(5) Satisfactory analytical and spectral data were obtained for all new compounds reported. Because of their instability, however, compounds 5c, 5d, and 5e were hydrolyzed to the corresponding formyl derivatives prior to analysis.

(6) For a closely related example, see A. I. Meyers and E. W. Collington, J. Am. Chem. Soc., 92, 6676 (1970).

(7) The coordination of alkali metal cations with neutral organic nucleophiles is, of course, a well-known phenomenon; cf. for example (a) N. S. Poonia and M. R. Truter, J. Chem. Soc., Dalton Trans., 2062 (1973). For a related example, see N. S. Poonia and B. P. Yadav, J. Org. Chem., 43, 2842 (1978), and references cited therein. (b) E. Piers and J. R. Grierson, ibid., 42, 3755 (1977). (c) M. Kool and G. W. Klumpp, Tetrahedron Lett., 1873 (1978).

(8) D. Hoppe, Angew. Chem., Int. Ed. Engl., 13, 789 (1974).

(9) U. Schöllkopf, D. Hoppe, and R. Jentsch, Angew. Chem., Int. Ed. Engl., 10, 331 (1971). See also U. Schöllkopf, H. H. Hausberg, I. Hoppe, M. Segal, and U. Reiter, Angew. Chem., Int. Ed. Engl., 17, 117 (1978) for related work in this area.

(10) K. Weinges, G. Craab, D. Nagel, and B. Stemmle, Chem. Ber., 104, 3594 (1971).

(11) R. D. Haworth, W. H. Perkin, and J. Rankin, J. Chem. Soc., 127, 1444 (1925).

(12) The corresponding methyl ester is a known compound and has previously been converted to 10; see ref 13a.

(13) M. Suzuki, T. Miyahara, R. Yoshioka, M. Miyoshi, and K. Matsumoto, Agric. Biol. Chem., 38, 1709 (1974); Chem. Ind. (London), 687 (1972); (b) G. A. Stein, H. A. Bronner, and K. Pfister, J. Am. Chem. Soc., 77, 700 (1955); (c) K. Freter, M. Götz, and K. Grozinger, J. Med. Chem., 15, 1072 (1972).

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Structures of Dictyodial and Dictyolactone, Unusual Marine Diterpenoids

Summary: The structures of dictyodial (1a), dictyodiol (1b), and dictyolactone (2) were deduced by spectroscopic means, primarily ^{13}C NMR and ^1H NMR spectroscopy, and from single-crystal X-ray diffraction experiments on 1b and 2. Dictyolactone (2) is produced by oxidation of 1b with pyridinium chlorochromate, showing that 1a, 1b, and 2 have the same absolute configuration.

Sir: Marine organisms have attracted considerable recent interest as sources of unusual and potentially useful natural products.[1] Extracts of brown algae of the genus *Dictyota* have been reported to have cytotoxic,[2] antibacterial,[3] and antiviral activities.[4] In this communication we wish to report the structures of two unusual diterpenoids, dictyodial (1a) isolated from the brown algae *Dictyota crenulata* and *D. flabellata,* and the closely related dictyolactone (2) isolated from the sea hare *Aplysia depilans* (Opisthobranchia). Dictyodial (1a) has

1a R = -CHO
1b R = -CH₂OH
2
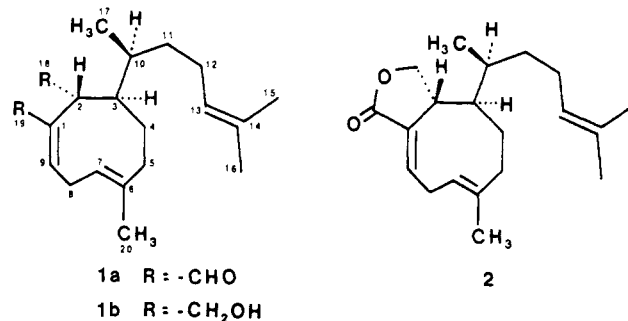
been isolated from two taxonomically and geographically distinct *Dictyota* species,[5,6] as a viscous oil, $[\alpha]^{25}_D$ −95° (c 1.2, $CHCl_3$). The mass spectrum of dictyodial (m/e 302) suggested the molecular composition $C_{20}H_{30}O_2$ and ^{13}C NMR spectral data (Table I) confirmed this formula.

Sharp doublets at δ 9.33 and 10.20 in the ^1H NMR spectrum (Table I) showed that two aldehydic protons were present. One had to occur as a disubstituted α,β-unsaturated enal group [λ_{max} (EtOH) 232 nm (ϵ 7300)] and a doublet of doublets at δ 6.95 showed that the enal olefinic proton was on the β carbon, oriented cis to the carbonyl, and adjacent to a methylene. Double resonance experiments proved that both aldehydic hydrogens were coupled to a methine proton at δ 3.04, suggesting part structure 3. Additional double resonance experiments allowed this structure to be expanded to 4 in which the methylene in 3 was further attached to an olefinic methine of a trisubstituted double bond. This olefinic proton,

Table I. Nuclear Magnetic Resonance Data for Dictyodial

carbon-13 chemical shift[a]	assignment[b]	proton chemical shift
203.5 (d)	18	10.20 (d, $J_{2,18}$ = 3 Hz)
194.2 (d)	19	9.33 (d, $J_{2,19}$ = 1 Hz[c])
157.4 (d)	9	6.95 (dd, $J_{9,8\beta}$ = 3.5, $J_{9,8\alpha}$ = 8.5 Hz)
148.5 (s)	1	
137.9 (s)	6	
130.9 (s)	14	
124.4 (d)	13	5.06 (tm,[d] $J_{13,12}$ = 7, $J_{13,16}$ = $J_{13,15}$ = 1.5 Hz)
122.3 (d)	7	5.35 (ddm, $J_{7,8\beta}$ = 11, $J_{7,8\alpha}$ = 3.5, $J_{7,20}$ = 1.5 Hz)
56.5 (dd)	8	3.27 (ddd, $J_{8\alpha,8\beta}$ = −16, $J_{8\beta,7}$ = 11, $J_{8\beta,9}$ = 3.5 Hz)
		2.98 (br ddd, $J_{8\alpha,8\beta}$ = −16, $J_{8\alpha,9}$ = 8.5, $J_{8\alpha,7}$ = 3.5 Hz)
48.5 (d)	3	1.7
40.7 (t)	5	2.25 (br d, $J_{5\alpha,5\beta}$ = −11.5, $J_{5\alpha,4\alpha}$ ∼ $J_{5\alpha,4\beta}$ ∼ 3 Hz)
		1.98 (td, $J_{5\alpha,5\beta}$ = −11.5, $J_{5\beta,4\alpha}$ = 11.5, $J_{5\beta,4\beta}$ = 6 Hz)
37.6 (t)	11	1.21 (dq, $J_{11,11'}$ = −13.5, $J_{11,12}$ = $J_{10,11}$ = 7)
		1.15 (dq, $J_{11,11'}$ = −13.5, $J_{11,12}$ = $J_{10,11}$ = 7)
32.7 (d)	10	2.43 (sextet,[e] $J_{10,11}$ = $J_{10,17}$ = 7 Hz)
29.1 (t)	4	1.68[f]
28.7 (d)	2	3.04 (dd,[g] $J_{2,19}$ = 1, $J_{2,18}$ = 3 Hz)
25.7 (t)	12	1.88 (quartet, $J_{12,13}$ = $J_{12,11}$ = 7 Hz)
25.4 (q)	16	1.57 (br m)
17.4 (q)	15	1.66 (br m)
17.1 (q)	20	1.77 (br m)
17.0 (q)	17	0.89 (d, J = 7 Hz)

[a] Relative to $CDCl_3$ (76.9 ppm) as an internal standard [value given in Levy and Nelson, "Carbon-13 NMR for Organic Chemists", p 23]. [b] Based on proton single frequency off-resonance decoupling experiments at 90 MHz (carbon-13) and proton spin–spin decoupling experiments at 100 and 360 MHz (proton). [c] W coupling. [d] Triplet of septets. [e] $J_{3,10}$ ∼ 0.5 Hz. [f] Obscured by methyl resonances. [g] $J_{2,3}$ = 0 Hz.

3

4
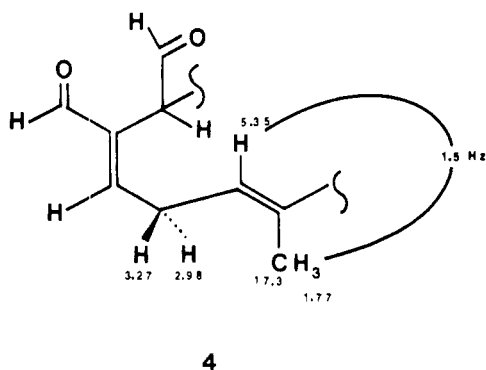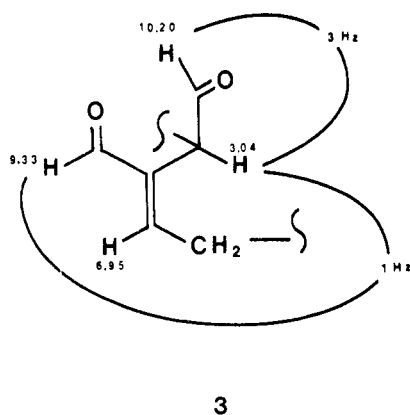
which resonated at δ 5.35, was coupled to a methyl group (δ 1.77) and the ^{13}C NMR chemical shift of the methyl group (δ 17.3) indicated that the geometry of the double bond was E.

Dictyodial also possessed fragment **5** as shown from decoupling experiments and comparison of chemical shifts with those of appropriate model compounds. A 1:5:10:10:5:1 sextet

5
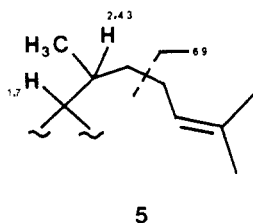
at δ 2.43, assigned to a methine bearing methyl and methylene groups, showed appreciable line sharpening when a methine proton at δ 1.7, obscured by olefinic methyl signals, was irradiated. This was further indicated by the appearance of a strong m/e 69 ion in the mass spectrum. Biogenetically the best structure that one could write with part structures **4** and **5** was **1a**. No relative stereochemistry could be assigned at C(10) and the absence of coupling between C(2)H and C(3)H suggested an ~90° dihedral angle or a trans disposition. The very small coupling of 0.5 Hz between C(3)H and C(10)H indicated that this dihedral angle was also ~90°. We were unable to crystallize dictyodial but the corresponding diol (**1b**) obtained by LiAlH₄ reduction was crystalline.

Dictyodiol (**1b**) crystallized in the orthorhombic space group $P2_12_12_1$ with *two* molecules of composition $C_{20}H_{34}O_2$ in the asymmetric unit. Cell constants were $a = 12.256$ (3), $b = 8.142$ (1), and $c = 38.101$ (4) Å. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using graphite monochromated Cu Kα (1.54178 Å) radiation and a variable speed ω scan. After correction for Lorentz, polarization, and background effects, only 1802 (61%) of the 2973 reflections surveyed were considered observed ($I \geq 3\sigma(I)$).
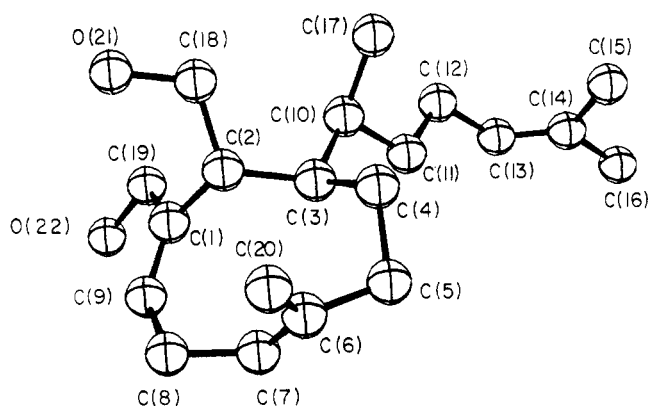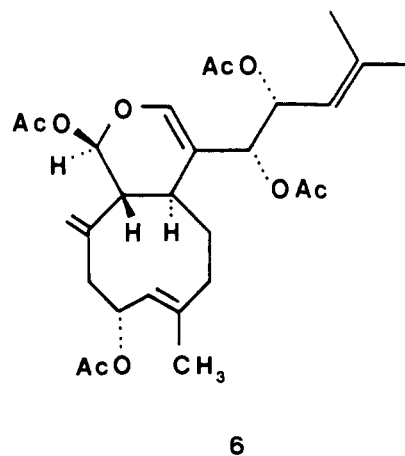

Figure 1. A computer-generated perspective drawing of dictyodiol (**1b**). Hydrogens are omitted for clarity and no absolute configuration is implied.

A phasing model was arrived at using a multisolution weighted tangent formula approach using magic integers.[7] The best model from this approach showed 35 of the 44 nonhydrogen atoms and the remaining atoms were easily located in subsequent electron density syntheses.[8] Hydrogen atoms were located on difference syntheses. Full-matrix least-squares refinements have converged to a conventional discrepancy index of 0.091 for the observed data.

The two molecules of dictyodiol (**1b**) in the asymmetric unit have the same configuration and conformation within experimental error. A drawing of the final X-ray model less hydrogens is given in Figure 1. The two hydroxyl groups of dictyodiol are involved in hydrogen bonds: O(22) is bonded to O(21′) of the other independent molecule (2.77 Å) and also to O(21′) ($-x, \frac{1}{2} + y, \frac{1}{2} - z$) (2.78 Å); O(21) is bonded to O(22′) ($x - 1, y, z$) (2.76 Å) and O(22′) ($-x, \frac{1}{2} + y, \frac{1}{2} - z$) (2.84 Å). There are no other abnormally short intermolecular contacts in dictyodiol. The solid-state conformation is similar to the solution-state conformation observed in dictyodial (**1a**) in that the C(2)H–C(3)H and C(3)H–C(10)H dihedral angles are ~90°. The X-ray experiment did not define the absolute stereochemistry but the relative stereochemistry is C(2)(R^*), C(3)(R^*), and C(10)(S^*). The C(6)–C(7) double bond has the E configuration and the C(1)–C(9) double bond also has the E configuration. This unusual diterpene skeleton was originally observed in the molecule xenicin (**6**) from the soft coral *Xenia elongata*.[9]

6

Investigation of the chemical constituents of the herbivorous sea hare *Aplysia depilans* has yielded a series of diterpenoids having an unusual perhydroazulene skeleton, pachidictyol A, and dictyols A–D,[10,11] which are also found in the brown alga *Dictyota dichotoma*,[12] the major dietary source
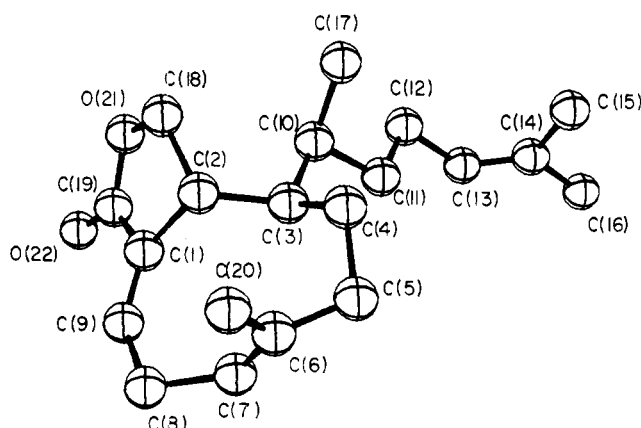
Figure 2. A computer-generated perspective drawing of dictyolactone (**2**). Hydrogens are omitted for clarity and no absolute configuration is implied.

Table II. Nuclear Magnetic Resonance Data for Dictytolactone (2)

carbon-13 chemical shift[a]	assignment[b]	proton chemical shift
172.5 (s)	19	
139.5 (d)	9	6.94 (dt, J = 7, 3 Hz)
136.4 (s)[c]	6	
135.4 (s)[c]	1	
131.1 (s)	14	
124.1 (d)	13	5.05 (br t, J = 7 Hz)
122.8 (d)	7	5.37 (dd, J = 10, 4 Hz)
67.8 (dd)	18	4.52 (d, J = 9.5 Hz)
		4.02 (dd, J = 9.5, 7.5 Hz)
47.1 (d)	3	
43.8 (d)	2	2.72 (br d, J = 7.5 Hz)
40.1 (t)	5	
37.2 (t)	11	1.23 (m)
32.5 (d)	10	
30.3 (t)	8	3.02 (complex signal, J_{gem} = −13 Hz)
28.6 (t)	4	
25.6 (t)	12	
25.4 (q)	16[c]	1.67 (br s)
17.5 (q, 2)	15, 20[c]	1.73 (br s)
17.1 (q)	17	0.95 (d, J = 6.5 Hz)

[a] Relative to $CDCl_3$ (76.9 ppm) as internal standard. [b] Based on chemical shift correlations, nondecoupled signal multiplicities, and model compounds. [c] These assignments may be reversed.

of the sea hare. Dictyolactone (**2**) was also isolated from *Aplysia depilans* collected in Naples.[13]

Dictyolactone (**2**) crystallized from hexane, mp 64–65 °C, $[\alpha]^{25}_D$ −165° (*c* 0.94, MeOH). Mass spectrometry suggested the molecular formula (*m/e* 302) $C_{20}H_{30}O_2$ and this was consistent with the elemental analysis (Found: C, 79.0; H, 10.2. $C_{20}H_{30}O_2$ requires: C, 79.5; H, 9.9.). The IR spectrum contained a band at 1740 cm⁻¹, which, together with the UV [λ_{max} (MeOH) 226 nm (ϵ 4771)], the ¹H NMR low-field olefinic signal at δ 6.94 (H(9), (Table II)) and the ¹³C NMR signals at δ 172.5 (C=O), C(19)) and 67.8 (dd, −C(18)H₂O−), indicated that dictyolactone was an α,β-unsaturated γ-lactone.

The ¹³C NMR spectrum contains 19 distinct lines with one degenerate signal at δ 17.5 for the two olefinic methyls. Table II gives an assignment of all signals based on comparison with dictyodial (**1a**), nondecoupled multiplicities, and other model compounds.[10,11,14,15] The ¹H NMR assignments are also given in Table II and have been confirmed by decoupling H(2) with H(18) and H(9) and H(8) with H(9) and H(7).

Dictyolactone (**2**) crystallized in the orthorhombic space

group $P2_12_12_1$ with two molecules in the asymmetric unit. The cell constants were a = 8.279 (4), b = 11.909 (13), and c = 37.143 (21) Å, isostructural with the unit cell of dictyodiol. All unique diffraction maxima with $2\theta \leq 114°$ were collected in the manner described for dictyodiol and 1634 (57%) of the 2863 reflections were judged observed.

A phasing model was arrived at by a multisolution weighted tangent formula approach[7] and refined by full-matrix least-squares refinements to a conventional crystallographic residual of 0.085 for the observed reflections.[8] Figure 2 is a computer-generated perspective drawing of one of the two identical dictyolactone (**2**) molecules in the unit cell. The configuration is very similar to that observed for the diol and the relative configurations at each of the chiral centers and double bonds are the same. Oxidation of dictyodiol (**1b**) with pyridinium chlorochromate (CH_2Cl_2, room temperature, 1.5 h) gave dictyolactone (**2**) as the major product. Thus the absolute configurations at C(2), C(3), and C(10) must be the same. While we have not found the algal source of dictyolactone (**2**), it is known that *Aplysia depilans* does feed on brown algae of the genus *Dictyota*.

The lipid extract of *Dictyota crenulata* shows good activity against Ehrlich ascites (EA) tumor in mice.[16] The major constituent, dictyodial (**1a**), is not responsible for the antitumor activity but does show good antibiotic activity against *Staphylococcus aureus* and *Bacillis subtilis* and antifungal activity against *Candida albicans*.[16] Dictyolactone (**2**) is inactive against EA.[16]

Supplementary Material Available: A 100-MHz ¹H NMR spectrum of dictyodial (**1a**), fractional coordinates and temperature factors, bond distances, and bond angles for dictyodiol (**1b**) and dictyolactone (**2**) (15 pages). Ordering information is given on any current masthead page.

References and Notes

(1) For recent reviews see: "Marine Natural Products, Chemical and Biological Perspectives", Vol. I, P. J. Scheuer, Ed., Academic Press, New York, 1978; "Marine Natural Products Chemistry", D. J. Faulkner and W. H. Fenical, Eds., Plenum Press, New York, 1977; and D. J. Faulkner, *Tetrahedron*, **33**, 1421 (1977).

(2) Y. Hashimoto, N. Fusetani, and K. Nozawa, *Proc. Int. Seaweed Symp., 7th*, 569 (1971).

(3) P. R. Burkholder, L. M. Burkholder, and L. R. Almodovar, *Bot. Mar.*, **11**, 149 (1968); I. S. Hornsey and D. Hide, *Br. Phycol. J.*, **9**, 353 (1974); T. Berti, G. Fassina, and S. Pignatti, *Giorn. Bot. Ital.*, **70**, 609 (1963).

(4) T. J. Starr, M. Piferrer and M. Kajima, *Tex. Rep. Biol. Med.*, **24**, 208 (1966).

(5) *Dictyota crenulata:* The alga was collected near Hauula Beach Park, Oahu, Hawaii. The wet seaweed (4.53 kg) was extracted with acetone and then with methylene chloride. The combined, concentrated extracts were distributed between methylene chloride and water. Evaporation of the methylene chloride left 63 g of an oily residue from which 4.4 g of dictyodial (**1a**) was obtained after successive chromatographies on Florisil with 20% chloroform/hexane, Bio-Beads SX-8 with benzene, and silica gel H with 1:1 chloroform/hexane.

(6) *Dictyota flabellata* (Collins) Setchell et Gardner: The alga was collected in Puerto Peñasco, Sonora, Mexico, June 1973 and 1975. Silica gel column chromatography followed by LC gives the dialdehyde as a viscous oil: see K. J. Robertson and W. Fenical, *Phytochemistry*, **16**, 1071 (1977) for the isolation of pachydictyol-A epoxide from the same source.

(7) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971). We thank Dr. L. Lessinger for a magic integer subroutine to the program MULTAN.

(8) The following library of crystallographic programs was used: C. R. Hubbard, C. O. Quicksall, and R. A. Jacobson, "The Fast Fourier Algorithm and the

Communications

Programs ALFF, ALFFDP, ALFFT and FRIEDEL", USAEC Report IS-2625, Iowa State University, Institute for Atomic Research, Iowa, 1971; W. R. Busing, K. O. Martin, and H. S. Levy, "A Fortran Crystallographic Least Squares Program", USAEC Report ORNL-TM-305, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965; C. Johnson, "ORTEP, A Fortran Thermal-Ellipsoid Plot Program", USAEC Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965.

(9) D. J. Vanderah, P. A. Steudler, L. S. Ciereszko, F. J. Schmitz, J. D. Ekstrand and D. van der Helm, *J. Am. Chem. Soc.*, **99**, 5780 (1977). We adopt the numbering scheme suggested by these authors. Other examples of this ring system are described in A. Groweiss and Y. Kashman, *Tetrahedron Lett.*, 2205 (1978), and Y. Kashman and A. Groweiss, *ibid.*, 4833 (1978). All of these examples of the xeniane skeleton have oxygen substitution at C(17) and C(18).

(10) L. Minale and R. Riccio, *Tetrahedron Lett.*, 2711 (1976).

(11) B. Danise, L. Minale, R. Riccio, V. Amico, G. Oriente, M. Piattelli, C. Tringali, E. Fattorusso, S. Magno, and L. Mayol, *Experientia*, **33**, 413 (1977).

(12) E. Fattorusso, S. Magno, L. Mayol, C. Santacroce, D. Sica, V. Amico, G. Oriente, M. Piattelli, and C. Tringali, *J. Chem. Soc., Chem. Commun.*, 575 (1976).

(13) *Aplysia depilans:* silica gel chromatography of the ether-soluble portion (20 g) of an acetone extract, not subjected to the saponification procedure, of homogenized digestive glands from three adult sea hares, collected in the Bay of Naples, gives 1.5 g of dictyolactone (**2**).

(14) G. Lukacs, F. Khuong-Hun, and C. R. Bennett, *Tetrahedron. Lett.* 3515 (1972).

(15) L. Radies, M. Kajatar-Peredy, S. Nozoe, and K. Kobayashi, *Tetrahedron Lett.* 4415 (1975).

(16) M. Kashiwagi and T. R. Norton, Department of Pharmacology, University of Hawaii, unpublished results.

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Photolysis of Nitrate Esters. Photochemically Initiated Inversion of Configuration

Summary: Photolysis of nitrate esters **1** and **2** in 2-propanol results in the formation of the corresponding alcohols while photolysis of nitrate ester **3** produces an alcohol with inverted configuration.

Sir: Nitrate esters of carbohydrates are compounds which are stable in the presence of a variety of reagents;[1] thus, they can be effective hydroxyl protecting groups, although they are used less frequently for this purpose than groups such as acetals, ketals, and carboxylic acid esters. One factor which limits the use of nitrate esters is the relatively vigorous conditions for their removal, which typically require heating with a nucleophile such as hydrazine or treating with a reducing agent such as lithium aluminum hydride.[1] The information available on the photolysis of nitrate esters suggests that alkoxy radicals are produced upon irradiation;[2] thus, irradiation in the presence of hydrogen donors is potentially a mild and effective technique for nitrate ester removal. In order to test this photochemical deprotection process (Scheme I), compounds **1-3** were synthesized[3] and irradiated.

Scheme I

$$RONO_2 \xrightarrow{h\nu} RO\cdot \quad \cdot NO_2 \xrightarrow[\text{donor}]{\text{hydrogen}} ROH$$
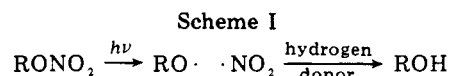
Photochemical reaction of each of the three nitrates **1-3** was conducted in the same manner. Corex-filtered irradiation of 1.0 g of material in 350 mL of 2-propanol under nitrogen with a 450-W Hanovia mercury lamp for 1 h resulted in complete disappearance of starting material and formation of a single photoproduct. Compound **1** quantitatively produced the
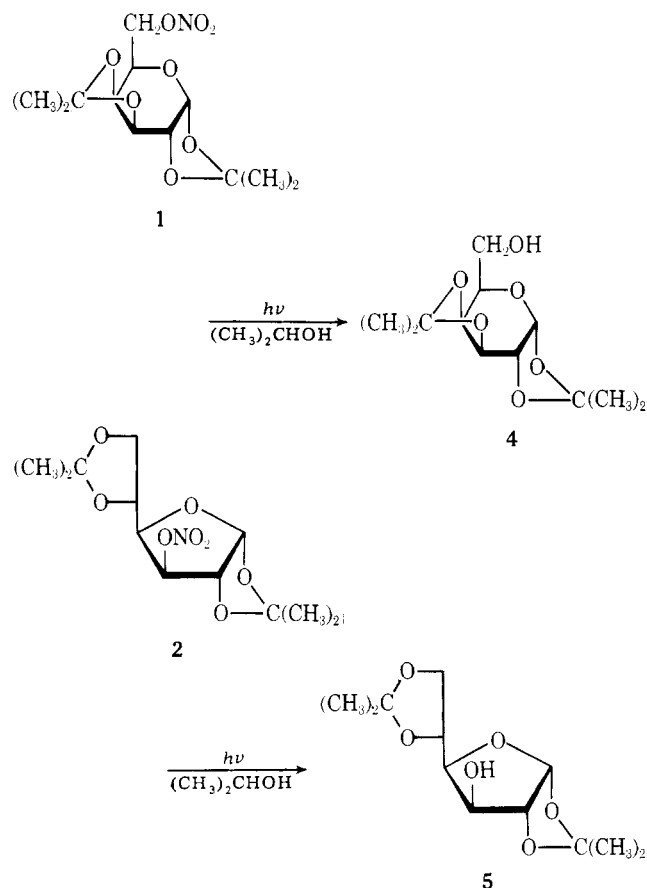
corresponding alcohol[4] **4** and compound **2** gave its corresponding alcohol[5] **5** in 92% yield. Surprisingly, however, irradiation of **3** did not result in the expected product **6** but rather the C_3 inverted alcohol **5** (100% yield). Identical results were obtained when compounds **1-3** were irradiated in butyl ether.

Although photochemical N–O bond homolysis followed by hydrogen abstraction from the solvent (Scheme I) explained satisfactorily the reactions of **1** and **2**, conversion of **3** into **5** required further explanation. Since one of the four bonds to C_3 must have been broken during reaction, the possible fragmentation of each of these four bonds needed to be considered. The C_3–O cleavage consistent with the exclusive formation

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