STEREOCHEMICAL STUDIES ON THE ELEMENE-TYPE SESQUITERPENES
FROM ACORUS CALAMUS L.

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The absolute configuration of epi- and isoshyobunone was established as 2 and 3, respectively, on the basis of their chemical and spectral data together with base-catalyzed isomerization of shyobunone (1) affording natural isoshyobunone and the enantiomer of natural epishyobunone. In addition, conformations of the base-catalyzed isomerization products (3, 6, 8, 9, and 11) are also discussed.

In connection with base-catalyzed equilibrium of shyobunone (1) and related sesquiterpenes,[1] further studies on the stereostructures of epi- and isoshyobunone were carried out. In the present paper, we wish to describe the absolute configuration of epi- and isoshyobunone. Furthermore, conformations of several elemene-type compounds are presented.

Previously, epishyobunone was regarded as the epimer of natural shyobunone only at C_2-position on the basis of its ORD data showing a strong negative Cotton effect, together with co-occurrence of shyobunone (1).[2] However, when treated with MeONa - MeOH (under reflux, 14 h), epishyobunone (2) was converted into unnatural isoshyobunone (4) ($[\alpha]_D^{23°} = +156°$) and its C_6-epimer (5). On the other hand, natural isoshyobunone (3) ($[\alpha]_D^{23°} = -159°$) and its C_6-epimer (6) were obtained in the case of shyobunone (1), whose absolute configuration had been established already in connection with α-santonin.[3] The reaction mixture of shyobunone was further separated by preparative TLC to give unnatural epishyobunone (7) in low yields,[1] whose physical data are completely identical with those of natural one except for a strong positive Cotton effect in its ORD curve. From the above facts, epishyobunone (2) should be the enantiomer of the C_6-epimer of shyobunone. This is in a complete agreement with Fråter's result.[4] Thus, the biogenesis and thermal reactions of these elemene-type sesquiterpenes are reasonably considered, as shown in Scheme 1. In the next step, the stereochemistry of isoshyobunone (3) and its C_6-epimer (6) is briefly discussed.

On catalytic hydrogenation using PtO_2 in AcOEt (room temp., overnight), isoshyobunone (3) and its epimer (6) were readily converted into the corresponding dihydro compounds (8) and (9), respectively [8: $C_{15}H_{26}O$ (m/e 222(M^+)); ν_{max}(film) 1680 and 1620 cm^{-1}; δ(CDCl$_3$) 0.68-1.0(9H, complex), 1.37(3H, s), 1.77(3H, s) and 1.84(3H, s); λ_{max}(MeOH) 253 nm (ϵ, 4640). 9: $C_{15}H_{26}O$ (m/e 222(M^+)); ν_{max}(film) 1700 and 1625 cm^{-1}; δ(CDCl$_3$) 0.72-1.0(9H, complex), 1.29(3H, s), 1.72(3H, s) and 1.86 (3H, s); λ_{max}(MeOH) 247 nm (ϵ, 2390)]. Dihydroisoshyobunone (8) was further reduced with LiAlH$_4$ in ether (room temp., overnight) to afford tetrahydroshyobunone (10) in 63% yield, which had been produced already from shyobunone (1) on catalytic hydrogenation.[2]

The CD data of isoshyobunone (3), C_6-epiisoshyobunone (6), dihydroisoshyobunone (8) and its epimer (9) are shown in Table 1. From these CD data, isoshyobunone and dihydroisoshyobunone both seem to adopt a conformation [A]. Interestingly, C_6-epiisoshyobunone (6) presumably adopts

a conformation [B] with an axial allyl group at C_3-position, while the corresponding dihydro compound (9) seems to be in a conformation [C].[5] In connection with these results, the conformation of 2,6-diepishyobunone (11), which also has an axial allyl group at the same position,[6] is described on the basis of its NMR spectral data using a lanthanide shift reagent [Eu(fod)$_3$].[7]

The induced shift ratios of eight protons were obtained by incremental addition of weighed Eu(fod)$_3$ to the substrate (11) in CDCl$_3$ containing TMS,[8] as shown in Table 2. The coordinate system was given to 11 according to Armitage's method (see Fig. 1).[9] Each ◢H value was calculated according to the following equation: ◢H = k(3cos$^2\theta$ - 1)·r^{-3}.

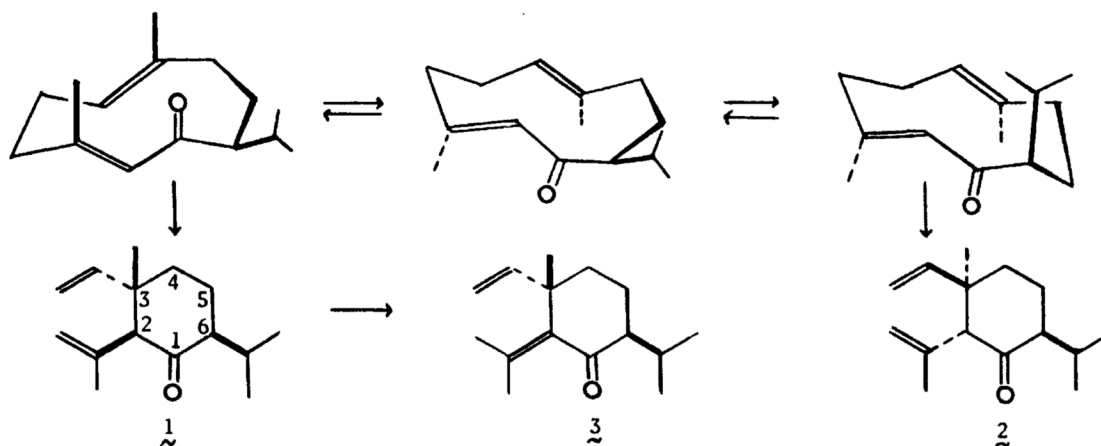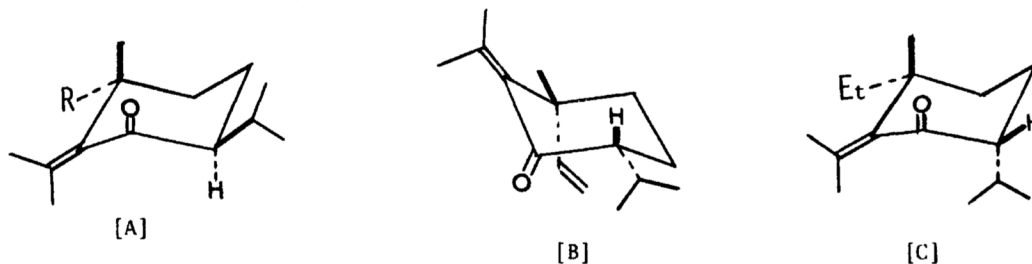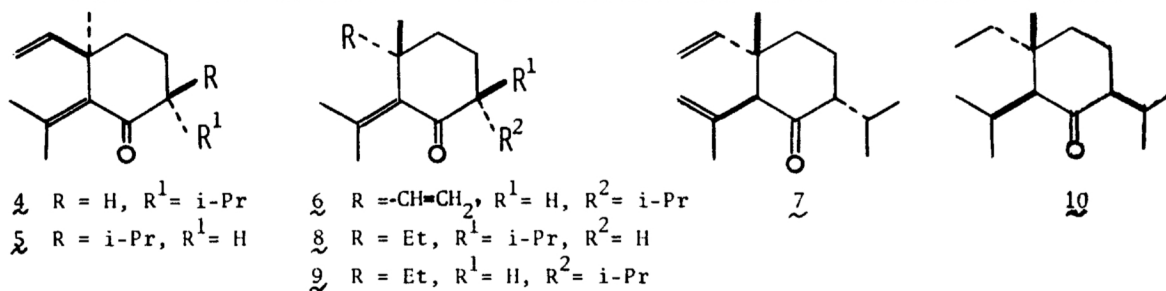Scheme 1.   Biogenesis of shyobunone and related sesquiterpenes

Table 1.   CD data of isoshyobunone and related compounds

Compound	$[\theta]$ x 10^{-2}		
	n $\longrightarrow \pi^*$	$\pi \longrightarrow \pi^*$	$\pi \longrightarrow \pi^*$
3	-50 (323 nm)	-141 (257 nm)	+48 (213 nm)
6	+62 (322 nm)	+108 (254 nm)	+126 (220 nm)
8	-105 (319 nm)	-348 (253 nm)	+322 (205 nm)
9	+30 (319 nm)	-161 (244 nm)	+97 (204 nm)

4 R = H, R^1= i-Pr
5 R = i-Pr, R^1= H

6 R =-CH=CH$_2$, R^1= H, R^2= i-Pr
8 R = Et, R^1= i-Pr, R^2= H
9 R = Et, R^1= H, R^2= i-Pr

7

10

[A]

[B]

[C]

In the first step, ΔH values were calculated for five protons (a - e) except for the three protons (f - h) attached to the vinyl group, and appropriate rotational angle of the isopropenyl group was examined. The results best fitted to the observed values were shown in Table 2. At this stage, two $\mathcal{L}$ values (300° and 60°) seem suitable. Then, ΔH values of the eight protons (a - h) were further calculated, and both appropriate conformation and position of the metal were examined. At this stage, one of the two conformations ($\mathcal{L}$ = 300°) was discarded in spite of a small agreement factor (0.030), because the compound (11) can not adopt this conformation which are much crowded with several carbon and hydrogen atoms. Thus, in consideration of the remaining conformation ($\mathcal{L}$ = 60°) the final results, in which the minimum agreement factor was 0.056, were obtained, as shown in Table 2. Finally, the positions of the metal, the isopropenyl group and the vinyl group are as follows: d = 3.4 Å, Ω = 100°, ϕ = 200°, $\mathcal{L}$ = 65° and β = 250°. Thus, the favorable conformation of 2,6-diepishyobunone can be depicted as 11,[10] in which the vinyl group and/or the isopropenyl group must adopt suitable positions to stabilize 11. Further studies on this point are in progress.

The CD spectra were taken on a JASCO J-20 spectropolarimeter using MeOH as the solvent.

Table 2

	H^a	H^b	H^c	H^d	H^e	H^f	H^g	H^h	$\mathcal{L}$	β
H (obsd)	7.32	5.06	3.81	6.52	2.35	4.42	1.00	1.77		
H (calcd)*	7.31	5.07	3.92	6.36	2.41				300°	
H (calcd)*	7.47	4.70	3.85	6.59	2.47				60°	
H (calcd)**	7.66	4.60	4.06	6.26	2.18	4.58	1.07	1.92	65°	250°

* For five protons (a - e); ** For eight protons (a - h).
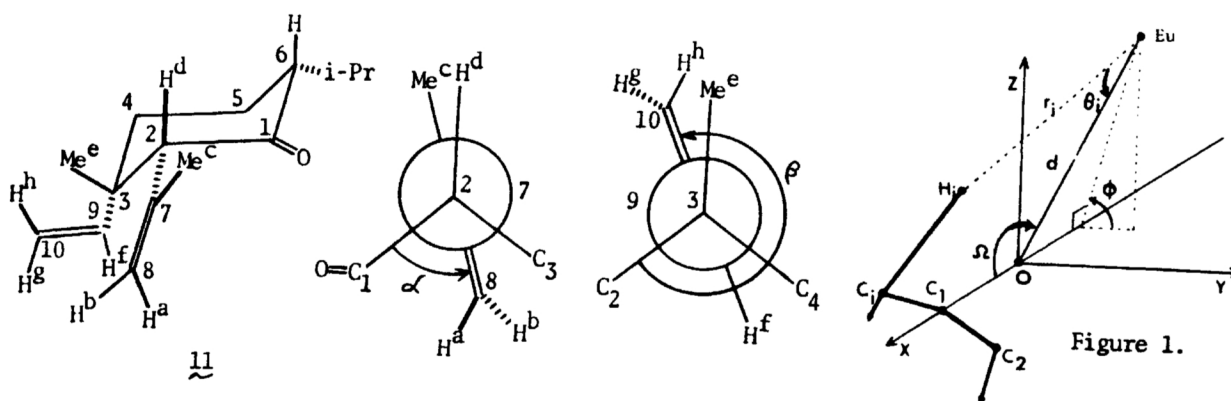
Figure 1.

References and Footnotes

1. To be published in the following paper.
2. S. Yamamura, M. Iguchi, A. Nishiyama, M. Niwa, H. Koyama, and Y. Hirata, Tetrahedron, 27, 5419 (1971); M. Niwa, A. Nishiyama, M. Iguchi, and S. Yamamura, Bull. Chem. Soc. Jpn., 48, 2630 (1975).
3. K. Kato, Y. Hirata, and S. Yamamura, Tetrahedron, 27, 5987 (1971).
4. Private communication from Dr. G. Fráter (SOCAR). We wish to thank him for the IR and NMR spectra of (±)-epishyobunone (G. Fráter, Chimia, 29, 528 (1975)).
5. As estimated from their molecular ellipticities, these chair-like conformations [A - C] must be distorted.
6. This compound is more stable than shyobunone (1) with an axial Me group at the same position, although the allyl group is considered to be more bulky than the Me group (see reference 1).
7. Y. Terada and S. Yamamura, Tetrahedron Lett., 1976, 4337.
8. Proton assignments were based on observed splitting and chemical shifts.
9. I.M. Armitage, L.D. Hall, A.G. Marshall, and L.G. Werbelow, J. Amer. Chem. Soc., 95, 1437 (1973)
10. The induced shift ratios of eight protons are constant regardless of the concentration of added $Eu(fod)_3$, and the NMR spectrum with a small amount of $Eu(fod)_3$ is quite similar to that of the original compound (11) in respect of the coupling constant and shape of each signal. Furthermore, the original CD spectrum of 11 in $CHCl_3$ was not varied in respect of its molecular ellipticity, on addition of $Eu(fod)_3$.