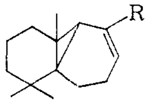
Biogenetically Assigned Structures of Thujopsene and Hinokiic Acid

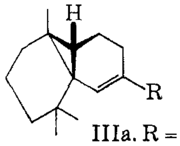
Sir:

The recent publication of Erdtman and Norin[1] on the tentative structures of thujopsene (Ia) and hinokiic acid (Ib) has prompted the authors to make a comment on the possible biogenesis of these sesquiterpenes.

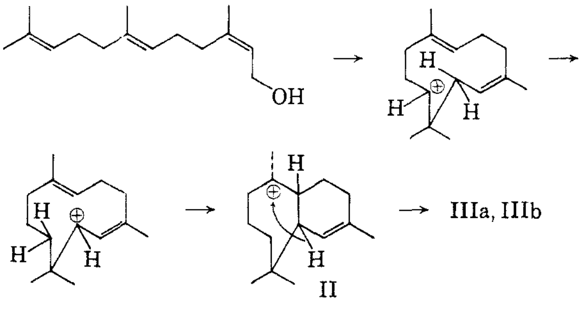
In the light of the ingenious idea of Ruzicka's biogenetic isoprene-rule[2] as extended by Eschenmoser,[3] Hendrickson[4] and others, it is quite attractive to consider that both thujopsene and hinokiic acid are derived from *cis*-farnesol according to the following scheme.



Ia. R = CH_3
Ib. R = COOH



IIIa. R = CH_3
IIIb. R = COOH



The bicyclic cation (II) is a probable intermediate stage for the production of longifolene as suggested by Hendrickson.[4] Regarding the conversion of II into the tricyclic compounds (IIIa and IIIb), a proton elimination assisted by the positive charge situated at the γ-carbon is assumed. Though this type of a cyclization is not very common,[5] the sterically-forced proximity of the α- and γ-carbon atoms concerned should be the cause of this rather unusual formation of the cyclopropane ring.

Such a consideration leads to the predicted absolute configurations of IIIa and IIIb for thujopsene and hinokiic acid, respectively. Those formulas are supported by almost all of the known reactions of the sesquiterpenes.[1,6] Full details will be published elsewhere.

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[1] H. Erdtman and T. Norin, *Acta Chem. Scand.*, **13**, 1124 (1959). The formula (Ia) had already been assigned to thujopsene by H. Kobayashi, S. Nagahama, and S. Akiyoshi [*Bull. Chem. Soc. Japan*, **32**, 202 (1959)] prior to the publication of the Swedish authors.

[2] L. Ruzicka, A. Eschenmoser, and H. Heusser, *Experientia*, **9**, 357 (1953).

[3] A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955). See also L. Ruzicka in Sir A. Todd, *Perspectives in Organic Chemistry,* Interscience, New York, 1956, p. 265.

[4] J. B. Hendrickson, *Tetrahedron*, **7**, 82 (1959).

[5] The formation of nortricyclene from 2-*exo*-norbornyl derivatives may be cited as an example of such a mode of deprotonation. See P. von Ragué Schleyer, *J. Am. Chem. Soc.*, 80, 1700 (1958).

[6] (a) S. Nagahama, H. Kobayashi, and S. Akiyoshi, *Bull. Chem. Soc. Japan,* **32**, 366 (1959) and earlier papers cited there. (b) O. Okuda, *J. Pharm. Soc. Japan,* **73**, 9 (1953) and earlier papers cited there.

Steroids and Related Natural Products. II. A Method for the Direct Conversion of Esters to Ethers[1,2]

Sir:

We wish to report a one-step procedure for converting an ester to its corresponding ether derivative. The reduction has been accomplishd employing a boron trifluoride etherate–lithium aluminum hydride reagent.[3] This novel reaction was first observed during the course of an investigation directed at determining the effect of boron trifluoride etherate–lithium aluminum hydride mixtures on the steroidal sapogenin spiroketal system.[4]

The ester in boron trifluoride etherate solution was added to a cooled suspension of lithium aluminum hydride in ethyl ether. After 45 min. at ice bath temperature followed by a 2-hr. period at reflux the product was isolated. This procedure has been used for the preparation of 3β-ethoxycholestane (0.17 g.),[5] colorless needles, $[\alpha]_D^{20}$ +23.8° (chloroform), m.p. 81–83° (*Anal.* Calcd. for $C_{29}H_{52}O$: C, 83.53; H, 12.58; 0, 3.89. Found: C, 83.47; H, 12.56; 0, 3.91), from 3β-acetoxycholestane (1.1 g.) and 3β-ethoxylanostane, colorless leaflets, m.p. 134–135°, $[\alpha]_D^{20}$ +53.2° (chloroform), 38% yield (*Anal.* Calcd. for $C_{32}H_{58}O$: C, 83.84; H, 12.66; 0, 3.49. Found: C, 83.62; H, 12.47; 0, 3.97), from

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[1] Consult G. R. Pettit and W. J. Bowyer, *J. Org. Chem.*, **25**, 84 (1960), for the first contribution to this series.

[2] This investigation was supported by Research Grants CY-4074(CI) and CY-4074(CISI), from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

[3] Similar reagents have been used recently for the hydroboration of olefins and as general reducing agents. *Cf.*, H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **82**, 681 (1960); S. Winstein, E. L. Allred, and J. Sonnenberg, *J. Am. Chem. Soc.*, **81**, 5833 (1959); H. C. Brown and K. Murray, *J. Am. Chem. Soc.*, **81**, 4108 (1959); H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 4106 (1959); F. Sondheimer and S. Wolfe, *Can. J. Chem.*, **37**, 1870 (1959); R. Dulou and Y. Chrétien-Bessière, *Bull. soc. chim. France*, 1362 (1959); S. P. Fore and W. G. Bickford, *J. Org. Chem.*, **24**, 920 (1959).

[4] *Cf.*, footnote 10 ref. 1.

[5] C. Djerassi, M. Shamma, and T. Y. Kan, *J. Am. Chem. Soc.*, **80**, 4723 (1958).