** → **18**).

The subject of many recent publications, the *cis,anti,cis*-tricyclo[6.3.0.0^{2,6}]undecane, or linearly fused tricyclopentanoid ring system, continues to attract attention. This is not surprising in view of the fact that several members of this class of sesquiterpenes, namely, hirsutic acid (**1**), coriolin B (**2**), and diketocoriolin B (**3**),



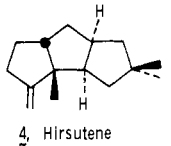
1, Hirsutic Acid



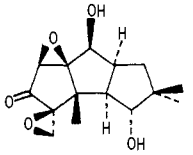
2, X = β-OH, α-H, Coriolin B
3, X = O, Diketocoriolin B

possess antibiotic and/or antitumor activity.[2]

Isolated as a mold metabolite from *Coriolus consors*, hirsutene (**4**) is thought to be the biogenetic precursor of hirsutic acid (**1**)



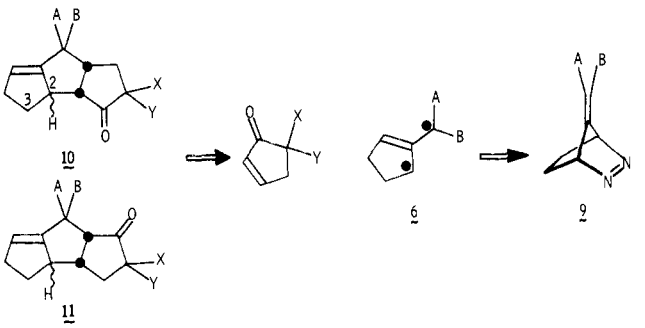
4, Hirsutene



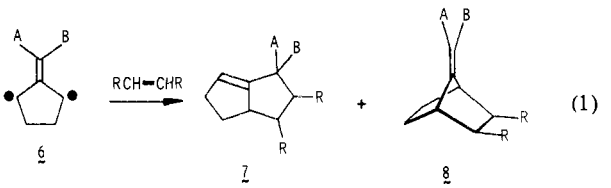
5, Coriolin

and coriolin (**5**).[3] A variety of different synthetic approaches directed toward the total synthesis of *dl*-hirsutene (**4**) have appeared. The first was reported by Nozoe and co-workers in 1976, and, like many of the routes which have been utilized to obtain the linearly fused tricyclopentanoid skeleton, their route was based upon the idea of annulating the third five-membered ring onto a preformed bicyclo[3.3.0]octane skeleton.[3] Two other syntheses, both devised to follow suspected biosynthetic pathways, appeared in 1976 and 1978.[4,5] Within the past year, three new syntheses have been completed, namely, the photocycloaddition–skeletal rearrangement pathway of Tatsuda,[6] the ketene cycloaddition–ring expansion route of Greene,[7] and most recently, the route of Kutchan and Wilson which was based upon the addition of an α-ketocarbene to a conjugated diene followed by a vinylcyclopropane to cyclopentene rearrangement.[8]

Scheme I. Intermolecular Diyl Trapping Route to Linearly Fused Tricyclopentanoids



Strategy. From the outset, it was our objective to develop an unusual, yet general, stereo- and regiospecific synthetic route to the linearly fused tricyclopentanoid skeleton founded upon the presumption that cyclopenta-1,3-diyls related to trimethylenemethane (e.g., **6**) might be useful synthetic intermediates. This presumption was based primarily upon the elegant mechanistic studies of Berson who demonstrated, inter alia, that, under the appropriate conditions, the diyls can be efficiently trapped by olefins bearing electron-withdrawing groups (the diylophile) to preferentially afford fused rather than bridged cycloadducts[9] (eq 1).



(1)

With these factors in mind, our initial strategy focused upon the use of cyclopentenone or a C_5 disubstituted cyclopentenone as the diylophile. Barring insurmountable difficulties, the plan

(1) Fellow of the Alfred P. Sloan Foundation, 1980–1982.

(2) Hirsutic acid: Comer, F. W.; McCapra, F.; Qureshi, I. H.; Scott, A. I. *Tetrahedron* **1967**, *23*, 4761. Trost, B. M.; Shuey, C. D.; Dininno, F. *J. Am. Chem. Soc.* **1979**, *101*, 1284. Hashimoto, H.; Tsuzuki, K.; Sakan, F.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1974**, 3745. Lansbury, P. T.; Wang, N. Y.; Rhodes, J. E. *Ibid.* **1972**, 2053. Hayano, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Ibid.* **1978**, 1991. Coriolin, coriolin B, diketocoriolin B: Takahashi, S.; Naganawa, H.; Iinuma, H.; Takita, T.; Maeda, K.; Umezawa, H. *Tetrahedron Lett.* **1971**, 1955–1958. Tanaba, M.; Suzuki, K.; Jankowski, W. C. *Ibid.* **1974**, 2271. Takeuchi, T.; Takahashi, S.; Iinuma, H.; Umezawa, H. *J. Antibiot.* **1971**, 24, 631. Nakamura, N.; Takita, T.; Umezawa, H.; Kunishima, M.; Nakayama, Y.; Iitaka, Y. I. *Ibid.* **1974**, *27*, 301. Kunimoto, T.; Umezawa, H. *Biochim. Biophys. Acta* **1973**, *318*, 78. Nishimura, Y.; Koyama, Y.; Umezawa, S.; Takeuchi, T.; Ishizuka, M.; Umezawa, H. *J. Antibiot.* **1977**, *30*, 59. Shibasaki, M.; Iseki, K.; Ikegami, S. *Tetrahedron Lett.* **1980**, 3587–3590. Danishefsky, S.; Zamboni, R. *Ibid.* **1980**, 3439–3442. Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Antibiot.* **1980**, *23*, 100. Danishefsky, S.; Zamboni, R.; Kahn M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097–2098. Hirsutene: Note ref 3–8 below. Capnellene: Kaisin, M.; Sheikh, Y. M.; Durham, L. J.; Djerassi, C.; Tursch, B.; Daloze, D.; Braekman, J. C.; Losman, D.; Karlsson, R. *Tetrahedron Lett.* **1974**, 2239. Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C.; Kaisin, M. *Ibid.* **1978**, 1671. Karlsson, R. *Acta Crystallogr., Sect. B* **1977**, *B33*, 1143. Norhirsutene: Lansbury, P. T.; Nazarenko, N. *Tetrahedron Lett.* **1971**, 1833.

(3) Nozoe, S.; Furukawa, J.; Sankawa, U.; Shibata, S. *Tetrahedron Lett.* **1976**, 195–198.

(4) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2795–2798.

(5) Hayano, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1978**, 1991–1994.

(6) Tatsuta K.; Akimoto, K.; Kinoshita, M. *J. Am. Chem. Soc.* **1979**, *101*, 6116–6118.

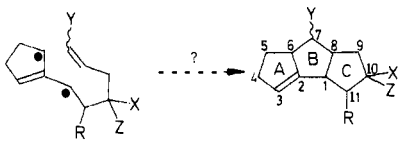
(7) Greene, A. E. *Tetrahedron Lett.* **1980**, 3059–3060.

(8) Hudlicky, T.; Kutchan, T.; Wilson, S. R.; Mao, D. T. "Abstracts of Papers", Second Chemical Congress of the North American Continent, Las Vegas, Nevada, Aug 1980; American Chemical Society: Washington, D.C., 1980; No. 246; *J. Am. Chem. Soc.* **1980**, *102*, 6351.

(9) Berson, J. A. *Acc. Chem. Res.* **1978**, *11*, 446–453 and references therein.

0002-7863/81/1503-2744$01.25/0

Scheme II. Intramolecular Diyl Trapping



was to convert the initially formed tricyclopentanoid into the desired natural product, in this case, hirsutene (**4**).

However, even at the outset, several potential difficulties can be envisaged. The first problem is regiochemical in nature and is concerned with the relationship between the B-ring substituent(s) and the C-ring carbonyl. In regard to a synthesis of hirsutene (**4**), this matter is of little concern since the carbonyl is destined to be removed. However, in the interest of developing a route of some potential generality, and in particular, a route which is amenable to the synthesis of the coriolins, the obtention of a regiochemical mixture of products would indeed be deleterious (note Scheme I).

Another potential problem concerns the establishment of the required anti,cis, rather than syn,cis ring fusion stereochemistry. A priori, there does not appear to be any compelling reason to suggest that the desired mode of cycloaddition should occur. Perhaps, if the wrong stereochemical outcome were to prevail, one could devise a means of converting the product to one with the proper arrangement. However, this would not constitute an appealing solution to the problem.

Yet another potential difficulty concerns the mode of functionalization of the A ring, for it can be seen that the location of the A-ring π bond in the initially formed tricyclopentanoid (**10** and **11**) is not well suited for the required elaboration and, in particular, the introduction of the angular methyl group found in all of the hirsutane sesquiterpenes.

In practice, all of the aforementioned problems proved to be real.[10c] For example, when the bicyclic azo compound **9** (A = B = CH_3) was refluxed for 1.0 h in the presence of a tenfold excess of cyclopentenone, a 90%–98% yield of a *regio- and stereochemical mixture* of tricyclopentanoids **10** and **11** was isolated. While some regio- and stereoselection was observed, the results did not bode well for the use of intermolecular diyl trapping in the total synthesis of linearly fused tricyclopentanoids.

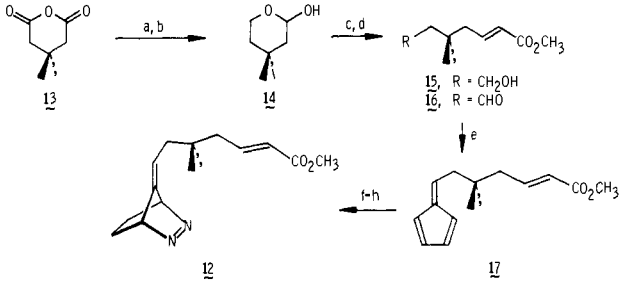
With the hope of being able to reap some of the entropic as well as regio- and stereochemical benefits which are so often associated with intramolecular processes, we decided to test the possibility of being able to construct the linearly fused tricyclopentanoid skeleton using an *intramolecular* diyl trapping reaction. It can immediately be seen from a comparison of Schemes I and II that if successful, the intramolecular route should provide a direct solution to a number of the problems which plague the intermolecular pathway. For example, the regiochemical problem of locating substituents on the B and C rings in the proper position for elaboration is solved since the relationship is fixed on the acyclic chain which contains the diylophile. Also, in contrast with the intermolecular approach, the A-ring π system ends up being located between C_2 and C_3, ideally situated for elaboration of the requisite functionality.

With these factors in mind and with *dl*-hirsutene (**4**) as the target molecule, we chose as the diyl precursor the bicyclic azo compound **12**.

Results and Discussion

Intramolecular Diyl Trapping Reactions. The basic problem in synthesizing **12** can be resolved into one involving construction of the acyclic chain in the form of the aldehyde **16** (note Scheme III). From **16**, reasonably standard methodology is utilized: specifically, fulvene formation,[11] Diels–Alder reaction, selective

Scheme III.[a] Synthesis of the Diyl Precursor 12

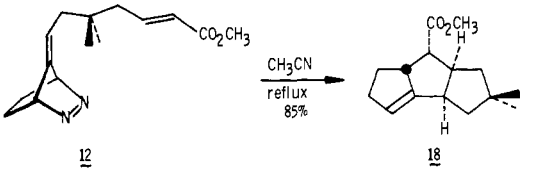


[a] Reagents: a, $NaBH_4$, THF, 0 °C, and then raise to room temperature, 74%; b, Dibah, ether, −20 °C, 76%; c, $Ph_3P{=}CHCO_2CH_3$, CH_3CN, reflux, 80%–96%; d, $C_5H_5NHCrO_3Cl$ (PCC), CH_2Cl_2, room temperature, 83%–92%; e, 2.5 equiv of cyclopentadiene, 1.5 equiv of Et_2NH, 1.0 equiv of **17**, absolute methanol, 5–10 °C, and then warm to room temperature, 91%; f, $Cl_3CCH_2O_2CN{=}NCO_2CH_2CCl_3$, ether, 0 °C; g, $KO_2CN{=}NCO_2K$, AcOH, 9–13 °C, 87%; h, e^- (−1.75 V vs. a silver/silver chloride reference electrode), DMF, 0.1 N $LiClO_4$, room temperature followed by cooling to 0 °C and the addition of 3.0 equiv of $K_3Fe(CN)_6$, 55%.

reduction of the C_5–C_6 π bond, and conversion of the dicarbamate into the azo linkage. At the outset, the latter conversion proved to be somewhat troublesome on occasion. However with the development of two new methods to accomplish the desired task (viz., $LiSCH_3$, HMPA at room temperature followed by $K_3Fe(CN)_6$ at 0 °C; and e^-, DMF, $LiClO_4$ at room temperature followed by $K_3Fe(CN)_6$ at 0 °C), this is no longer a problem.[10a,b]

We have previously described a synthesis of **12**;[10c] for completeness, it is outlined once again in Scheme III, and the details are presented in the Experimental Section. Two points, however, bear further comment. First, ring opening of lactol **14** with use of methyl (triphenylphosphoranylidene)acetate proceeds much more efficiently (ca. 90% vs. 40%) when the reaction is conducted in refluxing acetonitrile rather than in benzene as previously reported. Second, selective hydrogenation of the C_5–C_6 π bond of the Diels–Alder adduct of fulvene **17** and bis(2,2,2-trichloroethyl) azadicarboxylate is more effectively accomplished with the use of diimide at 0–15 °C than by using an atmospheric pressure hydrogenation over 10% Pd/C as reported previously. In general, there usually exists a rate preference for hydrogenation at C_5–C_6 rather than at C_7–C_8. However, when C_8 is tri- rather than tetrasubstituted, the rate difference becomes sufficiently small so that it is difficult to achieve the desired selectivity; in cases such as these, the use of diimide is preferred.

The Trapping Reaction. So that the viability of using an intramolecular diyl trapping route to synthesize linearly fused tricyclopentanoids could be tested, azo compound **12** was refluxed in acetonitrile for 6 h. A highly stereoselective reaction ensued; after removal of the solvent and chromatographic purification, tricyclopentanoid **18** was isolated in 85% yield (eq 2). In this



(2)

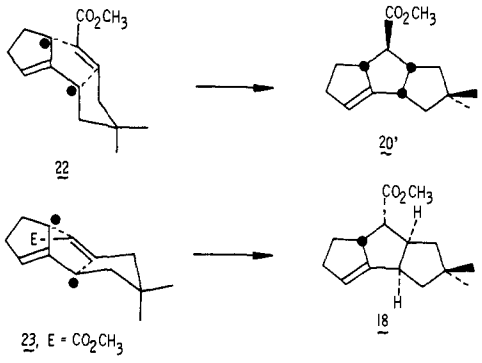
reaction, two new carbon–carbon bonds and two of the required three five-membered rings have been formed in a process which has served to generate four asymmetric centers in the proper relative stereochemical relationship required for elaboration to the naturally occurring systems. Indeed, from the practical viewpoint, the intramolecular diyl trapping reaction is decidedly superior to its intermolecular counterpart.

The ring-fusion stereochemical assignment was initially grounded upon the presumption that cis- rather than trans-ring

(10) (a) Little, R. D.; Venegas, M. G. *J. Org. Chem.* **1978**, *43*, 2921–2923. (b) Little, R. D.; Carroll, G. C. *Ibid.* **1979**, *44*, 4720–4722. (c) Little, R. D.; Bukhari, A.; Venegas, M. G. *Tetrahedron Lett.* **1979**, 305–308. (d) Venegas, M. G.; Little, R. D. *Ibid.* **1979**, 309–312. (e) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1979**, *101*, 7129–7130.

(11) (a) Freiesleben, W. *Angew. Chem.* **1963**, *75*, 576. (b) Büchi, G.; Berthet, D.; Decorzant, R.; Grieder, A.; Hauser, A. *J. Org. Chem.* **1976**, *41*, 3208.

Scheme IV



fusion ought to prevail, and upon ^1H NMR. The validity of the assignment has been substantiated through the conversion of **18** into *dl*-hirsutene (**4**) as described below. The ^1H NMR argument was based upon the appearance of a clean doublet at δ 2.58 corresponding to the methine hydrogen α to the ester group located at C_7. If it is assumed that the more stable cis-fused products form in the trapping reaction, then compounds **19–21** are the only

18, R = α-CO_2CH_3 **20**, R = α-CO_2CH_3
19, R = β-CO_2CH_3 **21**, R = β-CO_2CH_3

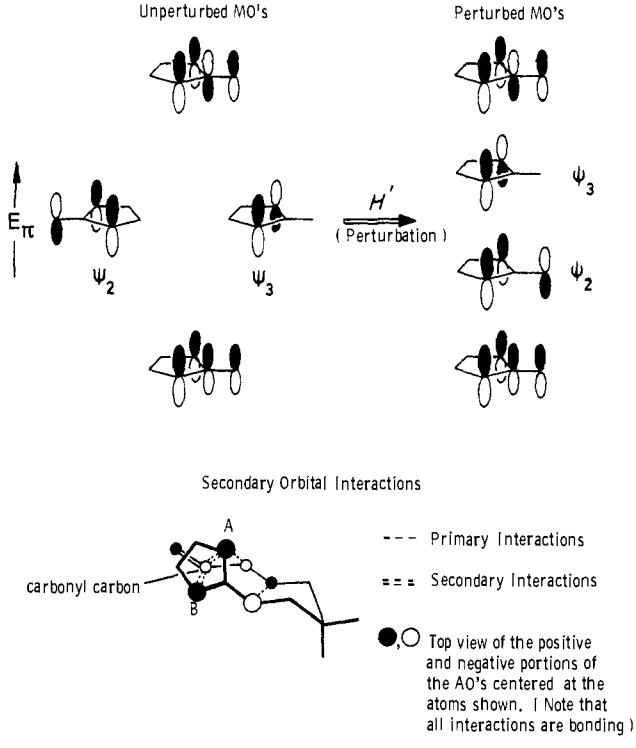
stereoisomers which could result. Of these, molecular models reveal that the dihedral angle between the hydrogen atoms located at C_7 and C_8 in **18** is 90°. Therefore, one would expect $J_{78} \approx 0$ and that H_7 should appear as a doublet, as observed. In each of the other compounds, more complex patterns would be anticipated.

Stereoselectivity. The stereoselectivity of the diyl trapping reaction can be rationalized with use of conformational and secondary orbital overlap arguments. First, if one assumes that the acyclic chain will preferentially adopt a pseudochair conformation, then the conformers **22** and **23**, illustrated in Scheme IV, are possible. Notice that a stereoretaining concerted trapping reaction involving **22** would lead to the production of a syn,cis-fused tricyclopentanoid **20'**, while **23** would be expected to lead to the observed anti,cis product **18**. Notice also that in **22**, the ester is exocyclic to the diyl ring whereas in **23**, it is endocyclic. Therefore, one would expect that steric interactions ought to disfavor the formation of **18**. On the other hand, conformer **23**, but not **22**, allows for the possible existence of secondary orbital interactions to occur between the diyl ring carbons and the ester carbonyl carbon atom.

So that the nature of the secondary orbital interactions can be illustrated, consider in turn, the diyl and the diylophile π-type MO's. The diyl MO's correspond to those of a perturbed trimethylenemethane, perturbed so that the symmetric orbital, $\psi_2(S)$, of the nominally degenerate pair of nonbonding MO's is the highest occupied orbital (HOMO). As illustrated by Schoeller, a through-space interaction between ψ_2 and the π-type orbitals of the ethano bridge leads to a stabilization of ψ_2, thereby making it, rather than ψ_3, the diyl HOMO.[12] Since the diylophile is an α,β-unsaturated ester, it follows that its LUMO has the same form as that of the LUMO of butadiene.

Scheme V illustrates the perturbation as well as a HOMO–LUMO diagram which portrays the *bonding* secondary orbital interactions which can take place between the ester carbonyl carbon and the diyl ring carbons A and B, when the pseudochair conformer **23** is utilized. To the extent that the secondary interactions lower the transition state energy of the path leading to **18**, one would predict its preferential formation.

Scheme V. Perturbation and Secondary Orbital Interactions



Finally, before closing this section, it is worthwhile to note that while the stereoselectivity rationale presented above is appealing, one obviously needs more evidence to substantiate the existence and determine the magnitude of the secondary interactions. Experiments are presently in progress, and the results will be reported at a later date.

Synthesis of *dl*-Hirsutene (4). With an efficient and selective means of tricyclopentanoid synthesis in hand, our objective turned toward the conversion of **18** into *dl*-hirsutene (**4**). It is obvious that the task requires the removal of the ester located at C_7 and elaboration of the A-ring π bond.

Treatment of **18** with diisobutylaluminum hydride (Dibah) under a variety of conditions invariably led to the production of mixtures of alcohol **24** and the desired aldehyde **25**. So that this problem could be circumvented, the ester was reduced directly to alcohol **24**, which was then oxidized to aldehyde **25** with the use of pyridinium chlorochromate (PCC) in dichloromethane.

Attempts to decarbonylate **25** with the use of Wilkinson's catalyst in refluxing 1,2-dichloroethane met with mixed success. A particularly annoying feature of the transformation was the fact that an olefin, isomeric with the desired product **26**, was also formed. Furthermore, for some unknown reason, the relative amounts of **26** and **26a** varied from run to run. It was reasoned that the C_{23} π bond was perhaps participating in the transformation and that it would be best to partially elaborate the A ring before removing the functionality at C_7.[13]

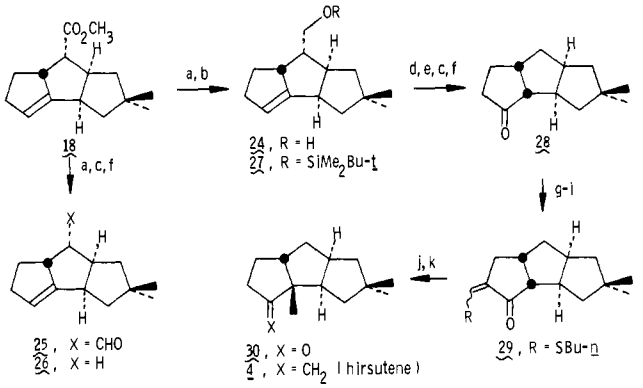
To this end, alcohol **24** was protected as the dimethyl *tert*-butyl silyl ether **27** and the $\Delta^{2,3}$ π bond was then elaborated with use of borane in THF followed by oxidation with PCC. While it is usually assumed that reactions occurring at the bridgehead of a linearly fused tricyclopentanoid proceed to afford the more stable cis- rather than trans-ring fusion,[14] the presence of the bulky silyl

(12) (a) Schoeller, W. W. *J. Chem. Soc., Perkin Trans. 2* **1979**, 366. (b) Siemionko, R.; Shaw, A.; O'Connell, G.; Little, R. D.; Carpenter, B. K.; Shen, L.; Berson, J. A. *Tetrahedron Lett.* **1978**, 3529–3532. (c) Siemionko, R.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 3870–3882.

(13) For examples and a mechanistic study of some of the complications which can arise upon the attempted decarbonylation of 4-pentenals, see: Campbell, R. E., Jr.; Lochow, C. F.; Vora, K. P.; Miller, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 5824–5830.

(14) For examples, see: Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097–2098. Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Antibiot.* **1980**, *33*, 100–102. Chang, S.; McNally, D.; Shary-Tehrany, S.; Hickey, M. J.; Boyd, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 3109–3118.

Scheme VI.[a] Total Synthesis of *dl*-Hirsutene (4)



[a] Reagents: a, $LiAlH_4$, Et_2O, room temperature, 0.5 h, quantitative; b, 1.2 equiv of *t*-$BuMe_2SiCl$, 2.5 equiv imidazole, DMF, room temperature, 67 h, 95%; c, 1.5~2 equiv of $C_5H_5NHCrO_3Cl$ (PCC), CH_2Cl_2, room temperature, 2 h, 67%–84%; d, 1.5 mol equiv of BH_3·THF, 0 °C–room temperature, 3.5 h, and then 9 equiv of PCC/Celite, CH_2Cl_2, room temperature, 54%–57%; e, 2.5 equiv of *n*-Bu_4NF, THF, room temperature, 1 h, 89%–93%; f, 1.2 equiv of $(Ph_3P)_3RhCl$, $ClCH_2CH_2Cl$, reflux, 54 h, 76%–91%; g, 2.5 equiv $NaOCH_3$, 2.0 equiv of EtOCHO, PhH, 0 °C–room temperature, 20 h, 96%; h, 1.5 equiv of *n*-BuSH, *p*-TsOH (cat), 5.5 equiv of $MgSO_4$, PhH, reflux, 20 h, 82%; i, 4 equiv of KO-*t*-Bu, *t*-BuOH, 20 equiv of CH_3I, 0 °C to reflux, 0.5 h, 62%; j, 25% KOH (aqueous), $HOCH_2CH_2OH$, reflux, 24 h, 51%; k, $Ph_3P{=}CH_2$, Me_2SO.

ether assures that the hydroboration will occur on the side away from it and guarantees that cis-ring fusion will result.

Cleavage of the silyl ether under standard conditions, followed by oxidation with PCC, set the stage for another attempt at removing the aldehyde located at C_7. This time, treatment of the ketoaldehyde with 1.2 equiv of Wilkinson's catalyst in refluxing 1,2-dichloroethane proceeded quite satisfactorily to afford ketone **28** in yields ranging from 76% to 91%. Unlike the decarbonylation of **25**, no side reactions were detected.

Finally, the synthesis was completed by introducing the C_2 angular methyl group with use of a standard series of reactions which involved the use of the blocking–alkylation–deblocking sequence illustrated in Scheme VI. Spectral data for norketone **30** proved to be identical with data kindly provided to us by Professor Hudlicky. Since **30** has previously been converted to *dl*-hirsutene (**4**) with use of a Wittig reaction,[3-8] the synthesis was complete.

Summary and Comments

The intramolecular diyl trapping reaction provides an efficient and selective means of constructing the linearly fused tricyclopentanoid system. It shows considerable promise for the application of the methodology to the synthesis of more complex naturally occurring systems—in both racemic and *chiral* forms.

From an examination of the route to hirsutene (**4**) which is described above, it is clear that the number of steps involved in the sequence could be decreased markedly if the ester located at C_7 of the initially formed tricyclopentanoid did not have to be removed. What would happen, for example, if the trapping reaction was carried out with use of an unactivated diylophile, viz., a terminal π bond? Is the presence of an electron-withdrawing group on the diylophile a necessary or merely a sufficient condition for the observation of stereoselectivity in intramolecular diyl trapping reactions? These and other questions form the subject of ongoing research efforts; the results of our studies will be reported in subsequent publications.

Experimental Section

Proton magnetic resonance spectra (^1H NMR) were obtained with the use of a Varian T-60, and on occasion, an FT-80 spectrometer. A Varian CFT-20 was used to obtain ^{13}C (^{13}C NMR) spectra; both fully decoupled and off-resonance decoupled spectra were recorded. Chemical shifts are given as parts per million (ppm) downfield from tetramethylsilane (Me_4Si) in δ units and coupling constants are given in cycles per second (Hz). The data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, br s = broad singlet, etc.), number of protons, coupling constants, and assignments.

Infrared (IR) spectra were recorded on a Perkin-Elmer 283 spectrometer.

High-resolution mass spectra or exact-mass measurements were obtained from an AEI MS902 or a ZAB 2-F mass spectrometer. The observed and calculated values for the ion of the given formula are reported. Low-resolution mass spectra were obtained from a Hewlett-Packard 5992A GC/MS system. The spectra are reported by giving the parent peak first (if it appeared), followed by the fragment peaks in order of decreasing mass.

Medium-pressure liquid chromatography (MPLC) was performed on a variety of Altex columns packed with E. Merck Silica Gel 60 (230–400 mesh, ASTM). The identity of the columns used (connected in series) are reported for each experiment. The distilled solvents (mixed by volume) were passed through the system with a FMI Model RPS 4 lab pump. The eluant was continuously monitored at 280 nm by using an Altex Model 150 monitoring system or TLC (E. Merck 60F-254, 70–230 mesh, ASTM). For gravity flow chromatography, E. Merck Silica Gel 60 (73–230 mesh, ASTM) was used. Florisil refers to Fischer 100-200 mesh gel.

Reagent grade solvents were used for all reactions. Anhydrous diethyl ether (Mallinkrodt) from freshly opened cans was sufficiently dry to be used without further treatment. In addition, acetonitrile and anhydrous methanol were purchased from Mallinkrodt and were used without further purification. Solvents referred to as "dry" were distilled from calcium hydride onto activated molecular sieves (4 Å). Tetrahydrofuran (THF) was tested for peroxides (EM test strips), collected from a calcium chloride prestill after refluxing for at least 1 day, and then distilled from sodium benzophenone ketyl. Pentane was distilled through a 30-cm glass column packed with glass helices.

Diisobutylaluminum hydride (Dibah, 1.02 M in hexane) and lithium aluminum hydride (LAH) were purchased from Ventron. Pyridinium chlorochromate (PCC), 3,3-dimethylglutaric anhydride, borane–tetrahydrofuran, Wilkinson's catalyst, and tetra-*n*-butylammonium hydroxide (40% aqueous solution used in the preparation of the corresponding fluoride) were purchased from Aldrich.

Cyclopentadiene was freshly distilled prior to use. Dipotassium azodicarboxylate was prepared from the corresponding commercially available amide, according to the procedure of Berson.[15] Bis(2,2,2-trichloroethyl) azadicarboxylate was prepared according to the procedure of Venegas and Little.[16]

Brine refers to a saturated solution of sodium chloride. Removal of the solvent "in vacuo" refers to the initial use of a rotary evaporator at water aspirator pressure followed by pumping on the material at 1 mm or less to remove the last traces of solvent.

Unless otherwise indicated, all reactions were conducted under an atmosphere of nitrogen.

5-Hydroxy-3,3-dimethylpentanoic Acid Lactone. To a cold (0 °C), stirred suspension of sodium borohydride (8.00 g, 211 mmol) in 40 mL of THF was added, over 0.5 h, a solution of 3,3-dimethylglutaric anhydride (**13**, 20.0 g, 141 mmol) dissolved in 100 mL of THF. The resulting solution was allowed to warm to room temperature and was stirred for 3.5 h. The solution was then cooled to 0 °C and was quenched by the addition of 70 mL of 6 N HCl. The solution was washed with brine (5 × 100 mL) and was then extracted with ether (3 × 75 mL). The combined ether extracts were dried ($MgSO_4$), and the solvent was removed in vacuo. The resulting oil was purified by chromatography on 60 g of silica gel. Elution with 70% ether in pentane afforded 11.11 g (61%) of 5-hydroxy-3,3-dimethylpentanoic acid lactone. ^1H NMR($CDCl_3$) δ 4.35 (t, 2 H, J = 6, CH_2OH), 2.30 (s, 2 H, CH_2CO_2R), 1.70 (t, 2 H, J = 6, $HOCH_2CH_2$), 1.10 (s, 6 H, *gem*-methyls); IR(NaCl, film) 3500, 2960, 1735 (br), 1395, 1372, 1230 cm^{-1}.

2-Hydroxy-4,4-dimethyltetrahydropyran (14). To a stirred solution of 5-hydroxy-3,3-dimethylpentanoic acid lactone (25.2 g, 197 mmol) in 500 mL of ether at −20 °C was added dropwise, over 1 h, a solution of Dibah (205 mL of 1.02 M = 209 mmol) in hexane. The resulting solution was stirred for an additional 0.5 h and was then quenched by the addition of 150 mL of methanol. The solution was allowed to warm slowly to room temperature and was stirred overnight. The resulting suspension was diluted with 250 mL of a 30% aqueous solution of sodium potassium tartrate and was stirred for 0.5 h. The organic layer was separated and was washed with 30% aqueous sodium potassium tartrate

(15) Berson, J. A.; Poonian, M. S.; Libbey, W. J. *J. Am. Chem. Soc.* **1969**, *91*, 5567.

(16) Little, R. D.; Venegas, M. G. *Org. Synth.*, in press. Preprints are available upon request.

(2 × 100 mL and 1 × 50 mL). The combined aqueous layers were then extracted with ether (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The resulting liquid was purified by trap-to-trap distillation (40 °C, <5 × 10^{-3} torr) to afford 19.43 g (76%) of 2-hydroxy-4,4-dimethyltetrahydropyran (**14**). ^{1}H NMR($CDCl_3$) δ 4.96 (m, 1 H, C*H*OH), 4.8 (d, 1 H, $J \approx 4$, O*H*), 4.18–3.37 (m, 2 H, CH_2O), 1.95–1.10 (m, 4 H, $CH_2C(CH_3)_2CH_2$), 1.05 (s, 6 H, CH_3CCH_3); IR(NaCl, film) 3390, 2950, 2870, 1555, 1385, 1365, 1195, 1115, 1080, 1030, 990 cm^{-1}.

Methyl 7-Hydroxy-5,5-dimethylhept-2-enoate (15). A stirred solution of the pyran **14** (12.0 g, 92.3 mmol) and methyl (triphenylphosphoranylidene)acetate (46.2 g, 138 mmol) in 600 mL of acetonitrile was heated to reflux for 34.5 h. Most of the solvent was removed in vacuo; 100 mL of ether was then added, and the mixture was stirred for 2 h. The resulting mixture was filtered, and the filtrate was washed with 50 mL of ether. The solvent was again removed in vacuo, and 50 mL of 70% ether in pentane was added. After 0.5 h of stirring, the resulting suspension was once again filtered and the filter cake was washed with 25 mL of 70% ether in pentane. The solvent was removed in vacuo, and the resulting material was purified by chromatography in two batches on 90 and 160 g of silica gel. Elution with 70% ether in pentane afforded 16.5 g (96%) of cis and trans (1:4, respectively) unsaturated hydroxy esters. Complete separation is readily achieved after the next step. ^{1}H NMR(trans, $CDCl_3$) δ 6.97 (overlapping dt, 1 H, J = 16 and 8, β-vinyl), 5.77 (dt, 1 H, J = 16 and 1, α-vinyl), 3.71 (s, 3 H, CO_2CH_3), 3.60 (t, 2 H, J = 8, CH_2OH), 2.90 (br s, 1 H, O*H*), 2.13 (dd, 2 H, J = 8 and 1, allylic CH_2), 1.53 (t, 2 H, J = 8, CH_2CH_2OH), 0.98 (br s, 6 H, *gem*-methyls); IR(NaCl, film) 3420, 2980, 1725, 1655, 1390, 1370 cm^{-1}; exact mass m/e 186.12473 (calcd for $C_{10}H_{18}O_3$, 186.12559).

Methyl (*Z*)- and (*E*)-7-Oxo-5,5-dimethylhept-2-enoate (16). To a stirred suspension of pyridinium chlorochromate (PCC, 13.9 g, 64.5 mmol) and 13.9 g of Celite in 90 mL of dichloromethane at room temperature was added a solution of methyl 7-hydroxy-5,5-dimethylhept-2-enoate (**15**, 8.00 g, 43.0 mmol) in 16 mL of dichloromethane. The resulting suspension was stirred for 2 h and was then diluted with 500 mL of ether. The resulting suspension was filtered through a pad of florisil which was rinsed with an additional 200 mL of ether. The solvent was removed in vacuo to afford an oil which was subjected to MPLC (17 mL/min, 15 × 250 mm and 25 × 1000 mm columns connected in series) on silica gel. Elution with 20% ethyl acetate in pentane afforded 1.34 g (17%) of the (*Z*) isomer and 5.19 g (66%) of the (*E*) isomer: ^{1}H NMR($CDCl_3$) δ 9.89 (t, 1 H, J = 3, C*H*O), 7.02 (overlapping dt, 1 H, J = 16 and 8, β-vinyl), 5.75 (dt, 1 H, J = 16 and 1, α-vinyl), 3.75 (s, 3 H, CO_2CH_3), 2.34 (d, 2 H, J = 3, CH_2CHO), 2.30 (dd, 2 H, J = 8 and 1, allylic CH_2), 1.15 (s, 6 H, *gem*-methyls); IR(NaCl, film) 2980, br carbonyl from 1710–1740, 1655, 1390, 1370 cm^{-1}; exact mass m/e 184.11015 (calcd for $C_{10}H_{16}O_3$, 184.10944).

6-[(*E*)-5-(Carbomethoxy)-2,2-dimethyl-4-pentenyl]fulvene (17). To a stirred solution of methyl (*E*)-7-oxo-5,5-dimethylhept-2-enoate (**16**, 5.19 g, 28.2 mmol) and freshly distilled cyclopentadiene (5.8 mL, 4.65 g, 70.5 mmol) in 50 mL of anhydrous methanol cooled in a 5–10 °C ice bath was added dropwise a solution of diethylamine (2.4 mL, 1.69 g, 23.1 mmol) in 40 mL of anhydrous methanol. The resulting solution was allowed to warm to room temperature where it was stirred for 2 h prior to cooling it to 0 °C and adding dropwise 3.4 mL of glacial acetic acid. Most of the solvent was removed in vacuo, and the resulting solution was extracted with 50 mL of ether and was washed with saturated aqueous sodium bicarbonate (2 × 25 mL) and brine (2 × 25 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo. The resulting oil was purified by chromatography on 120 g of neutral alumina (activity II). Elution with 7% ether/pentane afforded 5.96 g (91%) of 6-[(*E*)-5-(carbomethoxy)-2,2-dimethyl-4-pentenyl]fulvene (**17**) (it should be noted that reextraction of the aqueous layer affords another 1%–2% of the fulvene): ^{1}H NMR($CDCl_3$) δ 7.05 (overlapping dt, 1 H, J = 16 and 8, C*H*=$CHCO_2CH_3$), 6.70–6.10 (m, 5 H, fulvene ring H's), 5.78 (dt, 1 H, J = 16 and 1, CH=C*H*CO_2CH_3), 3.75 (s, 3 H, CO_2CH_3), 2.45 (d, 2 H, J = 8, C_6HCH_2), 2.17 (dd, 2 H, J = 8 and 1, $C(CH_3)_2CH_2$), 1.02 (br s, 6 H, *gem*-methyls); IR(NaCl, film) 2690, 1725, 1655, 1650, 1385, 1370 cm^{-1}; exact mass m/e 232.1475 (calcd for $C_{15}H_{20}O_2$, 232.1463).

***N,N'*-[Bis((2,2,2-trichloroethoxy)carbonyl)]-7-(*trans*-6-(carbomethoxy)-3,3-dimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]heptane.** To a stirred solution of 6-[(*E*)-5-(carbomethoxy)-2,2-dimethyl-4-pentenyl]-fulvene (**17**, 5.937 g, 25.59 mmol) in 7 mL of ether at 0 °C was added dropwise, over 15–30 min, a solution of bis(2,2,2-trichloroethyl) azodicarboxylate (9.699 g, 25.59 mmol) in 75 mL of ether. The resulting solution was stirred an additional 0.75 h and was then concentrated in vacuo to afford a quantitative yield of the desired Diels–Alder adduct which was used without purification in the next step of the sequence: ^{1}H NMR($CDCl_3$) δ 6.97 (overlapping dt, 1 H, J = 16 and 8, β-vinyl), 5.82 (dt, 1 H, J = 16 and 1, α-vinyl), 5.52 and 5.33 (br s, 2 H, bridgeheads), 6.87 (t, 2 H, J = 2, C_{56}), 5.33 (t, 1 H, J = 8, C_7=C*H*CH_2R), 4.85 (s, 4 H, $CO_2CH_2CCl_3$), 3.75 (s, 3 H, CO_2CH_3), 2.05 (d, 2 H, J = 8, CH_2CH=$CHCO_2CH_3$), 1.92 (d, 2 H, J = 8, $RC_8HCH_2CMe_2R$), 0.54 (s, 6 H, *gem*-methyls); IR(NaCl, film) 2960, 2930, broad carbonyl centered at 1735, 1660, 1440, 1385, 1300, 1290, 1120, 1060, 990 cm^{-1}.

To a stirred suspension of dipotassium azodicarboxylate (24.56 g, 127.9 mmol) and the Diels–Alder adduct (15.63 g, 25.58 mmol) in 100 mL of dry dichloromethane in an ice bath cooled to 9–13 °C was added dropwise, over 25 min, a solution of acetic acid (16 mL, 289 mmol) in 27 mL of dry dichloromethane. The mixture was stirred for an additional 1 h. The resulting suspension was filtered, and the filter cake was rinsed with 150 mL of ether. The solvent was removed in vacuo. ^{1}H NMR analysis indicated that approximately 60% of the Diels–Alder adduct was not hydrogenated; therefore, the reaction was continued. To a stirred suspension of the partially hydrogenated adduct and dipotassium azodicarboxylate (14.74 g, 76.74 mmol) in 60 mL of dry dichloromethane cooled in an ice bath to 9–13 °C was added dropwise, over 20 min, a solution of acetic acid (9.6 mL, 170 mmol) in 16 mL of dry dichloromethane. After 1 h of stirring, the resulting suspension was filtered and washed with 100 mL of ether. The solvent was removed in vacuo, and the resulting thick oil was purified by MPLC (silica gel, 16 mL/min, 15 × 250 and 25 × 1000 mm columns connected in series) in three portions. Elution with 40% ether in pentane afforded 13.62 g (87%) of the desired hydrogenated adduct: ^{1}H NMR($CDCl_3$) δ 6.93 (overlapping dt, 1 H, J = 16 and 8, β-vinyl), 5.80 (dt, 1 H, J = 8 and 1, α-vinyl), 5.45 (t, 1 H, J = 8, RC_7H=C*H*CH_2R), 5.08–4.48 (m, 6 H, $CO_2CH_2CCl_3$ and bridgeheads), 3.73 (s, 3 H, CO_2CH_3), 2.32–1.75 (m, 8 H, allylic CH_2's and CH_2CH_2), 0.92 (s, 6 H, *gem*-methyls); IR(NaCl, film) 2945, 2925, 2865, 1715, 1430, 1380, 1360, 1270, 1195, 1140, 1100 cm^{-1}; exact mass m/e 611.9878 (calcd for $C_{21}H_{26}O_6Cl_6N_2$, 611.99216).

7-(*trans*-6-(Carbomethoxy)-3,3-dimethylhex-5-enylidene)-2,3-diazabicyclo[2.2.1]hept-2-ene (12). *N,N'*-[bis(2,2,2-trichloroethoxy)-carbonyl)]-2,3-diaza-7-(*trans*-6-(carbomethoxy)-3,3-dimethylhex-5-enylidene)bicyclo[2.2.1]heptane (1.286 g, 2.09 mmol) was treated according to the method of Little and Carroll[10b] at a potential of −1.76 V (vs. Ag/AgCl) to afford an oil which was purified by chromatography on 80 g of silica gel. Elution with 30–100% ether in pentane afforded 300 mg (55%) of the azo compound **12**: ^{1}H NMR($CDCl_3$) δ 7.01 (dt, 1 H, J = 16 and 8, β-vinyl), 5.87 (dt, 1 H, J = 16 and 1, α-vinyl), 5.40 (br s, 1 H, bridgehead), 5.20 (t, 1 H, J = 8, C_7=C*H*R), 5.17 (br s, 1 H), bridgehead), 3.78 (s, 3 H, CO_2CH_3), 2.13 (2 H, γ to the ester), 1.90 (d, 2 H, J = 8, $HC_8CH_2CMe_2R$), 1.2 (m, 4 H, ethano bridge), 0.92 (s, 6 H, *gem*-methyls).

Methyl (3aα,6aβ,7α,7aα)-2,3,3a,5,6,6a,7,7a-Octahydro-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene-7-carboxylate (18). A stirred solution of azo compound **12** (300 mg, 1.14 mmol) in 500 mL of acetonitrile was refluxed for 6 h. The solvent was removed in vacuo to afford 260 mg of an oil which was purified by MPLC (16 mL/min, 15 × 250 mm and 25 × 1000 mm columns connected in series) on silica gel. Elution with 6% ether in pentane afforded 214 mg (85%) of tricyclopentanoids as a 9:1 mixture of two isomers. Complete separation of the isomers was accomplished by further chromatography under the same conditions. For tricyclopentanoid **18**: ^{1}H NMR($CDCl_3$) δ 5.2 (overlapping dt, 1 H, J = 2 and 3, vinyl), 3.61 (s, 3 H, CO_2CH_3), 2.58 (d, 1 H, J = 8, $CHCO_2CH_3$), 1.03 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3); IR(NaCl, film) 3050, 2950, 1735, 1370, 1160 cm^{-1}; ^{13}C NMR($CDCl_3$) 26.7, 25.9 and 28.2 (*gem*-methyls), 37.0, 39.9, 40.9 (CMe_2), 47.3, 47.6, 50.5, 50.7, 51.4 (CO_2CH_3), 51.6, 117.5 (CH_2CH=C), 154.5 (CH=CR_2), 175.1 (CO_2-CH_3); exact mass m/e 234.15891 (calcd for $C_{15}H_{22}O_2$, 234.16197).

(3aα,6aβ,7α,7aα)-2,3,3a,5,6,6a,7,7a-Octahydro-7-(hydroxymethyl)-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalene (24). To a stirred suspension of lithium aluminum hydride (48.0 mg, 1.27 mmol) in 4 mL of ether at room temperature was added dropwise, over 15 min, a solution of tricyclopentanoid **18** (281 mg, 1.20 mmol) in 3 mL of ether. After 45 min of stirring, the resulting suspension was cooled to 0 °C and was quenched by the dropwise addition of 6 mL of 5% HCl. The organic layer was separated, and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic solutions were dried ($MgSO_4$), and the solvent was removed in vacuo to afford a quantitative yield of the desired alcohol **24**: ^{1}H NMR($CDCl_3$) δ 5.20 (m, 1 H, vinyl), 3.80–1.05 (m, 12 H), 2.1 (s, 1 H, O*H*), 1.00 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3); IR(NaCl, film) 3330, 2940, 2840, 1730, 1460, 1380, 1365 cm^{-1}; exact mass m/e 206.1643 (calcd for $C_{14}H_{22}O$, 206.1671).

(3aα,6aβ,7α,7aα)-2,3,3a,5,6,6a,7,7a-Octahydro-2,2-dimethyl-7-((*tert*-butyldimethylsiloxy)methyl)-1*H*-cyclopenta[*a*]pentalene (27). To a stirred solution of *tert*-butyldimethylsilyl chloride (223 mg, 1.48 mmol) and tricyclopentanoid **24** (252 mg, 1.23 mmol) in 2 mL of DMF at room temperature was added, in one portion as a solid, imidazole (209 mg, 3.07 mmol). The reaction mixture was stirred at room temperature for 67 h.

Addition of 15 mL of brine, extraction with ether (3 × 10 mL), drying ($MgSO_4$), and concentration in vacuo afforded an oil which was chromatographed on 10 g of silica gel. Elution with 20% ether in pentane afforded 39.2 mg (15.5%) of the starting alcohol **24** and 320.2 mg (81.2%) of the desired protected alcohol: ^1H NMR($CDCl_3$) δ 5.07 (m, 1 H, vinyl), 3.72–1.06 (m 14 H), 0.99 and 0.86 (two s, 15 H, *t*-butyl and *gem*-methyls), –0.01 (s, 6 H, $SiMe_2$); IR(NaCl, film) 2950, 2920, 2850, 1465, 1385, 1365, 1255, 1095, 835 cm^{-1}.

(3aα,3bβ,6aβ,7α,7aα)-Decahydro-2,2-dimethyl-7-((*tert*-butyldimethylsiloxy)methyl)-1*H*-cyclopenta[*a*]pentalen-4-one. To a stirred solution of the silylated alcohol **27** (440 mg, 1.37 mmol) in 5.5 mL of THF at 0 °C was added, over 3 min, 2.2 mL of 0.94 M borane–THF. The ice bath was removed and the solution was allowed to warm to and stir at room temperature for 3.5 h. The solvent was removed in vacuo to afford an oil. The oil was dissolved in 15 mL of dichloromethane and was added to a stirred suspension of PCC (2.67 g, 12.4 mmol) and 2.67 g of Celite in 16 mL of dichloromethane at room temperature. After 2 h of stirring, the reaction mixture was diluted with 75 mL of ether and was filtered through a pad of florisil (Fischer). An additional 100 mL of ether was used to rinse the florisil. The solvent was removed in vacuo to afford an oil which was chromatographed on 40 g of silica gel. Elution with 18% ether in pentane afforded 263 mg (57%) of the desired ketone: ^1H NMR($CDCl_3$) δ 3.54 (d, 2 H, J = 7, CH_2O), 3.42–0.72 (m, 13 H), 0.99 and 0.86 (two s, 15 H, *gem*-methyls and *t*-butyl), –0.01 (s, 6 H, $Si(CH_3)_2$); IR(NaCl, film) 2930, 2900, 2860, 1735, 1460, 1410, 1385, 1365, 1250, 1100, 1005, 835, 810, 770 cm^{-1}.

(3aα,3bβ,6aβ,7α,7aα)-Decahydro-2,2-dimethyl-7-(hydroxymethyl)-1*H*-cyclopenta[*a*]pentalen-4-one. To a stirred solution of tetra-*n*-butylammonium fluoride[17] (354 mg, 1.35 mmol) in 2 mL of THF at 0 °C was added, over 2 min, a solution of (3aα,3bβ,6aβ,7α,7aα)-decahydro-2,2-dimethyl-7-((*tert*-butyldimethylsiloxy)methyl)-1*H*-cyclopenta[*a*]pentalen-4-one (182 mg, 0.542 mmol) in 3 mL of THF. The reaction mixture was allowed to warm to room temperature and was stirred for 1 h. To the resulting solution was added 20 mL of brine; the solution was then extracted with ether (3 × 10 mL). The combined ether extracts were washed with brine (3 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo to yield an oil which was chromatographed on 10 g of silica gel. Elution with ether afforded 112 mg (93%) of the desired product: ^1H NMR($CDCl_3$) δ 3.65 (d, 2 H, J = 6, CH_2O), 3.33–0.83 (m, 14 H), 1.07 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3); IR(NaCl, film) 3430, 2950, 2930, 2870, 1740, 1465, 1385, 1365, 1030 cm^{-1}.

(3aα,3bβ,6aβ,7α,7aα)-Decahydro-7-formyl-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalen-4-one. To a stirred suspension of PCC (290 mg, 1.34 mmol) and 290 mg of Celite in 2 mL of dichloromethane at room temperature was added a solution of (3aα,3bβ,6aβ,7α,7aα)-decahydro-2,2-dimethyl-7-(hydroxymethyl)-1*H*-cyclopenta[*a*]pentalen-4-one (149 mg, 0.672 mmol) in 3 mL of dichloromethane. The resulting mixture was stirred for 2 h and was then diluted with 15 mL of ether. The mixture was filtered through a pad of florisil which was rinsed with an additional 75 mL of ether. The solvent was removed in vacuo to afford an oil which was purified by chromatography on 9 g of silica gel. Elution with ether afforded 124 mg (84%) of the desired ketoaldehyde: ^1H NMR($CDCl_3$) δ 9.61 (d, 1 H, J = 1, CHO), 3.55–0.75 (m, 13 H), 1.10 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3); IR(NaCl, film) 2940, 2860, 2710, 1740, 1720, 1460, 1410, 1385, 1365, 1165 cm^{-1}.

(3aα,3bβ,6aβ,7aα)-Decahydro-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalen-4-one (28). A solution of tris(triphenylphosphine)rhodium(I) chloride (625 mg, 0.675 mmol) and (3aα,3bβ,6aβ,7α,7aα)-decahydro-7-formyl-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalen-4-one (124 mg, 0.563 mmol) in 16.6 mL of dry 1,2-dichloroethane was degassed via two freeze–pump–thaw cycles under argon. The resulting solution was refluxed for 40.5 h under an argon atmosphere. The solvent was removed in vacuo, 15 mL of ether was added, the resulting mixture was filtered, and the filter cake was washed with a small amount of ether. The solvent was removed in vacuo; the same procedure was repeated using 30% ether in pentane. After removal of the solvent in vacuo, the mixture was purified by chromatography on 10 g of silica gel. Elution with 30% ether in pentane afforded 99.3 mg (92%) of the desired decarbonylated ketone **28**: ^1H NMR($CDCl_3$) δ 3.33–0.82 (m, 14 H), 1.05 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3); IR(KBr disk) 2930, 1730, 1460, 1385, 1365 cm^{-1}; exact mass *m/e* 193.1563 (calcd for $C_{13}H_{20}O$, 193.1548).

(3aα,3bβ,6aβ,7aα)-Decahydro-5-formyl-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalen-4-one. To a stirred suspension of sodium methoxide (Mallinkrodt, 110 mg, 1.66 mmol) in 1 mL of benzene at room temperature was added a solution of ketone **28** (127.8 mg, 0.666 mmol) in 3.5 mL of dry benzene. The reaction mixture was stirred for 5 min and was then cooled to 0 °C by use of an ice bath. To the cold solution was added a neat solution of ethyl formate (0.11 mL, 98.6 mg, 1.33 mmol). The resulting mixture was allowed to warm to room temperature and stir overnight. The suspension was diluted with 25 mL of ether and washed with water (1 × 10 mL) and 2 M NaOH (2 × 6 mL). The combined aqueous extracts were acidified to pH 1 with 3 N HCl and were then extracted with ether (3 × 10 mL). The ether extracts were dried ($MgSO_4$), and the solvent was removed in vacuo to afford 141 mg (97%) of the desired product which was used in the next step without further purification: ^1H NMR($CDCl_3$) δ 11.17 (br s, 1 H, CHO*H*), 9.73 (br d, 1 H, C*H*O), 7.20 (m, 1 H, vinyl), 3.67–0.7 (m, 11 H), 1.03 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3); GC/MS (1% OV-101, 0.125 in. × 1 ft glass column) *m/e* 220 (parent), 192, 111 (base), 110, 93, 82, 77.

(3aα,3bβ,6aβ,7aα)-Decahydro-5-(*n*-butylthiomethylene)-2,2-dimethyl-1*H*-cyclopenta[*a*]pentalen-4-one (29). A stirred suspension of magnesium sulfate (424 mg, 3,53 mmol), *p*-toluenesulfonic acid (10 mg, 0.052 mmol), *n*-butylthiol (0.10 mL, 86.7 mg, 0.964 mmol), and (3aα,3bβ,6aβ,7aα)-decahydro-5-formyl-2,2-dimethyl-1*H*-cyclopenta[*a*]-pentalen-4-one (138.4 mg, 0.629 mmol) in 4.5 mL of dry benzene was heated to reflux for 20 h. The resulting mixture was filtered and diluted with 25 mL of ether and washed with saturated sodium bicarbonate (2 × 10 mL) and brine (3 × 10 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo to afford a brown solid which was purified by chromatography on 10 g of silica gel. Elution with 10% ether in pentane provided 152 mg (82%) of **29**: ^1H NMR($CDCl_3$) δ 7.42 (t, 1 H, J = 2, vinyl), 3.38–0.68 (m, 19 H), 1.02 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3); IR(NaCl, film) 3050, 2915, 2850, 1730, 1690, 1580, 1460, 1450, 1380, 1365, 1325, 1270, 1235, 1215, 1190, 1165, 1100, 1070, 1010, 890, 860, 830, 800, 785 cm^{-1}; GC/MS (0.125 in. × 1 ft glass column packed with 1% OV-101) *m/e* 292 (parent) 235, 109, 107, 95, 79, 72.

(3aα,3bβ,6aβ,7aα)-Decahydro-5-(*n*-butylthiomethylene)-2,2,3b-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-one. To a stirred solution of potassium *tert*-butoxide (2.07 mmol) in 1.5 mL of dry *tert*-butyl alcohol at room temperature was added compound **29** (148 mg, 0.507 mmol) in 3 mL of dry *tert*-butyl alcohol. After the solution was stirred at room temperature for 2 min, it was cooled to 0 °C. To the cooled solution was added, over 1 min, methyl iodide (0.64 mL, 1.47 g, 10.3 mmol). The resulting mixture was allowed to warm to room temperature and was then heated to reflux for 0.5 h. The suspension was washed with 25 mL of brine and was extracted with ether (3 × 10 mL). The combined ether extracts were dried ($MgSO_4$), and the solvent was removed in vacuo. The resulting solid was purified by chromatography on 12 g of silica gel. Elution with 8% ether in pentane afforded 28 mg (15 %) of starting material and 78 mg (50%) of the desired alkylation product: ^1H NMR($CDCl_3$) δ 7.45 (t, 1 H, J = 2, vinyl), 3.20–0.67 (m, 20 H), 1.05 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.97 (s, 3 H, angular methyl); IR (NaCl, film) 3005, 2915, 2865, 1730, 1695, 1585, 1455, 1380, 1365, 1290, 1275, 1230, 1210, 1185, 1155, 1100, 1010, 980, 890, 860, 840, 800, 780, 730 cm^{-1}; GC/MS (1% OV-101, 0.125 in. × 1 ft) *m/e* 306 (parent), 107, 95, 91, 81, 72.

(3aα,3bβ,6aβ,7aα)-Decahydro-2,2,3b-trimethyl-1*H*-cyclopenta[*a*]-pentalen-4-one (30). A stirred solution of (3aα,3bβ,6aβ,7aα)-decahydro-5-(*n*-butylthiomethylene)-2,2,3b-trimethyl-1*H*-cyclopenta[*a*]pentalen-4-one (68 mg, 0.22 mmol), 3 mL of 25% aqueous potassium hydroxide, and 4 mL of ethylene glycol was heated to reflux for 24 h. The resulting mixture was washed with 25 mL of brine and extracted with ether (3 × 10 mL). The combined ether extracts were washed with aqueous saturated sodium bicarbonate (2 × 8 mL) and brine (10 mL). The organic layer was then dried ($MgSO_4$), and the solvent was removed in vacuo. The resulting oil was purified by chromatography on 5 g of silica gel. Elution with 10% ether in pentane afforded 23 mg (51%) of the desired norketone **30** whose spectral properties nicely matched those kindly furnished to us by Professor Hudlicky: ^1H NMR($CDCl_3$) δ 3.1–0.73 (m, 13 H), 1.07 and 0.92 (2 s, 3 H each, *gem*-methyls), 0.95 (s, 3 H, angular methyl); IR(NaCl, film) 2935, 2860, 1760, 1550, 1380, 1365 cm^{-1}; GC/MS (0.125 in. × 1 ft glass OV-101 column) *m/e* 206 (parent), 162, 123, 108, 107, 105, 95, 94, 79, 77; ^{13}C NMR ($CDCl_3$) 224.5 (*C*=O), 59.3 (s, C α to C=O), 48.9, 46.8, 43.4, 41.9, 41.2 (*C*Me_2), 37.7, 34.2, 29.7, 29.3 and 26.6 (*gem*-methyls), 22.4, 17.3 (angular methyl).

Acknowledgment. Financial support for this work was provided by the Cancer Research Coordinating Committee of the University of California and by the National Cancer Institute, DHEW (Grant Number CA 21144-03), to whom we are most grateful. G.M. thanks the University of California, Santa Barbara, for the receipt of Patent Funds. Finally, we are pleased to acknowledge the receipt of spectral data, for comparison purposes, from Professor Tomas Hudlicky of the Illinois Institute of Technology.

(17) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.