pH 7 while poly A melted in a noncooperative manner at this pH.

The following general conclusions can be reached: methylation of the backbone in poly A does not interfere with the formation of a double-stranded structure at weakly acidic pH at intermediate temperatures and a partially ordered single-stranded structure at a pH close to 7. The absorption spectra (not shown) and more significantly the CD spectra of both forms of poly A and poly 2′-O-mA indicate a close similarity of the dissymmetric structures of the single- and double-stranded conformations of both polymers. The most significant difference between the two polymers, which is reflected in the melting and titration curves, is the considerable higher tendency of poly 2′-O-mA to form a double-stranded structure as compared to poly A under the same conditions. A number of reasons may be responsible for this difference. These include a change in solvation entropy, a shift in the position of the equilibrium between the *exo* and *endo* conformation of the ribose residues, and a change in the preferred orientation of the heterocyclic portion relative to the sugar due to the methylation of the backbone.

It has been suggested that the 2′-hydroxyl group may participate in the stabilization of the ordered structures of polyribonucleotides by the formation of hydrogen bonds to the phosphate groups of the backbone[11] or to various sites of the heterocyclic bases.[12] Beyond eliminating the 2′-hydroxyl groups as potential hydrogen bond donors, methylation of the backbone may change the relative importance of other factors contributing to the stabilization of polynucleotide structure in solution. The data so far obtained with poly 2′-O-mA therefore neither support nor clearly eliminate this hypothesis.

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(12) P. O. P. Ts'o, S. A. Rapaport, and F. J. Bollum, *Biochemistry*, **5**, 4153 (1966).

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The Synthesis of the Fungal Sex Hormone Antheridiol[1]

Sir:

The substance antheridiol is the first specific functioning steroidal sex hormone to be identified in the plant kingdom. This unique natural product, secreted by the female plant of the aquatic fungus *Achlya bisexualis*, induces the growth of antheridial hyphae in the male plant, thus initiating sexual reproduction in this species.[2]

The structure of antheridiol, depicted by **1**, was deduced by McMorris and collaborators mainly on the basis of spectroscopic evidence.[3] We wish to report the synthesis of two of the four possible 22,23 isomers of **1**. One of our synthetic compounds exhibits physical and biological properties in good agreement with the natural hormone, thereby confirming the structure (**1**) proposed for antheridiol.

Aldol condensation of 3-tetrahydropyran-2′-yloxy-22,23-bisnorchol-5-en-24-al (**2a**)[4,5] [mp 137–139°; $[\alpha]_D$ $-39°$] at $-78°$ in tetrahydrofuran with the anion of ethyl *trans*-3,4-dimethyl-2-pentenoate (**3**)[7] [bp 46–48° (0.7 mm)] generated by treatment of **3** with lithium triphenylmethide in tetrahydrofuran at $-20°$ followed by warming the reaction mixture to 0° (45–90 min) and work-up by acidification afforded the α,β-unsaturated lactone **4** (23%) [mp 208–212°; $[\alpha]_D$ $-62°$; ν_{max} 1710, 1630 cm^{-1}; nmr 0.71 (18-H), 1.02 (19-H), 1.12 (d, $J = 7$ Hz, isopropyl CH_3), 5.80 ppm (24′-H)]. Sequential treatment of lactone **4** with boiling 2% methanolic sodium hydroxide (5 hr) and dilute hydrochloric acid in aqueous methanol (15 min at 20°) provided the key intermediate, 3β-hydroxy-22,23-*trans*-dienoic acid **5a** (86%) [mp 213–215°; $[\alpha]d$ $-55°$; λ_{max} 262 mμ (log ε 4.28); ν_{max} 1680, 1635, 1595 cm^{-1}; nmr (100 MHz) in DMSO-d_6 0.69 (18-H), 0.94 (19-H), 1.04 (*d*, $J = 6.5$ Hz, 21-H and isopropyl CH_3), 5.50 (24′-H), 5.98 (q, $J_{20,22} = 9$ Hz, $J_{22,23} = 16$ Hz, 22-H), 7.35 ppm (d, $J_{22,23} = 16$ Hz, 23-H].

Retention of the natural 20*R* stereochemistry was confirmed by ozonolysis of the 5α,6α-epoxydienoic acid **5b**[9] to the amorphous 3β-hydroxy-5α,6α-oxido-22,23-bisnorcholan-24-al (**2b**) [$[\alpha]_D$ $-54°$; ν_{max} 2675, 1720 cm^{-1}; nmr (100 MHz) 0.66 (18-H), 1.06 (19-H), 1.09 (d, $J = 7.0$ Hz, 21-H): 2.91 (d, $J = 4.0$ Hz, 6β-H), 9.54 ppm (d, $J = 3.0$ Hz, 24-H); m/e 346 (M^+)] which was identical in all respects with the aldehyde obtained by ozonolysis of

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(1) Publication No. 355 from the Syntex Institute of Organic Chemistry.

(2) (a) T. C. McMorris and A. W. Barksdale, *Nature*, **215**, 320 (1967); (b) L. Machlis in "The Fungi," Vol. II, G. C. Ainsworth and A. S. Sussman, Ed., Academic Press, New York, N. Y., 1966, p 415.

(3) G. P. Arsenault, K. Biemann, A. W. Barksdale, and T. C. McMorris, *J. Amer. Chem. Soc.*, **90**, 5635 (1968). See also G. P. Arsenault, Abstracts, 16th Annual Conference on Mass Spectrometry and Allied Topics, Pittsburgh, Pa., May 1968, p 238.

(4) This substance was prepared by reducing methyl 3-tetrahydropyran-2′-yloxy-22,23-bisnorchol-5-en-24-oate with lithium aluminum hydride to the corresponding alcohol followed by oxidation with dimethyl sulfoxide–dicyclohexylcarbodiimide.[6]

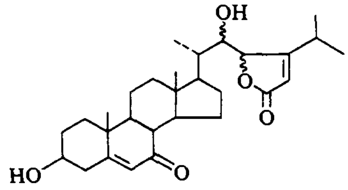
(5) Satisfactory elemental analyses were obtained for all fully characterized compounds. Nmr spectra were obtained on Varian A-60 and HA-100 spectrometers in deuteriochloroform solutions (10% w/v) containing tetramethylsilane as internal reference. Chemical shifts are reported as parts per million on the δ scale. We thank Miss J. Tremble for these determinations. In the presentation of data d = doublet, q = quartet, m = multiplet. Specific rotations are measured in chloroform solution, ultraviolet spectra in 95% ethanol, and infrared spectra in KBr disks. The mass spectra were obtained with an Atlaswerke CH-4 spectrometer equipped with a direct inlet system. Spectra were measured at an ionizing potential of 70 eV and an acceleration voltage of 3 kV. We thank Mr. J. Smith and Dr. L. Tökes for assistance with these measurements.

(6) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, **87**, 5661 (1965).

(7) This ester was prepared by Emmons alkylation of methyl isopropyl ketone with the anion of triethyl phosphonoacetate.[8]

(8) W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).

(9) This epoxide, prepared by the reaction of **5a** with 1 molar equiv of *m*-chloroperbenzoic acid in methylene dichloride, showed mp 196–197°; $[\alpha]_D$ $-65°$; λ_{max} 265 mμ (log ε 4.27); ν_{max} 1685, 1635, 1595 cm^{-1}.



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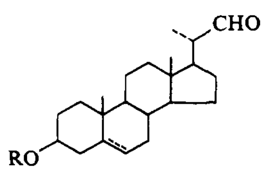
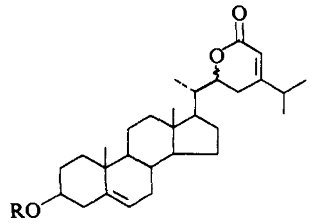
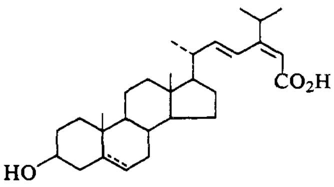


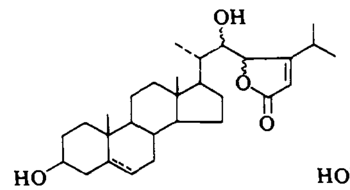
2a, R = tetrahydropyran-2'-yloxy; 5,6-double bond
b, R = H; 5α,6α-oxide



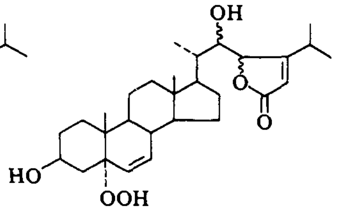
4, R = tetrahydropyran-2'-yl



5a, 5,6-double bond
b, 5α,6α-oxide



6a, 5α,6α-oxide
b, 5,6-double bond



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stigmasterol 5α,6α-oxide.[10]

Exposure of dienoic acid **5a** to 2.2 molar equiv of *m*-chloroperbenzoic acid in methylene chloride (72 hr at 20°) afforded a mixture of lactones[11] which was partially resolved by chromatography on silica gel into a pure epoxy-δ-lactone [mp 217–219°; 8%][12] and an epoxy-γ-lactone fraction, A.[13] Purification of the latter mixture by repeated crystallization yielded a homogeneous γ-lactone **6a** (6%) [mp 233–235°; [α]D −68°; λ_{max} 214 mμ (log ε 4.08); $\nu_{max}^{CHCl_3}$ 1740 cm^{-1}; nmr (100 MHz) 0.65 (18-H), 1.00 (d, J = 7.0 Hz, 21-H), 1.06 (19-H), 1.16, 1.21 (pair of d, J = 7 Hz, isopropyl CH_3), 2.91 (d, J = 4 Hz, 6β-H), *ca.* 3.5 (m; addition of D_2O gives d at 3.55 ppm; J = 9 Hz, 22-H), 4.89 (d, J = 9 Hz, 23-H), 5.77 ppm (24'-H)].

Regeneration of the 5,6 double bond of the epoxy-γ-lactone **6a** was accomplished by treatment with zinc dust–sodium iodide–acetic acid[14] to yield the corresponding Δ^5-γ-lactone **6b** (78%) [mp 203–204; [α]D −70°; λ_{max} 216 mμ (log ε 4.18); ν_{max} 1740 cm^{-1}; nmr (100 MHz) 0.72 (18-H), 1.02 (19-H), 1.04 (d, J = 7 Hz, 21-H), 3.60 (d, J = 9 Hz, 22-H), 4.92 (d, J = 9 Hz, 23-H), 5.37 (6-H), 5.79 ppm (24'-H)].

Hematoporphyrin-sensitized photooxygenation[15] of the latter product in pyridine solution gave rise to the Δ^6-5α-hydroperoxide **7** which without isolation was subjected to oxidative rearrangement by cupric acetate.[16] Purification of the resulting product by preparative tlc afforded 22,23-isoantheridiol (20%) [mp 273–277°; [α]D −125°; λ_{max} 225 mμ (log ε 4.27); ν_{max} 1740, 1645, 1625 cm^{-1}; nmr (100 MHz) 0.72 (18-H), 1.05 (d, J = 7 Hz, 21-H), 1.21 (19-H), 3.64 (broad d, J = 8.5 Hz, 22-H), 4.93 (d, J = 8.5 Hz, 23-H), 5.70 (6-H), 5.77 ppm (24'-H); m/e 470 (M^+), 344, 326, 298, 287, 269, 251].

Repetition of the last three stages of the synthesis on once crystallized material obtained from fraction A followed by preparative tlc afforded a mixture of two products. These were separable by fractional crystallization into the previously obtained 22,23-iso compound (5%) and antheridiol (**1**), 2.5% [mp 250–253°; λ_{max} 222 mμ (log ε 4.22); ν_{max} 1740, 1670 cm^{-1}; nmr ($CDCl_3$-MeOD 3:1) 0.70 (18-H), 1.17 and 1.22 (pair of d, J = 7 Hz, isopropyl CH_3), 1.20 (19-H), 4.95 (d, J = 8 Hz, 23-H), 5.69 (6-H), 5.77 ppm (24'-H); m/e 470 (M^+), 344, 326, 298, 287, 269, 251] whose physical properties were virtually identical with those reported by McMorris, *et al.*, for the natural product.[3] The synthetic material exhibited an activity in the same range as natural antheridiol in eliciting formation of antheridial hyphae on the male plant of *Achlya bisexualis*.[17]

Consideration of the mechanism of the reactions leading to the γ-lactone **6a** from the 22,23-*trans*-dienoic acid **5a** *via* an intermediate 22,23-epoxy acid requires that antheridiol possess the 22*R*,23*S* or 22*S*,23*R* configurations at these centers.

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[10] F. Radt, Ed., "Elsevier's Encyclopedia of Organic Chemistry," Vol. 14S, Elsevier Publishing Co., New York, N. Y., 1956, p 2192S.

[11] The crude product was obtained as follows. The epoxidation mixture was first shaken thoroughly with dilute sodium carbonate solution, the combined alkaline layers were acidified with 5% hydrochloric acid, and the resulting solution was extracted with ethyl acetate. The combined organic extracts were then washed with dilute sodium bicarbonate solution (to remove *m*-chlorobenzoic acid) and water, dried, and evaporated.

[12] The properties of this compound will be discussed in the full paper.

[13] Although this fraction is a mixture of the two 22,23 *erythro* epimers it moved as a single component in several tlc solvent systems.

[14] J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.*, 112 (1959).

[15] A. Nickon and J. F. Bagli, *J. Amer. Chem. Soc.*, **83**, 1498 (1961).

[16] G. O. Schenk, O. A. Neumüller, and W. Eisfeld, *Angew. Chem.*, **70**, 595 (1958).

[17] We are indebted to Drs. McMorris and Barksdale of the New York Botanical Garden, Bronx, N. Y., for kindly performing this assay.

[18] Syntex Postdoctoral Fellow: (a) 1967–1968; (b) 1968–1969.

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Photolysis of *cis,cis*-1,3-Cyclooctadiene

Sir:

Irradiation of *cis,cis*-1,3-cyclooctadiene has been reported to yield bicyclo[4.2.0]oct-7-ene.[1-3]

We wish to report the quantitative reinvestigation of this reaction, the results of which show these earlier observations to be incomplete. Our results indicate the major chemical transformation resulting from unsensitized photolysis[3] of *cis,cis*-1,3-cyclooctadiene (COD, **1**) is geometric isomerization to *cis,trans*-1,3-cyclooctadiene (**2**). Bicyclo[4.2.0]oct-7-ene (**3**) is formed,[4] as well as a small amount of *cis,cis*-1,4-cyclooctadiene (**4**).

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[1] R. Srinivasan, *J. Am. Chem. Soc.*, **84**, 4141 (1962).

[2] R. L. Cargill and W. G. Dauben, *J. Org. Chem.*, **27**, 1910 (1962).

[3] R. S. H. Liu, *J. Am. Chem. Soc.*, **89**, 112 (1967).

[4] Preliminary results indicate a quantum yield of 0.28 for formation of *cis,trans*-COD and 0.01 for formation of **3** after less than 10% conversion of **1**.