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INTERCONVERSION BETWEEN HIBAENE AND KAURENE*

A. YOSHIKOSHI, M. KITADANI[1] and Y. KITAHARA[2]
The Chemical Research Institute of Non-Aqueous Solutions,
Tohoku University, Sendai, Japan

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Abstract—Hibaene-α-epoxide, upon treatment with BF_3-etherate in benzene, undergoes skeletal rearrangement into the kaurane ring system, giving an unsaturated alcohol or a glycol, respectively. The unsaturated alcohol, after conversion to the corresponding unsaturated ketone, affords kaurane, isokaurene, and kaurane by Huang-Minlon reduction. It has also been found that an equilibrium mixture of kaurene, isokaurene and hibaene, in the ratio of 2:3:5, is produced when either kaurane or hibaene is heated in boiling xylene in the presence of iodine; thus the interconversion between hibaene and kaurene has been achieved. The stereochemistry of the intermediates in the transformation of hibaene to kaurene has been established.

INTRODUCTION

THE structure and stereochemistry of (−)-hibaene, one of the diterpenoid hydrocarbons from the essential oil of the leaves of Hiba (*Thujopsis dolabrata* Sieb. et Zucc.), has been determined as I[3] including the absolute configuration, and recently the total synthesis of I has been reported.[4] During the course of independent synthetic work on I, it appeared that (+)-kaurene (VIII)[5] or (+)-isokaurene (IX), a diterpenoid hydrocarbon differing from I in the stereochemistry of the C/D ring system, would be transformed into I through appropriate skeletal rearrangements.

From this point of view, the derivation of VIII from I was attempted first and was accomplished through an alternative skeletal rearrangement starting from hibaene-α-epoxide; the mechanism and the stereochemistry of the intermediates have also been clarified. Independently, Kapadi and Dev[6] found this rearrangement reaction starting from (+)-hibaene. This paper describes our results in detail. In addition, it has been demonstrated that kaurene (VIII) thus obtained gives an equilibrium mixture of VIII, IX, and I, which is also produced from I, by heating at the b.p. of xylene for 6 hr in the presence of iodine.

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[1] Present Address: College of General Education, Kobe University, Nada-ku, Kobe.

[2] Present Address: Department of Chemistry, Tohoku University, Sendai.

[3] Y. Kitahara and A. Yoshikoshi, *Tetrahedron Letters* 1771 (1964); *Bull. Chem. Soc. Japan* **38**, 735 (1965).

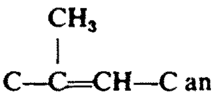
[4] R. E. Ireland and L. N. Mander, *Tetrahedron Letters* 2627 (1965).

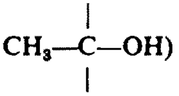
[5] For the total synthesis of kaurene (VIII), see R. A. Bell, R. E. Ireland and R. A. Partyka, *J. Org. Chem.* **27**, 3741 (1962); S. Masamune, *J. Am. Chem. Soc.* **86**, 288 (1964); C. Djerassi, P. Quitt, E. Mossetig, R. C. Cambie, P. S. Rutledge and L. H. Briggs, *J. Am. Chem. Soc.* **83**, 3720 (1961); B. E. Cross, R. H. B. Galt, J. R. Hauson and W. Klyne, *Tetrahedron Letters* No. 14, 145 (1962).

[6] K. H. Kapadi and Sukh Dev, *Tetrahedron Letters* 1255 (1965).

RESULTS AND DISCUSSIONS

The epoxide ring of hibaene-epoxide (II), readily prepared from (—)-hibaene (I) by perbenzoic acid oxidation,[3] is more likely to be α-orientated from a consideration of the steric interference of the angular Me group at C-10 to approach of the reagent and of preferential *exo*-side attack of the peracid on the double bond at C-15,16 corresponding to the C-6,7 position of a bicyclo[3.2.1]octane system; and this assignment is supported by the NMR spectrum.[7] A doublet at 9·56 τ (J = 10·5 c/s), which is not observed in the spectrum of I, could be attributed to the signal from one of the bridge-methylene protons at C-14 which has been shifted upfield through introduction of the α-(*exo*) epoxide ring, as observed in the NMR of *exo*-epoxy-bicyclo-[3.2.1] (or [2.2.2])octane and -bicyclo[2.2.1]heptane derivatives.[8]

The α-epoxide (II) was treated with BF_3-etherate in anhydrous benzene at room temperature overnight to give an unsaturated alcohol (III) in 88% yield and a small amount of a glycol (IV).[9] The spectroscopic data of the major product clearly support the assigned structure (III): absorption bands at 3540, 3445 (OH group) and 1645 cm^{-1} (double bond) in the IR spectrum,[10] and a doublet at 8·29 τ (J = 1·5 c/s, 3H, allylic Me) and a quartet at 5·07 τ (1H, vinyl proton) indicate the presence of the grouping  $C{-}\overset{\overset{CH_3}{|}}{C}{=}CH{-}C$ and the single peak in the NMR at 6·00 τ is due to a proton on a carbon atom (C-14) bearing a secondary OH group. Hence, rearrangement in the carbon skeleton in II apparently takes place during the formation of III.

When benzene saturated with water instead of anhydrous benzene was used as solvent in the above reaction, the major product was the glycol IV. Existence of a Me and a tertiary OH group on the same carbon atom (C-16) in IV was established by spectroscopic and chemical evidence: the NMR exhibits a peak at 8·66 τ (s, 3H,  $CH_3{-}\underset{|}{\overset{|}{C}}{-}OH$) which is not observed in the NMR of III and IV is readily dehydrated by iodine in boiling xylene to yield the unsaturated alcohol III. Therefore, it has been proved that the same skeletal rearrangement occurs in the formation of both III and IV.

The IR spectrum[11] of IV in CCl_4 reveals three O—H stretching absorption bands at 3500 (intermolecular hydrogen bonding), 3600 (intramolecular hydrogen bonding), and 3620 cm^{-1} (free OH group), and significant change in the relative intensities of these bands was observed by dilution: the intensity at 3500 cm^{-1} decreased, the intensity at 3620 cm^{-1} increased but that of the intramolecular hydrogen bonded OH group at 3600 cm^{-1} did not change. These facts obviously suggest that two OH groups

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[7] All NMR data were obtained at 60 Mc with a Varian A-60 Spectrometer using TMS as internal standard and CCl_4 was used as solvent.

[8] P. R. Jefferies, R. S. Rosich and D. E. White, *Tetrahedron Letters* 1853 (1963); K. Tori, K. Kitahonoki, Y. Takano, H. Tanida and T. Tsuji, *Ibid.* 559 (1964).

[9] Formation of a very small amount of ketonic substance was also detected but isolation and characterisation have not been done.

[10] IR spectra were taken with a Hitachi EPI-S Spectrophotometer using KBr disks unless otherwise stated.

[11] Taken with a Perkin-Elmer IR Grating Spectrophotometer Model 125.

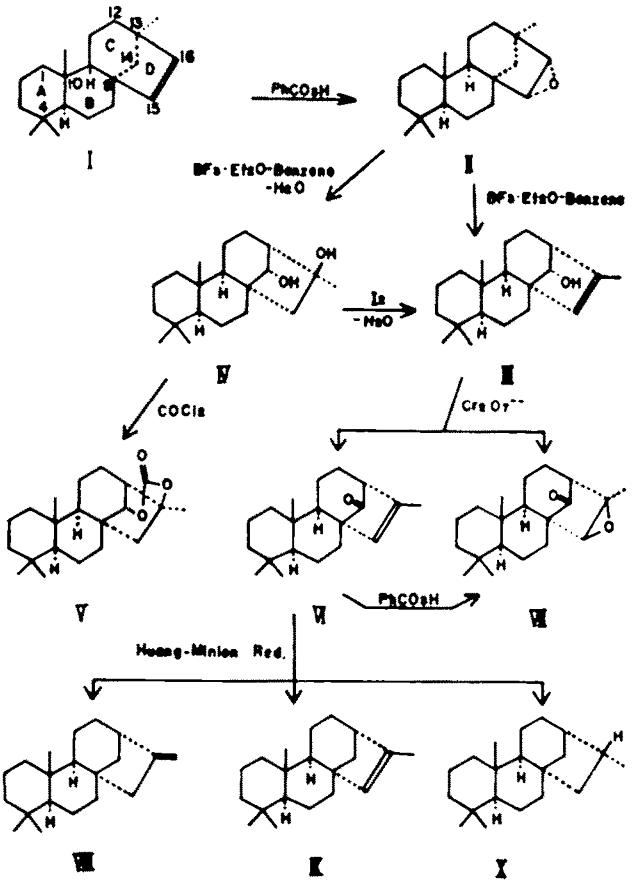

FIG. 1

in IV must have a *cis* configuration on the ring D (5-membered ring) capable of formation of intramolecular hydrogen bonding. This is decisively confirmed by the reaction of IV with phosgene producing a cyclic carbonate (V) in excellent yield.

Although final confirmation of the carbon framework (kaurane ring system) of III or IV is provided later through reactions yielding kaurene, isokaurene and kaurane, a possible mechanism in the rearrangement of II and the stereochemistry of III and IV may be considered at this stage.

A concerted reaction mechanism, which involves α-epoxide ring opening, migration of the 12,13-carbon–carbon bond, and then deprotonation (path a) or attack of a OH anion (path b) depending on the solvent used, might reasonably explain the skeletal rearrangement of II to III or IV as shown in Fig. 2. Thus, an α-configuration of the secondary OH group at C-14 in both III and IV is inevitable and the tertiary OH group of IV becomes β and has a 1,3-*cis* relationship to the secondary one of the 5-membered ring D, coinciding with the experimental results.

Two phase oxidation of III in ether with aqueous sulfuric acid–sodium bichromate at room temperature gave the corresponding unsaturated ketone (VI) in 73% yield