The Pauson–Khand Reaction in Triquinane Synthesis: Approaches to Pentalenene, Pentalenic Acid, and Silphinene

Elizabeth G. Rowley and Neil E. Schore*

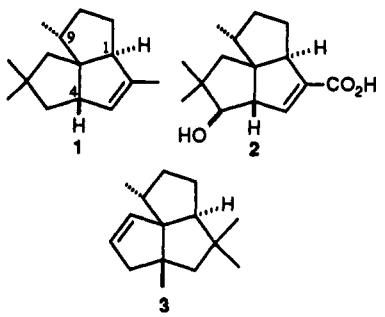
Department of Chemistry, University of California, Davis, California 95616

Received July 15, 1992

Substituted pentynylcyclopentene precursors for the synthesis of pentalenene, pentalenic acid, and silphinene by intramolecular Pauson–Khand cycloaddition reaction have been prepared from 2-methylcyclopentanone via 5-methylcyclopentenyllithium. Conjugate addition of the latter to BHT methacrylate followed by methylation were the key steps in enyne synthesis. Reaction of 4,4-dimethyl-5-(5-methylcyclopentenyl)-1-pentyne with $Co_2(CO)_8$ produces two diastereomeric triquinane enones in an overall yield of 51%, with the *exo*-9-methyl isomer predominating by ratio of 8:1. This material was converted into pentalenene in two steps. Pauson–Khand reaction of the TBDMS ether of 4,4-dimethyl-5-(5-methylcyclopentenyl)-1-pentyn-3-ol proceeds in 33% yield. Three of the four possible stereoisomeric products are formed, with two of them, making up ca. 80% of the product mixture, possessing the necessary *exo*-methyl stereochemistry at C-9 for further elaboration into pentalenic acid. A formal synthesis of the latter was completed by reduction of one of the enone isomers into a ketone which had previously been carried on to the natural product. Pd(0)-catalyzed coupling of 1-iodo-5-methylcyclopentene to 1-(trimethylsilyl)-1,4-pentadiyne and reduction over Lindlar's catalyst allowed efficient access to (*Z*)-1-(5-methylcyclopentenyl)-1-penten-4-yne, but the latter could not be induced to undergo Pauson–Khand cyclization, thus foiling a planned approach to silphinene.

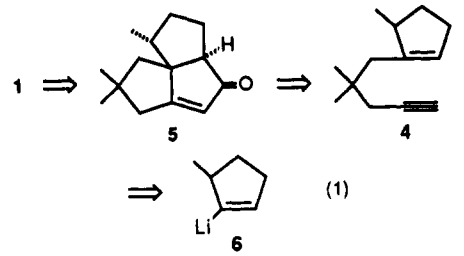
Introduction

The angularly fused triquinanes have proved to be challenging testing grounds for many cyclopentane syntheses. Several years ago we demonstrated the use of the Pauson–Khand cycloaddition reaction in the preparation of this ring system.[1,2] That initial approach used symmetrical precursors and was not applicable to most of the natural products in the compound class. In order to direct our efforts toward triquinane natural products we began an evaluation of methods for the synthesis of cycloaddition substrates derived from 1-(4-pentynyl)-5-methylcyclopentene.[3] We herein describe applications of this methodology to a total synthesis of (±)-pentalenene (**1**),[4-6] a formal total synthesis of (±)-pentalenic acid (**2**),[7-9] and an approach to (±)-silphinene (**3**).[10,11]



Results and Discussion

Pentalenene. For pentalenene, the simplest of the triquinanes under study, we chose a synthetic plan based on the synthesis and Pauson–Khand cycloaddition of an appropriately substituted enyne **4** giving tricyclic enone **5** (eq 1). Control of the configuration the C-9 methyl



group was expected to be dependent on steric interactions in the insertion of the substituted cyclopentene into the cobalt–alkyne complex during the Pauson–Khand process.

We used a modified Shapiro reaction to access the initial lithium reagent **6** in greater than 90% yield from the

(1) Reviews: (a) Pauson, P. L.; Khand, I. U. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 2. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Pauson, P. L. In *Organometallics in Organic Synthesis. Aspects of a Modern Interdisciplinary Field*; de Meijere, A., tom Dieck, H., Eds.; Springer: Berlin, 1988; p 233. (d) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081.

(2) Knudsen, M. J.; Schore, N. E. *J. Org. Chem.* **1984**, *49*, 5025.

(3) Schore, N. E.; Knudsen, M. J. *J. Org. Chem.* **1987**, *52*, 569.

(4) Isolation: Seto, H.; Yonehara, H. *J. Antibiot.* **1980**, *33*, 92.

(5) Syntheses: (a) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2869. (b) Misumi, S.; Matsumisha, H.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1982**, 855. (c) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4504. (d) Paquette, L. A.; Annis, G. D. *J. Am. Chem. Soc.* **1983**, *105*, 7358. (e) Piers, E.; Karunaratne, V. *J. Chem. Soc., Chem. Commun.* **1984**, 959. (f) Piers, E.; Karunaratne, V. *Can. J. Chem.* **1989**, *67*, 160. (g) Pattenden, G.; Teague, S. J. *Tetrahedron Lett.* **1984**, 3021. (h) Pattenden, G.; Teague, S. J. *Tetrahedron* **1987**, *43*, 5637. (i) Mehta, G.; Rao, K. S. *J. Chem. Soc., Chem. Commun.* **1985**, 1464. (j) Mehta, G.; Rao, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 8015. (k) Imanishi, T.; Ninbari, F.; Yamashita, M.; Iwata, C. *Chem. Pharm. Bull.* **1986**, *34*, 2268. (l) Hua, D. *J. Am. Chem. Soc.* **1986**, *108*, 3835. (m) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 800. (n) Hudlicky, T.; Natchus, M. G.; Sinai-Zingde, G. *J. Org. Chem.* **1987**, *52*, 4641. (o) Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G.; Ranu, B. C.; Papadopolous, P. *Tetrahedron* **1987**, *43*, 5685. (p) Ihara, M.; Katogi, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 2963.

(6) Preliminary communication: Schore, N. E.; Rowley, E. G. *J. Am. Chem. Soc.* **1988**, *110*, 5224.

(7) Isolation: Seto, H.; Sasaki, H.; Uzawa, J.; Takeuchi, S.; Yonehara, H. *Tetrahedron Lett.* **1978**, 4411.

(8) Syntheses: (a) Sakai, K.; Ohtsuka, T.; Misumi, S.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1981**, 355. (b) Ihara, M.; Katogi, M.; Fukumoto, K.; Kametani, T. *J. Chem. Soc., Chem. Commun.* **1987**, 721. See also ref 5m,o,p.

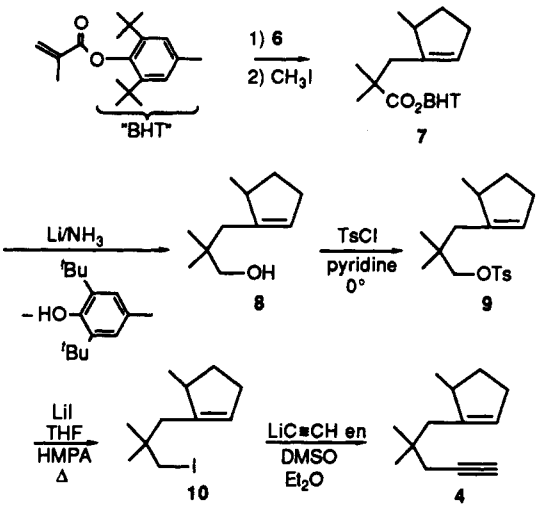
(9) Preliminary communication: Rowley, E. G.; Schore, N. E. *J. Organomet. Chem.* **1991**, 413, C5.

(10) Isolation: Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259.

(11) Syntheses: (a) Leone-Bay, A.; Paquette, L. A. *J. Org. Chem.* **1982**, *47*, 4173. (b) Paquette, L. A.; Leone-Bay, A. *J. Am. Chem. Soc.* **1983**, *105*, 7358. (c) Tsunoda, T.; Kodama, M.; Ito, S. *Tetrahedron Lett.* **1983**, *24*, 83. (d) Crimmins, M. T.; Mascarella, S. W.; Bredon, L. D. *Tetrahedron Lett.* **1985**, *26*, 997. (e) Crimmins, M. T.; Mascarella, S. W. *J. Am. Chem. Soc.* **1986**, *108*, 3438. (f) Sternbach, D. D.; Hughes, J. W.; Burdi, D. F.; Banks, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 2149. (g) Wender, P. A.; Ternansky, R. J. *Tetrahedron Lett.* **1985**, *26*, 2628. (h) Rao, Y. K.; Nagarajan, M. *Tetrahedron Lett.* **1988**, *29*, 107. (i) Rao, Y. K.; Nagarajan, M. *J. Org. Chem.* **1989**, *54*, 5678.

0022-3263/92/1957-6853$03.00/0

Scheme I



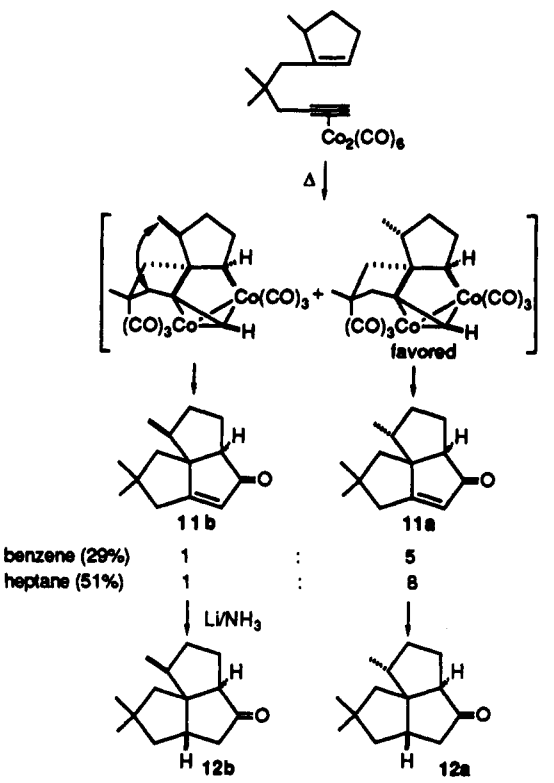
triisopropylbenzenesulfonyl (trisyl) hydrazone of 2-methylcyclopentanone.[12] Attempts to directly alkylate using either the appropriate pentynyl tosylate or iodide did not succeed.[3] Similarly, efforts to prepare a cycloaddition precursor by adding 6 to 2,2-dimethyl-5-(trimethylsilyl)-4-pentynal[13] also had to be abandoned because no effective way was found to reduce the highly hindered allylic alcohol function to a methylene group.

As an alternative approach, we investigated conjugate addition of the 5-methylcyclopentenyl group in some form to a methacrylate ester. If successful, quenching by methyl iodide followed by conversion of the carboxylate into an alkyne would lead to the required substrate. However, treatment of 5-methylcyclopentenylcopper,[14] formed by addition of a THF solution of 6 to phenylthiocopper[15] at −78 °C, with methacrylate gave only small amounts of unidentifiable material. Similarly, addition of 6 to dry CuI[16] followed by treatment with BF_3–etherate gave the corresponding cuprate reagent,[17] but its exposure to methyl methacrylate resulted in no observable reaction at all.

In 1986, Cooke reported that α,β-unsaturated esters of *tert*-butylphenol derivatives undergo conjugate addition reactions with a wide variety of organolithium reagents.[18] The *tert*-butyl groups block the carbonyl carbon and prevent 1,2 addition. The anisole derivative is generally the phenol of choice for this reaction because its esters can be cleaved oxidatively with ceric ammonium nitrate. Unfortunately, reaction of lithium 2,6-di-*tert*-butyl-4-methoxyphenoxide with methacryloyl chloride gave the ester (mp 64–65 °C) in only low yield, and 6 failed to undergo addition to this substrate, even at temperatures up to −20 °C.

As a consequence, 2,6-di-*tert*-butyl-4-methylphenyl (BHT) methacrylate was prepared and exposed to 6 in THF, followed by treatment with excess iodomethane at −78 °C, to give a 90% yield of BHT ester 7 (Scheme I). The usual method for cleaving a BHT ester is lithium aluminum hydride (LAH) reduction. However, neither LAH nor lithium triethylborohydride in THF reduced the ester group in 7, even upon extended treatment under forcing conditions. The steric hindrance associated with the quaternary α-carbon in 7 no doubt contributes to its resistance to reduction. Fortunately, dissolving metal reduction with either Li or Na succeeded.[19] The resulting neopentyl alcohol 8 was obtained in 30–45% yields.

Scheme II



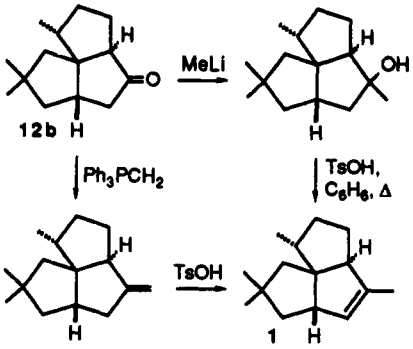
Alcohol 8 was converted to the enyne 4 following procedures based on work by Gibson and Erman.[20] Treating 8 with 2 equiv of *p*-toluenesulfonyl chloride in neat pyridine produced a 75% yield of tosylate 9 after 3 days. Refluxing sodium iodide in acetone failed to convert the tosylate into the corresponding neopentyl iodide 10. Instead, the tosylate was heated with LiI in THF and HMPA to give a 67% yield of 10.[21] Finally, displacement of the iodide with the lithium acetylide–ethylenediamine complex gave a 65% yield of enyne 4.

With 4 in hand we turned to the question of Pauson–Khand cycloaddition. We anticipated that the allylic methyl group on the cyclopentene ring of 4 would direct the bulky alkyne–cobalt complex to the opposite face of the double bond and thus provide the necessary stereocontrol. A study of models showed that the putative intermediate dimetallacycle suffers a 1,3-pseudodiaxial interaction between the methyl group and a propargylic hydrogen when the alkene inserts into the cobalt complex with the latter on the same face of the ring as the methyl substituent (Scheme II). This interaction is absent when the opposite face of alkene inserts.

In initial experiments, enyne 4 was treated with $Co_2(CO)_8$ at rt and cyclized in refluxing benzene. After 22 h a 29% yield of a mixture of two stereoisomeric enones 11a and b was isolated in a ca. 5:1 ratio, based on the appearance of two vinylic signals in the proton NMR at δ 5.76

(12) (a) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147. (b) Chamberlin, A. R.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 154.
(13) Magnus, P.; Principe, L. M. *Tetrahedron Lett.* **1985**, *26*, 4851.
(14) Kende, A. S.; Jungheim, L. N. *Tetrahedron Lett.* **1980**, *21*, 3849.
(15) Posner, G. H.; Brunelle, D. J.; Sinoway, L. *Synthesis* **1974**, 662.
(16) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788.
(17) Cf. Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.* **1982**, *47*, 119.
(18) Cooke, M. P. *J. Org. Chem.* **1986**, *51*, 1637.
(19) Greenfield, A.; Friedel, R. A.; Orchin, M. *J. Am. Chem. Soc.* **1954**, *76*, 1258.
(20) Gibson, T. W.; Erman, W. F. *J. Am. Chem. Soc.* **1969**, *91*, 4471.
(21) Stephenson, B.; Sollodie, G.; Mosher, H. S. *J. Am. Chem. Soc.* **1972**, *94*, 4184.

Scheme III



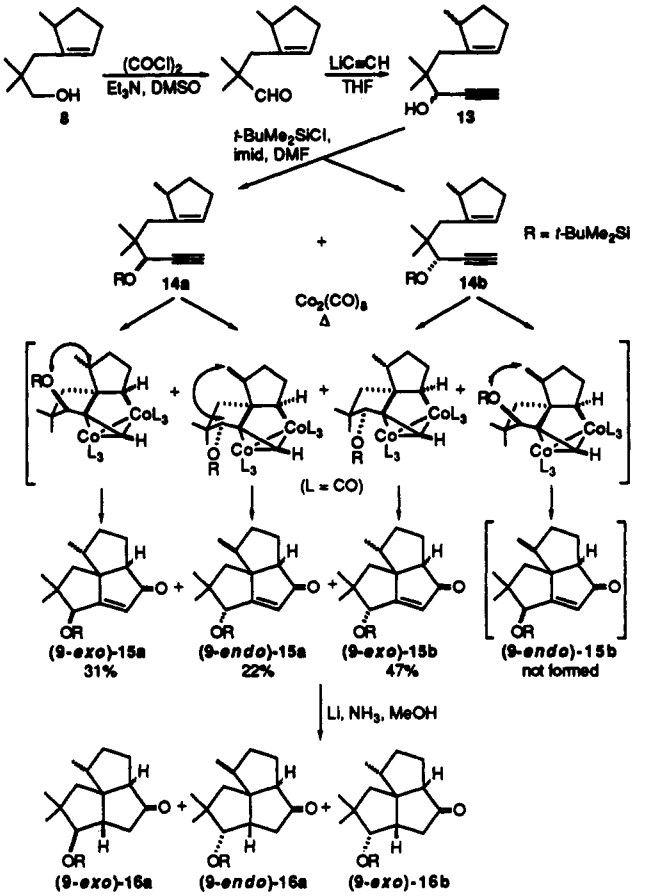
(major) and 5.89 (minor) ppm. Both the yield and the stereochemistry were improved by heating a heptane solution of the cobalt complex in a sealed tube:[22] a 51% yield of an 8:1 mixture was produced. The mixture was reduced with lithium in liquid NH_3 to produce two tricyclic ketones **12a** and **b**, which were found to be identical to intermediates in Piers' syntheses of pentalenene and *epi*-pentalenene.[5e,f] NMR comparisons[23] confirmed that the major product **12a** had the methyl group in the natural configuration.

Piers converted **12a** to pentalenene by reaction with methyllithium and then dehydration of the resulting tertiary alcohol. Competing enolate formation necessitates repeated treatment with the lithium reagent. Thus, in our hands approximately equal amounts of pentalenene and starting ketone were obtained even after three successive exposure to methyllithium, and the mass balance was rather poor. In a more successful approach we converted **12b** to the natural product by Wittig olefination followed by isomerism (Scheme III).[24] Use of a large excess of ylide and a further excess of the methyl phosphonium salt[25] allowed enolate reprotonation to occur in situ, improving the efficiency of the process and affording an overall yield of 45% of essentially pure pentalenene.

Pentalenic Acid. The substrate for a Pauson–Khand-based synthesis of **2** must contain oxygen functionality at the propargyl position. This aspect is easily addressed starting from the primary alcohol **8** used in the synthesis of **1**. Swern oxidation of **8** and treatment of the resulting aldehyde with freshly prepared lithium acetylide (the commercially available ethylenediamine complex did not work nearly as well) gave **13** as a ca. 55:45 mixture of diastereomers in 77% overall yield (Scheme IV). Unprotected propargyl alcohols have generally not performed well as Pauson–Khand cycloaddition substrates,[26] and while alcohol **13** was completely consumed upon treatment with $Co_2(CO)_8$ and heating, no indication of cyclization to an enone was observed.

The corresponding *tert*-butyldimethylsilyl ethers typically are better substrates.[27] Preparation of siloxy enyne **14** in the usual manner gave less than spectacular results (55–60% yields), perhaps a consequence of steric hindrance in the system (direct in situ silylation of the alkoxide

Scheme IV



formed by acetylide addition to the aldehyde, however, was even worse). The diastereomers of **14** were inseparable by the usual chromatographic methods. Thus, the mixture was carried through the Pauson–Khand process. Reaction of **14** with dicobalt octacarbonyl under the conditions used for cycloaddition of **4** (heptane, sealed tube, 115 °C, 19 h) gave a 33% yield of a mixture of enones. The ^1H NMR spectrum of the product showed three vinyl signals, indicating that three of the four possible diastereomers had been formed.

Several general improvements to Pauson–Khand methodology have been reported recently. An attempt to apply one of them, the dry state method of Smit and Caple,[28] to this problem proved fruitless. The $Co_2(CO)_6$ complex of **14** was adsorbed onto silica gel prepared with 10% water content and the resulting red powder heated until the red color disappeared (1 h at 80–90 °C was required). The reaction was very sluggish, did not go to completion, and afforded a poor mass balance: enones **15** were obtained in only ca. 15% yield while varying amounts of unreacted complexed and uncomplexed **14** were isolated, together with aromatic (alkyne trimerization?) side products.

The expected stereochemistry of cycloaddition of **14** may be predicted as follows. Using the analysis developed for the cycloaddition of **4**, one would expect enyne diaste-

(22) Magnus, P.; Principe, L. M.; Slater, M. J. *J. Org. Chem.* **1987**, *52*, 1483.

(23) We are extremely grateful to Prof. Edward Piers of the University of British Columbia for providing us with details of his conversion of **12** into **1** and for supplying IR and NMR spectra of these compounds for comparison purposes.

(24) (a) Short, R. P.; Revol, J.-M.; Ranu, B. C.; Hudlicky, T. *J. Org. Chem.* **1988**, *48*, 4453. (b) Hudlicky, T.; Natchus, M. G.; Sinai-Zingde, G. *J. Org. Chem.* **1987**, *52*, 4641.

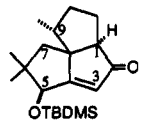
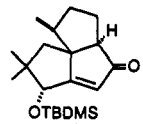
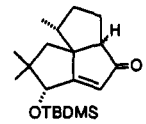
(25) Lund, E. C. Ph.D. Dissertation, 1987.

(26) Schore, N. E. Pauson–Khand Reaction. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991.

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

(28) (a) Smit, W. A.; Simonyan, S. O.; Tarasov, V. A.; Mikaelian, G. S.; Gybin, A. S.; Ibragimov, I. I.; Caple, R.; Froen, D.; Kregger, A. *Synthesis* **1989**, 472. (b) Smit, V. A.; Gybin, A. S.; Veretenov, S. O.; Shashkov, A. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987**, 232. (c) At the time these experiments were being carried out, the use of amine oxides to promote Pauson–Khand reaction at lower temperatures had yet not been reported.[28d,e] (d) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289. (e) Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S.-E. *Synlett* **1991**, 204.

Table I. Proton Chemical Shift Data for Enones 15

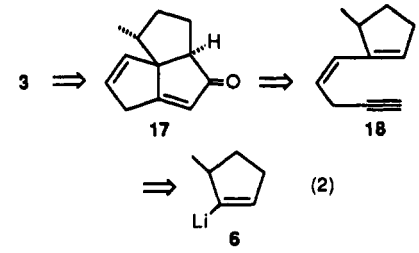
assignment	 OTBDMS (9-*exo*)-15a	 OTBDMS (9-*endo*)-15a	 OTBDMS (9-*exo*)-15b
H-3	5.83, s	6.03, d, J = 1.7 Hz	5.85, d, J = 1.7 Hz
H-5	4.04, s	4.50, d, J = 1.7 Hz	4.49, d, J = 1.7 Hz
H-1	2.41, m	2.44, m	2.43, m
H-7	2.07, d, J = 13.8 Hz	1.88, d, J = 13.8 Hz	2.02, d, J = 13.8 Hz
H-7	1.22, d, J = 13.8 Hz	1.63, d, J = 13.8 Hz	1.44, d, J = 13.8 Hz
CH_3-9	0.97, d, J = 7.2 Hz	0.93, d, J = 6.9 Hz	0.97, d, J = 7.2 Hz
CH_3-6	0.87 and 1.11, s	0.69 and 1.14, s	0.80 and 1.17, s
t-Bu-Si	0.86, s	0.91, s	0.90, s
CH_3-Si	0.01 and 0.07, s	0.06 and 0.07, s	0.05 and 0.07, s

reomer **14b** to give a more favorable ratio of enone products with respect to methyl stereochemistry at C-9 than the 88:12 ratio observed for **4**: if the alkene inserts into the cobalt complex such that the methyl group is on the endo face of the macrocycle, a severe steric interaction with the siloxy group at C-5 develops, and this pathway should be extremely disfavored. In contrast, the cycloaddition of **14a** should be less selective. Insertion placing the C-9 methyl group in an endo orientation experiences interference with a propargyl hydrogen, the same interaction seen in cycloaddition of **4**. However, the alternative mode of reaction suffers from a steric interaction between the tertiary hydrogen at C-9 and the siloxy group in the propargyl position. Thus, little preference is expected.

In the event, NMR data indicated that the three enones had formed in a 5:3:2 ratio. These were separated and tentatively characterized (Table I). It is generally observed that protons on the endo face of a bicyclo[3.3.0]-octane are shielded relative to those on the exo face.[3] Application of this guideline to the C-9 methyl group in this system does not give very clear-cut results, evidently due to the presence of the third ring: in the case of the enone precursors to pentalenene and *epi*-pentalenene (**11a** and **b**), the C-9 methyl protons are separated by only 0.05 ppm, appearing at δ 0.96 and 0.91 ppm, respectively. For enones **15**, the two major components both displayed C-9 methyl proton signals at δ 0.97, the minor component at δ 0.93, the corresponding ^{13}C signals at δ 14.5 vs δ 13.9. Still, the evidence was suggestive that two of the three enones formed in the cyclization of **14** had the desired *exo*-methyl configuration at C-9. Corroboration was found in the chemical shifts for the vinyl protons: in **11b** the *endo*-methyl group deshields this signal by 0.15 ppm. Similarly, the vinyl hydrogen in the minor isomer of **15** appears at δ 6.03, nearly 0.2 ppm downfield of the corresponding signals of the two major components. Stereochemistry at C-5 was more readily assigned using both chemical shift and coupling constant data: in bicyclo-[3.3.0]octenones of this type, $J_{H_{vinyl}-H_{allyl}}$ is ca. 2 Hz when the allylic hydrogen is exo and 0 Hz when it is endo.[29] The major isomer of **15**, in which $J_{H_3-H_5}$ is 1.7 Hz, is thus assigned structure (9-*exo*)-**15b**, evidently the sole expected product of cyclization of enyne **14b**. Similar coupling in the minor isomer sets the structures of the remaining two enones as cyclization products of **14a**, formed with much lower selectivity (ca. 3:2), as expected. Overall, enones possessing the same *exo*-methyl configuration at C-9 as pentalenic acid make up nearly 80% of the product mixture.

Reduction of the enone mixture with lithium in liquid NH_3 and methanol gave the corresponding tricyclic ketones **16**, together with variable but usually minor amounts of **12** from elimination of the siloxy substituent. The enones were separated and subjected to two-dimensional NMR experiments. Typical of these data (Table II) were nuclear Overhauser measurements indicating proximity between the C-9 methyl group and both the ring-fusion hydrogen at C-4 and the proton at C-5 only in isomer (9-*endo*)-**16a**. In contrast, in the two isomers with 9-exo stereochemistry, the most important interactions involving H-4 were with $H\text{-}3_{exo}$ in (9-*exo*)-**16a** and with H-5 in (9-*exo*)-**16b**. The identity of (9-*exo*)-**16a** with an intermediate in Hudlicky's pentalenic acid synthesis[5n,30] confirmed these assignments. The preparation of (9-*exo*)-**16a** thus represents a formal synthesis of the natural product. Note that (9-*exo*)-**16b**, the major isomer in this mixture, is also a viable pentalenic acid precursor because the alcohol may be inverted by an oxidation/selective reduction sequence.[5m,p,8b] Hudlicky also prepared ketone (9-*endo*)-**16b**, and the NMR spectrum of this isomer does not match the spectra of any product of our cycloaddition–reduction sequence. These results therefore provide strong confirmation that the interaction of the endo substituent at C-9 and the exo substituent at C-5 control the stereochemistry of this Pauson–Khand reaction.

Silphinene. Although the structure of silphinene has many similarities to that of pentalenene, the different positions of the double bond and the methyl groups has generally necessitated the use of completely different strategies for the synthesis of the two natural products. In contrast, the retrosynthetic plan we envisioned for silphinene using the intramolecular Pauson–Khand cycloaddition would use the same starting materials and the same key step as the pentalenene and pentalenic acid syntheses (eq 2).



The tricyclic enone **17** would be converted to silphinene by cuprate addition followed by Reetz's *gem*-dimethylation procedure on the carbonyl group.[31] Cycloaddition would test the feasibility of using a cis alkene in the chain connecting the two reactive parts of the cycloaddition precursor, as well as its effect on the stereocontrol with respect to the methyl group at C-9. While the pentalenene synthesis used the *gem*-dialkyl effect to hold the enyne in a reactive conformation, here the cis double bond might prove similarly useful.

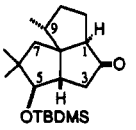
Several approaches to **18** were explored utilizing 5-methylcyclopentenecarbaldehyde, which was prepared

(29) (a) Veretenov, A. L.; Gybin, A. S.; Smit, W. A.; Chertkov, V. A.; Shashkov, A. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 1879. (b) Gybin, A. S.; Smit, W. A.; Veretenov, A. L.; Simonian, S. O.; Shashkov, A. S.; Struchkov, Y. T.; Kuz'mina, L. G.; Caple, R. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 2756.

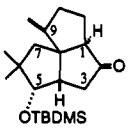
(30) We are extremely grateful to Prof. Tomas Hudlicky of the Virginia Polytechnic Institute for providing us with IR and NMR spectra of these compounds for comparison purposes.

(31) (a) Reetz, M. T.; Westermann, J.; Steinbach, R. *J. Chem. Soc., Chem. Commun.* **1981**, 237. (b) Reetz, M. T.; Westermann, J.; Kyung, S.-H. *Chem. Ber.* **1985**, *118*, 1050.

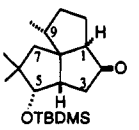
Table II. ^{1}H NMR Data and NOE Results for 16



(9-*exo*)-16a



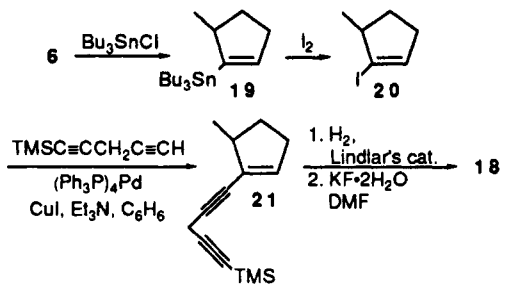
(9-*endo*)-16a



(9-*exo*)-16b

assignment	chemical shift, δ (ppm)	NOE interactions	chemical shift, δ (ppm)	NOE interactions	chemical shift, δ (ppm)	NOE interactions
H-5	3.37 (J_{4-5} = 9.5)		3.62 (J_{4-5} = 7.5)	H-3 exo, CH_3-9	3.64 (J_{4-5} = 5.4)	H-4
H-3 exo	2.48 (J_{3x-4} = 8.7, J_{gem} = 20.7)	H-4	2.72 (m)		2.23 (J_{3x-4} = 10.6, J_{gem} = 20.2)	
H-1	2.33 (m)		2.47 (m)		2.50 (m)	CH_3-6 endo
H-4	2.28 (m)	H-3 exo	2.55 (m)	CH_3-9	2.55 (m)	H-3 exo, 5
H-3 endo	1.95 (m)		2.05 (J_{3n-4} = 11.4, J_{gem} = 20.1)		1.97 (m)	
H-7 exo	1.85 (J_{gem} = 14.1)	CH_3-6 exo, 9	1.66 (J_{gem} = 13.2)	H-9	1.68 (J_{gem} = 13.5)	
H-9	1.52 (m)		1.73 (m)		1.50 (m)	
H-7 endo	1.24 (J_{gem} = 14.1)		1.52 (J_{gem} = 13.2)		1.42 (J_{gem} = 13.5)	
CH_3-6 exo	0.99 (s)	H-7 exo	0.96 (s)	H-5	0.96 (s)	
CH_3-9	0.97 (J = 6.6)	H-7 exo	0.94 (J = 6.3)	H-4,5	0.94 ($J \approx$ 6–7)	
CH_3-6 endo	0.92 (s)		0.82 (s)		0.94 (s)	H-1
t-Bu-Si	0.87 (s)		0.87 (s)		0.85 (s)	
CH_3-Si	0.04, 0.03 (s)		0.03, 0.01 (s)		0.03, 0.02 (s)	

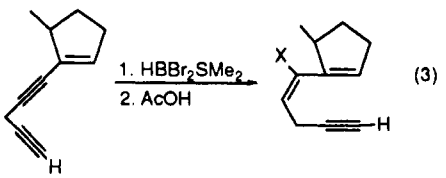
Scheme V



from **6** and dimethylformamide.[12a] However, a number of sequences utilizing Wittig and Peterson olefination procedures failed, for various reasons. For example, attempts to generate a 3-butynyl Wittig reagent from $(CH_3)SiC{\equiv}CCH_2CH_2P(C_6H_5)_3^+ I^-$ failed, due to preferred deprotonation at the propargylic position and elimination of triphenylphosphine.[32] More cumbersome sequences were briefly explored involving 2-butynyl systems,[33] which would require use of an acetylene zipper procedure.[34] These were eliminated due to results in model systems, which showed a reluctance of the triple bond in the intermediate 4,6-dien-2-ynes to move out of conjugation.

Instead, efforts were directed at making **18** from the commercially available 1-(trimethylsilyl)-1,4-pentadiyne. Methylcyclopentenyllithium **6** was converted to the tin derivative **19** and then iodide **20** using Paquette's method (Scheme V).[35] The latter was then coupled to the diyne using tetrakistriphenylphosphinepalladium(0) to give **21** in 90% yield.[36] The internal triple bond of **21** was hydrogenated with good chemo- and stereoselectively using a Lindlar catalyst.[37] The formation of the cis alkene product was confirmed by comparing the ^{1}H NMR spectrum of **18** with the spectra of *cis*- and *trans*-1-(1-propenyl)cyclopentene.[38] The hydrogen at the internal position of the diene moiety appears at δ 6.09 (d, J = 15.3 Hz) in the trans isomer of the latter. In the cis compound this signal is at δ 5.81 (d, J = 11.7 Hz), which compares well with that in **18**: δ 5.89 (d, J = 11.2 Hz). Overreduction of **21** to the corresponding triene occurred to a varying extent from reaction to reaction but was never completely eliminated. After desilylation to **18**, the triene side product was easily removed.

In an attempt to improve the selectivity of the reduction we briefly explored application of Brown's discovery that dibromoborane–methyl sulfide hydroborates internal alkynes much faster than terminal alkynes.[39] Treatment of the desilylated enediyne with dibromoborane followed by protonolysis gave a product whose ^{1}H NMR spectrum was similar to that of **18b**, except it was missing the signal for the proton at position X (eq 3). A likely explanation was that bromoboration rather than hydroboration was taking place, and that X was bromine.



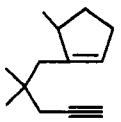
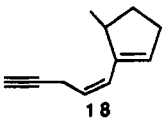
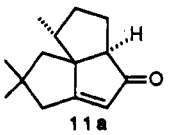
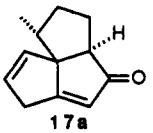
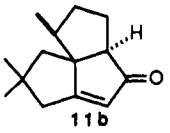
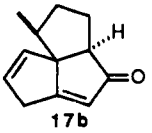
(3)

To test this assumption, the reaction was repeated with phenylacetylene. Indeed, ^{1}H NMR and mass spectral data indicated the *exclusive* formation of α-bromostyrene. The ^{11}B NMR spectrum of the dibromoborane used in this reaction (Aldrich) had the same chemical shift as reported by Brown, eliminating the possibility that tribromoborane was accidentally used in the reaction. Although a hydroborating agent that is selective for internal alkynes in the presence of terminal alkynes would be extremely useful, it is apparent that in this case hydrogenation using the Lindlar catalyst is the method of choice.

Finally, dienyne **18** was exposed to dicobalt octacarbonyl to give the red dicobalt hexacarbonyl complex. However, when the complex was submitted to several sets of cycloaddition conditions, no enone products were observed. The product mixture showed evidence for alkyne trimerization products and other unidentifiable materials, but no cyclopentenones were formed.

(32) See, however: Dharanipragada, R.; Fodor, G. *J. Chem. Soc., Perkin Trans 1* **1986**, 545.
(33) Haruta, R.; Ishiguro, M.; Furuta, K.; Mori, A.; Ikeda, N.; Yamamoto, H. *Chem. Lett.* **1982**, 1093.
(34) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, *97*, 891.
(35) Barth, W.; Paquette, L. A. *J. Org. Chem.* **1985**, *50*, 2438.
(36) Nicolaou, K. C.; Webber, S. E. *J. Am. Chem. Soc.* **1984**, *106*, 5734.
(37) Nicolaou, K. C.; Ladduwahetty, T.; Taffer, I. M.; Zipkin, R. E. *Synthesis* **1986**, 344.
(38) Inman, W. D.; Sanchez, K. A. J.; Chaidez, M. A.; Paulsen, D. R. *J. Org. Chem.* **1989**, *54*, 4872.
(39) (a) Brown, H. C.; Campbell J. B., Jr. *J. Org. Chem.* **1980**, *45*, 389. (b) Brown, H. C.; Chandrasekharan, J. *J. Org. Chem.* **1983**, *48*, 644.

Table III. Comparison of Pentalenene and Silphinene Cycloadditions

pentalenene	E (kcal/mol)	silphinene	E (kcal/mol)
 4	-0.2934	 18	2.0625
 11a	21.4877	 17a	29.3131
 11b	24.5819	 17b	30.4331

One possible reason for the failure of this cycloaddition is that dienyne 18 is more stable as an s-trans than an s-cis conformer, and the energy required to bring the cobalt–alkyne complex into a favorable conformation for Pauson–Khand reaction disfavors this process with respect to competing reactions. Molecular mechanics calculations on (*Z*)-1,3-pentadiene have shown that the barrier to rotation is 2.58 kcal/mol.[40] In addition, the s-cis conformation is not planar: the dihedral angle about the bond connecting the two double bonds is 46°.

A molecular mechanics investigation using Quanta 2.1 of the various conformations of 18 was thus undertaken. As expected, the s-trans conformer was found to be the most stable species, although a realistic value of the energy difference between it and that of 18 held in a planar s–cis conformation could not be obtained. As an alternative approach, the relative energies of the enyne cycloaddition precursors and enone products for the successful pentalenene cycloaddition and the unsuccessful silphinene reaction were calculated and compared (Table III).[41] A comparison of the change in energy in the reaction of 4 to make 11 and the reaction of 18 to make 17 is reasonable because the same bond-making and bond-breaking processes are involved. To be sure, hand-held models provide no indication that the two processes should differ in any major way. However, while the absolute energy values may be suspect, the calculations clearly indicate that the latter cyclization should be more difficult, even allowing for the unfavorable conformational effects. We presume that incorporation of an additional double bond in the type of polycyclic intermediate depicted in Schemes II and III introduces strain to such structures and, therefore, raises the energy barrier associated with their formation.[42] It is interesting to note that these calculations also indicate that the stereoselectivity of the silphinene cycloaddition, if it could be achieved, would probably not be as good as that observed for the pentalenene synthesis, as 3 kcal/mol separate **11a** and **11b** while **17a** and **17b** differ by only 1 kcal/mol.

Conclusions. The Pauson–Khand synthesis of pentalenene takes 10 steps from the readily available 2-methylcyclopentanone. Although reduction of the hindered ester is a low-yield process, the brevity of the synthesis is an attractive feature. In particular, use of allylic substitution in the cyclopentene ring to direct the stereochemistry of the Pauson–Khand reaction succeeds to a synthetically useful degree. Modification of the sequence in order to permit an approach to pentalenic acid is also successful, although the yield and stereoselectivity with respect to formation of useful Pauson–Khand cyclization products are (expectedly) somewhat lower. Silphinene is not directly acessible, evidently due to greater strain introduced in the cycloaddition of the dienyne precursor. Although alternative cyclization precursors containing oxygenated but exclusively single-bonded linkages between the ene and yne functions may be envisioned, our principal question had been answered: the Pauson–Khand process suffers from the presence of a cis alkene in the linkage. Nonetheless, the feasibility of application of this reaction to the synthesis of triquinanes has been established and identification of the key elements necessary for stereocontrol provided as well. We are currently developing routes to the pentalenolactones based on selective Pauson–Khand reaction. The results of these studies will be reported in due course.

Experimental Section[43]

Unless otherwise indicated, ^{1}H NMR data were obtained in $CDCl_3$ at 300 MHz. 2,4,6-Triisopropylbenzenesulfonyl hydrazide,[44] mp 118–120 °C, and 2-methylcyclopentanone 2,4,6-triisopropylbenzenesulfonylhydrazone,[3] mp 128–129 °C, were prepared as described previously. Molecular mechanics calculations were performed on a Silicon Graphics IRIS computer using Quanta (Polygen Corp.) Version 2.1 software and CHARMM energy minimization.[45]

2,6-Di-*tert*-butyl-4-methylphenyl Methacrylate (BHT Methacrylate).[46] To a solution of 2,6-di-*tert*-butyl-4-methylphenol (12.1 g, 55 mmol) in 100 mL of ether at 0 °C was added 35.0 mL of 1.6 M *n*-BuLi (56 mmol). After 15 m, 6.5 mL (67 mmol) of methacryloyl chloride was added and the mixture stirred and warmed to rt overnight. Saturated aqueous NH_4Cl (75 mL) was added, and the mixture was extracted with 3 × 50 mL of ether. The combined organic layers were washed with 2 × 100 mL of saturated aqueous NaCl and dried ($MgSO_4$). Filtration and solvent evaporation yielded 15.7 g of crude product. Recrystallization from hot ethanol and drying over P_2O_5 under vacuum gave 10.9 g (69%) of pure BHT methacrylate: mp 86–87 °C; ^{1}H NMR δ 7.11 (2 H, s), 6.36 (1 H, s), 5.80 (1 H, s), 2.32 (3 H, s), 2.09 (3 H, s), 1.30 (18 H, s); ^{13}C NMR δ 168.0, 146.0, 142.0, 136.9, 134.3, 127.5, 126.9, 35.1, 31.4, 21.5, 18.6; IR (mineral oil) 1726 cm^{-1}.

General Method for Preparing 5-Methylcyclopentenyllithium (6) in THF. To a solution of 2-methylcyclopentanone 2,4,6-triisopropylbenzenesulfonylhydrazone (henceforth referred to as "trisyl hydrazone") in THF (approximately 10 mL THF/g hydrazone) at −78 °C was added 2 equiv of *t*-BuLi. The orange-red solution was stirred for 1.5–2 h at −78 °C and 30 min at rt. Vigorous evolution of nitrogen accompanied formation of **6**.

2,6-Di-*tert*-butyl-4-methylphenyl 2,2-Dimethyl-3-(5-methylcyclopentenyl)propanoate (7). To a solution of BHT methacrylate (9.3 g, 32 mmol) in 150 mL of THF was added at −78 °C a solution of **6** prepared from 14.6 g (39 mmol) of trisyl hydrazone. The mixture was stirred at −78 °C for 30 min, and 10.0 mL (160 mmol) of methyl iodide was added. The reaction

(40) Tai, J. C.; Allinger, N. L. *J. Am. Chem. Soc.* **1976**, *98*, 7928.
(41) Boyd, D. B.; Lipkowitz, K. B. *J. Chem. Educ.* **1982**, *59*, 269. The energy described here is the minimization of a potential energy function including terms for bond stretching, bending, and twisting, electrostatic interactions, and nonbonded interactions.
(42) We are exploring ways to adapt either this or other software packages to handle species such as the cobalt complex of 18 and the putative metallocyclic intermediates, in order to obtain more realistic values for the energies associated with these transformations.
(43) For general procedures see ref 3.
(44) Cusack, N. J.; Reese, C. B.; Risius, A. C.; Roozpeiker, B. *Tetrahedron* **1976**, *32*, 2157.
(45) Brooks, B. R.; Bruccoleri, R. E.; Swaminathan, S.; Karplus, M. *J. Comput. Chem.* **1983**, *4*, 187. A bug in the software required that a structure be minimized, inverted, minimized again, and so on until the energies of the two enantiomers converged. It is not known how this problem affected the accuracy of the final minimized energy obtained in this fashion.
(46) Yamada, B.; Matsumoto, A.; Otsu, T. *J. Polym. Sci., Polym. Chem. Educ.* **1983**, *21*, 2241.

was stirred for 10 min at −78 °C, 10 min at rt, and treated with 1 mL of methanol and the solvent removed by rotary evaporation. The residue was partitioned between 150 mL each of water and CH_2Cl_2. The aqueous layer was extracted with 3 × 70 mL of CH_2Cl_2, and the combined organic layers were washed with 75-mL portions of saturated aqueous NH_4Cl and NaCl solutions. Drying ($MgSO_4$), filtration, and solvent removal yielded 11.1 g (90%) of a yellow oil that was sufficiently pure to be used in further reactions. For analytical purposes, a small amount was recrystallized from hexane to give **7** as a white solid: mp 56–59 °C; ^1H NMR δ 7.13 (2 H, s), 5.55 (1 H, br s), 2.72 (1 H, m), 2.62 (2 H, br s), 2.36 (3 H, s), 2.5–2.0 (4 H, series of multiplets), 1.44, 1.43 (6 H, two overlapping singlets), 1.38 (18 H, s), 1.08 (3 H, d, J = 6.8 Hz); IR (neat, film) 1744 cm^{-1}. Anal. Calcd for $C_{26}H_{40}O_2$: C, 81.20; H, 10.48. Found: C, 80.92; H, 10.46.

2-(2,2-Dimethyl-3-hydroxypropyl)-3-methylcyclopentene (8). NH_3 (150 mL) was condensed onto a few small pieces of sodium and then redistilled onto 6.5 g (283 mmol) of sodium. To this dark blue solution was added a mixture of 10.4 g (27 mmol) of **7** and 6.3 mL (108 mmol) of dry ethanol in 40 mL of ether. After the solution was stirred for 45 min, 4 mL of ethanol was added and the NH_3 allowed to evaporate. The sticky yellow residue was dissolved in 100 mL of saturated aqueous NH_4Cl and extracted with 6 × 30 mL of ether. The combined extracts were washed with 2 × 100 mL of saturated aqueous NaCl and dried ($MgSO_4$). After filtration and evaporation, 8.7 g of material was obtained whose NMR spectrum showed the presence of both BHT and **8**. Flash chromatography[47] with 35% ether in hexane afforded 1.6 g (36%) of alcohol **8**, sufficiently pure for further reactions. For analytical purposes, Kugelrohr distillation (8 mmHg, oven temperature 140–150 °C) gave pure **8**: ^1H NMR δ 5.37 (1 H, s), 3.32 (2 H, s), 2.8–1.8 (8 H, series of multiplets), 1.00 (3 H, d, J = 9.0 Hz), 0.89 (6 H, s). ^{13}C NMR δ 127.1, 104.9, 72.1, 42.4, 37.1, 32.9, 30.3, 24.8, 24.2, 19.4. IR (neat, film) 3379, 1457, 1419, 1262, 1038 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O$: C, 78.52; H, 11.98. Found: C, 78.48; H, 11.93.

2-[2,2-Dimethyl-3-[(*p*-toluenesulfonyl)oxy]propyl]-3-methylcyclopentene (9). To a solution of 1.3 g (7.7 mmol) of **8** in 13 mL of pyridine at 0 °C was added 2.8 g (15 mmol) of *p*-toluenesulfonyl chloride. The solution was stirred for 15 min and refrigerated for 3 days, producing a clear golden solution with a fine white precipitate. This mixture was poured into 50 g of ice and 30 mL of ether. After the ice had melted, the layers were separated and the water extracted with 5 × 15 mL of ether. The combined extracts were washed with 2 × 50 mL each of saturated aqueous NH_4Cl and saturated aqueous NaCl, dried ($MgSO_4$), and filtered. Dry heptane (20 mL) was added, and the solvents were removed by rotary evaporation to give 1.87 g (75%) of tosylate, which was used without further purification: ^1H NMR δ 7.78 (2 H, d, J = 9.0 Hz), 7.34 (2 H, d, J = 9.0 Hz), 5.24 (1 H, s), 3.67 (2 H, s), 2.45 (3 H, s), 2.6–1.0 (7 H, series of m), 0.93 (3 H, d, J = 6.0 Hz), 0.88 (3 H, s), 0.86 (3 H, s). ^{13}C NMR δ 144.7, 141.2, 129.8, 128.1, 127.9, 104.9, 66.8, 42.5, 36.6, 32.8, 30.3, 24.7, 24.2, 21.6, 19.4.

2-(2,2-Dimethyl-3-iodopropyl)-3-methylcyclopentene (10). A solution of 0.8 g (2.5 mmol) of tosylate **9** and 1.7 g (13 mmol) of LiI in 3 mL each of THF and HMPA was refluxed for 17 h. The mixture was partitioned between 20 mL each of hexane and water, and the layers were separated. The water layer was extracted with 5 × 15 mL of hexane, and the combined organic layers were washed with 2 × 40 mL of aqueous $Na_2S_2O_3$ and 50 mL of saturated aqueous NaCl. Drying ($MgSO_4$), filtration, and solvent evaporation gave 0.64 g of crude **10**. Filtration through a short silica column gave 0.47 g (67%) of **10**, pure enough for further use: ^1H NMR δ 5.45 (1 H, s), 3.18 (2 H, s), 2.7–1.2 (7 H, series of m), 1.03 (6 H, s), 0.99 (3 H, d, J = 9.0 Hz).

4,4-Dimethyl-5-(5-methylcyclopentenyl)-1-pentyne (4). To a suspension of 0.61 g (90%, 6 mmol) of lithium acetylide–ethylenediamine complex in 5 mL of DMSO and 1 mL of ether at 0 °C was added a solution of 0.66 g (2.4 mmol) of iodide **10** in 1 mL each of DMSO and ether. The mixture was stirred at rt for 3 days at which point 30 mL of hexane and 20 mL of saturated aqueous NH_4Cl were added and the layers separated. The water layer was extracted with 5 × 10 mL of hexane. The combined organic layers were washed with 25 mL of saturated aqueous NH_4Cl and saturated aqueous NaCl and dried ($MgSO_4$). Filtration and solvent removal gave 0.34 g of crude material, which was separated on the Chromatotron,[3] eluting with hexane to afford 0.05 g of unreacted **10** and 0.25 g (65%) of the highly volatile enyne **4**: ^1H NMR δ 5.40 (1 H, s), 2.61 (1 H, m), 2.23 (2 H, m), 2.05 (2 H, d, J = 2.7 Hz), 2.01 (2 H, s), 1.96 (1 H, t, J = 2.7 Hz), 1.40 (1 H, m), 0.99 (3 H, d, J = 9.0 Hz), 0.97 (3 H, s), 0.95 (3 H, s). ^{13}C NMR δ 146.0, 127.4, 82.8, 69.9, 42.5, 32.9, 31.7, 30.4, 27.4, 27.0, 19.5, 14.1. HR MS calcd for $C_{13}H_{20}$ 176.1566, found 176.1581.

2,10,10-Trimethyltricyclo[6.3.0.0^{1,5}]undec-7-en-6-one (11). To a solution of 0.10 g (0.57 mmol) of **4** in 20 mL of benzene was added 0.25 g (0.73 mmol) of $Co_2(CO)_8$. The solution was stirred under a CO atmosphere for 1.5 h at which point the solvent was removed from a small portion of the reaction mixture for the purpose of characterizing the cobalt–alkyne complex: ^1H NMR (90 MHz) δ 5.45 (1 H, br s), 5.33 (1 H, br s), 2.86 (2 H, br s), 2.6–0.5 (series of br m); IR (neat, film) 2091, 2048, 2018 cm^{-1}. The red-black solution was refluxed for 20 h, 10 mL of Florisil was added, and the solvent was evaporated. The resulting purple powder was added to the top of a Florisil column and eluted with hexane to remove the colored, nonpolar cobalt decomposition products. Elution with 300 mL of ether gave 0.035 g (29%) of pure tricyclic enone **11**. The ratio of the integrals of the two olefinic signals at δ 5.90 and 5.75 corresponding to the two stereoisomers was 17:83. MPLC with a 10:1 hexane–ethyl acetate solution separated the isomers. Minor isomer **11b**: ^1H NMR δ 5.90 (1 H, d, J = 1.8 Hz), 2.6–1.4 (10 H, series of m), 1.25 (3 H, s), 0.91 (3 H, d, J = 7.2 Hz), 0.88 (3 H, s). Major isomer **11a**: ^1H NMR δ 5.74 (1 H, d, J = 1.5 Hz), 2.5–1.3 (10 H, series of m), 1.22 (3 H, s), 0.98 (3 H, s), 0.96 (3 H, d, J = 7.5 Hz). ^{13}C NMR δ 191.7, 124.5, 64.8, 59.1, 44.5, 42.7, 39.7, 38.1, 32.9, 32.2, 31.1, 25.9, 17.3. IR (neat, film) 1701, 1636 cm^{-1}. Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 81.94; H, 10.02.

2,10,10-Trimethyltricyclo[6.3.0.0^{1,5}]undec-7-en-6-one (11) in Heptane. CO was bubbled through a solution of 0.22 g (1.3 mmol) of **4** in 7 mL of heptane for 30 min. $Co_2(CO)_8$ (0.46 g, 1.3 mmol) was added and the mixture stirred under CO for another hour. The solution was transferred to a sealed tube and heated (oil bath 110 °C) for 22 h. After cooling, the mixture was worked up as described above to give 0.15 g (51%) of **11**. The ratio of the integrals of the olefinic ^1H NMR signals of this product was 12:88.

2,10,10-Trimethyltricyclo[6.3.0.0^{1,5}]undecan-6-one (12).[5e] NH_3 (10 mL) was condensed over a small piece of lithium and then redistilled onto 13.5 mg (1.9 mmol) of lithium. A solution of **11** (35 mg, 0.17 mmol) in 1.5 mL of ether and 0.01 mL of methanol was slowly added and the mixture stirred for 2 h. Methanol (1 mL) was added and the NH_3 allowed to evaporate. Saturated aqueous NH_4Cl (5 mL) was added and the mixture extracted with 3 × 20 mL of ether. The extracts were washed with 25 mL of saturated aqueous NaCl and dried ($MgSO_4$). Filtration and evaporation gave 0.031 g (89%) of product: IR (neat, film) 1738, 1462 cm^{-1}. The IR spectrum showed no sign of overreduction to the alcohol. ^1H NMR δ 2.7–1.1 (13 H, series of overlapping m), 1.1–0.9 (9 H, singlets and doublets for methyl groups of the two isomers). The isomers in this mixture were not separated, but some NMR signals for methyl groups were identified. Major isomer **12a**: δ 1.08 (s), 1.00 (s), 0.96 (d, J = 6.9 Hz). Minor isomer **12b**: δ 1.02 (s). Except for differences in the relative intensities of the signals for the two isomers, the spectrum corresponded exactly to that of a 42:58 mixture of **12a** and **12b** obtained by Piers.[5e,f,23]

Pentalenene (1).[4] KH (0.74 g, 6.5 mmol, 35% in oil) was rinsed with hexane and allowed to react with 8 mL of DMSO for 10 min. Methyltriphenylphosphonium iodide (2.8 g, 6.9 mmol) was added and the mixture heated at 60 °C for 15 min. A solution of **12** (0.094 g, 0.46 mmol) in 2 mL of DMSO was added and the heating continued for 5 h. The mixture was poured into 100 mL of water and extracted with 5 × 20 mL ether. The combined ether extracts were washed with 2 × 30 mL of water and 3 × 30 mL of saturated aqueous NaCl. The ether was dried ($MgSO_4$), filtered, and evaporated to give 0.17 g of a yellow solid, which was dissolved in 3 mL of CH_2Cl_2 and stirred overnight with 0.08 g (0.47 mmol) of *p*-toluenesulfonic acid. Aqueous $NaHCO_3$ (2.5 mL) was added,

(47) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

and the layers were separated. The water layer was extracted with 3 × 5 mL of CH_2Cl_2 and the combined organic layers were washed with 10 mL of saturated aqueous NaCl and dried ($MgSO_4$). The mixture was filtered through a short column of silica gel and washed with 50 mL of ether. Evaporation yielded 0.042 g (45%) of pure pentalenene (the peaks for *epi*-pentalenene, if present, were too small to be observed): ^1H NMR δ 5.13 (1 H, s), 2.63 (1 H, m), 2.52 (1 H, d, J = 9.9 Hz), 1.9–1.1 (9 H, series of m), 1.59 (3 H, s), 0.96 (6 H, two overlapping s), 0.87 (3 H, d, J = 7.2 Hz); IR (neat, film) 1462, 1376, 1364 cm^{-1}.

4,4-Dimethyl-5-(5-methylcyclopentenyl)-1-pentyn-3-ol (13). To a solution of 1.0 mL (11 mmol) of oxalyl chloride in 25 mL of CH_2Cl_2 at −50 °C was added 1.4 mL of DMSO. After gas evolution had stopped, 1.5 g (8.9 mmol) of **8** dissolved in 10 mL of CH_2Cl_2 was added and the mixture stirred at −50 °C for 20 min. Triethylamine (8.8 mL) was added and the reaction allowed to stir at rt for 2 h. After addition of 70 mL of water, the layers were separated and the aqueous layer was extracted with 2 × 50 mL of CH_2Cl_2. The combined organic layers were washed with saturated aqueous NH_4Cl and NaCl and then dried ($MgSO_4$). Filtration and solvent evaporation produced 2.0 g of crude aldehyde. Flash column chromatography with 10% ether in petroleum ether gave 1.2 g (81%) of aldehyde which was used without further purification: ^1H NMR δ 9.50 (1 H, s), 5.30 (1 H, s), 2.25 (1 H, m), 2.22 (2 H, s), 2.2–1.1 (4 H, series of m), 1.04 (3 H, s), 1.02 (3 H, s), 0.94 (3 H, d, J = 6.6 Hz); ^{13}C NMR δ 206.2, 127.6, 41.9, 36.4, 32.7, 30.4, 22.3, 21.4, 19.2; IR (neat, film) 2848.3, 2702.6, 1726.5, 1456.4 cm^{-1}.

Acetylene was dried by passing through a −78 °C trap with concd H_2SO_4 and Drierite and then bubbled into a graduated cylinder containing 4 mL of THF at −78 °C. When the total volume reached 6 mL, the solution was transferred via cannula to a −78 °C flask containing 40 mL of THF. The system was then purged with nitrogen for 20 min to remove any acetylene vapor. *n*-BuLi (4.2 mL, 1.47 M, 6.2 mmol) was added to 10 mL of THF, cooled to −78 °C, and slowly added to the acetylene solution. After the mixture was stirred for 30 min, 0.84 g (5.1 mmol) of the above aldehyde dissolved in 10 mL of THF was added, and the reaction was allowed to stir at rt for 1.5 h, after which time 30 mL of 1 M HCl was added. After 20 min, the layers were separated and the aqueous layer was extracted with 4 × 20 mL ether. The combined organic layers were washed with saturated aqueous NH_4Cl and NaCl and then dried ($MgSO_4$). Filtration and evaporation yielded 0.93 g (95%) of crude **13**, which was purified by flash chromatography eluting with 1:5 ether/petroleum ether: ^1H NMR δ 5.43, 5.40 (1 H total, two s), 4.09, 4.06 (1 H total, two d, J = 2.1 Hz), 2.62 (1 H, m), 2.45 (1 H, app t, splitting = 1.8 Hz), 2.4–1.8 (5 H, series of m), 1.38 (1 H, m), 0.97 (9 H, overlapping s and d); ^{13}C NMR δ 128.1, 127.8, 74.2, 74.1, 70.3, 70.2, 42.5, 36.3, 32.8, 30.4, 30.3, 23.3, 22.7, 19.4; IR (neat, film) 3428.9, 3310.3, 2115.2, 1470.9, 1045.5, 653.0, 626.9 cm^{-1}.

3-(*tert*-Butyldimethylsiloxy)-4,4-dimethyl-5-(5-methylcyclopentenyl)-1-pentyne (14). A solution of 0.93 g (4.8 mmol) of **13**, 0.72 g (11 mmol) of imidazole, and 0.90 g (6.0 mmol) of *tert*-butyldimethylsilyl chloride in 3 mL of DMF was heated at 30 °C for 16 h. Water (25 mL) and ether (20 mL) were added, the layers were separated, and the aqueous layer was extracted with 4 × 20 mL ether. The combined organic layers were washed with saturated aqueous NH_4Cl (3 × 30 mL), water (30 mL), and saturated aqueous NaCl (2 × 30 mL) and then dried ($MgSO_4$). Filtration and solvent evaporation gave 1.4 g of an orange liquid. Flash chromatography with petroleum ether gave 0.85 g (57%) of pure **14**: ^1H NMR δ 0.06 and 0.07 (total 3 H, two s), 0.12 and 0.13 (total 3 H, two s), 0.88 (9 H, s), 0.91 (3 H, s), 0.92 (3 H, s), 0.96 (3 H, d, J = 6.6 Hz), 1.2–2.3 (6 H, series of m), 2.35 (1 H, app t, splitting = 2.0 Hz), 2.59 (1 H, m), 4.01 (1 H, br s), 5.35 and 5.38 (total 1 H, two s); ^{13}C NMR δ 111.9, 73.5, 71.1, 70.8, 42.7, 35.7, 33.0, 30.4, 25.8, 23.0, 22.8, 19.5, −19.6; IR (neat, film) 3312.2, 1472.8, 1252.0, 1089.9, 838.2, 627.9 cm^{-1}; HR MS calcd for $C_{19}H_{34}OSi$–$(CH_3)_3C$ 249.1675, found 249.1672.

9-(*tert*-Butyldimethylsiloxy)-2,10,10-trimethyltricyclo[6.3.0.0^{1,5}]undec-7-en-6-one (15). To a solution of 0.30 g (0.98 mmol) of enyne **14** in 3 mL of heptane under a CO atmosphere was added 0.36 g (1.1 mmol) of $Co_2(CO)_8$, and the mixture was stirred under CO for 1 h. The red solution was transferred to a sealed tube and heated at 115 °C for 19 h. Approximately 5 g of Florisil was added and the heptane evaporated. The resulting purple powder was placed at the top of a Florisil column and eluted with 700 mL of petroleum ether and 700 mL of ether. Several 100-mL fractions were collected, and fractions 10–14 consisted of 0.17 g of a brown liquid containing enones **15**. Further purification by MPLC eluting with a solution of 5% ether in petroleum ether gave 24 mg of (**9-*endo*)-15a** (retention time: 33.0 min), 51 mg of (**9-*exo*)-15b** (38.4 min), and 34 mg of (**9-*exo*)-15a** (57.8 min), a total of 0.110 g (33% yield): ^1H NMR, see Table I; IR (neat, film) 1709.1 cm^{-1}; HR MS calcd for $C_{20}H_{34}O_2Si$ – $(CH_3)_3C$ 277.1623, found 277.1620.

9-(*tert*-Butyldimethylsiloxy)-2,10,10-trimethyltricyclo[6.3.0.0^{1,5}]undecan-6-one (16).[8c] Approximately 25 mL of NH_3 was condensed over a small piece of lithium and then redistilled onto 40 mg (5.7 mmol) of lithium. Enone **15** (71 mg, 0.22 mmol) and 0.03 mL (0.74 mmol) of methanol were dissolved in 1 mL of ether and added to the NH_3 solution. The reaction was stirred at −33 °C for 1 h, 2 mL of methanol added, and the NH_3 allowed to evaporate. Saturated aqueous NH_4Cl (10 mL) was added to the yellow residue and the mixture extracted with 4 × 5 mL ether. The combined extracts were washed with 2 × 10 mL of saturated aqueous NH_4Cl and 10 mL of saturated aqueous NaCl. The ether solution was then dried ($MgSO_4$), filtered, and evaporated giving an oil which was purified by MPLC, eluting with a solution of 5% ether in petroleum ether to give 44 mg (59%) of ketones **16** (retention times for (**9-*exo*)-16a** and (**9-*endo*)-16a**: 9.6 min; for (**9-*exo*)-16b**: 12.8 min). The ethyl acetate wash of the column contained 9.7 mg of enone **12a**, corresponding to 22% of the starting material: ^1H NMR of **16**, see Table II; ^{13}C NMR (**9-*exo*)-16a** δ 86.9, 62.7, 48.3, 43.6, 42.8, 41.6, 34.0, 28.7, 26.2, 25.9, 22.4, 14.5, −3.8, −4.2; (**9-*endo*)-16a** δ 192.2, 82.5, 63.6, 52.0, 46.7, 43.0, 41.2, 34.5, 30.8, 29.3, 26.5, 23.0, 13.9, −3.8, −4.2; (**9-*exo*)-16b** δ 82.5, 63.0, 47.1, 44.2, 43.7, 38.4, 34.2, 28.5, 26.0, 24.4, 14.5, −4.1; IR (neat, film) 1736.2 cm^{-1}. Anal. Calcd for $C_{20}H_{36}O_2Si$: 71.37 C, 10.78 H. Found: 71.41 C, 10.84 H.

5-Methyl-1-(tri-*n*-butylstannyl)cyclopentene (19). To a THF solution of **6** prepared as described earlier from 9.0 g (24 mmol) of trisyl hydrazone at −78 °C was added 6.8 mL (24 mmol) of tri-*n*-butyltin chloride. The reaction was allowed to warm to rt, stirred overnight, and quenched with 4 mL of water and the THF removed by rotary evaporation. The solid white residue was dissolved in 130 mL of water and 100 mL of hexane, and the layers were separated. The water was extracted with 5 × 50 mL of hexane. The extracts were washed with 3 × 60 mL of aqueous $CuSO_4$ and 2 × 60 mL of saturated aqueous NaCl. Drying ($MgSO_4$) and solvent evaporation gave 11.9 g of a purple liquid which was chromatographed on silica, eluting with hexane, to give 6.5 g (73%) of **19**: ^1H NMR δ 5.81 (1 H, s), 2.78 (1 H, m), 2.32 (2 H, m), 2.01 (1 H, m), 1.6–1.1 (19 H, series of m), 1.00 (3 H, d, J = 6.9 Hz), 0.88 (9 H, t, J = 7.3 Hz); ^{13}C NMR δ 140.3, 46.2, 34.0, 32.5, 29.3, 27.5, 21.9, 13.7, 9.5.

1-Iodo-5-methylcyclopentene (20). To a solution of 2.3 g (6.2 mmol) of **19** in 40 mL of ether at 0 °C was added dropwise a solution of 1.9 g (7.4 mmol) of iodine dissolved in 50 mL of ether. The reaction was stirred overnight and then washed twice with 50 mL of aqueous $NaHSO_3$, 3 × 30 mL of aqueous KF, and 2 × 50 mL of saturated aqueous NaCl. After drying ($MgSO_4$) and solvent evaporation, 2.2 g of a product was obtained whose ^1H NMR spectrum showed no starting material but considerable tin-containing side products. Kugelrohr distillation (85–100 °C/20 mmHg) yielded 0.9 g (69%) of pure iodide: ^1H NMR δ 6.04 (1 H, s), 2.75 (1 H, m), 2.26 (2 H, m), 2.10 (1 H, m), 1.52 (1 H, m), 1.02 (3 H, d, J = 6.9 Hz).

1-(5-Methylcyclopentenyl)-5-(trimethylsilyl)-1,4-pentadiyne (21). To a solution of 2.0 g (9.6 mmol) of **20** in 5 mL of benzene was added 0.44 g (0.38 mmol) of tetrakis(triphenylphosphine)palladium(0) followed by 0.95 mL (12 mmol) of propylamine. The mixture was stirred at rt for 30 min. 1-(Trimethylsilyl)-1,4-pentadiyne (2.6 g, 19 mmol) was added to the reaction mixture followed by 0.81 g (4.3 mmol) of cuprous iodide, and the reaction was heated for 17 h at 35 °C. The gray solids were filtered off and washed with hexane, 5 mL of silica was added to the filtrate, and the solvents were evaporated. The resulting brown powder was put at the top of a silica column and eluted with hexane to give 1.9 g (90%) of **21**: ^1H NMR δ 5.95 (1 H, s), 3.34 (2 H, s), 2.70 (1 H, m), 2.32 (2 H, m), 2.08 (1 H, m), 1.40 (1

H, m) 1.08 (3 H, d, J = 7.5 Hz), 0.13 (9 H, s); ^{13}C NMR δ 136.5, 100.0, 85.0, 84.9, 42.7, 32.1, 31.8, 19.7, 11.7, −0.1; IR (neat, film) 2183, 1454, 1408, 844 cm^{-1}.

(*Z*)-1-(5-Methylcyclopentenyl)-1-penten-4-yne (18). A mixture of 0.12 g (0.56 mmol) of **21**, 0.02 g of Lindlar catalyst, 0.01 g of quinoline, and 2 mL of heptane was placed in a flask and attached to a hydrogenation apparatus. The system was flushed three times with hydrogen, filled again with hydrogen, and sealed. Measurable uptake of hydrogen ceased after 3 h at 759 mmHg and 22 °C. The catalyst was filtered off and washed with hexane, and the solvents were evaporated, giving 0.15 g of crude material. Chromatography on silica, eluting with hexane, gave 0.088 g (73%) of impure silylated dienyne, which was used directly in the next step: ^{1}H NMR δ 5.87 (1 H, d, J = 11.4 Hz), 5.60 (1 H, s), 5.52 (1 H, d of t, J = 11.4, 6.9 Hz), 3.13 (2 H, d, J = 6.9 Hz), 2.70 (1 H, m), 2.22 (3 H, series of m), 1.41 (1 H, m), 0.99 (3 H, d, J = 6.6 Hz), 0.13 (9 H, s). This material contained a small amount of the triene overreduction product: ^{1}H NMR δ 6.28 (1 H, d of t, J = 13.9, 7.1 Hz), 5.84 (1 H, d, J = 11.7 Hz), 5.58 (1 H, s), 5.52 (1 H, d of t, J = 13.9, 1.2 Hz), 5.43 (1 H, d of t, J = 11.7, 7.0 Hz), 3.06 (2 H, d of t, J = 1.2, 7.0 Hz), 2.71 (1 H, m), 2.35 (2 H, m), 2.09 (1 H, m), 1.45 (1 H, m), 1.01 (3 H, d, J = 7.2 Hz), 0.11 (9 H, s).

To a solution of 1.3 g (13.8 mmol) of potassium fluoride dihydrate in 8 mL of DMF was added 0.20 g (0.92 mmol) of impure dienyne dissolved in 2 mL of DMF. After being stirred for 3.5 h, the reaction mixture was poured into 30 mL of 1 M HCl and extracted with 5 × 15 mL ether. The extracts were washed with 3 × 50 mL of water and 2 × 50 mL of saturated aqueous NaCl. Drying ($MgSO_4$), filtration, and solvent evaporation gave 0.16 g of crude product that was further purified by MPLC with hexane to yield 0.053 g (41%) of **18**: ^{1}H NMR δ 5.89 (1 H, d, J = 11.2 Hz), 5.63 (1 H, s), 5.53 (1 H, d of t, J = 11.2, 7.0 Hz), 3.06 (2 H, d of t, J = 2.0, 7.0 Hz), 2.71 (1 H, m), 2.5–2.0 (3 H, series of m), 1.98 (1 H, t, J = 2.5 Hz), 1.43 (1 H, m), 0.99 (3 H, d, J = 6.9 Hz); ^{13}C NMR δ 129.7, 126.2, 125.5, 92.8, 68.0, 42.0, 32.3, 31.3, 19.9, 18.8; IR 3310, 2120, 631 cm^{-1}.

α-Bromostyrene by Bromoboration of Phenylacetylene Using Dibromoborane.[48] To a solution of 0.07 g (0.7 mmol) of phenylacetylene in 2 mL of 1,2-dichloroethane at 0 °C was added 0.7 mL (1 M in CH_2Cl_2, 0.7 mmol) of dibromoborane–methyl sulfide complex. The reaction was stirred for 20 min at 0 °C and 30 min at rt. Glacial acetic acid (0.2 mL) was added and the mixture refluxed for 2.5 h. The reaction was cooled in an ice bath, and 2 mL of 2.5 M sodium hydroxide solution was added. The mixture was dissolved in 3 mL of water and extracted with 3 × 5 mL of hexane. The combined hexane layers were washed with 2 × 10 mL of saturated aqueous $NHCl_4$ and 10 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Filtration and solvent evaporation gave 0.10 g of yellow liquid. The NMR spectrum of this crude product showed no phenylacetylene and no styrene: ^{1}H NMR δ 7.57 (2 H, m), 7.32 (3 H, m), 6.10 (1 H, d, J = 2.0 Hz), 5.77 (1 H, d, J = 2.0 Hz). Low-resolution GC/MS showed only one major product of this reaction: base peak m/e 103 (loss of Br); other peaks at m/z 182 and 184 (M^+), 77, 63, and 51.

Representative Attempted Synthesis of 2-Methyltricyclo[6.3.0.0^{1,5}]undeca-7,10-dien-6-one (17). A mixture of 0.11 g (0.75 mmol) of dienyne **18** and 0.25 g (0.75 mmol) of $Co_2(CO)_8$ in 5 mL of heptane was stirred under CO for 1 h. The mixture was transferred to a sealed tube and heated at 115 °C for 18 h. After the reaction had cooled, 10 mL of Florisil was added and the solvents were evaporated. The purple solids were loaded onto a Florisil column and eluted with 300 mL of hexane, 450 mL of ether, and 200 mL of ethyl acetate, collecting 50-mL fractions. None of these fractions had NMR spectra displaying any vinyl protons although some did have peaks in the aromatic region. No carbonyl signals were observed in any of the IR spectra of these fractions.

Acknowledgment. We thank the National Institutes of Health (Grant GM26294) and the Chevron Research Corporation for financial support of this research. This material is based upon work supported under a National Science Foundation Graduate Fellowship to E.G.R. We also express our appreciation to Professors E. Piers and T. Hudlicky for supplying copies of spectra and to Professors R. Caple and W. Smit for providing results prior to publication.

Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra of compounds lacking elemental analysis data (17 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(48) (a) Hanzlick, R. P.; Hilbert, J. M. *J. Org. Chem.* **1978**, *43*, 610. (b) Hara, S.; Dojo, H.; Takinami, S.; Szuki, A. *Tetrahedron Lett.* **1983**, *24*, 731.

Spongian Pentacyclic Diterpenes. Stereoselective Synthesis of (−)-Dendrillol-1

Antonio Abad,* Manuel Arnó,* Ana C. Cuñat, M. Luisa Marín, and Ramón J. Zaragozá

Departamento de Química Orgánica, Universidad de Valencia, Dr. Moliner 50, 46100-Burjasot, Valencia, Spain

Received June 22, 1992

A formal total synthesis of the spongian diterpene (−)-dendrillol-1 (**3**), through a consice approach that could be used for the synthesis of other pentacyclic spongian diterpenes, is reported. The synthesis is based on the intramolecular acetalization of an acid–dialdehyde **4**, which is prepared from (+)-podocarp-8(14)-en-13-one (**5**) via a sequence of transformations involving (a) introduction of a latent dialdehyde unit on **5** by photochemical reaction with acetylene, (b) reductive carboxylation at C-13 of photoadduct **6** to obtain acid **18**, and (c) elaboration of the dialdehyde moiety at C-8 and C-14 of **18** by ozonolysis. Several procedures that have been examined for the reductive carboxylation at C-13 of **6** are described. A simple three-step procedure to effect the conversion of a podocarp-8-en-13-one system into a C-17-functionalized beyerane compound is also reported.

Introduction

A family of diterpenes sharing the hypothetical spongian carbon skeleton (**1**) have been reported from various marine organisms.[1] In recent years, a small group of novel spongian pentacyclic terpenoids have been isolated from various marine sponges[2] and nudibranches.[3] These compounds have a common skeleton represented by **2** with

(1) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 251; **1984**, *1*, 551; **1986**, *3*, 1; **1987**, *4*, 539; **1988**, *5*, 613; **1990**, *7*, 269; **1991**, *8*, 97.

(2) (a) Molinski, T. F.; Faulkner, D. J. *J. Org. Chem.* **1986**, *51*, 1144. (b) Schmitz, F. J.; Chang, J. S.; Hossain, M. B.; van der Helm, D. *J. Org. Chem.* **1985**, *50*, 2862. (c) Karuso, P.; Taylor, W. C. *Aust. J. Chem.* **1986**, *39*, 1629. (d) Karuso, P.; Bergquist, P. R.; Cambie, R. C.; Buckleton, J. S.; Clark, G. R.; Rickard, C. E. F. *Aust. J. Chem.* **1986**, *39*, 1643. (e) Gunasekera, S. P.; Schmitz, F. J. *J. Org. Chem.* **1991**, *56*, 1250.

0022-3263/92/1957-6861$03.00/0