The Structure and Stereochemistry of Trichokaurin, a New Diterpenoid from *Isodon trichocarpus* Kudo

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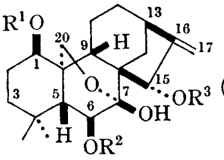
RECENTLY we isolated eight diterpenoids from *Isodon japonicus* Hara (Japanese name: "Hikiokoshi") and *I. trichocarpus* Kudo (Japanese name: "Kurobana-hikiokoshi") (Labiatae), and elucidated the structures of five of them.[2]

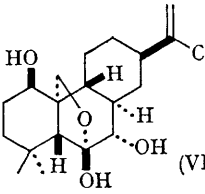
We isolated a new kaurene-type diterpenoid, which was given the name trichokaurin, from *I. trichocarpus*. Trichokaurin (I) [$C_{24}H_{34}O_7$, m.p. 184—185° (decomp.), $[\alpha]_D^{17}$ −93°] has a secondary hydroxyl group [ν_{max}(KBr) 3550, 3450, and 3350 cm.$^{-1}$, δ 3·58 p.p.m. ($CDCl_3$) (1H, triplet, *J* = 2·0 c./sec., >C*H*OH)], a tertiary hydroxyl group [ν_{max}(KBr) 3550, 3450, and 3350 cm.$^{-1}$, δ 3·83 p.p.m. ($CDCl_3$) (1H, broad, $\geqslant$ CO*H*)], an exocyclic methylene group [δ 5·04 and 4·91 p.p.m. ($CDCl_3$) (each 1H, doublets of doublets, *J* = 2·0 and 1·0 c./sec.)], two secondary acetoxyl groups [δ 2·19, 2·06 (each 3H, singlet), 5·21 (1H, doublet, *J* = 7·0 c./sec., coupling with a doublet at δ 1·93 p.p.m.), and 5·62 p.p.m. ($CDCl_3$) (1H, triplet, *J* = 2·0 c./sec., coupling with signals at δ 5·04 and 4·91 p.p.m.)] and an ether-type methylene group [δ 3·93 p.p.m. ($CDCl_3$) (2H, singlet, –C*H*$_2$–O–)].

Hydrolysis with 1/50 N-sodium hydroxide in methanol of trichokaurin or its acetate (II), $C_{26}H_{36}O_8$, m.p. 189—191° (decomp.) [δ 2·18, 2·09, and 2·06 p.p.m. ($CDCl_3$) (each 3H, singlet)] gave mainly an oily hemiketal aldehyde (VI) [ν_{max}(KBr) 1690 and 1625 cm.$^{-1}$, δ 6·26, 5·98 (each 1H, singlet) and 9·51 p.p.m. ($CDCl_3$) (1H, singlet)], besides a tetraol (III), $C_{20}H_{30}O_5$, m.p. 247—249° (decomp.) [ν_{max}(KBr) 3500, 3300, and 3050 cm.$^{-1}$]. A satisfactory yield of the expected tetraol (III) was achieved by the reaction of (I) or (II) with $LiAlH_4$. The aldehyde (VI) on acetylation gave a triacetate (VII), $C_{26}H_{36}O_8$, m.p. 116—120° (decomp.) [ν_{max} (KBr) 2700, 1740, 1690, and 1620 cm.$^{-1}$, δ 2·16, 2·14, 1·99 (each 3H, singlet), and 2·43 p.p.m. ($CDCl_3$) (1H, singlet, C-5–H)].

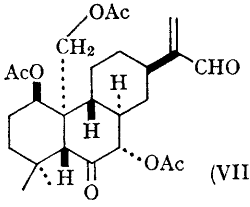
Periodate oxidation of tetraol (III) in methanol afforded a hemiacetal lactone (IX) [ν_{max}(KBr) 3400 and 1700 cm.$^{-1}$, δ 5·32 [1H, singlet, C-6–*H*], 5·05 (2H, multiplet, =C*H*$_2$), 4·92 [1H, quartet, *J* = 3·0 and 5·0 c./sec., C-15–*H*], and 3·89 p.p.m. ($CDCl_3$) (2H, AB type, *J* = 10·0 c./sec., –C*H*$_2$–O–)] as a major product, and an aldehyde lactone (VIII) [ν_{max}(KBr) 3450, 2725, and 1705 cm.$^{-1}$, δ 9·92 p.p.m. ($CDCl_3$) (1H, doublet, *J* = 4·0 c./sec.)] as a minor one. The latter on treatment with weak acid was easily converted into the former. The hemiacetal (IX) on hydrogenation using Adams' catalyst followed by oxidation with Jones' reagent



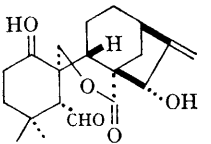
(I: $R^1 = H, R^2 = R^3 = Ac$)
(II: $R^1 = R^2 = R^3 = Ac$)
(III: $R^1 = R^2 = R^3 = H$
(IV: $R^1 = R^2 = Ac, R^3 = H$)
(V: $R^1 = R^3 = H, R^2 = Ac$)



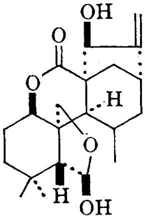
(VI)



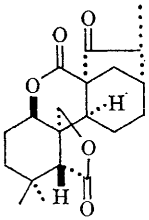
(VII)



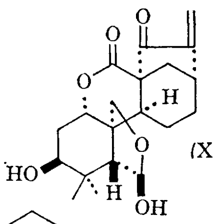
(VIII)



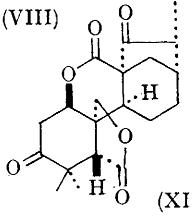
(IX)



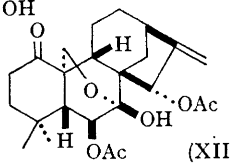
(X)



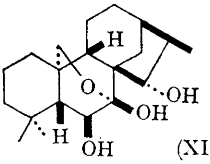
(XI)



(XII)



(XIII)



(XIV)

yielded a crystalline keto-dilactone (X), m.p. 199—201° [ν_{max}(KBr) 1775, 1740, and 1705 cm.$^{-1}$]. The latter proved to be identical with dihydro-1-*epi*-3-deoxydehydroenmein (X), m.p. 199—204°, prepared by thioketalization and subsequent desulphurization from dihydro-1-*epi*-bisdehydroenmein (XII)[3] which can be derived from enmein (XI).[3,4] Thus, it was clarified that trichokaurin can be represented as formula (I), although the stereochemistry of the hydroxyl groups at C-6 and C-15 remains unresolved.

Acetylation of tetraol (III) gave a crystalline diacetate (IV), $C_{24}H_{34}O_7$, m.p. 175—178° [δ 2·18, 2·07 (each 3H, singlet), 4·62 (1H, broad, C-1-*H*), and 5·27 p.p.m. ($CDCl_3$) (1H, doublet, $J = 6{\cdot}0$ c./sec., C-6-*H*)] and an oily 6-monoacetate (V) [δ 2·12 (3H, singlet), 5·15 (1H, doublet, $J = 6{\cdot}0$ c./sec., C-6-*H*), and 3·46 p.p.m. ($CDCl_3$) (1H, broad, C-1-*H*)]. The fact that 6-monoacetate was obtained suggests β-hydroxyl stereochemistry at C-6, because acetylation of α-hydroxyl at C-6 would be more difficult than that of β-hydroxyl at C-1. The coupling constants (5·5—7·0 c./sec.) of C-6-H in the several derivatives also support β- rather than α-stereochemistry of the hydroxyl group at C-6.

1-Keto-derivative (XIII), an oxidation product of trichokaurin, $C_{24}H_{32}O_7$, m.p. 177—179° [ν_{max} (KBr) 3400, 1740, 1700, and 1655 cm.$^{-1}$] was converted into triol (XIV), $C_{20}H_{32}O_4$ 232—235° [ν_{max}(KBr) 3400 cm.$^{-1}$, δ 4·18 (1H, doublet, $J = 5{\cdot}5$ c./sec., C-6-*H*) and 4·31 p.p.m. (C_5D_5N) (1H, doublet, $J = 5{\cdot}0$ c./sec., C-15-*H*] through a series of reactions; thioketalization, desulphurization accompanied with saturation of exocyclic methylene, and reaction with $LiAlH_4$. The coupling constant of the proton at C-15 indicated the *trans* relationship between the hydrogens at C-15 and C-16. On the basis of stereochemical considerations, the methyl group on C-16 should be in the β-orientation.[5] Thus the α-orientation is assigned to the hydroxyl group at C-15.

From the foregoing evidence, we suggest the structure (I) for trichokaurin.

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[5] L. H. Briggs, B. F. Cain, E. C. Cambie, B. R. Davis, P. S. Rutledge, and J. K. Wilmshurst, *J. Chem. Soc.*, 1963, 1345.