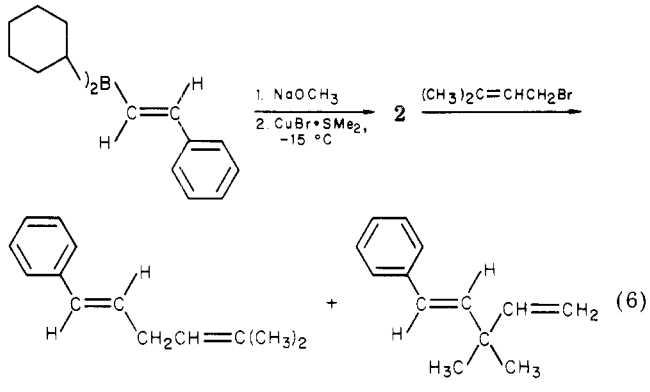
Table II. Preparation of 1,4-Dienes from Allylic Chlorides

alkyne	allylic chloride[a]	product	yield,[b] %
1-hexyne	allyl chloride	(4*E*)-1,4-nonadiene (6)	90
3-hexyne	allyl chloride	(4*E*)-4-ethyl-1,4-heptadiene	93
cyclohexylacetylene	3-chloro-2-methylpropene	(1*E*)-1-cyclohexyl-4-methyl-1,4-pentadiene	(89)
5-chloro-1-pentyne	2,3-dichloropropene	(4*E*)-2,8-dichloro-1,4-octadiene	(83)

[a] In each case, the allylic chloride was converted into the corresponding allylic iodide by treatment with 1.5 equiv of sodium iodide in THF at 25 °C. The halide was used in 10% excess. [b] GC analysis, isolated yields in parentheses.

may be circumvented easily by conversion of the allylic chlorides in situ to the more reactive iodides. Thus, stirring allyl chloride with excess sodium iodide in THF at 25 °C results in a quantitative conversion to the iodide within 20 h. Simple decantation of the solution of allyl iodide into a second flask containing the copper reagent derived from **5** provides the diene **6** in a yield of 91%. This technique proved to be generally applicable with comparable efficiency to other allylic chlorides (Table II).

To determine whether or not allylic transposition accompanies the coupling reaction, we treated the intermediate copper complex from (1*E*)-β-styryldicyclohexylborane with prenyl bromide (eq 6). A mixture of two isomeric



(6)

3:1 ratio
90% overall yield

1,4-dienes is obtained in a combined yield of 90% with the predominant product resulting from a direct S_N2 attack. Although the S_N2' product appears highly sterically disfavored, its presence indicates the reaction can proceed by both pathways.

In summary, the reactive alkenylcopper complexes generated from alkenyldialkylboranes easily undergo cross-coupling with allylic halides in excellent yield, with very high stereospecificity. In addition, there are several advantages of the method over related 1,4-diene syntheses employing other alkenylmetallic reagents.[6] First, there is no need to isolate or to purify the reactive intermediate. Second, only stoichiometric amounts of both the alkenylborane and allylic halide are required for efficient coupling. Finally, many reactive functional groups, not tolerated by the harsher reaction conditions required by many of the other procedures, are readily accommodated.

We are presently examining reactions of the copper complexes from such alkenylboranes with other electrophiles, including nonactivated alkyl halides. The mechanism and exact nature of the reactive copper intermediate are also under active investigation.

(6) Aluminum: (a) Lynd, R. A.; Zweifel, G. *Synthesis* **1974**, 658. (b) Baba, S.; Van Horn, D. E.; Negishi, E. *Tetrahedron Lett.* **1976**, 1927. Boron: (c) Yamamoto, Y.; Yatagai, H.; Sonoda, A.; Murahashi, S. I. *J. Chem. Soc., Chem. Commun.* **1976**, 452. Mercury: (d) Larock, R. C.; Bernhardt, J. C.; Driggs, R. J. *J. Organomet. Chem.* **1978**, *156*, 45. Copper: ref 2.

Registry No. 1, 72161-18-3; 3, 72161-19-4; 5, 69322-45-8; 6, 60835-96-3; 7, 30651-68-4; 8, 72161-20-7; 1-hexyne, 693-02-7; 9-BBN, 280-64-8; allyl bromide, 106-95-6; (*Z*)-1-hexen-1-yldicyclohexylborane, 56962-83-5; (*Z*)-1,4-nonadiene, 54068-77-8; (*E*)-β-styryldicyclohexylborane, 62072-25-7; prenyl bromide, 870-63-3; 3-hexyne, 928-49-4; (*E*)-4-ethyl-1,4-heptadiene, 72161-21-8; 4-acetoxy-1-butyne, 56703-55-0; 1-iodo-1-hexyne, 1119-67-1; 1-nonyne, 3452-09-3; (*Z*)-4-(trimethylsilyl)-1,4-dodecadiene, 72175-02-1; allyl chloride, 107-05-1; cyclohexylacetylene, 931-48-6; 3-chloro-2-methylpropene, 563-47-3; 5-chloro-1-pentyne, 14267-92-6; 2,3-dichloropropene, 78-88-6; (*E*)-1-cyclohexyl-4-methyl-1,4-pentadiene, 72161-22-9; (*E*)-2,8-dichloro-1,4-octadiene, 72161-23-0.

Herbert C. Brown,* James B. Campbell, Jr.

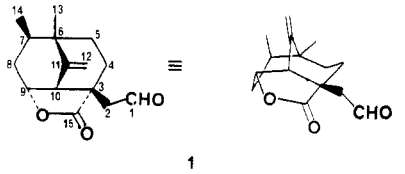
Richard B. Wetherhill Laboratory
Purdue University
West Lafayette, Indiana 47907

Received August 20, 1979

Upial, a Sesquiterpenoid Bicyclo[3.3.1]nonane Aldehyde Lactone from the Marine Sponge *Dysidea fragilis*

Summary: The structure of upial (**1**), a sesquiterpenoid marine natural product, is deduced from spectral correlations and chemical transformations.

Sir: The marine sponge genus *Dysidea* has become noted for a broad spectrum of metabolites which include bromophenols, sesquiterpenoids, and thiazole derivatives.[1] We wish to report the structure and properties of upial[2] (**1**), a nonisoprenoid sesquiterpene aldehyde lactone with



1

the rare bicyclo[3.3.1]nonane skeleton, isolated from the Kaneohe Bay, Oahu, sponge *Dysidea fragilis*.[3] Fresh sponge was freeze-dried (1 kg) and consecutively extracted with petroleum ether and dichloromethane. The latter extract after chromatography on BioBeads SX-8[4] (C_6H_6), followed by reversed-phase chromatography on BioBeads SX-12[4] (THF/CH_2Cl_2, 3:2) and high-pressure LC on μ-

(1) (a) Minale, L.; Cimino, G.; DeStefano, S.; Sodano, G. *Fortsch. Chem. Org. Naturst.* **1976**, *33*, 1-72 and references therein. (b) Kazlauskas, R.; Murphy, P. T.; Wells, R. J. *Tetrahedron Lett.* **1978**, 4949-50, 4951-2. (c) Charles, C.; Braekman, J. C.; Daloze, D.; Tursch, B.; Declercq, J. P.; Germain, G.; Van Meerssche, M. *Bull. Soc. Chim. Belg.* **1978**, *87*, 481-6.

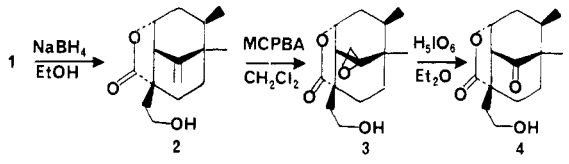
(2) Pronounced o͞opēăl, after the Hawaiian 'ūpī = sponge.

(3) Identified by Dr. P. R. Bergquist.

(4) BioRad Laboratories, Richmond, CA.

0022-3263/80/1945-0552$01.00/0

Scheme I



Partisil,[5] yielded upial (1) as a colorless oil, $[\alpha]^{25}_D$ +92.6 (*c* 0.27, $CHCl_3$), in 0.002% yield from dried animal. Spectral data secured the composition of $C_{15}H_{20}O_3$ (high-resolution mass spectrum, *m/e* 248.142; calcd 248.141) and its trifunctional character, aldehyde [1725 cm^{-1}; δ 9.74 (1 H, dd, J = 0.6, <0.5 Hz), 199.5 (d)], δ-lactone [1765 cm^{-1}; δ 4.98 (1 H, ddd J = 9.5, 6, 4 Hz for H-9), 180.8 (s), 78.4 (d)], and *exo*-methylene [905 cm^{-1}; δ 4.94 (1 H, d, J = 1 Hz), 4.81 (1 H, d, J = 1 Hz), 147.5 (s), 111.3 (t)],[6] thus encompassing all three oxygens and all four directly observable elements of unsaturation.

The remaining two carbocyclic rings were further adumbrated by a series of reactions (vide infra) and by double resonance studies. Irradiating the ^1H signal at δ 4.98 (H-9) caused the collapse to a singlet of a one-proton doublet (J = 9.5 Hz) at δ 3.03 (H-10) and simplified to doublets of doublets two signals at δ 2.24 (1 H, ddd, J = 15, 6.5, 4 Hz) and 1.50 (1 H, ddd, J = 15, 7, 6 Hz) assigned to the C-8 methylene protons, which are geminally coupled by 15 Hz. Irradiation of the signal at δ 1.50 (H-8_α) partially decoupled an obscured one-proton signal at δ 1.93 (qdd, J = 7, 7, 6.5 Hz), now attributable to H-7. This signal could in turn be decoupled to an observable broad triplet by irradiation of the signal arising from the secondary C-14 methyl (3 H d, J = 7 Hz). These experiments define the >C(10)H–C(9)H–C(8)H_2–C(7)H–C(14)H_3 sequence in 1.

Scheme I outlines the reactions which establish the remaining carbon skeleton of 1 except for two contiguous methylenes (C-4,5). Reduction of 1 (10.6 mg) with $NaBH_4$ (EtOH) furnishes upiol (2) in 87% yield. The spectral data[7] of 2 confirmed the identity of the alcohol and firmly placed the aldehyde function next to a methylene (C-2), since the AB system of 1 [δ 2.95 (1 H, dd, J = 19, <0.5 Hz), 2.71 (1 H, dd, J = 19, 0.6 Hz)], now assignable to CH_2-2, had moved upfield and was no longer discernible. A new AB pattern in the ^1H NMR spectrum of 2 [δ 3.80 (1 H, dt, J = 13, 6 Hz), 3.76 (1 H, dt, J = 13, 6 Hz)] arises from the newly formed C-1 methylene. Treatment of upiol (2) with *m*-chloroperbenzoic acid (MCPBA) in methylene chloride yielded upiol epoxide (3, 84%) stereoselectively.[8] Periodate oxidation of 3 cleaved the epoxide and furnished upiolone (4; $C_{14}H_{20}O_4$, *m/e* 252) in poor (48%) yield. The infrared spectrum (CH_2Cl_2) of this ketol lactone ($C_{14}H_{20}O_4$, *m/e* 252) (3450, 1765, 1720 cm^{-1}) placed the keto function, and hence its precursor, the *exo*-methylene, on a six-membered ring. Proton chemical shift comparison of compounds 1–4 proves that CH-10, shifted substantially downfield to δ 3.59 (1 H, d, J = 9.5 Hz), and CH_3-13, shifted to δ 1.31 (3 H, s), must be adjacent to the carbonyl and that C-6, bearing a methyl group, and CH-10 complete a carbocyclic six-membered ring.[9] Furthermore, the downfield shifts of H-10 in 1 (δ 3.03) and in 2 (δ 3.11) provide additional evidence for its allylic nature. Correct placement of the C-4,5 methylenes in upial (1) is aided by consideration of its ^{13}C NMR ($CDCl_3$) spectrum, which displays only three singlet resonances at δ 180.8 (assigned to the lactone carbonyl), 46.9, and 37.9. The quaternary carbon signal at δ 46.9 must be assigned to C-3, which is α to the lactone carbonyl, and the δ 37.9 resonance must arise from C-6, which bears the C-3 methyl group. If these two carbons are to be fully substituted, they must be the termini of the C-4,5 methylene bridge and thus form the second carbocyclic six-membered ring. C-3, furthermore,

Table I. LIS Data for Upiol (2)[a]

H	δ	$\Delta\delta$	θ	r_{calcd}, Å	r_{measd}, Å	% r
1	3.8	9.2				
2	1.88	5.9	33	4.7	4.7	0.43
4_α	1.7	4.1	25	5.8	6.0	3.2
4_β	1.6	3.8	21	6.2	6.2	0.96
5_α	1.6	2.1	10	8.0	7.8	2.6
5_β	1.5	1.7	18	8.3	8.2	1.1
7	2.15	1.15	12	9.7	9.5	1.8
8_α	2.1	1.9	11	8.2	8.1	1.7
8_β	1.5	1.6	17	8.5	8.8	3.6
9	4.84	1.48	30	7.8	7.6	1.8
10	3.11	3.7	30	5.7	6.0	4.8
12_α	5.02	1.4	34	7.5	7.3	2.6
12_β	4.82	1.1	28	8.8	8.6	2.9
13	1.02	0.95	23	9.7	9.4	2.9
14	0.81	0.80	27	9.9	9.4	5.1

[a] Chemical shifts (δ), Eu(fod)$_3$-induced chemical shifts ($\Delta\delta$, ppm), oxygen-europium-hydrogen angles (θ, deg), calculated and measured europium-hydrogen distances, and percent deviation of calculated from measured distances.

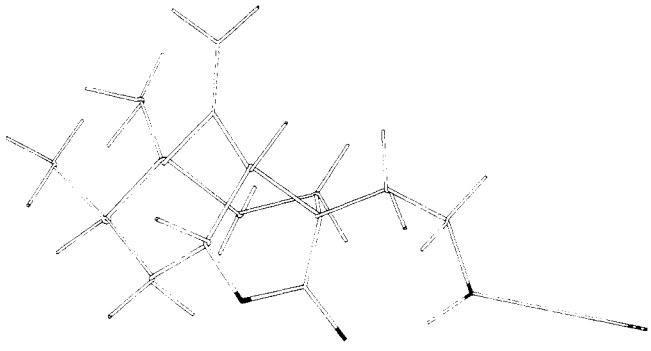
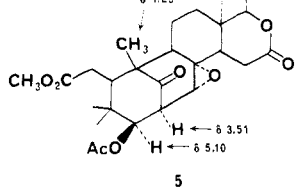


Figure 1. Dreiding model of the Eu(fod)$_3$–upiol complex.



5

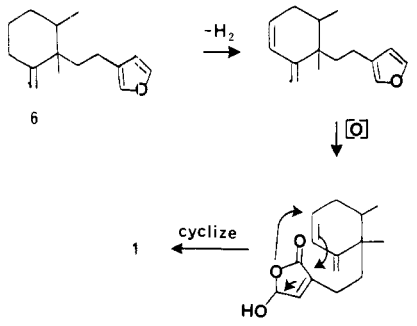
(5) Whatman, Inc., Clifton, NJ.

(6) Other spectral data: ^1H NMR (100 MHz, $CDCl_3$) AB system δ 2.95 (1 H, dd, J = 19, <0.5 Hz, H-2_α), and 2.71 (1 H, dd, J = 19, 0.6 Hz, H-2_β), 1.93 (1 H, qdd, J = 7, 7, 6.5 Hz, H-7), 1.9–1.5 (complex), 1.03 (3 H, s, H_3-13), 0.81 (3 H, d, J = 7 Hz, H_3-14); ^{13}C NMR (25.2 MHz, $CDCl_3$) δ 50.8 (t), 49.1 (d), 46.9 (s), 39.6 (d), 39.4 (t), 37.9 (s), 36.1 (t), 30.6 (t), 24.6 (q), 19.0 (q); mass spectrum, *m/e* 220.154 (M – CO), 204.112 (M – C_2H_4O), 91 ($C_7H_7^+$).

(7) Mass spectrum ($C_{15}H_{22}O_3$) *m/e* 250 (M^+), 232 (M – H_2O), 206 (M – CO_2), 91 ($C_7H_7^+$, 100%); IR (CH_2Cl_2) 3420, 1760, 895 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 5.02 (1 H, d, J = 1.5 Hz, H-12_α), 4.84 (1 H, ddd, J = 8.5, 6, 5 Hz, H-9), 4.82 (1 H, d, J = 1.5 Hz, H-12_β), 3.80 (1, H, br, exchangeable), AB system 3.80 (1 H, dt, J = 13, 6 Hz, H-1_α) and 3.76 (1 H, dt, J = 13, 6 Hz, H-1_β), 3.11 (1 H, d, J = 8.5 Hz, H-10), 1.02 (3 H, s, H_3-13), 0.81 (3 H, d, J = 7 Hz, H_3-14).

(8) Mass spectrum, ($C_{15}H_{22}O_4$) *m/e* 266 (M^+), 236 (M – CH_2O), 222 (M – CO_2), 105 ($C_8H_9^+$, 100%); 91 ($C_7H_7^+$, 100%); IR (CH_2Cl_2) 3450, 1763 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 4.90 (1 H, ddd, J = 9, 5, 4 Hz, H-9), 3.80 (2 H, br t, J = 6 Hz, H_2-1), 2.90 (1 H, d, J = 4 Hz, H-12_α), 2.59 (1 H, d, J = 4 Hz, H-12_β), 2.43 (1 H, d, J = 9 Hz, H-10), 2.30–1.90 (9 H, complex), 0.94 (3 H, d, J = 7 Hz, H_3-14), 0.75 (3 H, s, H_3-13).

(9) Other ^1H NMR ($CDCl_3$) signals of 4: δ 5.00 (1 H, ddd, J = 9.5, 6, 4 Hz, H-9), 3.78 (2 H, br t, J = 7 Hz, H_2-1), 2.50–1.50 (9 H, complex), 1.20 (3 H, d, J = 7 Hz, H_3-14).



must bear the aldehydic side chain. An excellent model compound for upiolone (**4**) is the limonoid triterpene xylocarpin (**5**),[10] which includes a bicyclo[3.3.1]nonanone structure with an infrared carbonyl band at 1720 cm^{-1}.

Structure **1** of upial was conclusively confirmed by a lanthanide-induced-shift study (LIS) of upiol (**2**) with $Eu(fod)_3$. Existence of the C-4,5 methylenes was shown by decoupling the shifted spectrum. Semiquantitative analysis of the shift data (Table I) allowed stereochemical assignments as shown.[11] The LIS study and the observed coupling constants support the chair–boat conformation of the bicyclo[3.3.1]nonane system, in perfect agreement with coupling constants extrapolated from the Karplus curve. Figure 1 reproduces a Dreiding model of the europium complex with upiol.

In addition to the limonoid xylocarpin (**5**),[10] a terrestrial sesquiterpene, clovanediol,[12] also possesses the bicyclo[3.3.1]system. Upial (**1**) may be biogenetically related to a sponge sesquiterpenoid, microcionin-4 (**6**), which Minale and co-workers[13] isolated from *Microciona toxystila*.

Acknowledgment. We thank Mr. James Loo for assistance with NMR measurements, Mr. Norman Liu for assistance with mass spectral determinations, and the National Science Foundation for financial support.

Registry No. 1, 72378-77-9; 2, 72378-78-0; 3, 72378-79-1; 4, 72378-80-4.

(10) Okone, D. A.; Taylor, D. A. H. *J. Chem. Soc. C* **1970**, 211–3.

(11) Aliquots of $Eu(fod)_3$ in $CDCl_3$ were added to **2** in $CDCl_3$, and the 100-MHz spectrum was recorded. The induced shifts ($\Delta\delta$) were determined by plotting the chemical shift of each proton signal against the molar quantities of $Eu(fod)_3$ added. Distances and angles were measured by using a Dreiding model of **2** after fixing the europium–oxygen bond distance at 2.7 Å and the carbon–oxygen–europium bond angle at about 120°. Methyl protons were treated as a single proton with a bond length of 1.94 Å from the ring carbons.

(12) Gupta, A. S.; Dev, S. *Tetrahedron* **1971**, *27*, 635–44.

(13) Cimino, G.; DeStefano, S.; Guerriero, A.; Minale, L. *Tetrahedron Lett.* **1975**, 3723–6.

Gary Schulte, Paul J. Scheuer*

Department of Chemistry
University of Hawaii at Manoa
Honolulu, Hawaii 96822

Oliver J. McConnell

Skidaway Institute of Oceanography
Savannah, Georgia 31406

Received August 13, 1979