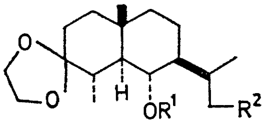
# Syntheses of Shyobunone, Preisocalamendiol, and Related Sesquiterpenes

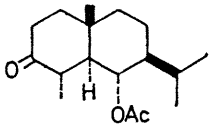
By KUNIKI KATO and YOSHIMASA HIRATA
(*Chemical Institute, Nagoya University, Chikusa, Nagoya, Japan*)
and SHOSUKE YAMAMURA*
(*Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya, Japan*)

*Summary* Shyobunone, preisocalamendiol, and related sesquiterpenes have been synthesized from (−)-santonin.

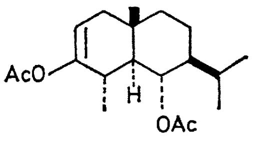
SEVERAL new sesquiterpenes have been isolated from *Acorus calamus* L. (Japanese name, Shyobu).[1] The biogenetic relationship among them is of considerable interest, and the syntheses of these optically active sesquiterpenes were required for biogenetic model reactions. We report here their syntheses from the known dihydroxy-acetal (I),[2] which has previously been obtained from (−)-santonin.



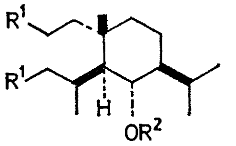
(I) $R^1 = H, R^2 = OH$
(II) $R^1 = Ac, R^2 = OH$
(III) $R^1 = Ac, R^2 = I$
(IV) $R^1 = Ac, R^2 = H$



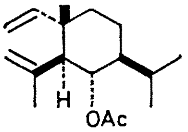
(V)



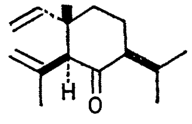
(VI)



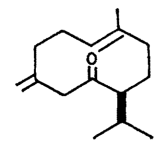
(VII) $R^1 = OH, R^2 = H$
(VIII) $R^1 = OMs, R^2 = Ac$
(IX) $R^1 = I, R^2 = Ac$



(X)



(XI)



(XII)

Acetylation of (I) with acetic anhydride–pyridine (100°, overnight) followed by partial hydrolysis with 5% methanolic potassium hydroxide (room temp., 10 min.) afforded a hydroxy-monoacetate (II), m.p. 150—152°, $\nu_{max}$ (Nujol) 3600, 3350 br., 1725, and 1255 $cm^{-1}$, which was treated with mesyl chloride–pyridine (0°, 1 hr., and then at room temp., 1 hr.), and then heated with a large excess of sodium iodide in acetone under reflux overnight to give an iodo-acetate (III), m.p. 108—109°. Reduction of (III) with sodium borohydride in dimethyl sulphoxide at room temperature for 1 hr.,[3] and then at 80° for 15 min., produced a monoacetoxy-acetal (IV), m.p. 144—145° (in a sealed tube), which was then heated in aqueous acetic acid (80°, 3 hr.) to afford an acetoxy-ketone (V), m.p. 118—119°. Yields of the reaction products are almost quantitative in each step.

A degradation of the ring A of (V) and its conversion into shyobunone were carried out as follows.[4] When heated with isopropenyl acetate–conc. $H_2SO_4$ under reflux, (V) gave in 87% yield an oily enol acetate (VI), $\nu_{max}$ (film) 1760, 1740, 1690, 1240, and 1215 $cm^{-1}$, which was ozonized in diethyl ether at −78°, and then treated with lithium aluminium hydride (0°, 1 hr. and room temp., another 1 hr., and then under reflux, 2 hr.) to give in 70% yield a triol (VII), m.p. 140—141°, $\nu_{max}$ (Nujol) 3300 br. $cm^{-1}$. Under essentially the same conditions as described in the case of (I), (VII) was converted in three steps into a monoacetoxy-dimesylate (VIII), m.p. 98—100°. One of two mesyl groups in (VIII) was resistant to substitution by sodium iodide: when heated with sodium iodide in ethyl methyl ketone under reflux for 3 days, (VIII) could be quantitatively converted into the corresponding di-iodo-compound (IX), m.p. 70—71°. Finally, dehydrohalogenation of (IX) was effected with 1,5-diazobicyclo[5,4,0]undec-5-ene (80°, 24 hr.) to give in 39% yield an oily acetoxy-diene (X), $\nu_{max}$ (film) 3100, 1740, 1635, 1235, 905, and 890 $cm^{-1}$, which was almost quantitatively converted into shyobunone (XI) when treated with lithium aluminium hydride at room temperature followed by oxidation with Jones' reagent (room temp., 30 min.).[5] The synthetic compound thus obtained was identical with an authentic sample of shyobunone (g.l.c., t.l.c., and i.r. spectrum).

The synthesis of shyobunone (XI) also means the syntheses of epi- and iso-shyobunone.[1] Furthermore, when (XI) was heated in a sealed tube (160—180°, 20 min.), preisocalamendiol (XII) was obtained, in *ca.* 30% yield, in a pure state.[1,6] This is the first example of the synthesis of a naturally occurring germacrone-type sesquiterpene.

All compounds gave satisfactory physical data.

(*Received, July 20th,* 1970; *Com.* 1178.)

---

[1] M. Iguchi, A. Nishiyama, H. Koyama, S. Yamamura, and Y. Hirata, *Tetrahedron Letters*, 1968, 5315; *ibid.*, 1969, 3729; M. Iguchi, A. Nishiyama, S. Yamamura, and Y. Hirata, *ibid.*, 1970, 855.

[2] D. M. Simonovic, A. S. Rao, and S. C. Bhattacharyya, *Tetrahedron*, 1963, **19**, 1061.

[3] R. O. Hutchins, D. Hoke, J. Keogh, and D. Koharski, *Tetrahedron Letters*, 1969, 3495.

[4] L. J. Patil and A. S. Rao, *Tetrahedron Letters*, 1967, 2273 and references cited therein.

[5] G. H. Kulkarni, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron*, 1964, **20**, 1301.

[6] M. Iguchi, A. Nishiyama, S. Yamamura, and Y. Hirata, *Tetrahedron Letters*, 1969, 4295.