On the Stereochemistry of the Acetoxy-group at C-15 in Trichokaurin

By EIICHI FUJITA,* TETSURO FUJITA, and MASAYUKI SHIBUYA
(*Institute for Chemical Research, Kyoto University, Takatsuki, Osaka-fu, Japan*)

RECENTLY, we isolated from *Isodon* species two new diterpenes[1,2] possessing the kaurene nucleus. One of them was named trichokaurin and a structure for it was suggested [formula (I)].[1] At that time, the α-stereochemistry of the acetoxy-group at C-15 was tentatively assigned on the assumption that the methyl group at C-16 of the triol (II) which was derived from trichokaurin through a series of reactions—that is, oxidation to a 1-oxo-derivative, thioketalization, subsequent desulphurization accompanied by saturation of the exocyclic methylene group, and reaction with $LiAlH_4$—should have the β-orientation;[3] the hydroxy-group at C-15 of the triol (II) was shown to have a *trans*-relationship to the methyl group at C-16 on the basis of an n.m.r. investigation.

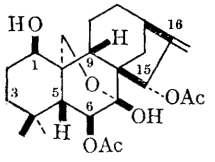
We reached the conclusion that the assignment was incorrect, from the evidence given below, and hence the structure and absolute configuration of trichokaurin should be revised to formula (III).

The 1-methylsulphonate (IV) [$C_{25}H_{36}O_9S$, m.p. 190—191° (decomp.), δ 3·06 p.p.m. ($CDCl_3$) (3H, singlet, OSO_2CH_3)] of trichokaurin on oxidation with the Lemieux–Johnson reagent[4] gave a ketone (V) [$C_{24}H_{34}O_{10}S$, m.p. 192—193° (decomp.), ν_{max} (KBr) 1750 cm.$^{-1}$ (five-membered-ring ketone)]. Treatment of the compound (V) with Me_2SO afforded an unsaturated compound (VI) [$C_{23}H_{30}O_7$, m.p. 203—204° (decomp.), δ 5·80 and 5·30 p.p.m. ($CDCl_3$), AB part of ABX_2, *cis*-$CH:CH{\cdot}CH_2$]. The hydrogenation of (VI) in the presence of Adams' catalyst yielded a saturated product (VII)† [$C_{23}H_{32}O_7$, m.p. 186—187° (decomp.)], which was reduced with $LiAlH_4$ to give tetraol (VIII) [m.p. 195—200° (decomp.), ν_{max} (KBr) 3350 cm.$^{-1}$ (OH)]. The latter on acetylation gave a diacetate (IX) [$C_{23}H_{34}O_7$, m.p. 205—206° (decomp.)]. In the n.m.r. spectrum ($CDCl_3$) of the diacetate (IX), a doublet of doublets [$J = 3{\cdot}5$ (coupling with O*H*) and 9·0 c./sec.] appeared at δ 4·26 p.p.m. which was assigned to the proton at C-15, and a quartet ($J = 6{\cdot}5$ and 9·0 c./sec.) also appeared at δ 4·97 p.p.m. which was assigned to the proton at C-16. The stereomodel allowed only one reasonable assignment of the stereochemistry, the hydrogens at C-15 and C-16 being in *cis*-relationship and both having α-orientation.

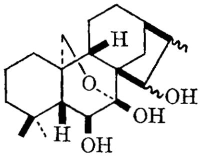
The chemical confirmation was accomplished by the following conversion. 1-Oxotrichokaurin (X) on $LiAlH_4$ reduction gave tetraol (XI), m.p. 240—243° (decomp.), which was oxidized with $NaIO_4$ to yield an enmein-type product (XII) [m.p. 265—269° (decomp.), ν_{max} (KBr) 3450 and 1700 cm.$^{-1}$, δ 5·36 (1H, singlet, C-6–*H*) and 4·48 p.p.m. ($CDCl_3$) (1H, triplet, $J = 9{\cdot}0$ c./sec., C-1–*H*)]. A partial acetylation and hydrogenation in the presence of Adams' catalyst of (XII) afforded a compound, m.p. 270—272° (decomp.), which proved to be identical with tetrahydroisodocarpin 6-acetate (XIII) [$C_{22}H_{32}O_6$, m.p. 271—273° (decomp.), ν_{max} (KBr) 3350, 1735, and 1710 cm.$^{-1}$, δ 6·17 (1H, singlet, C-6–*H*), 4·93 (1H, doublet,

---

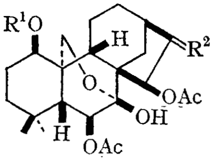
† The compound (VII) was originally prepared as a key intermediate for the purpose of the conversion of trichokaurin into (−)-kaurene and diterpene alkaloids. See following Communication.



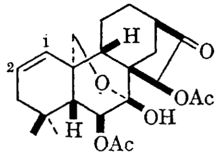
(I)



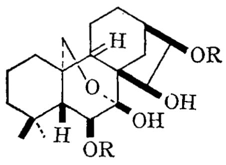
(II)



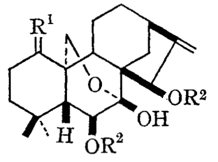
(III) R^1=H, R^2=CH_2
(IV) R^1=SO_2Me, R^2=CH_2
(V) R^1=SO_2Me, R^2=O



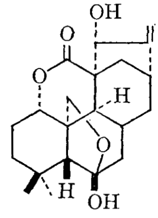
(VI)
(VII) with 1,2 saturated



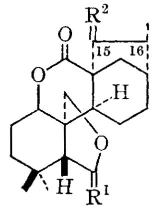
(VIII) R=H
(IX) R=Ac



(X) R^1=O, R^2=Ac
(XI) R^1=α-OH, β-H; R^2=H



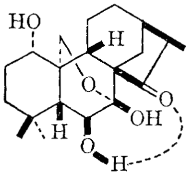
(XII)



(XIII) R^1=α-H, β-OAc R^2=α-OH, β-H
(XIV) R^1=α-H, β-OH; R^2=O
(XV) R^1=α-H, β-HO R^2=α-OH, β-H
(XVI) R^1=R^2=O

$J = 10{\cdot}0$ c./sec., C-15–H), 4·44 (1H, triplet, $J = 9{\cdot}0$ c./sec., C-1–H), and 0·94 p.p.m. ($CDCl_3$) (3H, doublet, $J = 7{\cdot}0$ c./sec., C-16–CH_3)] by the i.r. and n.m.r. comparison and mixture melting-point determination. Compound (XIII) was derived from dihydroisodocarpin (XIV) by $NaBH_4$ reduction to diol (XV) [ν_{max} ($CHCl_3$) 3400 and 1710 cm.$^{-1}$, δ 4·86 p.p.m. ($CDCl_3$) (1H, doublet, $J = 10{\cdot}0$ c./sec., C-15–H], and subsequent partial acetylation. Moreover, the compound (XIII) derived from trichokaurin on oxidation with Jones' reagent gave a product which was shown to be identical with the known dilactone (XVI).[5] Since the absolute configuration of the methyl group at C-16 in dihydroisodocarpin (XIV) has been established,[5] the α-configuration of the hydroxy-group at C-15 in tetrahydroisodocarpin 6-acetate (XIII) is supported by the coupling-constant value [see n.m.r. data of (XIII)] which suggested the *cis*-relationship between the hydrogens at C-15 and C-16, and also from the foregoing conversion from (XIV) *via* (XIII) into (XVI) which indicated non-inversion of the methyl group at C-16. Thus, the acetoxy-group at C-15 in trichokaurin must have β-orientation as shown in formula (III).

Further evidence was provided by the following: tetraol (XI) was treated with 15% HCl to afford quantitatively a saturated ketone (XVII) [m.p. 244—246° (decomp.), ν_{max} (KBr) 1715 cm.$^{-1}$, δ 6·54 (1H, doublet, $J = 11{\cdot}0$ c./sec., C-6–OH), 4·13 (1H, quartet, $J = 5{\cdot}5$ and 11·0 c./sec., C-6–H), and 1·08 p.p.m. (C_5D_5N) (3H, doublet, $J = 6{\cdot}0$ c./sec., C-16–CH_3)], which supports[6] the β-configuration of the acetoxy-group at C-15 in trichokaurin. The structure of the ketone (XVII) was confirmed chemically by its conversion into dihydroisodocarpin (XIV)[5] through oxidation with $NaIO_4$. In the ketone (XVII), an unusual i.r. absorption for the five-membered-ring ketone is due to hydrogen-bonding with the hydroxyl group at C-6, just as in the case of oridonin,[2] and this fact confirms again the β-assignment of the acetoxy-group at C-6 in trichokaurin.



(XVII)

(*Received, March 20th, 1967; Com. 271.*)

---

[1] E. Fujita, T. Fujita, and M. Shibuya, *Chem. Comm.*, 1967, 148.
[2] E. Fujita, T. Fujita, H. Katayama, and M. Shibuya, *Chem. Comm.*, 1967, 252.
[3] L. H. Briggs, B. F. Cain, R. C. Cambie, B. R. Davis, P. S. Rutledge, and J. K. Wilmshurst, *J. Chem. Soc.*, **1963**, 1345.
[4] R. Pappo, D. S. Allen, jun., R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, 1956, **21**, 478.
[5] E. Fujita, T. Fujita, and M. Shibuya, *Tetrahedron Letters*, **1966**, 3153.
[6] C. Djerassi, C. R. Smith, A. E. Lippman, S. K. Figdor, and J. Herran, *J. Amer. Chem. Soc.*, **1955**, **77**, 4801.