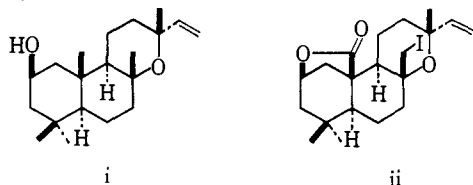


tation of its formation support Vb as the most likely structure.^{11,12}

The availability of substances of structure type IIIb opens an easy route to the highly oxygenated diterpenic constituents of *Sciadopitys verticillata*¹³ and diterpene alkaloids. The transformation products of friedanol can be of aid in the determination of the structures of the friedelanic triterpenes of *Siphonodon australe* Benth.^{14,15}

(11) Whereas in principle the friedanol skeleton should permit three 1,5-hydrogen shifts to take place, no products of overoxidation of established constitution derived from such changes have been isolated. However, two of the minor products, C₃₀H₄₈O [mp 341–343°; no C=O (infrared), no C=C (infrared, pmr)] and C₃₀H₄₈O₂ [mp 284–285°; no C=O, C=C (infrared)], may be such representatives.

(12) Both transformations Ia → IIb and IV → Vb illustrate V-shaped chemical billiard shots. The consequence of a linear shot is portrayed by ii (mp 162–164° dec), one of the products of lead tetracetate–iodine oxidation (followed by Jones oxidation) of 2β-hydroxymanoyl oxide (i).



(13) M. Sumimoto, *Tetrahedron*, **19**, 643 (1963); C. Kaneko, T. Tsuchiya, and M. Ishikawa, *Chem. Pharm. Bull. (Tokyo)*, **11**, 271 (1963).

(14) Reference cited in footnote 10.

(15) The authors are indebted to the National Science Foundation for support of this work, to Drs. C. Djerassi, O. E. Edwards, M. Fétizon, and P. Grant for samples of compounds used in this work, and to Dr. W. Hargrove for mass spectral determinations.

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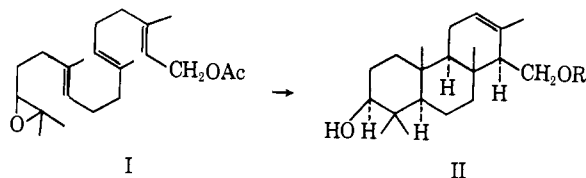
Laboratory Cyclization of Geranylgeranyl Acetate Terminal Epoxide

Sir:

With the demonstration that squalene 2,3-oxide is converted enzymatically in good yield to lanosterol and cholesterol,¹ the study of simpler terpene terminal epoxides² gains added interest and importance, especially in the sense that they are implicated as biological precursors of other 3-hydroxylated polycyclic systems. In this publication we describe the terminal epoxide of geranylgeranyl acetate (I) and its reactivity under nonenzymic conditions, including formation of a 3-hydroxylated tricyclic terpenoid (II, R = Ac)

(1) (a) E. J. Corey and W. E. Russey, *J. Am. Chem. Soc.*, **88**, 4750 (1966); E. E. van Tamelen, J. D. Willett, R. B. Clayton, and K. E. Lord, *ibid.*, **88**, 4752 (1966).

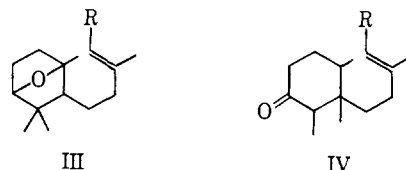
(2) E. E. van Tamelen, A. Storni, E. J. Hessler, and M. Schwartz, *ibid.*, **85**, 3295 (1963); E. E. van Tamelen, M. Schwartz, E. J. Hessler, and A. Storni, *Chem. Commun.*, 409 (1966); E. E. van Tamelen and R. M. Coates, *ibid.*, 413 (1966).



featuring six asymmetric centers specifically oriented in the relationship characteristic of the natural product series.³

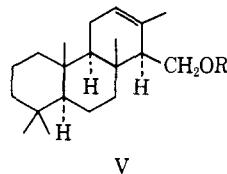
trans,trans,trans-Geranylgeraniol was obtained from *trans,trans*-farnesol by modification of the Ruzicka procedure.⁴ *N*-Bromosuccinimide oxidation of geranylgeranyl acetate in aqueous tetrahydrofuran⁵ provided the terminal bromohydrin, which on treatment with potassium carbonate in methanol gave the terminal epoxide of the free alcohol (over-all yield 45%).

Conversion to the oily acetate (I) was followed by cyclization, carried out by exposure to 0.2 molar equiv of stannic chloride in benzene for 5 min at ca. 0°. After routine work-up and chromatography of the resulting mixture on silica gel, various entities were isolated, including a hydrocarbon fraction (~5%), cyclic ether III (~5%), monocyclic ketone IV (~27%), and a mixture consisting (by nmr) of acyclic terminal



chlorohydrin (~27%) and tricyclic diol monoacetate (~10%). Isolation and purification of the latter was facilitated by conversion of crude fractions to *p*-nitrobenzoate, which was subjected to preparative tlc on silver nitrate–silica gel. Saponification of the chromatographed diol diester provided tricyclic diol II (R = H), the mass spectrum of which was entirely consistent with the assigned structure.

Reliable chemical evidence for the molecular and stereochemical nature of the tricyclic substance II was obtained by conversion to a transformation product (V) also derivable in a rational manner from the



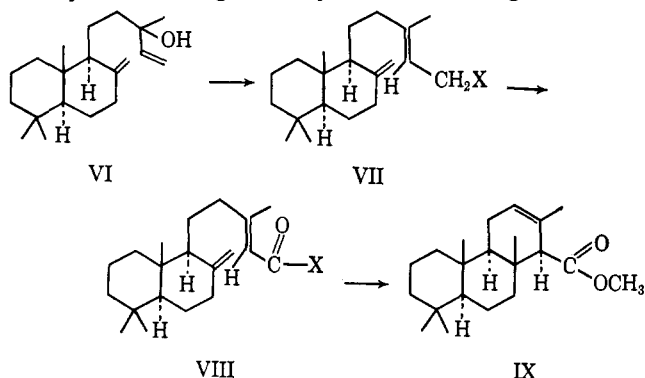
naturally occurring manool (VI). The synthetic monoester was oxidized by Jones reagent to the corresponding keto acetate, which was subjected to the ethylene dithioketalization–Raney nickel hydrogenolysis se-

(3) Nonoxidative conversion of acyclic polyenes to tricyclic substances in the natural product category have been reported by (a) A. Eschenmoser, "Biosynthesis of Terpenes and Sterols," Ciba Foundation Lectures, G. E. W. Wolstenholme and M. O'Conner, Eds., J. and A. Churchill, Ltd., London, 1959, p 224, (b) W. S. Johnson, N. P. Jensen, and J. Hooz, *J. Am. Chem. Soc.*, **88**, 3859 (1966); W. S. Johnson and R. B. Kinnel, *ibid.*, **88**, 3861 (1966).

(4) L. Ruzicka and G. Firmenich, *Helv. Chim. Acta*, **22**, 392 (1939). In our hands, formation of ethyl geranylgeranate (50:50 *cis-trans* α,β-unsaturated ester mixture, by vpc) was carried out by addition of ethoxyacetylene to farnesylacetone, followed by hydrolysis with dilute sulfuric acid (over-all yield >95%). After enrichment (≥90% by vpc) of the all-*trans* isomer by chromatographic means, geranylgeraniol was prepared by lithium aluminum hydride reduction.

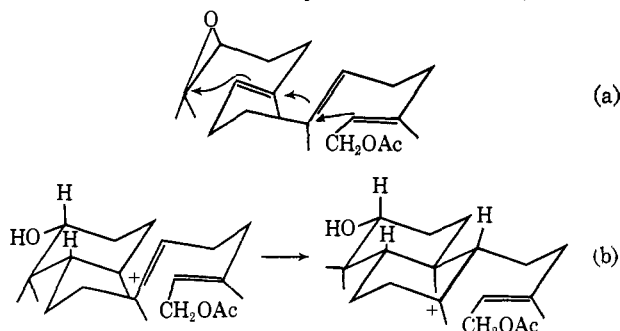
(5) E. E. van Tamelen and T. J. Curphey, *Tetrahedron Letters*, 121 (1962).

quence. Purification (tlc) of the *p*-nitrobenzoate (V, R = COC₆H₄-*p*-NO₂) was employed in order to obtain tricyclic alcohol which, as the acetate, appeared substantially homogeneous (single peak with a slight shoulder on vpc over Apiezon at 270°). Alternatively, alcohol V resulted from the synthetic sequence VI → VII (X = Br) → VIII (X = OAc) → VIII (X' = H) → VIII (X' = OCH₃) → IX → V, the penultimate step closely resembling the cyclization of agathic acid



to isoagathic acid, substances of established structure and stereochemistry.⁶ The unsaturated methyl ester IX, a well-defined crystalline substance of mp 108–110°, provided on lithium aluminum hydride reduction noncrystalline but stereochemically homogeneous tricyclic alcohol V (R = H). The vpc, infrared, and mass spectral behavior of the alcohols (II, R = H) derived from the two sources were, within experimental error, identical. Since the nmr spectrum of synthetic II reveals axial hydrogen (broad peak τ 6.67–7.15, $J = \sim 7$ cps) at C-3,⁷ the stereochemistry of II is established at all positions as shown.⁸

Although the methyl substitution pattern of squalene oxide directs laboratory cyclization principally to tricyclic product with a five-membered C ring,⁹ the "head-to-tail" arrangement of all isoprene units in geranylgeraniol permits formation of a hydrophenanthrene system through involvement of three centers with chemically preferred, *t*-carbocationic properties. In the sesquiterpene series, it has been demonstrated that monocyclic products obtained by cyclization of terminal epoxide are not separately converted under original cyclization conditions to bicyclic products formed concurrently from the epoxide, and therefore are not intermediates.⁷ By the same token, further



(6) S. Bory, M. Fétizon, and P. Laszlo, *Bull. Soc. Chim. France*, **30**, 2310 (1963).

(7) Cf. E. E. van Tamelen and E. J. Hessler, *Chem. Commun.*, 411 (1966).

(8) Spectral (mass, infrared, and/or nmr) characteristics of all substances described are consistent with the assigned structures.

(9) E. E. van Tamelen, J. Willett, M. Schwartz, and R. Nadeau, *J. Am. Chem. Soc.*, **88**, 5937 (1966).

cyclization under original conditions of mono- or bicyclic material produced from geranylgeranyl acetate epoxide is unlikely; consequently we believe that the tricyclic diol II monoacetate arises from epoxide I by (a) a synchronized cyclization, (b) a stepwise sequence involving mono- or bicyclic carbonium ions, or (c) a sequential combination of mechanisms a and b.

Acknowledgment. The authors are grateful to the National Science Foundation and the National Institutes of Health for grant support.

(10) National Institutes of Health Predoctoral Fellow, 1964–1965 academic year.

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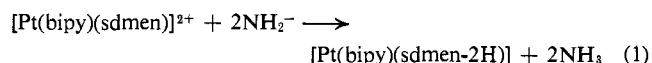
Received October 12, 1966

Reactions of Deprotonated Ligands. II. The *in Situ* Synthesis of Bipyridyl(*N,N,N',N'*-tetramethylethylenediamine)platinum(II) Chloride^{1,2}

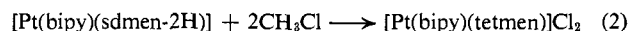
Sir:

In connection with studies on the effect of methyl substitution upon the deprotonation of coordinated ethylenediamine, we had need for an authentic specimen of [Pt(bipy)(tetmen)]Cl₂. Conventional methods of synthesis, *e.g.*, treatment of [Pt(bipy)X₂] with tetmen or [Pt(tetmen)X₂] with bipy, and other direct approaches that seemed reasonable failed to provide the desired product.

We have, however, produced the complex by an indirect route which, as far as we are aware, is unprecedented in the sense of producing *in situ* a ligand that apparently cannot be introduced directly. This was done by producing [Pt(bipy)(sdmen)]I₂ by a known method,³ removing both remaining protons from the nitrogen atoms using methods described elsewhere⁴



and methylating the deprotonated species as described in an earlier communication.⁵



Attempts to form the corresponding iodide by using methyl iodide in reaction 2 led to the desired product, but (as shown by X-ray diffraction and infrared spectral data) it was contaminated with [Pt(bipy)₂I₂]. By taking advantage of the lesser tendency for chloride to coordinate with platinum(II) and carrying out reaction 2 at 7°, only very small quantities of by-product [Pt(bipy)Cl₂] resulted; this was eliminated essentially completely by carrying out the reaction at -12°. The experimental evidence is as follows.

To establish that [Pt(bipy)(sdmen)]I₂ is unreactive toward the deprotonation reaction medium, a 0.54-g sample was treated with anhydrous liquid ammonia

(1) This work was supported by the U. S. Atomic Energy Commission and the Robert A. Welch Foundation.

(2) bipy = 2,2'-bipyridyl; en = ethylenediamine; en-H = a deprotonated en ligand, and similarly for sdmen; sdmen = *N,N'*-dimethylethylenediamine; tetmen = *N,N,N',N'*-tetramethylethylenediamine.

(3) G. W. Watt and D. G. Upchurch, *Inorg. Nucl. Chem. Letters*, **2**, 363 (1966).

(4) G. W. Watt and J. K. Crum, *J. Am. Chem. Soc.*, **87**, 5366 (1965).

(5) G. W. Watt and D. G. Upchurch, *ibid.*, **87**, 4212 (1965).