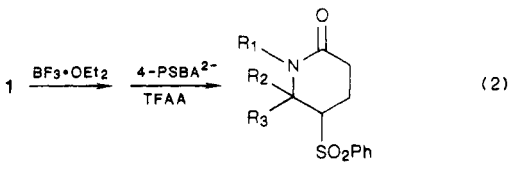
Table I. Boron Trifluoride Promoted Addition of 2 to Imines



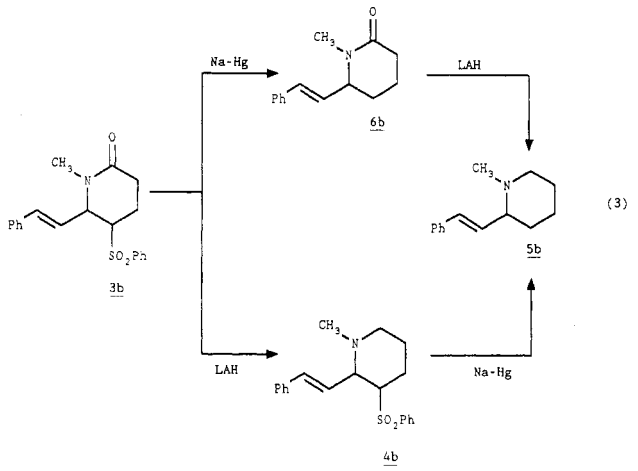
(2)

3a-f

entry	R_1	R_2	R_3	yield,[a] %	mp, °C
3a	*n*-Pr	*n*-Pr	H	70	150
3b	CH_3	PhCH=CH	H	82	116
3c	CH_3	Ph	H	90	155
3d	$PhCH_2$	*n*-Pr	H	66	124–5
3e	$PhCH_2$	$-(CH_2)_5-$		78	187
3f	CH_3	citryl[b]	H	85	136

[a] Isolated yields. [b] Citryl = $(CH_3)_2C{=}CHCH_2CH_2(CH_3)C{=}CH$.

present, there is scant information available on β-amido or β-amino sulfone eliminations, but it is reasonable to assume that lactams **3a–f** could be cleaved by this process. We examined both possibilities with the 6-cinnamyl lactam **3b** (eq 3) as this allylic system should be most sensitive



(3)

to the reaction conditions.[10d] Prior reduction of lactam **3b** to piperidine **4b** with LAH[11] and subsequent treatment with 6% sodium amalgam in methanol[12] afforded a 60% overall yield of desulfonylated product **5b**.[13] More interestingly, direct desulfonylation[10a] of the lactam **3b** yields 2-piperidone **6b** (93%). Treatment with LAH converted the lactam to piperidine **5b** (71%), suggesting this methodology will accommodate a wide variety of structural manipulation without ring scission.[14] The trans geometry of the olefin was preserved in all transformations. Further structural evidence was provided by conversion of lactam **3c** (Na–Hg then LAH; 55% overall) into the known 1-methyl-2-phenylpiperidine.[15]

The efficiency of this process and the ready availability of imines promises to provide a facile route to piperidine-containing natural products. We are currently examining this aspect and extension to chiral substrates.

Acknowledgment. We wish to thank Loyola University of Chicago for the purchase of the Varian 300-MHz NMR instrument used in this study. D.L.C.G. wishes to thank the Graduate School and R.K. wishes to thank Baxter Healthcare Corporation for financial support.

Supplementary Material Available: NMR spectral data for compounds **3a–f**, **4**, **5**, and **6** are available (10 pages). Ordering information is given on any current masthead page.

(10) (a) Julia, M.; Paris, M.-J. *Tetrahedron Lett.* **1973**, 4833. (b) Kocienski, P.; Lythgoe, B.; Ruston, S. *J. Chem. Soc. Perkin Trans. 1* **1978**, 829. (c) Kocienski, P. J.; Lythgoe, B.; Waterhouse, I. *J. Chem. Soc. Perkin Trans. 1* **1980**, 1045. (d) Kocienski, P. *Phosphorus Sulfur* **1985**, *24*, 97 and references therein.

(11) (a) Moffett, R. B.; White, L. *J. Org. Chem.* **1952**, *17*, 407. (b) Micovic, V. M.; Mihailovic, M. L. *J. Org. Chem.* **1953**, *18*, 1190. (c) Schopf, C.; Wust, W. *Justus Liebigs Ann. Chem.* **1959**, *626*, 153. (d) Uffer, A.; Schlitter, E. *Helv. Chim. Acta* **1948**, *31*, 1397.

(12) (a) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477. (b) The conditions employed for the reductive removal of sulfone group on the lactam did not use NaH_2PO_4 as a heterogeneous scavenger of base.

(13) (a) Compound **5b**: bp 92 °C (0.3 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25–1.3 (m, 1 H), 1.48 (dq, *J* = 3.5, 1 H), 1.56–1.65 (m, 3 H), 1.70–1.75 (m, 1 H), 1.99 (dt, *J* = 4 and 11.3, 1 H), 2.21 (s, 3 H), 2.44 (dt, *J* = 3 and 8, 1 H), 2.88 (d, *J* = 8, 1 H), 6.12 (dd, *J* = 16 and 9, 1 H), 6.45 (d, *J* = 16, 1 H), 7.15–7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 23.9, 26.0, 33.5, 44.6, 56.5, 68.0, 126.2, 127.2, 128.5, 130.5, 133.7, 137.2. Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.43; H, 9.69; N, 6.89. (b) Hasiak, B. *Bull. Soc. Chim. Fr.* **1976**, *9–10*, 1526.

(14) 5-Phenylsulfonyl lactam **3b** (1 mmol) was dissolved in 5 mL of dry methanol and chilled to 0 °C; 6% Na–Hg amalgam (finely crushed) was added portionwise with vigorous stirring over 0.25 h. After an additional 0.25 h of mixing, the reaction mixture was filtered through Celite, diluted with ether, extracted, and dried. Compound **6b**: bp 166 °C (0.3 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.78–2.04 (m, 4 H), 2.40 (q, *J* = 8 and 13.6, 2 H), 2.91 (s, 3 H), 4.01 (q, *J* = 11.2 and 5.4, 1 H), 6.07 (dd, *J* = 15.8 and 7, 1 H), 6.42 (d, *J* = 16, 1 H), 7.21–7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 17.8, 29.2, 32.1, 33.4, 61.3, 126.3, 127.8, 128.5, 129.0, 131.6, 170.3.

(15) Physical and spectral properties (picrate, mp 171 °C) were identical with literature values [in this example, initial reduction of the lactam followed by removal of the phenylsulfonyl moiety led to significant ring opened product]. (a) Hasiak, B. *Bull Soc. Chim. Fr.* **1976**, *9–10*, 1531. (b) Buechel, K. H.; Korte, F. *Chem. Ber.* **1962**, *95*, 2438.

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Isobraunicene, Wolficene, and Isowolficene. New Cyclic 1′–3 Fused Isoprenoids from *Botryococcus braunii*

Summary: Three new isoprenoid hydrocarbons, isobraunicene (**2**), wolficene (**3**), and isowolficene (**4**), were isolated from the Berkeley strain of *Botryococcus braunii*. ^1H NMR and mass spectra indicate the compounds contain terminal methylenecyclohexane rings like that in braunicene (**1**). Isobraunicene is a C_{32} regioisomer of **1** with the ring at the opposite end of the isoprenoid chain. Wolficene and isowolficene are C_{31} regioisomers with methylenecyclohexane rings at the same ends of the chain as **1** and **2**, respectively.

Sir: The B form of *Botryococcus braunii*, a fresh water colonial green alga, produces and accumulates a family of 1′–3 linked isoprenoid hydrocarbons, which constitute up to 75% of its biomass.[1–3] Pulse-chase experiments indicate that a parent C_{30} triterpene formed by condensation of two farnesyl residues is successively methylated by *S*-adenosyl

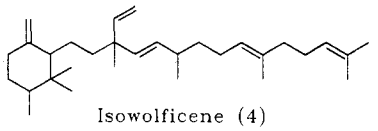
(1) Maxwell, J. R.; Douglas, A. G.; Eglington, G.; McCormick, A. *Phytochemistry* **1968**, *7*, 2157–2171.

(2) Huang, Z.; Wolf, F. R.; Poulter, C. D.; Somers, T. C.; White, J. D. *J. Am. Chem. Soc.* **1988**, *110*, 3959–3964.

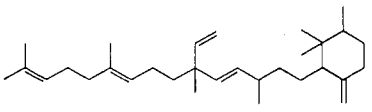
(3) Metzger, P.; David, M.; Casadevall, E. *Phytochemistry* **1987**, *26*, 129–134.

0022-3263/88/1953-5390$01.50/0

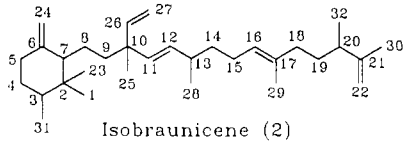
methionine to yield higher members of the botryococcene family.[4] Although approximately 30 different botryococcenoids have been identified by GCMS, the compounds are difficult to separate, and only 11 have been assigned structures.[4,5] Recently, we[1,6] and Murakami et al.[7] described the isolation and characterization of braunicene (1), a new dimethylated triterpene from the Berkeley isolate of *B. braunii*, which contains a trans-substituted methylenecyclohexane moiety identical with that in γ-irone. We now report structures for three new botryococcenoids[8] with methylenecyclohexane rings, isobraunicene (2), wolficene (3), and isowolficene (4).



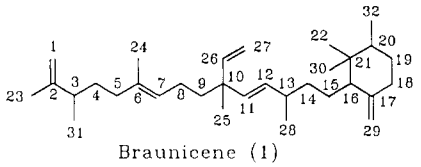
Isowolficene (4)



Wolficene (3)



Isobraunicene (2)

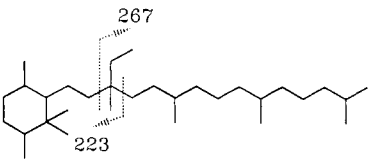


Braunicene (1)

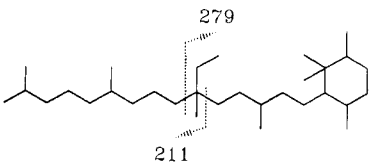
Chromatography on silica gel with hexane separated crude hexane extracts of stationary-phase cultures of *B. braunii* into three groups. The first to elute contained braunicene (76%) and three unknowns (**2**, 20%; **3**, 2%; and **4**, 2%). HPLC on 5 μm ODS Hypersil (acetonitrile) gave pure fractions of the four components. Mass spectra (EI, 17 eV) of **1** and **2** had molecular ions at m/z 438 ($C_{32}H_{54}$), while **3** and **4** had molecular ions at m/z 424 ($C_{31}H_{52}$). High-resolution mass spectra were consistent with these formulas.

Comparisons of the 500-MHz ^1H NMR spectra of **2**–**4** with that of braunicene (Table I) indicated that all of the hydrocarbons contained the unusual methylenecyclohexane moiety. The ^1H NMR spectrum of **2** was very similar to that of **1**, although close inspection revealed slight differences in chemical shifts and coupling patterns for protons at C9, C11, C12, C25, C26, and C27.[9] Almost identical differences were evident in the ^1H spectra of **3** and **4**. ^1H NMR spectra for **1** and **3** were virtually superimposable except for changes associated with methylation at C3. Braunicene (**1**, C_{32}) had a doublet at 1.01 ppm (methyl at C3), a multiplet at 2.12 ppm (allylic proton at C3), and a broad three-proton resonance at 4.68 ppm (olefinic protons at C1 and C29). In wolficene (**3**, C_{31}) these features were replaced by resonances at 1.61 and 1.69 ppm (methyls at C2), a broad signal at 5.10 ppm (proton at C3), and a one-proton signal at 4.68 ppm. A similar comparison was made between ^1H spectra for **2** and **4** where resonances at 1.02 (methyl at C20) and 2.12 (allylic proton at C20) were replaced by signals at 1.61, 1.69 (methyls at C21), and 5.11 ppm (olefinic proton at C20). In addition, the three-proton resonance at 4.69 ppm in **2** was replaced by a one-proton signal in **4**. These observations led us to suspect that **1**, **2** and **3**, **4** were regioisomer pairs where methylation and methylation/cyclization had occurred at opposite ends of the parental chain.

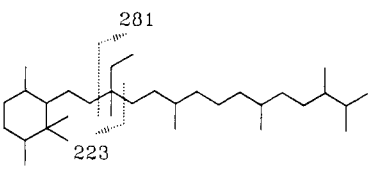
The locations of the cyclohexane rings in **1**–**4** were established from mass spectra of fully saturated derivatives. GLPC indicated that hydrogenation of each with activated platinum gave four isomers in the relative ratio of 4:1:4:1. ^1H NMR spectra of the mixtures showed that no double bonds remained, and GC mass spectra of the components in each mixture had fragmentation patterns with only small differences in peak intensities. We presume that the hydrogenation products from each of **1**–**4** were diastereomers formed upon generation of new chiral centers at C6 and C17. Characteristic fragments were seen for cleavages at C10 in all of the alkanes. The mixture of braunicane (**5**) and wolficane (**7**) diastereomers had fragment ions at m/z 225 and 211 (M − $C_{16}H_{31}$), respectively, resulting from cleavage between C10 and C11 with loss of fragments containing the cyclohexane ring. Major fragments at m/z 279 (M − 169 ($C_{12}H_{25}$) for **5** and M − 155 ($C_{11}H_{23}$) for **7**)



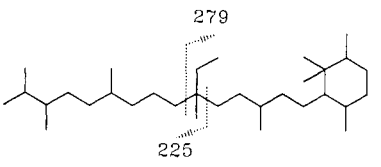
Isowolficane (8)



Wolficane (7)



Isobraunicane (6)



Braunicane (5)

(4) Wolf, F. R.; Nemethy, E. K.; Blanding, J. H.; Bassham, J. A. *Phytochemistry* **1985**, *24*, 733–737.

(5) Metzger, P.; Casadevall, E.; Pouet, M. J.; Pouet, Y. *Phytochemistry* **1985**, *24*, 2995–3002.

(6) Huang, Z.; Poulter, C. D. *J. Org. Chem.* **1988**, *53*, 4089–4094.

(7) Murakami, M.; Nakano, H.; Yamaguchi, K.; Konosu, S.; Nakayama, O.; Matsumoto, Y.; Iwamoto, H. *Phytochemistry* **1988**, *27*, 455–457.

(8) Wolficene and isowolficane are named in recognition of the contributions of Fred Wolf in this area.

(9) The numbering system initially used for braunicene[2,6] was changed to reflect the addition of methyls to a parental C_{30} isoprenoid skeleton and to facilitate comparisons among compounds.[10] With the 1′-branch of the 1′–3 linkage placed on the right, the parental hydrocarbon chain is numbered from left to right, followed by left to right numbering of the nonchain isoprenoid carbons. The nonisoprenoid carbons are then numbered from left to right.

(10) Metzger, P.; Casadevall, E. *Tetrahedron Lett.* **1983**, *24*, 4013–4016.

Table I. ^{1}H NMR Spectral Data of 1–4[a]

assignment[b]	1	2	3	4
1	4.69	0.87	1.61	0.87
3	2.12	1.60	5.10	1.60
4	1.35, 1.47	1.21, 1.47	2.06	1.21, 1.47
5	1.89	2.05	1.97	2.04
7	5.10	1.59	5.12	1.60
8	1.91	1.29, 1.40	1.91	1.29, 1.41
9	1.37	1.09, 1.28	1.39	1.09, 1.28
11	5.33	5.31	5.33	5.32
12	5.18	5.16	5.19	5.16
13	2.04	2.09	2.04	2.09
14	0.98, 1.19	1.29	0.97, 1.18	1.30
15	1.44, 1.31	1.97	1.32, 1.43	1.96
16	1.63	5.11	1.63	5.13
18	2.07, 2.10	1.90	2.08	1.98
19	1.21, 1.47	1.36, 1.48	1.22, 1.46	2.06
20	1.62	2.12	1.61	5.11
22	0.87	4.69	0.87	1.61
23	1.66	0.74	1.69	0.74
24	1.58	4.52, 4.69	1.58	4.52, 4.68
25	1.08	1.05	1.08	1.05
26	5.81	5.78	5.81	5.78
27	4.95, 4.96	4.91, 4.93	4.94, 4.96	4.92, 4.94
28	0.95	0.97	0.95	0.97
29	4.52, 4.68	1.58	4.52, 4.68	1.59
30	0.75	1.67	0.74	1.69
31	1.01	0.78	0.78	0.78
32	0.78	1.02		

[a] Spectra were taken in $CDCl_3$ with TMS as an internal standard on a Varian VXR-500 MHz spectrometer. [b] Proton assignments refer to directly attached carbons.

were also observed for cleavage between C9 and C10. Similarly, isobraunicane (**6**) and isowolficane (**7**) diastereomers had fragments at m/z 281 and 267 ($M - C_{12}H_{23}$), respectively, from cleavage between C9 and C10 with loss of the cyclohexane ring and ions at m/z 223 (loss of $C_{16}H_{33}$ for **6** and $C_{15}H_{31}$ for **8**) resulting from cleavage between C10 and C11. Since those fragments that contained a degree of unsaturation also contained a cyclohexane ring, it was possible to establish regioisomeric relationships for the structures of **1–4**.

Both possible C_{31} and C_{32} regioisomers formed by methylation and methylation/cyclization of the terminal trisubstituted double bonds in the parent C_{30} botryococcene have now been isolated from stationary-phase cultures of the Berkeley isolate of *Botryococcus braunii*. Given the rich variety of methylation patterns in the hydrocarbons whose structures have been determined to date, it is quite possible that the methylase and methylase/cyclase enzymes in the alga have broad substrate specificities and there are not unique biosynthetic routes to the polymethylated botryococcenoids. It will be of interest to see if other varieties of *B. braunii* also produce botryococcenoids containing methylenecyclohexane moieties.

Acknowledgment. We wish to thank Dr. Fred Wolf of Amoco Corp. for his generous assistance in establishing the cultures in our laboratory. This work was supported by the National Institutes of Health, Grant GM 21328.

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Additions and Corrections

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Wim H. Kruizinga, John Bolster, Richard M. Kellogg,* Johan Kamphuis,* Wilhelmus H. J. Boesten, Emmo M. Meijer, and Hans E. Schoemaker. Synthesis of Optically Pure α-Alkylated α-Amino Acids and a Single-Step Method for Enantiomeric Excess Determination.

Page 1826. The final sentence of ref 5 should be replaced with "The microorganism can be obtained from the American Type Culture Collection (ATCC 25795)".