be separated and purified by vacuum distillation and they do not appear to isomerize on heating.

Dipole moment measurements form the main basis of our structural assignments of the isomers of VII. The locking of the ring by equatorial methyl groups in these compounds offers the advantage that dipole moment contributions from other conformers are negligible. Furthermore, since the P=O moment exceeds by a factor of at least two that of a $PNMe_2$ or POMe group,[8] the overall moments of VIIa and IXa should be comparable but larger than those of VIIb and IXb and this is confirmed in Table I. That the

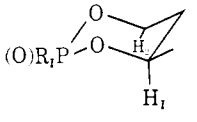
Table I. Dipole Moments[a] and ^{31}P Chemical Shifts[b] of Cyclic Phosphorus Compounds

Compd	μ, D	$\delta^{31}P$
IXa	6.11 ± 0.05	+7.06
IXb	4.69 ± 0.05	+4.98
VIIa	5.80 ± 0.1	−3.49
VIIb	4.05 ± 0.1	−6.58

[a] Measured at 25° in benzene using the apparatus and procedure described in A. C. Vandenbroucke, R. W. King, and J. G. Verkade, *Rev. Sci. Instrum.*, **39**, 558 (1968). [b] Measured in benzene relative to 85% H_3PO_4.

stereochemistries of the comparison compounds IXa and b are as shown is fixed by the established[1,2] configurations of Ia and Ib and the conclusion that oxidation of cyclic phosphorus systems proceeds with retention of configuration.[9,10] Since the same oxidation procedure produced Xa and Xb from IIa and IIb, their stereochemistries at phosphorus are also established with considerable firmness. If the reasonable assumption can be made that IIIa,b oxidized with retention of configuration at phosphorus, then VIIb (and by implication VIIIb) is thermodynamically more stable than the a isomer. This conclusion arises from the observation of a 10:1 IIIb to IIIa ratio in the first step of the equilibrium process represented in reaction 1. That the 1:10 ratio of IIIa to IIIb is very likely the equilibrium ratio is indicated by the production of this ratio in two different reactions (1 and 2) carried out at rather different temperatures. Moreover, the ratio did not change upon heating to 120° for 18 hr nor on vacuum distillation on a spinning band column.

Additional strong support for the above configurational assignments of VIIa,b and IXa,b comes from the lanthanide-induced pmr shifts of H_1 and H_2 in the isomers of VIII and X. Because these particular protons apparently experience greater downfield shifts when the P=O group is axial,[2,11] such deshielding



should be more pronounced in VIIIb and Xb than in their a counterparts and the data in Table II confirm this.

The ^{31}P chemical-shift progression to lower applied

Table II. Lanthanide[a] Shift Behavior of Selected Protons in Cyclic Phosphorus Compounds[b]

Compd	$\Delta\delta H_1$[c]	$\Delta\delta H_2$[c]
VIIIa	2.3	2.3
VIIIb	5.3	4.6
Xa	3.3	3.0
Xb	5.1	4.5

[a] Tris(1,1,1,2,2,3,3-heptafluoro-4,6-octanedione)europium(III) ($Eu(fod)_3$). [b] The downfield increments were obtained by comparing spectra of $CDCl_3$ solutions of these compounds with $CDCl_3$ solutions 0.2 *M* in compound and 0.1 *M* in $Eu(fod)_3$. [c] Relative to TMS.

fields from IXa and VIIa to their respective b isomers (Table I) seems to parallel the change in configuration at phosphorus.

In contrast to pentavalent phosphorus a and b isomers where X = oxygen and R = aryl, alkyl, or alkoxy, the P=O group prefers the axial position when R = NMe_2. In preliminary acid-catalyzed hydrolysis experiments on VIIa and VIIb, for instance, VIIb is observed by pnmr spectroscopy to convert to VIIa while VIIa hydrolyzes without apparent isomerization. Pnmr and stereospecific reaction studies have led to the conclusion that the equatorial NR_2 axial P=O stereochemistry is also preferred for relatively nonrigid 1,3,2-dioxaphosphorinanes in solution[5,12,13] and preliminary X-ray work indicates that the same is true in the solid state.[14]

Acknowledgment. The authors thank the National Science Foundation for generous support of this work in the form of a grant to J. G. V. and a Traineeship to J. A. M.

(8) C. P. Smyth, "Dielectric Behavior and Structure," McGraw-Hill, New York, N. Y., 1955.
(9) D. Z. Denney, G. Y. Chen, and D. B. Denney, *J. Amer. Chem. Soc.*, **91**, 6838 (1969).
(10) W. G. Bentrude and J. H. Hargis, *ibid.*, **92**, 7136 (1970).
(11) K. C. Yee and W. G. Bentrude, *Tetrahedron Lett.*, 2775 (1971).
(12) R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc. C*, 3033 (1968).
(13) H. Horton and W. Wadsworth, Jr., *J. Amer. Chem. Soc.*, **92**, 3785 (1970).
(14) W. Wadsworth, Jr., private communication.

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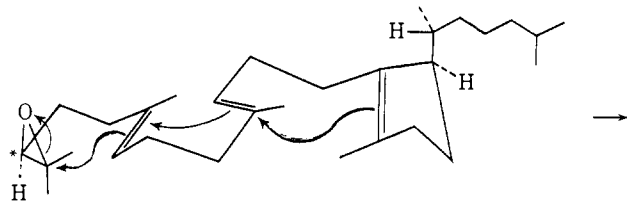
Biogenetic-Type Total Synthesis. 24,25-Dihydrolanosterol, 24,25-Dihydro-$\Delta^{13(17)}$-protosterol, Isoeuphenol, (−)-Isotirucallol, and Parkeol

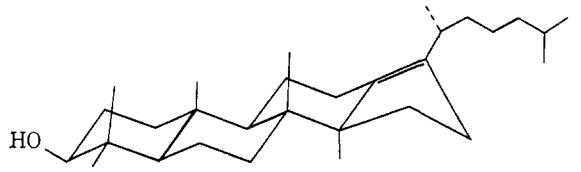
Sir:

In the biogenesis of the euphol and lanosterol classes, it is assumed that enzyme-controlled all-chair folding of squalene 2,3-oxide (**1**)[1] prefigures generation of the former type, while the chair–boat–chair conformation determines production of the latter category.[2] In order to pursue total synthesis in this area and also realize the closest simulation so far of the biological cyclization process, we have sought to employ the parallel, abiological reaction of a selected oxide **1** variant.[3] We now report the nonenzymic transforma-

(1) For a review dealing with the function of squalene 2,3-oxide in nature, see E. E. van Tamelen, *Accounts Chem. Res.*, **1**, 111 (1968).
(2) For the basic stereochemical interpretation, see (a) G. Stork and A. W. Burgstahler, *J. Amer. Chem. Soc.*, **77**, 4068 (1955), and (b) A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955).



α-2a



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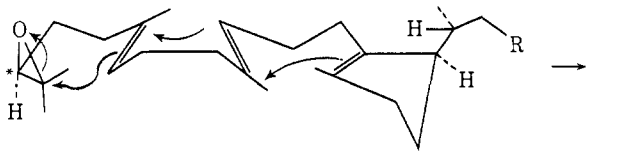
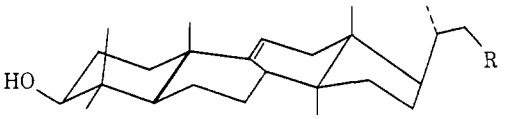


β-2a, R = $(CH_2)_2CH(CH_3)_2$
7a, R = $CH_2CH{=}C(CH_3)_2$

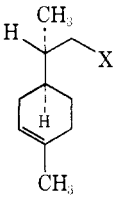
4



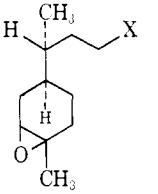
5, R = $(CH_2)_2CH(CH_3)_2$
8, R = $CH_2CH{=}C(CH_3)_2$

tion of the totally synthetic epoxide epimer (*)-**2a**—with concurrent stereorational generation of five new asymmetric centers—to not only isoeuphenol (**3**), presumably reflecting the polychair conformation (α-**2a**) of reacting epoxide, but also 24,25-dihydro-$\Delta^{13(17)}$-protosterol (**4**) and 24,25-dihydroparkeol (**5**), apparently arising as a consequence of chair–boat–chair folding (β-**2a**), cyclization, and (in the case of **5**) termination by a CH_3–H migration sequence akin to that occurring in the biological process. Abiological tricyclization of **2b**, the C-3(*) epimer of **2a**, yields only (−)-isotirucallenol (**6**), the enantiomer of naturally derived material,[4] again a consequence of the all-chair arrangement. Similarly, synthetic epoxide **7a** affords parkeol (**8**), while **7b**, the C-3(*) epimer of **7a**, gives rise to (−)-isotirucallol (**9**).[5]

The cyclohexenyl alcohol **10a**, prepared from (*S*)-(−)-limonene as previously described,[6] was converted by the Lee method[7] (93%) to the corresponding bromide **10b** [bp 70° (0.4 mm); nmr δ 0.99 (d, 3, J = 6.5 Hz, CH_3CH), 1.62 (s, 3, $CH_3C{=}C$), 3.40 (q of d, 2, J_{AB} = 13 Hz, J_{AX} = 4 Hz, J_{BX} = 6 Hz, CH_2Br)], which, on treatment with malonic ester anion at 80° in DMSO for 1 hr, gave rise to the diester **10c** (66%) [bp 120° (0.1 mm); nmr δ 0.86 (d, 3, J = 6.5 Hz, CH_3CH), 3.47 (d of d, 1, J_{AX} = 6 Hz, J_{AY} = 9.5 Hz, $CH(COOMe)_2$), 3.73 (s, 6, $(COOCH_3)_2$)]. Decarbomethoxylation of **10c** was carried out (81%) by heating with NaCN[8,9] in DMSO solution at 130°, and the resulting monoester was quantitatively reduced by $LiAlH_4$ to the corresponding alcohol **10d** [ir (film) 3320 cm^{-1}; nmr δ 0.85 (d, 3, J = 6 Hz, CH_3CH), 1.63 (br s, 3, $CH_3C{=}C$), 3.61 (t, 2, J = 6.5 Hz, CH_2OH), 5.37 (br, 1, C=CH)]. On oxidation with *m*-chloroperbenzoic acid in CH_2Cl_2 at 0°, **10d** was transformed (95%) to a 1:2.2 mixture of α:β epoxides **11a** (separable by glc, 3% OV-225, 110°) [nmr δ 0.82 and 0.83 (two d, 3, CH_3CH of diastereomers), 1.30 (s, 3, CH_3C–O), 2.97 (d, J = 5 Hz, H(c-C(O)C of β-epoxide), 3.03 (br s, HC–O of α-epoxide), 3.60 (t, 2, J = 6 Hz, CH_2 OH)], which mixture was further oxidized by Collins reagent[10] in CH_2Cl_2 to the aldehyde **11b** [ir (film) 2710, 1720 cm^{-1}; nmr δ 0.81 and 0.83 (two d, J = 6 Hz, CH_3CH), 1.29 (s, 3, CH_3C–O), 9.74 (t, 1, J = 1.5 Hz, CHO)]. By means of a Wittig reaction with triphenylphosphonium isopropylide, aldehyde **11b** was converted to diene monoxide mixture **11c** (56% from **5a**) [bp 90° (bulb-to-bulb) (0.04 mm); nmr δ 1.30 (s, 3, CH_3C–O), 1.60 and 1.68 (two s, 6, $(CH_3)_2C{=}C$), 5.08 (br t, 1, J = 7 Hz, C=CH)]. Treatment of the epoxide mixture **11c** with 3% $HClO_4$ in THF at room temperature for 3 hr effected conversion (92%) to an 8.4:1 (diaxial:diequatorial hydroxyls) mixture of diastereoisomeric trans glycols (**12**) (separable by column chromatography on silica) [nmr: diaxial OH δ 0.86 (d, 3, J = 6 Hz, CH_3CH), 1.22 (s, 3, CH_3COH), 3.57 (br s, 1, HCOH); diequatorial OH δ 0.83 (d, 3, J = 6 Hz, CH_3CH), 1.15 (s, 3, CH_3COH), 3.50 (d of d, 1, J = 4 Hz, J = 11 Hz, HCOH)], which mixture was subjected to sodium metaperiodate in THF–H_2O for 18 hr at 60°. The resulting ketoaldehyde [ir



10a, X = OH
b, X = Br
c, X = $CH(COOCH_3)_2$
d, X = $(CH_2)_2OH$



11a, X = CH_2OH
b, X = CHO
c, X = $CH{=}C(CH_3)_2$

(3) For earlier nonenzymic synthesis and polycyclization of terpenoid terminal epoxides, see *inter alia* (a) E. E. van Tamelen and T. J. Curphey, *Tetrahedron Lett.*, 121 (1962); (b) E. E. van Tamelen, A. Storni, E. J. Hessler, and M. Schwartz, *J. Amer. Chem. Soc.*, **85**, 3295 (1963); (c) E. E. van Tamelen, J. Willett, M. Schwartz, and R. Nadeau, *ibid.*, **88**, 5937 (1966); (d) E. E. van Tamelen and R. G. Nadeau, *ibid.*, **89**, 176 (1967); (e) E. E. van Tamelen, G. M. Milne, M. I. Suffness, M. C. Rudler-Chauvin, R. J. Anderson, and R. Achini, *ibid.*, **92**, 7202 (1970).

(4) Isotirucallol and isotirucallenol (Δ^{24}-dihydroisotirucallol) are, respectively, the C-20 epimers of isoeuphol and isoeuphenol (Δ^{24}-dihydroisoeuphol).

(5) Reaction mechanism detail is not known, and products **3**, **4**, **5**, **6**, **8**, and **17** may result from cyclization initiated on and controlled by an entirely preformed all-chair or chair–boat–chair acyclic conformer, or they may originate by sequential appearance of appropriate individual conformational units, each of which precedes a discrete cyclization leg.

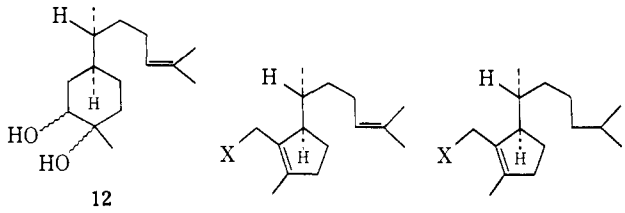
(6) B. A. Pawson, H-C. Cheung, S. Gurbaxani, and G. Saucy, *J. Amer. Chem. Soc.*, **92**, 336 (1970).

(7) J. B. Lee and T. J. Nolan, *Can. J. Chem.*, **44**, 1331 (1966).

(8) See A. P. Krapcho, G. A. Glynn, and B. J. Grenor, *Tetrahedron Lett.*, 215 (1967), for examples of decarboethoxylation by this means. We found that milder conditions were necessary to effect efficiently the reaction.

(9) It is convenient to convert bromide **10b** to monoester by carrying out in DMSO sequential alkylation and decarbomethoxylation in a "one-flask" reaction.

(10) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).



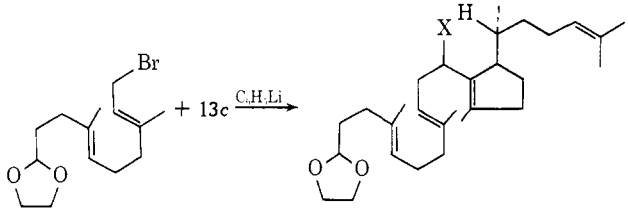
12

13a, X = OH
b, X = Br
c, X = $(n\text{-}C_4H_9)_3P^+Br^-$

16a, X = OH
b, X = Br

(film) 2270, 1715 cm^{-1}; nmr δ 2.12 (s, 3, CH_3CO), 9.74 (t, 1, J = 1.5 Hz, CHO)] was heated in benzene at reflux with piperidine–acetic acid and thereby transformed (63%) to the cyclopentenaldehyde, which was reduced directly by means of $NaBH_4$ to the alcohol **13a** (63% from 12) [bp 95° (0.04 mm); nmr δ 0.83 (d, 3, J = 6.5 Hz, CH_3CH), 3.99 (br, d, 1, J = 12 Hz, CHOH), 4.26 (d, 1, J = 12 Hz, CHOH)].

After formation[7] of bromide **13b** from alcohol **13a**, coupling was carried out, as previously described,[11] between trisnoracetal **14**[12] and the ylide derived by



14

15a, X = $(n\text{-}C_4H_9)_3P^+Br^-$
b, X = H

treatment with phenyllithium of phosphonium salt **13c**. The coupling product **15a**[13] (29%) [nmr δ 0.97 (br t, 9 J = 4 Hz, CH_3CH_2O), 4.85 (t, 1, J = 4.5 Hz, OCHO)] was reduced with lithium–ethylamine to tetraeneacetal **15b** (80%) [nmr δ 0.90 (d, 3, J = 7 Hz, CH_3CH), 3.89 (m, 4, OCH_2CH_2O), 4.84 (t, 1, J = 4.5 Hz, OCHO), 5.11 (br m, 3, C=CH)]. The aldehyde obtained by perchloric acid hydrolysis of **15b** (91%) was converted by diphenylsulfonium isopropylide[14] (80%) to epoxide **7**, presumably a *ca.* 50:50 mixture of C-3 epimers (*) (**7a,b**) inseparable by chromatographic means.

Exposure of epoxide **7** to 2.5 equiv of $SnCl_4$ in CH_3NO_2 at 0° for 1.5 hr resulted in formation of a product complex from which there was isolated by means of a combination of tlc (silica; three elutions with 7% EtOAc–petroleum ether, R_f 0.34) and preparative vpc (6-ft 3% OV-17, 260°) methods, (−)-isotirucallol (**9**) (18%):[15] mp 140–143° (MeOH–H_2O) [ir (CCl_4) 3640, 2950, 1450, 1370, 1020 cm^{-1}; nmr (C_6D_6) δ 0.81, 0.91, 1.04, 1.10, 1.18 (ratio 2:1:1.5:0.5:1), 1.60 and 1.70 (br s, 6, CH_3C=C), 3.05 (br m, 1, HCOH), 5.25 (m, 1, C=CH); mass spectrum (70 eV) calcd for $C_{30}H_{50}O$, 426.3860; found, 426.3838]. Acid-catalyzed isomerization (1% $HClO_4$ in HOAc, 55° for 12 hr) of natural (+)-tirucallol acetate afforded (+)-isotirucallol acetate; the latter, when hydrolyzed, gave (+)-isotirucallol, the glc and mass spectral properties of which were identical with those of (−)-isotirucallol resulting from cyclization of **7**. Identification as **9** was confirmed by catalytic hydrogenation (10% Pd/C–C_2H_5OH) to (−)-isotirucallenol (**6**), mp 142–144° (MeOH–H_2O), indistinguishable from that obtained by cyclization of epoxide **2b** (see below). Admixture with (+)-isotirucallenol (mp 143.5–145.5°)[16] gave melting point depression (range 120–130°). A second preparative vpc product, further purified by $AgNO_3$–silica tlc, was identified as parkeol (**8**) (2%)[15] by vpc, gas chromatographic–mass spectral, ir, and mixture melting point comparison of its acetate (mp 161–163°) with authentic parkeyl acetate (mp 162–165°), as well as hydrogenation (10% Pd/C) to Δ^{24}-dihydroparkeol; identical (vpc, gas chromatography–mass spectra) with an authentic sample of **5**.

In order to obtain dihydroepoxide **2**, the cyclopentenyl alcohol **13a** was selectively hydrogenated (5% Pt/C) to allylic alcohol **16a** (90%) [bp 75° (bulb-to-bulb) (0.1 mm); nmr ($CDCl_3$) δ 0.85 (d, 6, J = 6 Hz, $(CH_3)_2$-CH), 0.90 (d, 3, J = 6 Hz, CH_3CH), 3.98 (br d, 1, J = 12 Hz, CHOH), 4.30 (d, 1, J = 12 Hz, CHOH)], and the corresponding bromide **16b**[5] was subjected to a reductive coupling sequence similar to ones described elsewhere.[17,18] Attachment of the terminal epoxide unit, as above with **15b**, completed the synthesis of the **2a,b** mixture [nmr ($CDCl_3$) 1.25 and 1.28 (two s, 6, $(CH_3)_2C$–O), 2.70 (t, 1, J = 6 Hz, HC–O)].[19]

As with **7a,b**, cyclization of epoxide **2a,b**, followed by tlc separation of products, yielded a tetracycle fraction (R_f 0.23; 30% weight recovery) comprising (vpc) isoeuphenol (**3**) (3.5%), 24,25-dihydro-$\Delta^{13(17)}$-protolanosterol (**4**) (2%), and 24,25-dihydroparkeol (**5**) (3.5%), all from epoxide **2a**,[15] and (−)-isotirucallenol (**6**) (43%) from epimer **2b**.[15] After further purification by preparative vpc (6-ft 3% OV-17, 245°), the identity of **6** was established by ir, nmr, high- and low-resolution mass spectra, glc (three columns), and melting point comparison with an authentic specimen of (+)-isotirucallenol.[20] Isoeuphenol (**3**) from cyclization of **2a** was identical with authentic material[21] as indicated by vpc coinjections (3% OV-17, 3% OV-25, 3% OV-225) and gas chromatographic–mass spectral comparison. Synthetic dihydroparkeyl acetate (mp 173–175°) was indistinguishable from an authentic sample (mp 175–176°)[22] (mmp 173–175°; coinjection on 3% OV-17, 3% OV-25; identical gas chromatography–mass spectra). Likewise, dihydroprotolanosterol (**4**) proved to have the same vpc retention times (3% OV-17, 3% OV-25) and gas chromatography–mass spectra as the authentic compound.[23] Since $BF_3 \cdot Et_2O$–CH_3NO_2 treat-

(11) E. H. Axelrod, G. M. Milne, and E. E. van Tamelen, *J. Amer. Chem. Soc.*, **92**, 2139 (1970).
(12) K. B. Sharpless, R. P. Hanzlik, and E. E. van Tamelen, *ibid.*, **90**, 209 (1968).
(13) Because of difficulties in purification, a combustion analysis on the phosphonium salt was not attempted.
(14) E. J. Corey, M. Jautelat, and W. Oppolzer, *Tetrahedron Lett.*, 2325 (1967).
(15) Yield based upon reaction of one epoxide epimer.
(16) J. S. Mills, *J. Chem. Soc.*, 2196 (1956).
(17) E. E. van Tamelen, R. A. Holton, R. E. Hopla, and W. E. Konz, *J. Amer. Chem. Soc.*, **94**, 8228 (1972).
(18) E. E. van Tamelen, M. P. Seiler, and W. Wierenga, *ibid.*, **94**, 8229 (1972).
(19) All new compounds described in this paper gave satisfactory combustion analysis.
(20) J. S. Mills, *J. Chem. Soc.*, 2196 (1956).
(21) M. C. Dawson, T. G. Halsall, and R. E. H. Swayne, *ibid.*, 590 (1953).
(22) W. Voser, M. Montavon, Hs. H. Gunthard, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **33**, 1893 (1950).
(23) (a) G. Visconti di Modrone, Ph.D. Thesis, ETH, Zurich, 1968; (b) T. Hattori, H. Igarashi, S. Iwasaki, and S. Okuda, *Tetrahedron Lett.*, 1023 (1969).

ment of authentic dihydro-$\Delta^{13(17)}$-protolanosterol (**4**) (or its acetate)[24] resulted in formation (70–80%) of dihydroparkeol (**5**)[25] (or acetate), the realization of the same transformation (vpc and gas chromatographic–mass spectral comparisons) when synthetic tetracycle **4** was subjected to such conditions confirms its identification as **4**. In that terpenoid **5** has been previously converted[26] to 24,25-dihydrolanosterol (**17**), the present work also constitutes a direct total synthesis of the latter natural product.[27]

Although generation of either the 9,10 trans or cis rearrangement in the hydronaphthalene framework arising from polycyclization of terpenoid terminal epoxides has been previously observed,[28] the formation of tetracycles **4**, **5**, and **8** from epoxides **2a** and **7a** represents the first *tric*yclization featuring the 9,10 cis outcome and thus emerges as a close simulation of the biosynthetic conversion of squalene oxide to the presterol, and thence to the lanosterol level. The results described herein thus not only constitute total syntheses of tetracycles **3**, **4**, **5**, **6**, **8**, and **17**, but also suggest that biological chair–boat–chair construction rests on a palpable, purely chemical foundation, the function of the lanosterol cyclase enzyme being in part to optimize this particular folding–cyclization process.

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(24) The observation that $SnCl_4$–CH_3NO_2 also effects, albeit in lower yield, conversion of **4** to **5** permits that **5** may be generated from **4** under the conditions when **4** is formed from **2**.

(25) S. Uyeo, J. Okada, S. Matsunaga, and J. W. Rowe, *Tetrahedron*, **24**, 2859 (1968).

(26) Despite the considerable difference in melting point from literature values and the unmistakable mass spectral retro Diels–Alder cleavage exhibited by the derived Δ^1-3-ketone indicative of a Δ^7 double bond, the epoxide cyclization product reported by E. E. van Tamelen and J. W. Murphy, *J. Amer. Chem. Soc.*, **92**, 7204 (1970), is indistinguishable from dihydroparkeol (**5**).

(27) The synthesis of lanosterol from cholesterol was achieved by R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *ibid.*, **79**, 1131 (1957).

(28) Cis and/or trans: E. E. van Tamelen, A. Storni, E. J. Hessler, and M. Schwartz, *ibid.*, **85**, 3295 (1963); E. E. van Tamelen and R. M. Coates, *Chem. Commun.*, 13, 413 (1966); E. E. van Tamelen and J. P. McCormick, *J. Amer. Chem. Soc.*, **91**, 1847 (1969). Trans: E. E. van Tamelen and R. G. Nadeau, *ibid.*, **89**, 176 (1967); E. E. van Tamelen, G. M. Milne, M. I. Suffness, M. C. Rudler-Chauvin, R. J. Anderson, and R. S. Achini, *ibid.*, **92**, 7202 (1970). Cis: ref 17.

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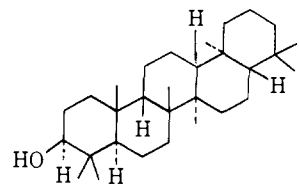
Biogenetic-Type Total Synthesis. *dl*-Tetrahymanol

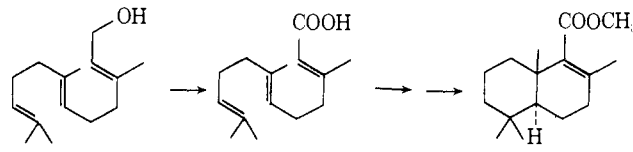
Sir:

Incorporating five carbocyclic rings and nine asymmetric centers, the protozoan metabolite tetrahymanol (**1**)[1,2] presents a considerable challenge for



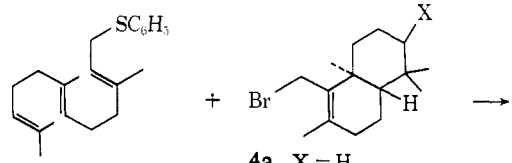
1

laboratory construction by efficient means. We have now completed a *dl*-tetrahymanol total synthesis—the first of a pentacarbocycle featuring ring formation solely by polyolefin cyclization methods—which comprises ten steps starting from farnesol (**2**), or seven steps from previously described, available starting material **3**.[3a]



2 3

Bicyclic bromide **4a**, prepared by $LiAlH_4$ reduction of **3** to allyl alcohol followed by treatment with hydrobromic acid,[3b] was used without purification to alkylate (THF for several hours in the range −35 to 20°) the anion of phenyl thioether **5**,[4] prepared by sequential



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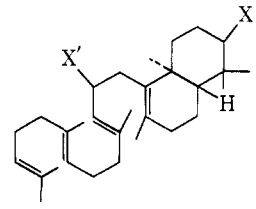
4a, X = H
b, X = $OCH_2C_6H_5$



6a, X′ = SC_6H_5; X = H
b, X′ = H; X = H
c, X′ = SC_6H_5; X = $OCH_2C_6H_5$
d, X′ = H; X = OAc

in situ treatment of *trans,trans*-farnesol with methyllithium, *p*-toluenesulfonyl chloride, and lithium thiophenoxide. The trans,trans alkylation product **6a** [nmr (CCl_4) δ 7.07 (5, s), 4.97 (3, m), 3.90 (1, m), 0.87 (12, m)] (65%) was reductively desulfurized (100%)[4] with Li–$C_2H_5NH_2$ at −78° to a *ca.* 50:50 mixture of the desired 2,6,10,14-tetraene **6b** [nmr (CCl_4) δ 5.02 (3, m), 0.92 (3, s), 0.87 (3, s), 0.82 (3, s)] and the 2,6,11,14 isomer [nmr (CCl_4) δ 2.65 (2, d, J = 2 Hz)], separated by gc or preparative tlc ($AgNO_3$–SiO_2). Presumably because of adverse steric influences in the environment of the Δ^{14} tetrasubstituted bond, selective oxidative attack[5] on the terminal Δ^2 trisubstituted site

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