

span a phospholipid bilayer and are well suited for transmembrane electron transfer in artificial photosynthetic membranes. In fact, porphyrin-based triads have been found to demonstrate photo-driven transmembrane electron transfer.⁶ The chlorophyll-based triads have a much larger effective absorption cross section due to the efficient singlet energy transfer and the greatly increased oscillator strength in the Q-bands and therefore are potentially much more effective in model photosynthetic systems.

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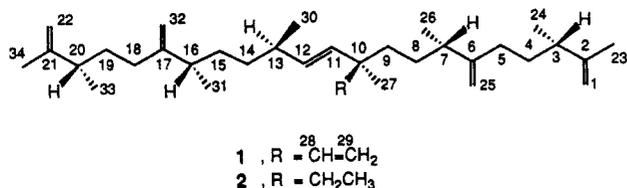
Absolute Configuration of (-)-Botryococcene

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The green alga *Botryococcus braunii* (Kützing) is found throughout the world under a wide range of climatic conditions.¹ The unusual morphology and composition of this organism has been investigated and its involvement in the formation of a variety of carboniferous deposits, including petroleum, has been postulated.² Of particular chemical interest is the finding that *B. braunii* produces a mixture of C₃₀-C₃₆ hydrocarbons of terpenoid origin that constitutes up to 90% of the dry weight of the alga.³ The major component of this mixture, botryococcene, was shown by Eglinton et al. through degradation and spectral analysis to possess the gross structure depicted in 1.⁴ Our interest in the

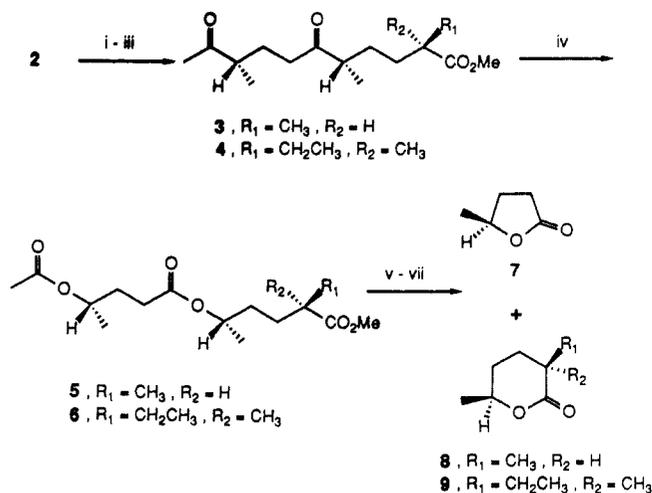


total synthesis of 1, as well as the biosynthetic events leading to incorporation of the four non-mevalonoid methyl groups and the unusual coupling of the farnesyl moieties, required that we establish the configuration of the six stereogenic centers in the molecule. We now report that the absolute configuration of botryococcene is 3*S*,7*S*,10*S*,13*R*,16*S*,20*S*.

Selective reduction of botryococcene (1) with diimide afforded the known dihydro derivative 2⁴ which, upon exhaustive ozonolysis followed by an oxidative workup and treatment with diazomethane, gave 3 and 4. After chromatographic separation, these diketone esters were each subjected to Baeyer-Villiger oxidation to furnish triesters 5 and 6, respectively. Saponification of 5, followed by acidification, afforded a pair of hydroxy acids which were converted to a 1:1 mixture of γ - and δ -lactones 7 and 8. Similar treatment of 6 yielded 7 and the δ -lactone 9 (Scheme I).

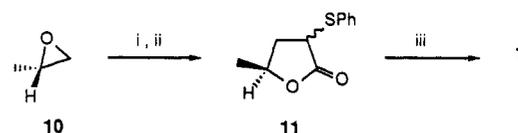
The absolute configurations of 7-9 were determined by correlation with the optically pure substances synthesized from (*S*)-(-)-propylene oxide (10).⁵ Thus, opening of 10 with the dilithio dianion of 2-thiophenoxyacetic acid,⁶ followed by lac-

Scheme I^a



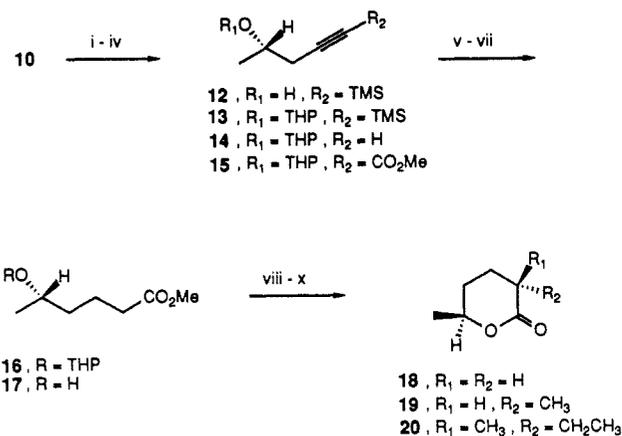
^a (i) O₃, CH₂Cl₂/MeOH/EtOAc (10:5:1), -78 °C; (ii) CrO₃, H₂S-O₄, Me₂CO, 0 °C, 2 h; (iii) CH₂N₂, Et₂O, 25 °C (3, 38%; 4, 40% from 2); (iv) mCPBA, NaHCO₃, CH₂Cl₂, 25 °C, 5 days then Δ , 24 h (5, 64%; 6, 83%); (v) KOH, aqueous THF, 25 °C, 24 h; (vi) aqueous HCl; (vii) C₆H₆, 4- Å sieves, Δ , 3 h, (7,8 1:1), 80%; 7,9 (1:1), 86% from 5 and 6, respectively).

Scheme II^a



^a (i) PhSCH₂CO₂H, 2 equiv of LDA, THF, -78 °C; (ii) C₆H₆, *p*-TsOH, Δ (80% from 10); (iii) Raney nickel (W6), MeOH, Δ , 6 h (78%).

Scheme III^a



^a (i) Me₃SiC \equiv CH, *n*-BuLi, THF, -78 °C, 6 h (97%); (ii) DHP, *p*-TsOH, CH₂Cl₂, 25 °C, 3 h (90%); (iii) *n*-Bu₄NF, THF, 25 °C, 1 h (78%); (iv) *n*-BuLi, ClCO₂Me, THF, -78 \rightarrow 25 °C, 2 h (92%); (v) H₂, 10% Pd/C, EtOAc, 25 °C (97%); (vi) *p*-TsOH, MeOH, 40 °C, 1.5 h; (vii) K₂CO₃, azeotropic removal of MeOH with C₆H₆, 25 °C; (viii) *P*-TsOH, C₆H₆, 4- Å sieves, Δ , 2 h (78% from 16); (ix) LDA, MeI, THF, HMPA, -78 \rightarrow -40 °C, 4 h (92%); (x) LDA, EtI, THF, HMPA, -78 \rightarrow -40 °C, 4 h (87%).

tonization, gave 11 which was desulfurized with Raney nickel to yield (4*S*)-7 (Scheme II).⁷ For synthesis of the δ -lactones 8 and 9, (*S*)-propylene oxide was reacted with lithium trimethylsilylacetylide to afford 12 which was converted to its tetrahydropyranyl

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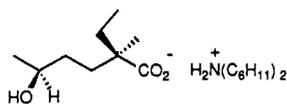
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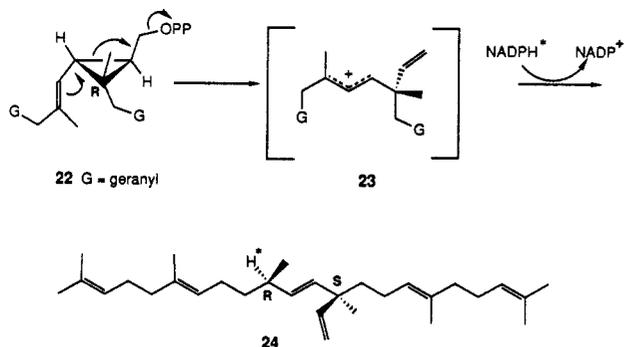
ether **13**. Removal of the silyl group and carbomethoxylation of the resulting pentyne **14** gave **15**. This ester was hydrogenated to the saturated derivative **16**, from which the tetrahydropyranyl ether was removed by methanolysis and the crude hydroxy ester **17** lactonized to (5*S*)-**18**.⁸ Methylation⁹ of **18** gave **8** and **19** (3:2, respectively), which were separated by gas-liquid chromatography and identified by comparison of their ¹H NMR spectra with published data.¹⁰ Alkylation of the mixture of **8** and **19** with ethyl iodide gave the 2*R*,5*S* and 2*S*,5*S* lactones **9** and **20** (3:1) which were separated by HPLC (μ -Porasil) (Scheme III). The major diastereomer **9** was found to correspond with the lactone obtained from botryococcene and was shown to be trans by an X-ray crystal structure of the dicyclohexylamine salt, **21**, of the derived hydroxy acid.¹¹



21

A parallel series of transformations from (*R*)-(+)-propylene oxide¹² provided the enantiomers of **7-9**. The absolute configurations of the lactones obtained from botryococcene were then determined from the ¹H NMR spectra (400 MHz) of 1:1 mixtures of natural and synthetic lactones in the presence of tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) [Eu(hfc)₃].¹³ Progressive induced shifts of the methyl signals were observed with increasing Eu(hfc)₃ concentration for unmatched lactones.

The absolute configuration of botryococcene has important biogenetic implications. Taken with the incorporation studies of Casadevall¹⁴ and Wolf,¹⁵ our results show that the four non-mevalonoid methyl substituents are installed sequentially at the *si* face of the trisubstituted double bonds of the intact triterpenoid precursor. Further, the 10*S*,13*R* configuration of **1** is consistent with a biosynthesis via (*R,R,R*)-presqualene pyrophosphate (**22**) but deviates from the pathway to squalene in the subsequent collapse of **22** to **23**. This variant, which has precedent in the chemistry of monoterpenes containing an "irregular" linkage of isoprene units,¹⁶ would be terminated by delivery of a hydrogen atom (presumably from NADPH) to C-13 from the *si* face of the allylic system.



22 G = geranyl

23

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Supplementary Material Available: Spectral data for compounds **1-21** (7 pages). Ordering information is given on any current masthead page.

Facile Cyclization of the Valeronitrile Group Bound to a Nickel Macrocycle

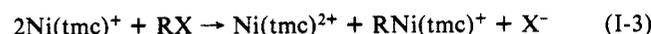
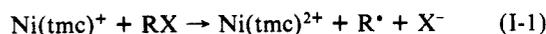
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The formation of cyclic alkyl products in reactions of transition-metal complexes with linear cyclizable alkyl halides has been considered reliable evidence for the involvement of free radicals in these reactions.¹⁻⁹ The underlying assumption that the products were determined exclusively by the competition between radical cyclization and capture by the metal seems to have been correct in the work reported. On the other hand, several literature reports provide undeniable evidence of cyclizations/rearrangements of carbanions^{10,11} and organometallic complexes in aprotic solvents.¹²⁻¹⁹ Thus the formation of cyclic products from linear cyclizable precursors does not constitute sufficient evidence for the involvement of free radicals in a reaction.²⁰

Scheme I



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 (22) The complex is [(1*R*,4*R*,8*S*,11*S*)-1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane]nickel. Under the reaction conditions (pH ~ 12) the nickel(II) complex is a mixture of aquo and hydroxo species [pK_a 11.93; Herron, N.; Moore, P. *Inorg. Chim. Acta* **1979**, *36*, 89]; for simplicity it is referred to as Ni(tmc)²⁺ throughout.