

ACID CATALYZED ISOMERIZATION OF
 α -CUBEBENE, α -COPAENE AND α -YLANGENE

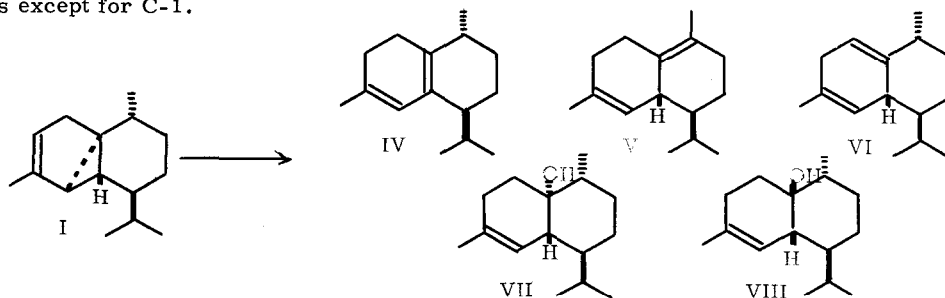
Yoshimoto Ohta, Keiko Ohara and Yoshio Hirose

The Institute of Food Chemistry
Dojimanaka, Kita-ku, Osaka, Japan

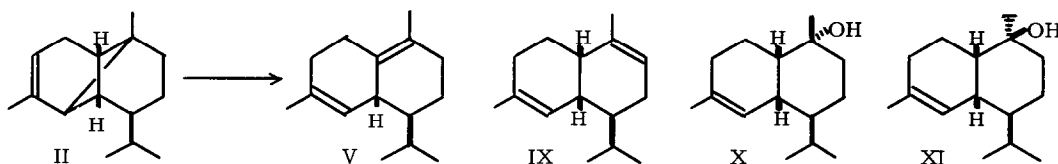
(Received in Japan 11 June 1968; received in UK for publication 22 June 1968)

Generally it is accepted that sesquiterpene hydrocarbons containing a cyclopropane or a cyclobutane ring adjacent to a double bond in their molecule are sensitive to the action of mineral acids. In this communication, we wish to report the acid catalyzed isomerization of α -cubebene (I), α -copaene (II) and α -ylangene (III), since it seems of importance to examine the behavior of these tricyclic hydrocarbons under such condition for making clear the mutual relation among those closely related compounds of cadalene type.

A), Isomerization of α -cubebene (I): When a solution of α -cubebene isolated from cubeb oil, $[\alpha]_D -20.0^\circ$, in 80% aqueous dioxane which was 0.012N in hydrochloric acid was warmed at 50° for 2 hrs, three hydrocarbons, cadina-4,6(1)-diene (IV), δ -cadinene (V)^{*1)} and cadina-1,4-diene (VI), were obtained in a ratio of about 1 : 4 : 1 together with a smaller amount of sesquiterpene alcohols, cubenol (VII) and epi-cubenol (VIII) in a ratio of about 1 : 2. Identification of these hydrocarbons was attained by comparison of their i. r. spectra and Rts in GLC with those of the authentic samples obtained from cubenol by dehydration⁽¹⁾. The $[\alpha]_D$ values of these hydrocarbons, (IV); -67.8° , (V); $+42.5^\circ$ ^{*2)} and (VI); -21.9° , accord with those of them from cubenol, (V); $+84.7^\circ$ and (VI); -23.2° . Cubenol (VII), $[\alpha]_D -32.1^\circ$, and epi-cubenol (VIII), $[\alpha]_D -116.4^\circ$, derived from α -cubebene also have the same absolute configuration with those of the natural products, $[\alpha]_D -24.8^\circ$ and -95.7° , respectively⁽¹⁾. It was thus confirmed that all of α -cubebene (I), cubenol (VII) and epi-cubenol (VIII) have the same configuration at all points except for C-1.

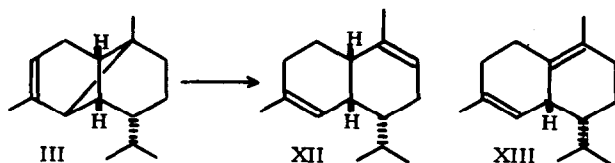


B), Isomerization of α -copaene (II). The cyclobutane ring of α -copaene or α -ylangene is more stable than the cyclopropane ring of α -cubebene and, indeed, α -copaene (II) was recovered unchanged under the same condition employed for the isomerization of α -cubebene. Treatment of α -copaene isolated from cubeb oil, $[\alpha]_D -19.0^\circ$, with 0.1N sulfuric acid in 80% aqueous dioxane under reflux for 2 hrs gave two hydrocarbons V and IX in a ratio of about 2 : 1. Purified samples of V and IX were identified with δ -cadinene and α -muurolene, respectively, by comparing their i. r. and n. m. r. spectra and Rts in GLC with those of the authentic samples. The values of optical rotation of V and IX, $+67.1^\circ$ and -62.5° , respectively, are in agreement with those of natural (+)- δ -cadinene ($+94^\circ$)⁽²⁾ and (-)- α -muurolene (-52.5°)⁽³⁾. Besides these hydrocarbons, a small amount of two sesquiterpene alcohols, identified with δ -cadinol (X)⁽⁴⁾ and T-muurolol (XI)⁽⁵⁾, were obtained in a ratio of 1 : 1, $[\alpha]_D -101.8^\circ$ and -99.4° , respectively (natural product, -102.3°)⁽⁶⁾ and -102.9°)⁽⁵⁾, respectively).

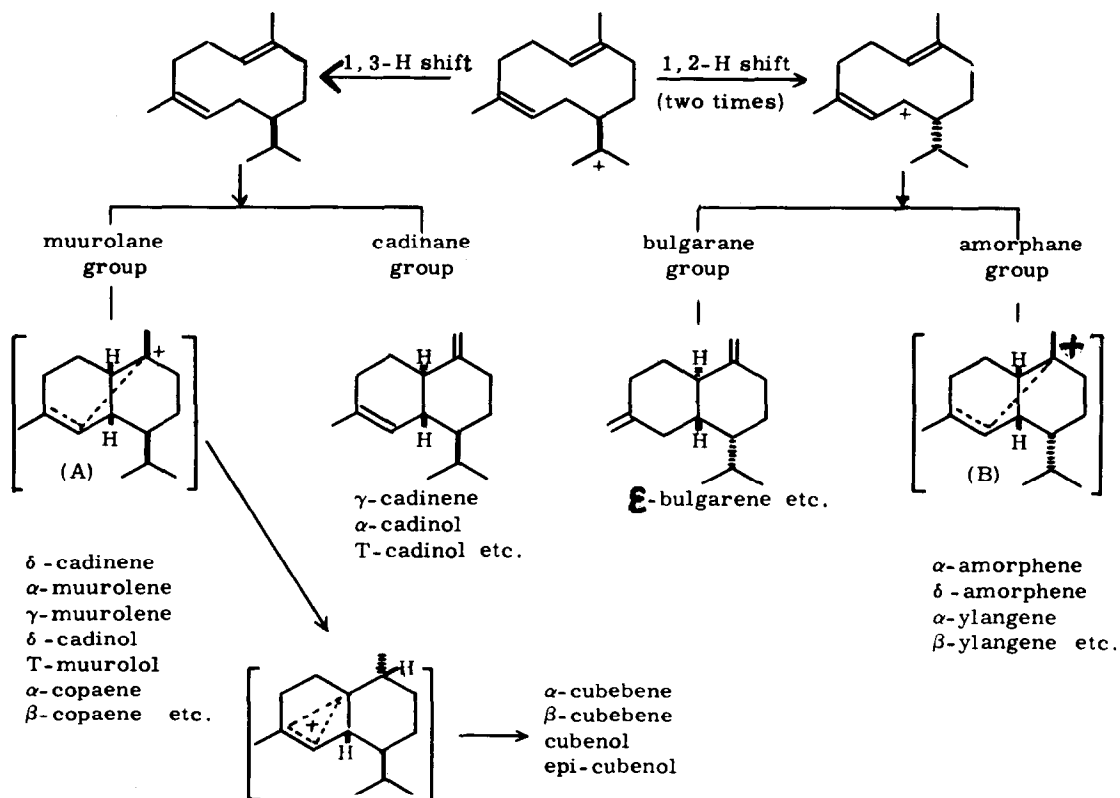


C), Isomerization of α -ylangene (III): On treatment under the same condition, α -ylangene (III) isolated from the fruits of *Schisandra chinensis*, $[\alpha]_D +55.6^\circ$, afforded two new sesquiterpene hydrocarbons, XII and XIII, both $C_{15}H_{24}$, in a ratio of about 2 : 1. The hydrocarbon (XII), named α -amorphene, $[\alpha]_D -127.6^\circ$, shows ν_{max} at 1670, 815 and 770cm^{-1} . Its n. m. r. spectrum (in CCl_4) exhibited unusual splitting of isopropyl signals at 52.5, 54.6, 59.4 and 61.2cps, broad singlet of two olefin methyl groups at 1.64ppm and signals of two vinyl protons at 5.10 and 5.33ppm. XII yielded two tetrahydro derivatives by hydrogenation with platinum oxide in acetic acid, and one of them shows an i. r. spectrum identical with that of iso-cadinane which was obtained from γ -amorphene by Herout and his colleagues⁽⁷⁾. Another tetrahydro derivative is considered to be its isomer having a different orientation of methyl group at C-4 or C-10. On consideration of the spectral data and the nature of the isomerization reaction, its structure was concluded to be XII.

The hydrocarbon XIII, named δ -amorphene, $[\alpha]_D +16.1^\circ$, shows absorption maxima at 1660, 1640 and 830cm^{-1} and n. m. r. signals at 0.94ppm (6H, d., $J=6.0\text{cps}$, isopropyl group), 1.61ppm (6H, broad s., two olefin methyl groups) and 5.35ppm (1H, broad s., one vinyl proton). These spectral data show the presence of a trisubstituted double bond and a tetrasubstituted one, each of them bearing a methyl substituent. On hydrogenation (platinum oxide in acetic acid), XIII again yielded two tetrahydro derivatives which were identical with those obtained from α -amorphene (XII)^{*3}. Thus, the structure of this hydrocarbon was concluded to be XIII.



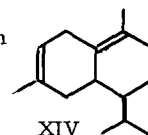
Most of sesquiterpenoids of cadalene type carry a β -oriented hydrogen atom on C-6 carbon atom and these compounds are divided into four groups according to the orientation of isopropyl group at C-7 and the nature of ring fusion (cadinane, muurolane, amorphane and bulgarane). Now, some interesting facts call our attention, that is, 1), there have been found no compounds in nature which have the trans ring junction and a double bond at C-9, 2), most commonly encountered alcohols have recently been proved to have the functional group on the right hand ring of cadalenic skeleton, and 3), as in the cases of cubenol (VII) and epi-cubenol (VIII) in cubeb oil, and δ -cadinol (X) and T-muurolol (XI) in the oil of Taiwania cryptomerioides



Hayata, epimeric pair of sesquiterpene alcohols often coexist in one essential oil. These facts and the results of above mentioned isomerization reactions enable us to presume that the anti-elimination of a hydrogen atom and S_N1 like attack of water molecule to carbonium ion are likely involved in the genesis of these sesquiterpenoids. In the cases of muurolane and amorphane group, we can imagine the transition state (A) and (B), respectively, that are responsible for the intermediate states in the isomerization of α -copaene (II) and α -ylangene (III), respectively. Through the transition state (A), δ -cadinene, α - and γ -muurolene, α - and β -copaene will be formed by elimination of a hydrogen atom, and δ -cadinol and T-muurolol by hydration. Further, α - and β -cubebene, cubenol and epi-cubenol will be produced from (A) via shift of the hydrogen atom from C-1 to C-10. Similarly, the compounds of amorphane group, α -, δ - and γ -amorphene and α - and β -ylangene, are to be formed via the transition state (B). As to the genesis of the compounds having trans ring junction, those of cadinane and bulgarane group, it is impossible to proceed through such a transition state as (A) or (B), and only a hydrogen atom on C-15 carbon atom seems to be allowed for elimination to form γ -type hydrocarbons.

In this way, the mutual relation became evident between the tricyclic compounds, α -cubebene, α -copaene and α -ylangene, and the bicyclic ones of cadalene type, and, according to our opinion, δ -cadinene should reasonably be put into the muurolane group.

*1), As to the structure of δ -cadinene, the one (XIV) presented by Vlahov et al.⁽⁸⁾ instead of the hitherto accepted one (V), was inconsistent with our results. Concurrently, δ -cadinene obtained from the oil of *Chamaecyparis obtusa*, $[\alpha]_D +80.1^\circ$, was converted into 5-methyl cadalene via hydroboration-oxidation, oxidation with chromium trioxide, methylation with methyl lithium and dehydrogenation. Thus, the structure of δ -cadinene was reconfirmed as V, and the same conclusion was arrived by S. Dev⁽⁴⁾ and Sutherland⁽⁹⁾ based on the independent experimental results.



*2), Rather low $[\alpha]_D$ value of this δ -cadinene is due to the contamination with a hydrocarbon which is supposed to be cadina-5,10(1)-diene. Details of this new compound will be presented in a full paper.

*3), In this case, the sterical unfavorability of the resultant bulgarane skeleton (axial isopropyl) seems imperative to refuse otherwise more stable trans ring fusion product.

Acknowledgement: The authors are indebted to Dr. Y. T. Lin for the i. r. spectra of δ -cadinol and T-muurolol.

REFERENCES

- 1), Y. Ohta and Y. Hirose, *Tetrahedron Letters*, 2973 (1967).
- 2), V. Herout, T. Kolos and J. Priva, *Chem. Listy*, **47**, 440 (1953).
- 3), A. Zabza, M. Romanuk and V. Herout, *Coll. Czech. Chem. Comm.*, **31**, 3373 (1966).
- 4), B. A. Nagasampagi, L. Yankov and Sukh Dev, *Tetrahedron Letters*, 1913 (1968).
- 5), Y. S. Cheng, Y. H. Kuo and Y. T. Lin, *Chem. Comm.*, 565 (1967).
- 6), W. G. Dauben, B. Winstein, P. Lin and B. Anderson, *Tetrahedron* **15**, 217 (1961).
- 7), O. Motl, M. Romanuk and V. Herout, *Coll. Czech. Chem. Comm.*, **31**, 2025 (1966).
- 8), R. Vlahov, M. Holub and V. Herout, *ibid.*, **32**, 822 (1967).
- 9), D. W. Connell, R. P. Hildebrand and M. D. Sutherland, *Tetrahedron Letters*, 519 (1968).