whose oxidation product showed no further change in rotation, the fraction was considered to be optically pure.

The physical properties of 2-*l*,4′D,8′D-α-tocopherol are given in Table I. It has a slight positive rotation of 0.36°. However, the specific rotation (−24°) of its oxidation product is opposite in sign to that of the oxidation product from natural *d*-α-tocopherol and the 2-*d*,4′D,8′D-α-tocopherol prepared *via* the fractionation procedure. The rotations of the *l*-acetate and acid succinate esters were negative and lower in value than the corresponding *d*-esters.

Melting points for the *l*-acetate and acid succinate were lower than for the corresponding *d*-esters.

The 2-*d*,4′D,8′D-α-tocopherol prepared by the fractionation procedure was judged to be identical with natural *d*-α-tocopherol from the data shown in Table I for the free tocopherols, oxidation products, crystalline acetates and acid succinates.

This procedure for preparing 2-*l*,4′D,8′D-α-tocopherol makes it available for determining the relation between stereochemical configuration and vitamin E activity of α-tocopherol in human and animal nutrition. Such studies are in progress.

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RECEIVED JUNE 13, 1962

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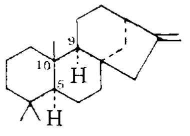
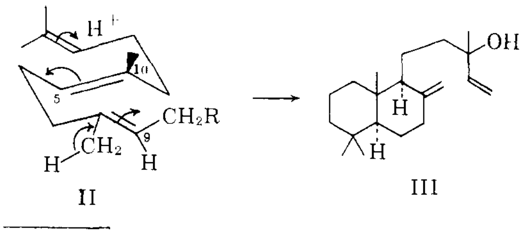
## STEREOCHEMISTRY OF THE DITERPENOIDS: ABSOLUTE CONFIGURATION OF CAFESTOL[1]

*Sir:*

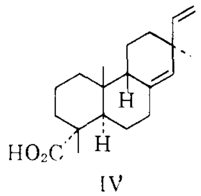
The recent disclosure[2] of the absolute configurations of steviol, kaurene and the diterpene alkaloids, together with the unequivocal assignment of absolute stereochemistry (I) to phyllocladene,[3,4a] suggests a concerted *trans-anti* cyclization in the biosynthesis of the diterpenoids from a geranylgeraniol precursor[5] (II → III). Earlier speculations[4,5,6] regarding the stereochemical nature of the primary diterpenoids cyclization have, however, been tempered by the presence of a small but important group of $C_{20}$ compounds which apparently[6] possessed a *syn*-9,10 backbone. These include isopimaric acid (IV),[7] rosenonolactone (V)[8] and its relatives (VI, VII), gibberellic acid (VIII)[9], eperuic acid (IX),[10] rimuene (X),[11a,b] cafestol (XI),[4a,12] and kahweol (XII).[4a]



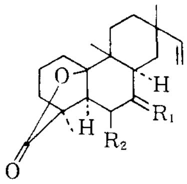
I



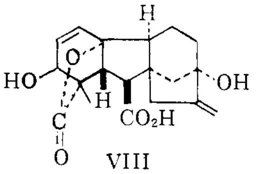
II III



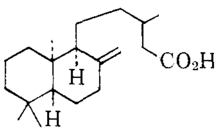
IV



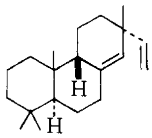
V, $R_1 = O$
$R_2 = H$
VI, $R_1 = H_2$
$R_2 = OH$
VII, $R_1 = H_2$
$R_2 = H$



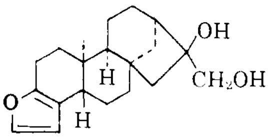
VIII



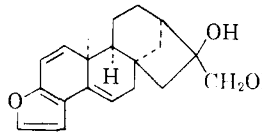
IX



X



XI



XII

We now suggest that the entire family of di-, tri- and tetracarbocyclic diterpenoids is based on the backbone of rings A and B in the *trans-anti* configuration (as III and its mirror image). The exceptions to the 9,10-*anti* configuration can be eliminated as follows.

Stereospecific syntheses[11b] of structure (IV) epimeric at $C_9$ and $C_{13}$ representing rimuene have demonstrated that the proposed formulation is untenable and suggest that the isomerism of (IV) and (X) with their respective relatives is structural.[13] A process such as XIII→VII[14] in the biosynthesis

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[1] Circular Dichroism Studies. II. Part I: F. McCapra, A. I. Scott, G. A. Sim and D. W. Young, *Proc. Chem. Soc.*, in press, 1962.

[2] C. Djerassi, P. Quitt, E. Mosettig, R. C. Cambie, P. S. Rutledge and L. H. Briggs, *J. Am. Chem. Soc.*, **83**, 3720 (1961).

[3] P. K. Grant and R. Hodges, *Tetrahedron*, **8**, 261 (1960).

[4] (a) C. Djerassi, M. Cais and L. A. Mitscher, *J. Am. Chem. Soc.*, **81**, 2386 (1959); (b) E. Wenkert and J. W. Chamberlain, *ibid.*, p. 688.

[5] L. Ruzicka, *Experientia*, **9**, 357 (1953); *Proc. Chem. Soc.*, 341 (1959).

[6] W. B. Whalley, *Tetrahedron*, **18**, 43 (1962).

[7] (a) B. Green, A. Harris and W. B. Whalley, *J. Chem. Soc.*, 4715 (1958); O. E. Edwards and R. Howe, *Canad. J. Chem.*, **37**, 760 (1959).

[8] A. Harris, A. Robertson and W. B. Whalley, *J. Chem. Soc.*, 1799, 1807 (1958); W. B. Whalley, B. Green, D. Arigoni, J. J. Britt and C. Djerassi, *J. Am. Chem. Soc.*, **81**, 5520 (1959).

[9] B. E. Cross, *J. Chem. Soc.*, 3022 (1960); G. Stork and H. Newman, *J. Am. Chem. Soc.*, **81**, 5518 (1959).

[10] C. Djerassi and D. Marshall, *Tetrahedron*, **1**, 238 (1957); J. A. Barltrop and D. B. Bigley, *Chem. and Ind.*, 1447 (1959).

[11] (a) E. Wenkert and P. Peak, *J. Am. Chem. Soc.*, **83**, 998 (1961); (b) R. F. Church and R. E. Ireland, *Tetrahedron Letters*, **14**, 493 (1961).

[12] R. A. Finnegan and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 4342 (1960).

[13] The revised structure for isopimaric acid (Edwards, *et al.*, *J. Org. Chem.*, **27**, 1930 (1962): Ireland, *et al.*, *ibid.*, **27**, (1962) is in full accord with our prediction.

[14] A. J. Birch, R. W. Rickards, H. Smith, A. Harris and W. B. Whalley, *Tetrahedron*, **7**, 241 (1959).

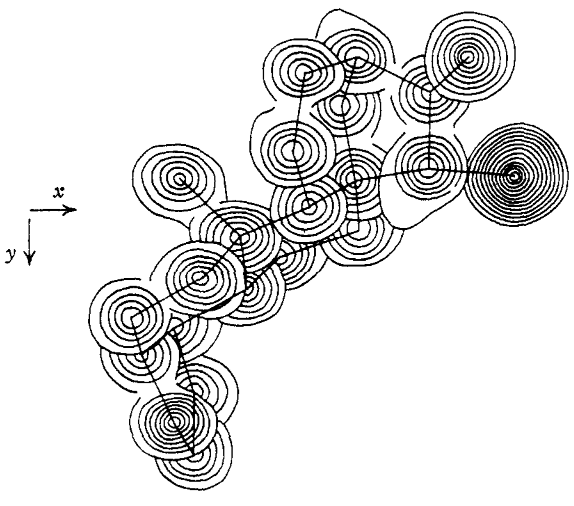


Fig. 1.—The fourth three-dimensional electron-density distribution over the molecule of the bromo-derivative (XVII) drawn parallel to (001).

of the *Trichothecium roseum* metabolites V–VII removes them from the category of diterpenes of exceptional $C_9$ orientation.

The assignment of stereochemistry has been assisted by the development[15] of optical rotatory dispersion. However, the method may be restricted where assignments rely on comparative studies of O.R.D. curves of molecules which are not amenable to octant rule[16] treatment. Therefore structures VIII, IX and XI whose "abnormal" $C_9$ configurations are based mainly on the results of comparison of O.R.D. curves attracted our attention.

It has been shown[1] that gibberellic acid is XIV, derivable from the antipode of *trans-anti* precursor (III) without prior migration of the $C_{10}$ methyl group[14] and we now report a revised stereochemistry (XV) for cafestol. A bromo derivative[4a] of epoxynorcafestanone (XVI) was subjected to X-ray crystallographic analysis and found to have the constitution and relative stereochemistry shown in (XVII).

The bromo derivative (XVII) crystallizes in the orthorhombic system with cell dimensions $a$ = 10.10, $b$ = 14.75, $c$ = 11.18 Å. There are four molecules of $C_{19}H_{27}O_2Br$ in the unit cell ($D_{\text{meas.}}$ = 1.462 g. cm.$^{-3}$, $D_{\text{calc.}}$ = 1.464 g.cm.$^{-3}$) and the space group is $P2_12_12_1$–$D_2^4$. Three-dimensional X-ray intensity data were recorded on equi-inclination Weissenberg photographs and estimated visually.

The co-ordinates of the bromine atom were determined from Patterson syntheses and the remaining atoms (other than hydrogen) were then located by evaluating three-dimensional electron-density distributions. The fourth such distribution is shown in Fig. 1. The average discrepancy between observed and calculated structure amplitudes is 21%. Further refinement is proceeding.

Simultaneous confirmation came from comparison of the circular dichroism data[17] of (XVI) with those of reference compounds. Previous C.D. studies with ketones derived from gibberellic acid showed that in spite of the virtual identity of the O.R.D. curves of gibberic (XVIII) and epigibberic (XIX) acids,[18] the C.D. curves of these epi-

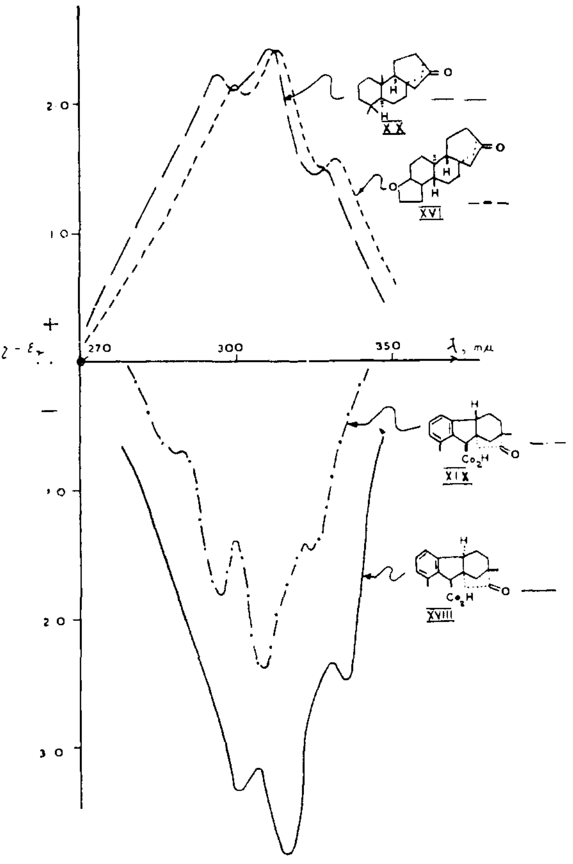
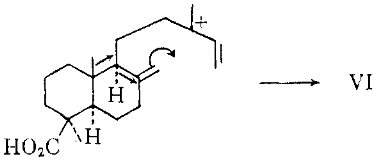
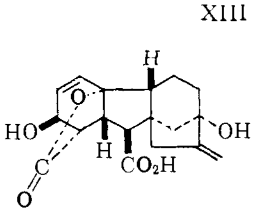


Fig. 2.



XIII



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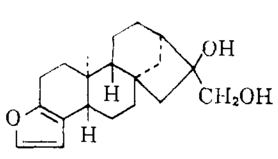
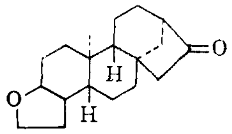
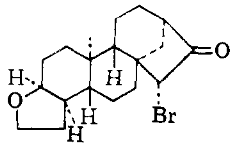


XV



XVI



XVII

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[15] See C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., New York, N. Y., 1960, and later papers of C. Djerassi and his colleagues.

[16] W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961).

[17] We propose the abbreviation C.D. for circular dichroism. For leading references see *Tetrahedron*, **13**, 1 (1961).

[18] J. F. Grove, J. MacMillan, T. P. Mulholland and W. B. Turner, *J. Chem. Soc.*, 3049 (1960).

mers reflected the change of configuration of the $C_9$ hydrogen atom (see Fig. 2). Thus in XVIII a bathochromic displacement of the ellipticity maxima relative to XIX is observed. Similarly, although the O.R.D. curves of XX and of XVI are coincident,[12] the red shift of the dichroism is apparent in epoxynorcafestanone, leading to the assignment of $C_9$ $\beta$-oriented hydrogen.

The remaining exception to $C_{9,10}$-*anti*-configuration is eperuic acid.

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RECEIVED MAY 18, 1962

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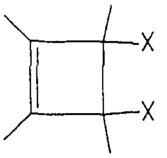
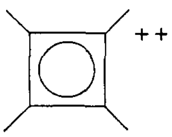
## 1,2,3,4-TETRAMETHYL-2-CHLOROCYCLOBUTENYL CATION

*Sir:*

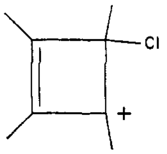
The reaction of 1,2,3,4-tetramethyl-3,4-dichlorocyclobutene (Ia) with silver hexafluoroantimonate in liquid sulfur dioxide was studied in an effort to prepare the tetramethylcyclobutadienyl dication (II), a species which it was presumed would be of exceptional stability as a result of the delocalization energy of its $\pi$-electron system and the salutary effect of its four methyl substituents.[1] However, at −70°, although a ready reaction did take place between the reactants (typically, 0.29 mmole of Ia and 0.72 mmole of $AgSbF_6$ in 0.7 ml. of $SO_2$), the amount of silver chloride isolable by filtration of the reaction mixture, contained in a sealed tube, through a sintered glass disc, was only one mole per mole of the dichloride.[2]



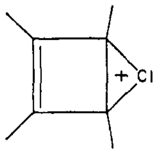
Ia (X = Cl)
b (X = Br)
c (X = F)



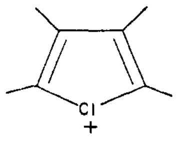
II



III



IV



V

The derivative formed upon quenching the reaction mixture with an excess of tetramethylammonium chloride (by destroying a break-seal connecting two chambers of a sealed tube) proved to be the initial starting material, Ia (65–69% yield by sublimation), identified by melting and mixed melting points. The structure of the organic moiety produced on treatment of Ia with $AgSbF_6$ was determined by examination of the nuclear magnetic resonance (n.m.r.) spectrum of the $SO_2$ solutions at −63° (Fig. 1).[3] Of the possibilities for the nature of the product in solution, II is eliminated by the complexity of the spectrum, and Ic, while not eliminated by the spectral pattern, is excluded by the chemical shifts.[4] Ic and II are also eliminated by the observed precipitation of less than the stoichiometrically required two moles of AgCl. A likely species to be observed in the $SO_2$ solutions is 1,2,3,4-tetramethyl-2-chlorocyclobutenyl cation (III)—an analogous preparation was used to make the 7-norbornadienyl cation[5]—and the n.m.r. spectrum does speak for a product of this structure.[6]

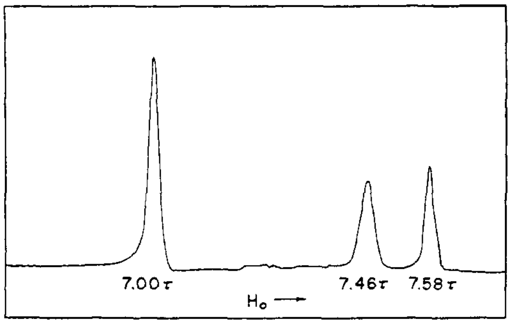


Fig. 1.—N.m.r. spectrum of III in liquid $SO_2$ at −63°; the areas under the peaks as measured planimetrically are from left to right 2.1:0.98:0.92.

The ion does not possess the structure IV or V, and if III, IV, and V are in equilibrium, this implies that III is the most stable.[7] The resolution of the components in the n.m.r. spectrum indicates that, although in other cases chloronium ions are presumably more stable than the corresponding $\alpha$-chlorocarbonium ions, in this case the symmetrical ion, IV, is, compared to the cyclobutenyl cation, III, at a considerable energetic disadvantage. The rate of interconversion of four equivalent structures for III by chlorine migration is less than 10 sec.$^{-1}$; the corresponding free energy of activation and, therefore, the barrier separating

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[1] (a) *Cf.* the heptamethylbenzenonium ion of W. v. E. Doering, M. Saunders, H. G. Boyton, H. W. Earhart, E. F. Wadley, W. R. Edwards, and G. Laber, *Tetrahedron*, **4**, 178 (1958). (b) The synthesis of tetraphenylcyclobutadienyl dication has possibly been realized: H. H. Freedman and A. M. Frantz, Jr., "Abstracts of Papers Presented to the American Chemical Society, Washington, D. C., March, 1962," p. 26-O.

[2] The yield in four runs was 1.25 ± 0.04 moles of AgCl per mole of Ia, probably greater than 1.00 as a result of incomplete separation of the filtrate from the AgCl. Allowing the tube to warm to room temperature for the AgCl isolation would then precipitate a second mole.

[3] Tropylium hexafluoroantimonate was used as an internal standard, and a correction was applied for its chemical shift (0.55 τ) with respect to internal tetramethylsilane (TMS), determined separately, for TMS was itself destroyed in the reaction mixture.

[4] The high intensity band should appear at 8.35 τ. The dichloro compound in $CCl_4$ solution has bands of equal intensity at 8.35 and 8.27 τ relative to internal TMS, and the dibromo compound at 8.35 and 7.97.

[5] P. R. Story and M. Saunders, *J. Am. Chem. Soc.*, **82**, 6199 (1960).

[6] The chemical shifts are consistent with those of known methyl substituted alkenyl cations: N. C. Deno, H. G. Richey, Jr., J. D. Hodge, and M. J. Wisotsky, *J. Am. Chem. Soc.*, **84**, 1498 (1962).

[7] Since IV and V are of relatively high energy, it is unlikely that they are true intermediates in the unusual dimerization reaction used to prepare the dichloro compound Ia by chlorination of dimethylacetylene (*cf.* J. D. Roberts and C. M. Sharts, "Organic Reactions," John Wiley and Sons, Inc., 1962, Vol. 12, p. 17). It is probable that along a reaction path heading for IV or V some displacement irreversibly leads to III and by-passes the former species.