

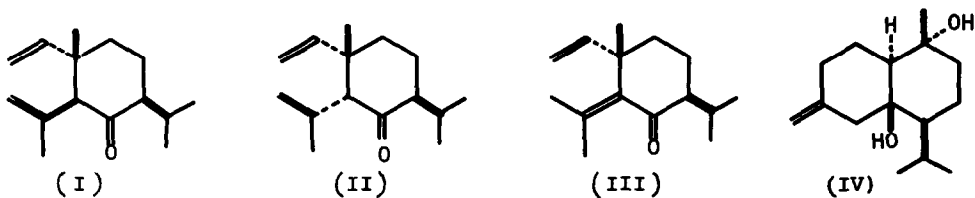
CONVERSION OF ELEMENE-TYPE SESQUITERPENES INTO CADINENE-TYPE COMPOUNDS
AND FORMATION OF TEN-MEMBERED GERMACRONE-TYPE INTERMEDIATES

Masanobu Iguchi and Atsuko Nishiyama
Faculty of Pharmacy, Meijo University; Tenpakucho, Showaku, Nagoya, Japan

Shosuke Yamamura and Yoshimasa Hirata
Chemical Institute, Nagoya University; Chikusaku, Nagoya, Japan

(Received in Japan 1 September 1969; received in UK for publication 15 September 1969)

In the previous papers,^{1,2} we reported the structures of three monocyclic sesquiterpenes [shyobunone(I), epishyobunone(II) and isoshyobunone(III)] as well as a bicyclic diol [isocalamendiol(IV)]. From a biogenetic point of view, we attempted the syntheses of germacrone-type compounds from monocyclic sesquiterpenes(I, II and III) as well as the isocalamendiol(IV).*

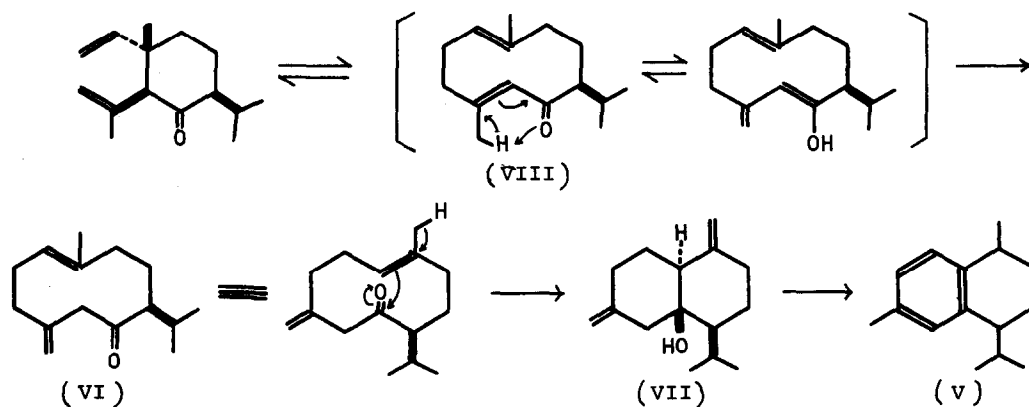


In general, elemene-type sesquiterpenes, having both a vinyl group and an isopropenyl group, are known to be thermally in a certain equilibrium with the corresponding ten-membered ring isomers.³ However, the latter are ready to

* An isopropyl group at C₆-position has been suggested to be in an equatorial configuration(see ref.2). This is confirmed by thermal rearrangement of I, the stereochemistry of which is already known, into dehydroxyisocalamendiol (VII).

take a Cope rearrangement leading to the corresponding elemene-type compounds.³

When heated in a sealed tube under various conditions (see the Table), shyo-bunone (I) afforded three important products, one of which could be assigned as calamenene (V). The structures of the remaining compounds (VI and VII) were elucidated by the following physical data. VI : relative retention* 2.08; m/e 220(M^+); ν_{\max}^{film} 3080, 1705($>C=O$), 1642 and 897 cm^{-1} ; $\delta_{\text{ppm}}^{\text{TMS}}(\text{CCl}_4)$ 0.86(3H, d, $J = 6.7\text{cps}$) and 0.91(3H, d, $J = 6.7\text{cps}$)($-\text{CH}-\overset{\text{Me}}{\text{Me}}$), 1.37(3H, near s)($-\text{CH}=\overset{\text{Me}}{\text{C}}-\text{Me}$), 2.83(1H, d, $J = 15\text{cps}$) and 3.24(1H, d, $J = 15\text{cps}$)($=\overset{\text{C}}{\text{C}}-\text{CH}_2-\overset{\text{C}}{\text{C}}=O$), 4.84(1H, br. s) and 4.95(1H, br. s)($>C=CH_2$) and 4.9 ~ 5.3(1H, br.)($>C=CH-$). VII : relative retention* 2.63; m/e 220(M^+); ν_{\max}^{film} 3550($-\text{OH}$), 3080, 1645 and 890 cm^{-1} ; $\delta_{\text{ppm}}^{\text{TMS}}(\text{CDCl}_3)$ 0.90(3H, d, $J = 6.7\text{cps}$) and 0.93(3H, d, $J = 6.7\text{cps}$)($-\text{CH}-\overset{\text{Me}}{\text{Me}}$), and 4.60(1H, br. s) and 4.7 ~ 4.9(3H, br. m)($2 \times \text{H}_2\text{C}=\overset{\text{C}}{\text{C}}-$). Particularly, the compound (VII) was completely identical with the dehydration product of isocalamendiol (IV), as described later. Similarly, thermal rearrangements of epishyobunone (II) as well as isoshyobunone (III) also gave a mixture of V, VI and VII. The relative ratio of the reaction products in the Table indicates the plausible mechanism for the formation of these compounds (V, VI and VII), as shown below.**



* The numerical values of relative retention were obtained *vs.* calamenene (V) as an internal standard [stationary phase: 5% PEG 20M (on Neopak 1A, 60~80 Mesh); carrier gas: N_2].

** Thermal equilibrium must be present among three monocyclic ketones (I, II and III).

Table. Thermal Isomerization of Shyobunone(I)

Condition		Product (%) ^a								
Temp. (°C)	Time (min.)	Unidentified compounds		V	II	III	I	VI	VII	
		(0.42) ^b	(0.66)	(1)	(1.10)	(1.25)	(1.33)	(2.08)	(2.63)	
220	0	-	-	-	-	-	100	-	-	
	6	0	2	0	10	42	10	19	17	
	14	0	7	1	6	32	6	11	37	
	20	0	7	3	6	27	0	7	50	
	40	1	7	19	4	14	0	0	55	
	100	6	7	38	0	0	0	0	48	
180	3	-	-	-	-	-	100	-	-	
	15	0	1	0	12	24	28	29	6	
	50	0	2	0	5	34	9	31	17	
	90	0	3	0	4	41	1	24	27	
	210	0	0	5	12	4	22	0	7	50

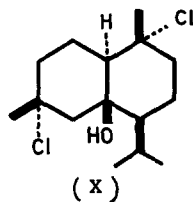
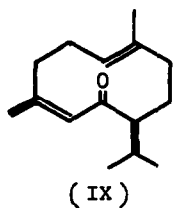
a. Peak area of gas-liquid chromatogram (PEG 20M, 115°, N₂, flame-ionizer detector) was served as an approximate value of content(%).

b. Relative retention of each product is shown in parenthesis.

In the above mechanism, isolation of a plausible intermediate(VIII) has been attempted without success. However, we could make another new germacrone-type compound(IX) from isocalamendiol(IV), according to the following manner. When treated with POCl₃-pyridine(0°, 2 hr.), isocalamendiol(IV) afforded, in 91% yield, a dehydration product(VII), which was then allowed to stand at -20° for 1.5 hr. in diethyl ether saturated with dry hydrogen chloride to give a quantitative yield of the dichloride(X), m.p. 89~90°; m/e 220(M⁺ - 2HCl); ν_{\max}^{KBr} 3560 cm⁻¹(-OH); $\delta_{\text{ppm}}^{\text{TMS}}(\text{CDCl}_3)$ 0.92(6H, d, J = 6.9cps)(-CH<_{Me}), 1.64(3H, s)(Me-C-Cl) and 1.69(3H, s)(Me-C-Cl). Furthermore, treatment of X with *t*-BuOK-*t*-BuOH(room temperature, 1.5 hr.)⁴ afforded, in 73% yield,* a germacrone-type compound(IX), the structure of which was confirmed by its physical data [relative retention 2.63; m/e 220(M⁺); ν_{\max}^{film} 1681(α, β -unsaturated ketone) and 1635cm⁻¹; $\lambda_{\max}^{\text{MeOH}}$ 241(ϵ : 5460) and 208m μ (ϵ : 3750); $\delta_{\text{ppm}}^{\text{TMS}}(\text{CCl}_4)$ 0.90(6H, d, J = 6.8cps)(-CH<_{Me}), 1.43(3H, d, J = 1.5cps)(Me-C=CH-), 1.78(3H, d, J = 1.7cps)(Me-C=CH-CO), 4.95(1H, br. t, J = 7.8cps)(CH=C-Me) and 5.93(1H, q, J = 1.7cps)(Me-C=CH-CO)].

* The formation of IX in high yield indicates that the chlorine atom at C₉-position must be in an equatorial configuration.⁴

Finally, this compound(IX) was easily converted into calamenene(V) under milder conditions(110°, 25 min.) than that of shyobunone(I) as well as VI. This fact is in good agreement with the given structure(IX) which can take a favourable conformation for a bond formation between C₅ and C₁₀- carbon atoms.



All compounds gave satisfactory physical data and elemental analyses.

We thank Dr. A. Tatematsu (Meijo University) for the measurement of high resolution mass spectra.

REFERENCES

1. M.Iguchi, A.Nishiyama, H.Koyama, S.Yamamura and Y.Hirata, *Tetrahedron Letters*, 5315(1968).
2. M.Iguchi, A.Nishiyama, H.Koyama, S.Yamamura and Y.Hirata, *Tetrahedron Letters*, in press.
3. A.S.Rao, A.Paul, Sadgopal and S.C.Bhattacharyya, *Tetrahedron*, 13, 319(1961); G.H.Kulkarni, G.R.Kelkar and S.C.Bhattacharyya, *Tetrahedron*, 20, 1301(1964); K.Takeda, H.Minato and M.Ishikawa, *J.Chem.Soc.*, 4578(1964); H.Ishii, T.Tozoy, M.Nakamura and K.Takeda, *Tetrahedron*, 24, 625(1968); R.V.H.Jones and M.D.Sutherland, *Aust.J.Chem.*, 21, 2255(1968); K.Morikawa and Y.Hirose, *Tetrahedron Letters*, 869(1969).
4. P.S.Wharton and G.A.Hiegel, *J.Org.Chem.*, 30, 3254(1965).