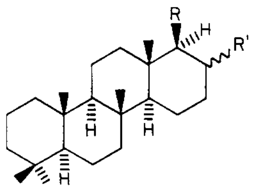
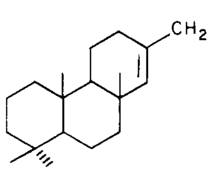
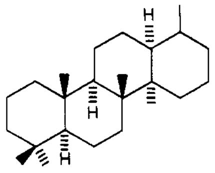


9a, R = R' = Me
b, R = Me; R' = H
c, R = H; R' = Me



A



10

skeleton different from that attributed to it. The absence of peaks in the range between the M–CH_3 ion and m/z 206 is reminiscent of the mass spectral behavior of hopanes[27b] and, in fact, the MS of the $C_{24}H_{42}$ hydrocarbon is essentially identical with that of a C_{24} secohopane **10** recently synthesized by Albrecht and co-workers[26c] and shown to be the lowest member of a C_{24}–C_{27} series occurring in sediments and petroleums.

Acknowledgment. This study was supported in part by a National Science Foundation Grant (CHE-7801 191).

Supplementary Material Available: Experimental details on synthesis and ^{1}H NMR and mass spectra of all new compounds described in this work (11 pages). A table listing the ^{13}C NMR spectra of **2a,b**, **3a,b**, **5**, and (*Z*)-**5**, **6a,b,e,f** and **7** is included. Ordering information is given on any current masthead page.

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(29) A copy of the computer-generated GC/MS of the $C_{24}H_{42}$ hydrocarbon kindly sent to us by Dr. Whitehurst had peaks at m/z (relative intensities approximate) 330 (10), 315 (10), 274 (1), 251 (1), 206 (12), 191 (68), 177 (38), 163 (8), 150 (23), 137 (25), 136 (28), 123 (42), 109 (78), 97 (100), 95 (59), 81 (49), 69 (21), and 67 (18). For the MS of **10**, see ref 26c.

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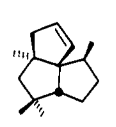
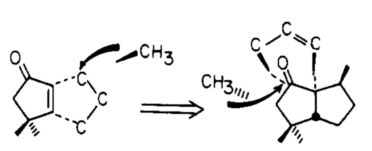
Total Synthesis of Racemic Silphinene

Summary: The tricyclic sesquiterpene silphinene (**1**) has been synthesized in fully stereocontrolled fashion from 4,4-dimethylcyclopentenone by a twofold five-ring annulation sequence in 15 steps and 10% overall yield.

Sir: Highly condensed polycyclopentanoid (polyquinane[2]) natural products have come to represent an increasingly important class of natural products. Considerable interest has been paid to the total synthesis of these substances because of their appealing and frequently intricate molecular architecture which has often mandated the development of new strategies. One of the more recent additions to this class is silphinene (**1**), a sesquiterpene hydrocarbon isolated in 1980 by Bohlmann and Jakupovic from *Silphium perfoliatum.*[3] The structural assignment to **1** was based on its ^{1}H NMR spectrum and those of select oxidation products. Central to the derived formula is a tricyclo[$6.3.0.0^{4,8}$]undecene ring system possessing four logistically placed methyl groups. As such, silphinene is recognizable as a congener of isocomene[4,5] and pentalenene[6] whose directed syntheses we have completed earlier. Importantly, however, the unique stereodisposition of the double bond and pendant alkyl groups within **1** necessitates the implementation of an entirely different protocol. In this connection, we have now developed a short and notably efficient synthetic approach to **1** that fully confirms its assigned structure.



1



2 3

From the retrosynthetic perspective, we viewed **1** to be potentially accessible from 4,4-dimethylcyclopentenone (**2**).[7] Insertion of a three-carbon chain across the double bond was first to be implemented in a manner that would ultimately permit stereochemically clean introduction of a secondary β-methyl substituent. Judicious selection of functional groups was required, since the first cyclopentannulation was to be followed by a second to establish the tricyclic skeleton (see **3**). Because the latter ring-forming maneuver installs both an endocyclic olefinic center and angular α-methyl group, it appears to have different requirements from the first. Nevertheless, we anticipated the possibility of exploiting similar high-yielding aldol condensations in both contexts to achieve the needed stereo- and regiochemical control.

Central to the overall scheme is the ready availability of the Grignard reagent derived from 2-(2-bromoethyl)-1,3-dioxane[8] and the efficiency with which this reactive intermediate undergoes CuBr·Me_2S-promoted conjugate addition to α,β-unsaturated enones.[9] Following admixture of these reagents with **2** in THF at −78 °C, the product was directly hydrolyzed (HCl, H_2O, THF) to give **4** (78%).[10] Since spontaneous dehydration is not encountered in β-hydroxy ketones of this type, conversion to **5** required formation of the mesylate and elimination with DBU in CH_2Cl_2 (76%; Scheme I).

Consideration was next given to the desirability of introducing the angular methyl group while simultaneously setting the stage for the second cyclopentannulation. To this end, **5** was treated with methyllithium and the tertiary allylic alcohol so formed was directly oxidized with PCC and Celite in CH_2Cl_2.[11] With the isolation of **6**, the feasibility of interring allylic rearrangement–oxidation was demonstrated for the first time.[12] Although the tertiary

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(1) National Institutes of Health Postdoctoral Fellow, 1981–1982.

(2) Paquette, L. A. *Forschr. Chem. Forsch.* **1979**, *79*, 41.

(3) Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259.

(4) Paquette, L. A.; Han, Y. K. *J. Org. Chem.* **1979**, *44*, 4014; *J. Am. Chem. Soc.* **1981**, *103*, 1835.

(5) For additional isocomene syntheses, see: (a) Oppolzer, W.; Bättig, K.; Hudlicky, T. *Helv. Chim. Acta* **1979**, *62*, 1493; *Tetrahedron*, **1981**, *37*, 4359. (b) Pirrung, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 7130; **1981**, *103*, 82. (c) Dauben, W. G.; Walker, D. M. *J. Org. Chem.* **1981**, *46*, 1103.

(6) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4504.

(7) Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, *10*, 273.

(8) Stowell, J. C. *J. Org. Chem.* **1976**, *41*, 560.

(9) For the earliest report of conjugate addition reactions of the related dioxolane, see Marfat, A.; Helquist, P. *Tetrahedron Lett.* **1978**, 4217.

(10) (a) Each new compound exhibits infrared and ^{1}H NMR spectra (90, 200, or 300 MHz) fully compatible with its assignment. Analytical samples gave satisfactory C/H combustion analysis and/or appropriate high-resolution mass spectral parent ions. (b) All yields recorded herein are based upon isolated materials which exhibit one spot on TLC (>95% purity).

(11) Boeckman, R. K., Jr., personal communication.

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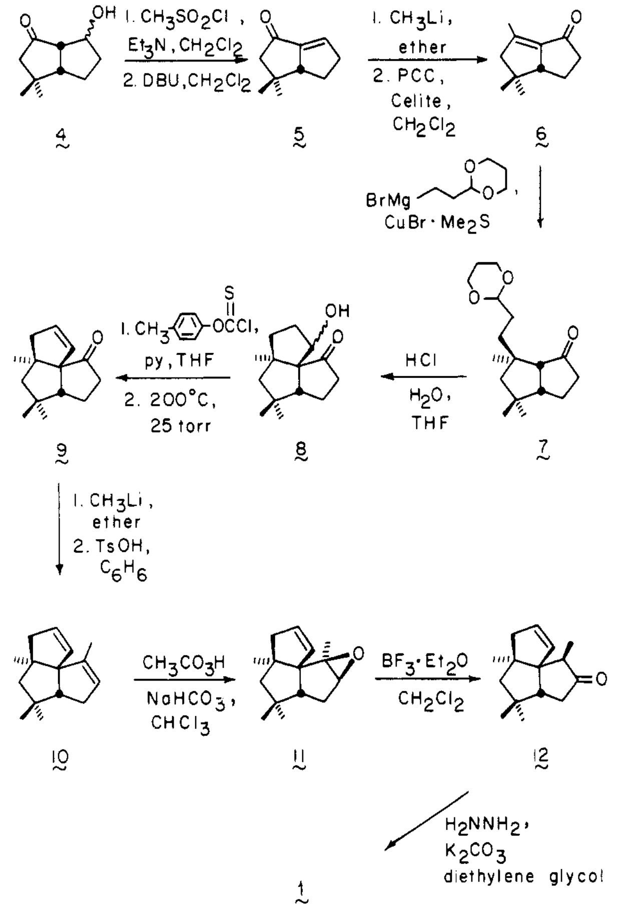
Scheme I



hydrogen in **6** is the only stereochemical anchor in the molecule, it as usual proved adequate to direct clean entry of the cuprate reagent from the β face. Following the isolation of **6** (68%), its exposure to aqueous acid afforded in turn the tricyclic hydroxy ketone **8** (71%).

With ample quantities of **8** in hand, dehydration of this intermediate was next broached. The more customary conditions for effecting elimination of water could not be implemented here because of ready retroaldolization. To our delight, however, condensation of **8** with 4-methylphenyl thiochloroformate in dry pyridine led quantitatively to the thiocarbonate ester whose pyrolysis at 200 °C and 25 torr delivered **9** with preservation of the tricyclic framework (84%).[13]

Following arrival at **9**, stereocontrolled introduction of a secondary β-methyl group was undertaken. Ample precedent exists to suggest that any scheme involving catalytic hydrogenation would generate the α isomer predominantly if not exclusively.[4,5] Such methodology had, therefore, to be avoided for this reason and because the second lesser substituted double bond had to be preserved. On the other hand, no difficulty in the form of structural isomerization was encountered during acid-catalyzed dehydration of the tertiary alcohol produced by methyllithium addition to **9**. When diene **10** (73%) was in turn subjected to the action of buffered peracetic acid (1 equiv) in CHCl$_3$ at 0 °C, the β-epoxide **11** was obtained exclusively (100%). Evidently, the reactivity of the trisubstituted double bond in **10** is sufficiently heightened to be the sole detectable site of electrophilic attack.[14]

Exposure of **11** to BF$_3$·Et$_2$O in C$_6$H$_6$ at room temperature overnight[15] resulted in stereospecific rearrangement to **12** (95%), with the secondary methyl group occupying the thermodynamically more stable quasi-equatorial position. Epimer contamination was also not encountered during the ensuing Wolff–Kishner reduction of **12** with potassium carbonate and hydrazine hydrate in hot diethylene glycol.[16] Following isolation of the resulting hydrocarbon (83%) by preparative VPC, its spectra proved identical with those of natural silphinene.[17]

In summary, the first total synthesis of silphinene has been achieved in a fully stereocontrolled manner from **2** in 15 steps and 10% overall yield. The carbon skeleton **1** is developed by twofold conjugate addition of a functionalized organocopper reagent and subsequent aldol cyclization. In addition to highlighting the utility and efficiency of this methodology for polyquinane construction, the route also provides a practical solution to the ready introduction of vicinal quaternary carbon centers onto polycyclic frameworks.[18]

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(12) For earlier precedent, consult the following: (a) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682. (b) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1980**, *64*, 104 and relevant references cited therein.

(13) Gerlach, H.; Huong, T. T.; Müller, W. *J. Chem. Soc., Chem. Commun.* **1972**, 1215.

(14) Eletti-Bianchi, G.; Centini, F.; Re, L. *J. Org. Chem.* **1976**, *41*, 1648.

(15) (a) Schostarez, H.; Paquette, L. A. *Terahedron* **1981**, *37*, 4431; *J. Am. Chem. Soc.* **1981**, *103*, 722. (b) Henbest, H. B.; Wrigley, T. I. *J. Chem. Soc.* **1957**, 4765.

(16) Hansen, H.-J.; Sliwka, H.-R.; Hug, W. *Helv. Chim. Acta* **1979**, *62*, 1120.

(17) Copies of these spectra were kindly provided to us by Professor Bohlmann whom we thank.

(18) This research was generously financed by the National Institutes of Health (Grant GM-28468) to whom we are indebted.

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Micelle-Induced Chemoselectivity: A Probe for Sites of Solubilization and Water Penetration

Summary: The potential and limitations of micellar differentiation between reactive sites in a molecule are delineated and then related to questions of micelle structure and sites for solubilization.

Sir: As part of our study of micelle-induced selective chemistry, we have previously demonstrated the ability of anionic micelles to promote both the selective monomercuration of nonconjugated dienes and the micelle-enhanced transformation of dienes into cyclic ethers.[1] Both of these observations were attributed to the anisotropic solubilization of an initially formed alkylmercurial in a relatively water-poor environment. The work we report herein further elucidates the requirements for reaction-site selectivity in terms of substrate structure and demonstrates that this selectivity is a new diagnostic for substrate solubilization that may help interpret data bearing on the question of water penetration into micellar aggregates.

In earlier work[1] we used 1 equiv of Hg(OAc)$_2$ in sodium lauryl sulfate (SLS) micelles to bring about the monofunctionalization of limonene (I) and 4-vinylcyclohexene

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(1) Link, C. M.; Jansen, D. K.; Sukenik, C. N. *J. Am. Chem. Soc.* **1980**, *102*, 7798.

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