Terpenoids. Part XXV.[1] Structures and Absolute Configurations of Isodoacetal, Nodosinin, and Odonicin, Novel Diterpenoids of *Isodon japonicus*

By **Eiichi Fujita,* Manabu Taoka, Yoshimitsu Nagao,** and **Tetsuro Fujita,** Institute for Chemical Research, Kyoto University, Uji, Kyoto-Fu 611, Japan

On the basis of spectroscopic data and chemical evidence, the structure and absolute configuration of isodoacetal (1a), nodosinin (6), and odonicin (11) have been established. The first two are B-secokaurene derivatives and the third is *ent*-6α,15α-diacetoxy-7β,20-epoxy-7α-hydroxykaura-2,16-dien-1-one. Chemical interconversions between isodoacetal and nodosinin have been accomplished.

WE have previously reported the isolation from *Isodon japonicus* Hara of the diterpenoids oridonin,[2] sodoponin,[1,3] enmein,[4] enmein 3-acetate,[4b] isodocarpin,[5] nodosin,[6] isodonal,[1,3] epinodosin,[1,3] epinodosinol,[1,3] and isodotricin,[7] and have determined their structures and absolute configurations. The first two belong to the kaurene derivatives, and the latter eight are B-secokaurene- (enmein-) type compounds. Further investigation of the same plant has led to isolation of three new diterpenoids: isodoacetal, nodosinin, and odonicin.

Isodoacetal, m.p. >300°, $[\alpha]_D$ −134°, $C_{22}H_{28}O_6$ (analysis and mass spectrum), contains two tertiary methyl groups [δ 1·06 and 1·07 (each 3H, s)], a secondary acetoxy-group [$\nu_{max.}$ 1740 and 1235 cm^{-1}, δ 2·09 (3H, s, Ac) and 6·30 (1H, t, *J* 2·5 Hz, C*H*·OAc)], a methylene group between a tertiary carbon atom and an oxygen atom [δ 3·69 and 4·28 (each 1H, AB-type, *J* 8 Hz)], an exocyclic methylene group [$\nu_{max.}$ 1660 and 875 cm^{-1}, δ 5·11 (2H, m)], a δ-lactone system [$\nu_{max.}$ ($CHCl_3$) 1725 cm^{-1}, δ 4·90 (1H, dd, *J* 7·0 and 9·0 Hz)], and an acetal group [δ 5·30 (1H, s)]. These data led to the assignment of a B-secokaurene skeleton to this diterpenoid.

By analogy with recent examples, the exocyclic methylene group was placed at C-16. An n.m.r. decoupling experiment showed that the proton on the acetoxylated secondary carbon atom was coupled to the exocyclic methylene protons; hence the acetoxy-group is at C-15.

The δ-lactone system was placed between C-8 and C-1 by analogy with the enmein-type diterpenoids found hitherto. Two methyl groups were expected to be at C-4. The AB-type signal already mentioned and a singlet at δ 5·30 in the n.m.r. spectrum were assigned to the C-20 methylene protons and the C-6 proton, respectively, and an oxygen bridge was assumed to connect C-6 and C-20. Thus, five oxygen functions were characterized. The remaining oxygen atom was assigned to the acetal system constituting a sixth ring by joining C-6 and C-11. Thus the structure (1) was assigned, with stereochemistry (1a) or (1b) for isodoacetal. Dreiding models of structures (1a) and (1b) showed that the torsion angle between C(5)H and C(6)H was about 90°, explaining the singlet signal of the 6-proton.

The stereochemistry at C-15 was assigned on the basis of the coupling constant ($J_{15.16}$) of 10·5 Hz for dihydroisodoacetal, indicating the *cis*-relationship between 15- and 16-H.† The 11-H signal of isodoacetal was observed as a multiplet, *J* 11·5, 8·5, and 7·5 Hz. Decoupling experiments enabled $J_{9.11}$ to be evaluated as 8·5 Hz.‡ When the C(11)–O bond has the stereochemistry shown in formula (1b), ring C can exist only

† Hydrogenation of C-16 exocyclic methylene group in enmein-type diterpenoids always occurs from the *exo*-side of the bicyclo[3.2.1]octane system.[4-6]

‡ In the case of dihydroisodoacetal, $J_{9.11}$ was 9 Hz.

[1] Part XXIV, E. Fujita, T. Fujita, M. Taoka, H. Katayama, and M. Shibuya, *Chem. and Pharm. Bull (Japan)*, **1973**, **21**, 1357.

[2] E. Fujita, T. Fujita, H. Katayama, M. Shibuya, and T. Shingu, *J. Chem. Soc. (C)*, 1970, 1674; E. Fujita, T. Fujita, and H. Katayama, *ibid.*, p. 1681.

[3] E. Fujita, T. Fujita, M. Taoka, H. Katayama, and M. Shibya, *Tetrahedron Letters*, 1970, 421.

[4] (*a*) E. Fujita, T. Fujita, K. Fuji, and N. Ito, *Tetrahedron*, 1966, **22**, 3423; (*b*) E. Fujita, T. Fujita, and M. Shibuya, *J. Pharm. Soc. Japan*, 1967, **87**, 1076.

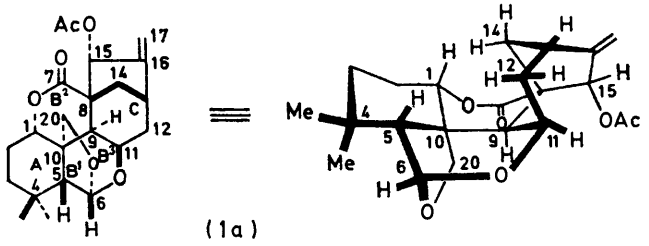
[5] E. Fujita, T. Fujita, and M. Shibuya, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 1573.

[6] E. Fujita, T. Fujita, and M. Shibuya, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 509.

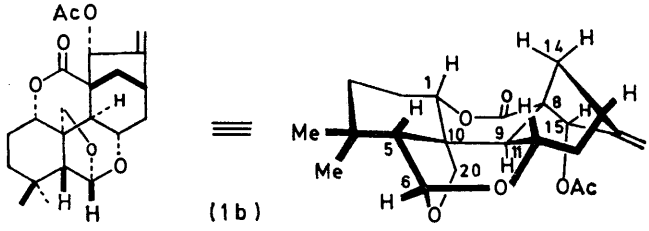
[7] E. Fujita, T. Fujita, Y. Okada, S. Nakamura, and M. Shibuya, *Chem. and Pharm. Bull. (Japan)*, 1972, **20**, 2377.

as a boat form. In this case, the dihedral angle between C(9)H and C(11)H is *ca.* 160°, which satisfies the observed coupling constant. Nuclear Overhauser effects, however, were not observed * between 5-H and 11-H and between 11-H and 14-H, contrary to expectations. On the other hand, such an effect was observed * between 5-H and 12β-H, as expected for formula (1a) with ring C in a chair form and a β-C–O bond at C-11. The 12β-H signal was sought for by a decoupling experiment. Irradiation at the 11-H frequency clarified the chemical shifts of the 12-protons. INDOR experiments showed that the chemical shifts of 14α-H (monitored by 14β-H) and of the C-2 methylene protons were very close to that of 12β-H, but these protons are not located in positions such that one would expect a nuclear Overhauser effect with 5-H. Thus, the formula (1a) was considered to be more reasonable. The large value of $J_{9,11}$ and the small Overhauser effect between 5- and 12β-H can be explained in terms of a half-chair conformation of ring C, in which the 12-methylene group protrudes, so that the torsion angle between C(9)H and C(11)H is *ca.* 10—20° and the distance between 5-H and 12β-H is greater than in a normal chair form. If ring C were in a normal chair form in the dihydroisodoacetal 16α-Me and 11-H would be close, whereas a half-chair conformation would make these two distant. As expected, a nuclear Overhauser effect between 16α-Me and 11-H was not observed.

When isodoacetal was refluxed for 2 h in methanol–chloroform containing hydrochloric acid, a crystalline product was obtained. This proved to be identical



(1a)



(1b)

with the acetal (2) prepared from dihydronodosin (4). The mechanism shown for this rearrangement in Scheme 1 follows that established [8b] for the garryfoline–cuauchichicine rearrangement.[8a] The authentic acetal (2) was prepared from dihydronodosin (4) [6] by heating in methanolic hydrochloric acid under reflux (Scheme 2).

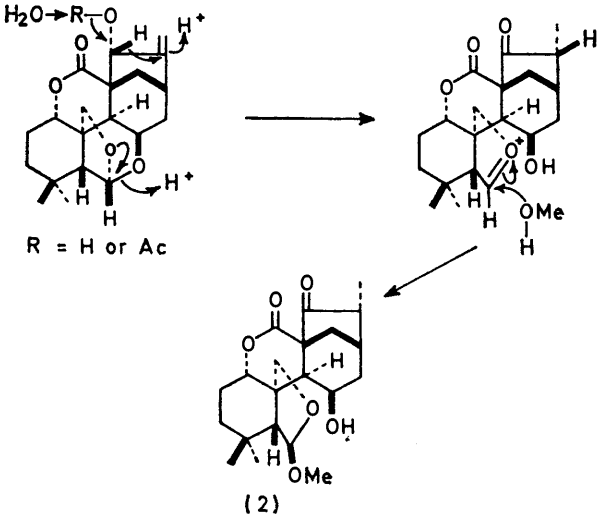
Nuclear Overhauser effect data for isodoacetal *

Signal irradiated (δ)	19-Me (1·03)		1-H (5·08)		11-H (4·53)	5-H (2·47)
Signal observed	5-H		5-H	14β-H	5-H 14β-H	11-H
Intensity increase (%)	10		6	9	Nil Nil	Nil
Signal irradiated (δ)	14β-H (2·37)		12β-H (1·90)		12α-H (2·10)	
Signal observed	11-H		5-H		5-H	
Intensity increase (%)	Nil		7		Nil	

* Spectra at 100 MHz; solutions in [$^2H_5$]pyridine. As isodoacetal is hardly soluble in pyridine, the concentration used was 1—2% (w/v). In this solution, however, the 14β-H showed a paramagnetic shift compared to that measured in chloroform, and this made the measurements more convenient.

The foregoing facts established the structure and absolute configuration of isodoacetal as (1a).

Nodosinin, $C_{23}H_{32}O_7$, m.p. 281—284°, $[\alpha]_D^{26}$ −211°, contains two tertiary methyl groups [δ 1·03 and 1·00



(2)

SCHEME 1

(each 3H, s)] and a methylene group between a tertiary carbon atom and an oxygen atom [δ 3·75 and 3·98 (2H, ABq, *J* 9 Hz)]. I.r. absorption at 1708 cm^{-1} and an n.m.r. triplet [δ 5·47 (*J* 8 Hz)] assigned to an axial proton on a secondary oxygenated carbon atom suggested the presence of a δ-lactone system. Thus a B-secokaurene-type skeleton was deduced for nodosinin.

In addition to the foregoing, the presence of an exocyclic methylene group [δ 5·10 and 4·98 (each 1H)], a secondary acetoxy-group [$\nu_{max.}$ 1750 cm^{-1}, δ 2·10 (3H, s, Ac) and 6·30 (1H, t, *J* 2·5 Hz, C*H*·OAc)], a methoxy-group [δ 3·30 (3H, s)], an acetal system {δ 4·83 [1H, s, $CH(OR)_2$]} and a secondary hydroxy-group [$\nu_{max.}$ 3480 cm^{-1}, δ 4·47 (1H, m, C*H*·OH)] was deduced.

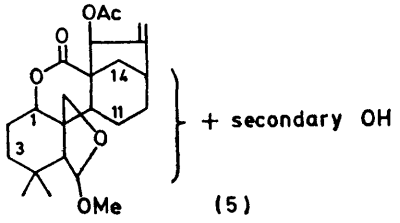
The locations of the exocyclic methylene at C-16 and of the acetoxy-group at C-15 were assumed, because

* See Table.

[8] (*a*) C. Djerassi, C. R. Smith, A. E. Lippman, S. K. Figdor, and J. Herran, *J. Amer. Chem. Soc.*, 1955, **77**, 4801; (*b*) M. F. Barnes and J. MacMillan, *J. Chem. Soc.* (*C*), 1967, 361.

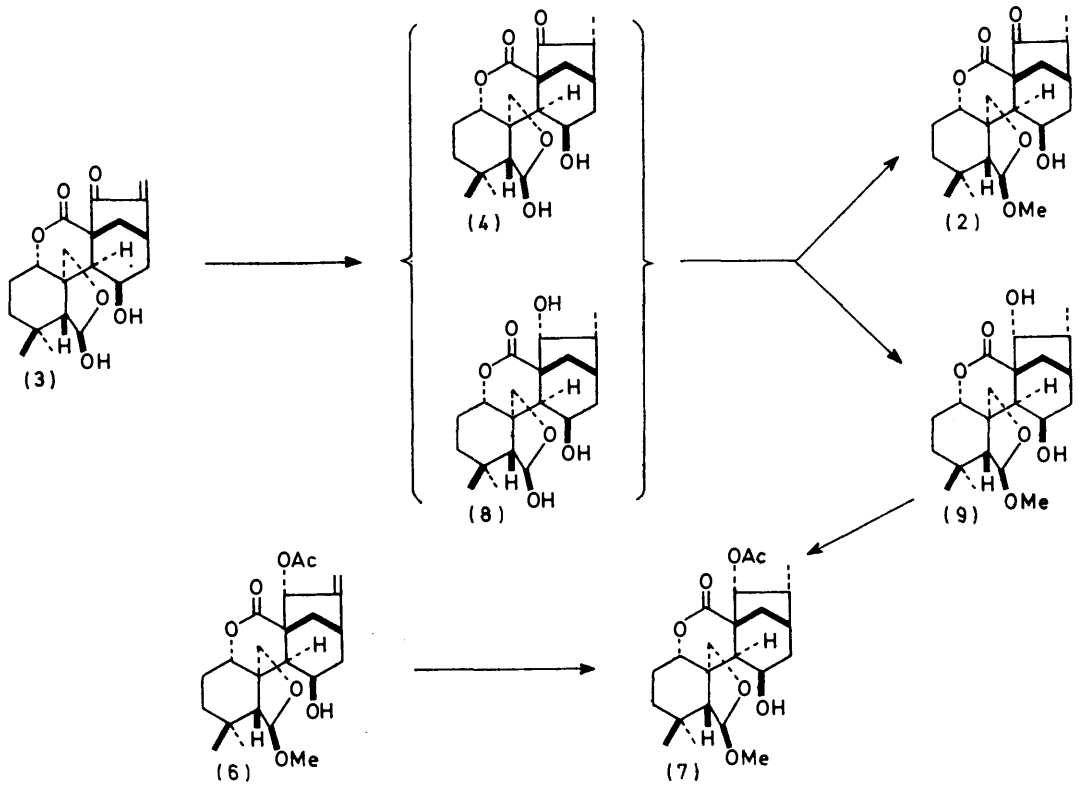
their n.m.r. patterns were very similar to those of isodoacetal.

In nodosinin the absence of a hemiacetal hydroxy-group was inferred, because the diterpenoid was not easily acetylated. We deduced the presence of a methyl acetal involving the ether-type methylene at C-20 and a methoxy-group at C-6. Thus, the partial structure (5) was formulated for nodosinin.



(5)

The n.m.r. signal (δ 5·47) of 1-H of nodosinin was at considerably lower field than that (δ 4·90) of isodoacetal. This paramagnetic shift was considered to be due to the remaining secondary alcohol function. With assumption of the usual stereochemistry common among B-seco-kaurene-type diterpenoids known hitherto, a reasonable position where the secondary hydroxy-group could deshield the 1-H was sought for by use of a Dreiding model. 3β-Axial, 14β-quasiaxial,* and 11β-quasiaxial positions appeared possible. The 14β-position was rejected because this would give the 14α-H signal as a doublet instead of a multiplet in the n.m.r. spectrum. The spectrum of nodosinin showed doublets at δ 2·65 (*J* 4·3 Hz) and 2·82 (*J* 11·5 Hz). Assignment of the former to 9-H and of the latter to 14β-H with an 11β-hydroxy-group was able to explain all the foregoing facts. The paramagnetic shift of 9-H was attributed to the effects of the surrounding oxygen atoms of the acetal and 15α-OAc, and that of 14β-H was assumed due to the 'flagpole' OH at C-11, as in the case of nodosin.[6] Assumption of a 3β-axial OH was not able to give such a satisfactory explanation. Thus formula (6) was suggested for nodosinin.



SCHEME 2

Catalytic hydrogenation of nodosinin gave the dihydro-derivative (7), identical with a product derived from tetrahydronodosin (8) by acetalization with methanol in acidic medium followed by acetylation (Scheme 2). This established the structure and absolute configuration of nodosinin as (6).

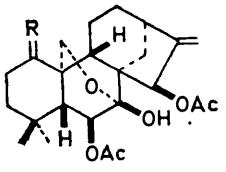
Interconversions of isodoacetal and nodosinin were achieved as follows. Isodoacetal (1a) in methanol–chloroform was refluxed in the presence of hydrochloric acid to yield nodosinin (6) in 19% yield; nodosinin (6) was heated in aqueous acetic acid to give isodoacetal (1a) in 27% yield.

* Ring C is most likely present as a boat form as in enmein (*cf.* ref. 9).

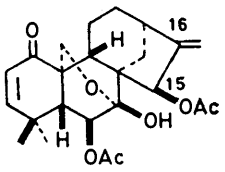
[9] Y. Iitaka and M. Natsume, *Tetrahedron Letters*, 1964, 1257; *Acta Cryst.*, 1966, **20**, 197.

Odonicin, m.p. 193—195°, $[\alpha]_D^{26}$ −193°, $C_{24}H_{30}O_7$ (mass spectrum and analysis) contains two tertiary methyl groups [δ 1·11 and 1·23 (each 3H, s)] and a methylene group [δ 4·02 and 4·18 (each 1H, AB-type, *J* 10 Hz)] between an ether-type oxygen atom and a tertiary carbon atom. A tertiary alcoholic function was suggested by i.r. and n.m.r. data [$\nu_{max.}$ 3420 cm^{-1}, δ 3·43 (1H, s, removed by deuteroxide)]. These findings led to assignment of a kaurene- rather than B-seco-kaurene-type skeleton to this diterpenoid.

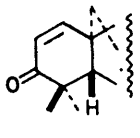
The presence of an exocyclic methylene group was inferred [δ 4·90 and 5·08 (each 1H, m), $\nu_{max.}$ 900 cm^{-1}] and this was placed at C-16 by analogy with the kaurene-type diterpenoids [2,3,10,11] found hitherto from *Isodon* species. In addition, the presence of two secondary acetoxy-groups was deduced [$\nu_{max.}$ 1740, 1720, and 1255 cm^{-1}, δ 2·10 and 2·20 (each 3H, s), 5·68 (1H, t, *J* 2·5 Hz), and 5·36 (1H, d, *J* 9 Hz)]; these were placed at C-15 and C-6 by analogy with trichokaurin (10).[10] That odonicin has a conjugated ketone group is suggested by u.v. ($\lambda_{max.}$ 227·5 nm), i.r. ($\nu_{max.}$ 1665 and 820 cm^{-1}), and n.m.r. data [δ 5·95 and 6·73 (each 1H, AB-type *J* 10 Hz)]. The tertiary hydroxy-group and ether-type methylene group were assigned as 7-hemiacetal hydroxy- and 20-methylene-groups. Thus, odonicin could be formulated as (11) or (12) (or an antipode).



(10) R = α-H, β-OH
(15) R = O



(11)



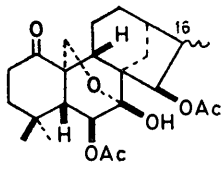
(12)

Catalytic hydrogenation of odonicin gave a crystalline product which showed one spot on t.l.c. Its n.m.r. spectrum, however, showed it to be a mixture of 15,16-*trans*- (13) and *cis*- (14) isomers in the ratio 5 : 2. Catalytic hydrogenation of the 1-keto-analogue (15)[10] of trichokaurin also gave a mixture of 15,16-*trans*- (13) and *cis*- (14) isomers, showing the same i.r. spectrum. Thus the structure of odonicin was elucidated as (11).

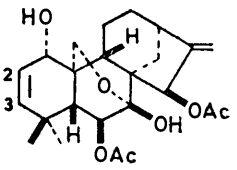
An attempt to convert the didehydrotrichokaurin (15) into odonicin (11) by dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone [12] was unsuccessful. Attempted hydrolysis of odonicin followed by garryfoline–cuauchichicine rearrangement,[8,10] with methanolic hydrochloric acid, was not successful; an unknown product which appeared to have a rearranged ring D but also a modified ring A was formed. Reduction of odonicin with lithium aluminium hydride gave several products, from which we thought it unlikely that a high yield of the desired product (18) could be obtained.

[10] E. Fujita, T. Fujita, M. Shibuya, and T. Shingu, *Tetrahedron*' 1969, **25**, 2517.
[11] E. Fujita and M. Taoka, *Chem. and Pharm. Bull* (*Japan*,) 1972, **20**, 1752.

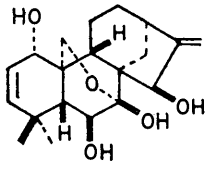
Reduction of odonicin with sodium borohydride gave a product which was apparently homogeneous (t.l.c.). An n.m.r. investigation showed it to be a mixture of dihydro- (16) and tetrahydro- (17) [13] derivatives in the ratio *ca.* 2 : 3; this was confirmed by Jones oxidation



(13) 16α-Me
(14) 16β-Me

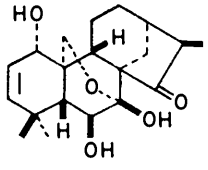


(16)
(17) 2,3-Dihydro

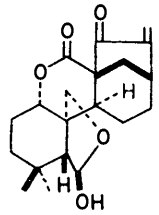


(18)
(19) 2,3-Dihydro

to a 1 : 1 mixture of odonicin (11) and its didehydro-derivative (15). Treatment of the mixture of (16) and (17) with lithium aluminium hydride afforded deacetylated products, (18) and (19), which on treatment with hydrochloric acid in methanol yielded a mixture of compounds (20) and (21). Hydrogenation of this mixture gave a homogeneous product, shown to be *ent*-7β,20-epoxy-1β,6α,7α-trihydroxykauran-15-one (21),[10] previously derived from trichokaurin (10). Thus, odonicin was identified as *ent*-6α,15α-diacetoxy-7β,20-epoxy-7α-hydroxykaura-2,16-dien-1-one (11). Since compound (21) has been converted [2,10] into isodocarpin



(20)
(21) 2,3-Dihydro



(22)

(22),[5] the foregoing conversion completes a conversion of odonicin (11) into isodocarpin (22).

EXPERIMENTAL

M.p.s were taken on a micro hot-stage apparatus. Unless otherwise stated, i.r. spectra were recorded for KBr discs with a Hitachi EPI-S2 spectrometer and n.m.r. spectra with a Varian A-60, T-60, or HA-100 spectrometer for solutions in deuteriochloroform (tetramethylsilane as internal standard). Mass spectra were determined with a JMS-OISG double-focusing spectrometer.

[12] P. J. Kropp, *J. Org. Chem.*, 1964, **29**, 3110.
[13] E. Fujita, T. Fujita, and Y. Nagao, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 2343.

Rotations were measured with a JASCO DIP-180 automatic polarimeter. Extracts were dried over Na_2SO_4. Mallinckrodt silicic acid or Kieselgel 0·05—0·2 mm (Merck) was used for column chromatography. T.l.c. plates were coated with Silica Gel G (nach Stahl; Merck) or Nakarai Silica Layer G.

Ethereal Extraction and Isolation of Diterpenoids from the Dried Leaves and Stems of Isodon japonicus *and Isolation of New Diterpenoids.*—The air-dried leaves and stems (8 kg) of *Isodon japonicus* Hara, collected in Kochi in August 1969, were digested in ether (75 l) for a few months. The filtrate was evaporated to leave a syrup (800 g), which was dissolved in methanol and treated with charcoal. Concentration of the solution and removal of the precipitate (mainly enmein) was repeated; a total of 40 g of precipitate was removed. The filtrate was evaporated and the residue was dissolved in ethyl acetate and shaken with aqueous 10% sodium carbonate to remove acidic substances. The usual work-up gave a crude extract (81 g), which was column-chromatographed (SiO_2; 1·5 kg). Careful separation of the fraction which showed spots between those of enmein and β-sitosterol on t.l.c. led to isolation of isodoactal, nodosinin, odonicin, another minor diterpenoid, enmein 3-acetate, nodosin, and enmein. From the foregoing precipitate (3·8 g), pure enmein (1·9 g) was isolated. The yields of the new diterpenoids per kg of dried plant source were 43 (isodoacetal), 8·5 (nodosinin), 46 (odonicin), and 4·2 mg (unnamed diterpenoid).

Isodoacetal (1a).—Recrystallization from methanol yielded pure *isodoacetal* as needles, m.p. >300°, $[\alpha]_D^{17}$, −134° (*c* 1 in $CHCl_3$), $\nu_{max.}$ 1740, 1660, 1235, and 875 cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 1725 and 1215 cm^{-1}, δ (100 MHz) 5·11 (2H, m, *J* 1·0 and 2·5 Hz, 17-H_2), 4·57—4·03 (1H, m, *J* 11·5, 8·5, and 7·5 Hz, 11-H), 2·95br (1H, s, 13-H), 2·87 (1H, d, *J* 8·5 Hz, 9-H), and 2·29 (1H, s, 5-H) (Found: C, 67·7; H, 7·5%; M^+, 388·189. $C_{22}H_{28}O_6$ requires C, 67·65; H, 7·75%; *M*, 388·189).

Catalytic Hydrogenation of Isodoacetal.—To a solution of isodoacetal (5 mg) in methanol (10 ml) was added platinum oxide (catalytic amount). The mixture was stirred overnight in an atmosphere of hydrogen and then filtered. The filtrate was concentrated to precipitate crystals (3 mg) of *dihydroisodoacetal*, m.p. 284—290° (decomp.) (crystal form changed above 260°), $\nu_{max.}$ 1740 and 1245 cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 1740 and 1230—1210 cm^{-1}, δ 6·02 (1H, d, *J* 10·5 Hz, 15-H), 5·30 (1H, s, 6-H), 4·96 (1H, t, *J* 7 Hz, 1-H), 4·57—4·0 (1H, m, 11-H), 4·27 and 3·68 (each 1H, AB-type, *J* 8 Hz, 20-H_2), 2·79 (1H, d, *J* 9 Hz, 9-H), 2·30 (1H, s, 5-H), 2·07 (3H, s, OAc), 1·09 (6H, s, 4-Me_2), and 0·88 (3H, d, *J* 7 Hz, 16-Me) (Found: M^+, 390·204. $C_{22}H_{30}O_6$ requires *M*, 390·204).

Conversion of Nodosin (3) *into the Methyl Acetals* (2) *and* (9).—To a solution of nodosin (3) (723 mg) in methanol (40 ml) was added platinum oxide (58 mg); the mixture was stirred for 24 h in an atmosphere of hydrogen. The u.v. absorption of the conjugated system disappeared. The mixture was filtered and evaporated *in vacuo*; t.l.c. of the residue (727 mg) showed two spots. To a solution of this substance (717 mg) in methanol (10 ml), conc. hydrochloric acid (1 drop) was added, and the mixture was heated under reflux for 20 min. Work-up gave a crude product (700 mg) from an ethyl acetate extract. Column chromatography on silica gel (dichloromethane–acetone, 9 : 1) gave two fractions. The crystals (390 mg) obtained from the first fraction were recrystallized to yield the *acetal* (2) as needles, m.p. 245—248 and 276—278°, $[\alpha]_D^{26}$ −237° (*c* 0·038 in $CHCl_3$), $\nu_{max.}$ 3500 (OH), 1750 (cyclopentanone), and 1700 cm^{-1} (δ-lactone), δ 5·20 (1H, t, *J* 8 Hz, 1-H), 4·80 (1H, s, 6-H), 4·45br (1H, s, 11-H), 4·05 and 3·91 (each 1H, AB-type, *J* 10 Hz, 20-H_2), 3·26 (3H, s, OMe), 2·28 (1H, s, 5-H), 1·73 (1H, s, 11-OH), 1·13 (3H, d, *J* 7 Hz, 16-Me), and 1·05 and 1·00 (each 3H, s, 4-Me_2) (Found: C, 66·45; H, 7·9. $C_{21}H_{30}O_6$ requires C, 66·65; H, 8·0%). The crystals (239 mg) obtained from the second fraction gave the *acetal* (9) as long needles, m.p. 107—109° (from methanol), $\nu_{max.}$ 3450 (OH), 1700 (δ-lactone), and 1050 cm^{-1} (C–O), δ 5·42 (1H, t, *J* 9 Hz, 1-H), 4·96 (1H, m, changed to doublet by D_2O, *J* 10 Hz, 15-H), 4·83 (1H, s, 6-H), 4·40 (1H, m, changed to triplet by D_2O, *J* 5 Hz, 11-H), 3·92 (2H, s, 20-H_2), 3·29 (3H, s, OMe), 2·75 (1H, d, *J* 11 Hz, 14β-H), 2·64 (1H, d, *J* 5 Hz, 9-H), 2·35 (1H, s, 5-H), 1·05 and 1·00 (each 3H, s, 4-Me_2), and 0·84 (3H, d, *J* 6·5 Hz, 16-Me) (Found: C, 63·55; H, 8·25. $C_{21}H_{32}O_6,H_2O$ requires C, 63·3; H, 8·6%).

Partial Acetylation of the Acetal (9).—A solution of acetal (9) (17 mg) in acetic anhydride–pyridine (1 : 1; 1 ml) was set aside for 45 h. Ethanol was added to decompose the excess of reagent, and the solvent was evaporated off. Chromatography of the residue (18 mg) on a silica gel column (dichloromethane–acetone, 95 : 5) gave the acetate (7) (8 mg) and unchanged starting material (9 mg). The *acetate* was recrystallized from methanol; yield 6 mg, m.p. >300° (crystal form changed at 275°) (Found: M^+, 422·227. $C_{23}H_{34}O_7$ requires *M*, 422·230).

Treatment of Isodoacetal (1a) *with Acidic Methanol.*—To a solution of isodoacetal (1a) (21 mg) in methanol (6 ml) and chloroform (2 ml), conc. hydrochloric acid (6 ml) was added, and the mixture was refluxed for 2 h. Work-up gave a crude product, which was chromatographed on a silica gel column (dichloromethane) to yield crystalline material (15 mg) which formed needles, m.p. 245—248 and 275—278° (from methanol), $[\alpha]_D^{26}$ −237° (*c* 0·016 in $CHCl_3$), $\nu_{max.}$ 3500, 1750 (cyclopentanone), 1700 (δ-lactone), and 1055 cm^{-1}, identical with the 6-*O*-methyldihydronodosin (m.p., mixed m.p., i.r. and n.m.r. spectra).

Nodosinin (6).—Recrystallization from methanol yielded pure *nodosinin* as needles, m.p. 281—284° (crystal form changed at 265—270°), $[\alpha]_D^{26}$ −211° (*c* 0·11 in $CHCl_3$), $\nu_{max.}$ 3480, 1750 (OAc), 1708 (δ-lactone), 1235 (OAc), and 1055 cm^{-1}, δ 2·30 (1H, s, 5-H) (Found: C, 65·75; H, 7·6%; M^+, 420·210. $C_{23}H_{32}O_7$ requires C, 65·7; H, 7·6%; *M*, 420·214).

Catalytic Hydrogenation of Nodosinin.—To a solution of nodosinin (7 mg) in methanol (5 ml), platinum oxide (catalytic amount) was added. The mixture was stirred for 23 h in an atmosphere of hydrogen, then filtered. The filtrate was evaporated *in vacuo* to leave a crystalline mass (5·5 mg), which yielded dihydronodosinin (7) as needles, m.p. >300° (from methanol) (crystal form changed at 275°), $\nu_{max.}$ 3470 (OH), 1740 (OAc), 1705 (δ-lactone), 1240, and 1050 cm^{-1}, δ (C_5D_5N) 6·35br (1H, s, 11-OH), 6·35 (1H, d, *J* 10 Hz, 15-H), 5·95 (1H, t, *J* 8·5 Hz, 1-H), 5·03 (1H, s, 6-H), 4·80br (1H, s, 11-H), 4·10 (2H, s, 20-H_2), 3·40 (3H, s, OMe), 3·23 (1H, d, *J* 12 Hz, 14β-H), 2·93 (1H, d, *J* 4 Hz, 9-H), 2·67 (1H, s, 5-H), 2·10 (3H, s, OAc), 1·01 and 1·00 (each 3H, s, 4-Me_2), and 0·80 (3H, d, *J* 7 Hz, 16-Me) (Found: M^+, 422·229. Calc. for $C_{23}H_{34}O_7$: *M*, 422·230), identical with the acetal acetate (7) prepared from nodosin (3) (m.p., mixed m.p., i.r. and n.m.r. spectra).

Conversion of Isodoacetal (1a) *into Nodosinin* (6).—To a

solution of isodoacetal (1a) (11 mg) in methanol (2 ml) and chloroform (1 ml) was added 20% hydrochloric acid (9 ml). The mixture was refluxed for 2·5 h. Work-up including neutralization and extraction with chloroform gave a crude product (10 mg) which was shown to be a mixture (three spots on t.l.c.). Column chromatography (SiO_2; CH_2Cl_2) and purification gave crystals (2 mg), m.p. 281—284° (crystal form changed at 265—270°), $[\alpha]_D^{26}$ −210° (*c* 0·005 in $CHCl_3$), identical with authentic nodosinin (6) (m.p., mixed m.p., i.r. spectrum, and t.l.c.).

Conversion of Nodosinin (6) *into Isodoacetal* (1a).—A solution of nodosinin (6) (15 mg) in acetic acid (2 ml) and water (0·5 ml) was heated at 80° for 1 h. After 1 h at room temperature, water (5 ml) was added and the mixture was extracted with dichloromethane. Work-up gave a crystalline product (13·5 mg), which was shown to be a mixture (four spots on t.l.c.). Chromatography on a silica gel column (dichloromethane) separated pure crystals (4 mg) (from the first eluted fraction). Recrystallization from methanol gave isodoacetal, m.p. >300°, identical (i.r. spectrum, mixed m.p., and t.l.c.) with authentic material.

Odonicin (11).—Recrystallization from methanol gave *needles*, m.p. 193—195°, $[\alpha]_D^{26}$ −193° (*c* 0·114 in $CHCl_3$), $\lambda_{max.}$ (MeOH) 227·5 nm (ε 8200), δ 2·65 (1H, d, *J* 9 Hz, 5-H) (Found: C, 66·8; H, 7·0%; M^+, 430·195. $C_{24}H_{30}O_7$ requires C, 67·0; H, 7·0%; *M*, 430·199).

Catalytic Hydrogenation of Odonicin.—To a solution of odonicin (47 mg) in methanol (15 ml) was added platinum oxide (catalytic amount), and the mixture was stirred for 2 days in an atmosphere of hydrogen (the u.v. absorption of the conjugated ketone had then disappeared). The mixture was filtered and evaporated; t.l.c. of the residue (50 mg) exhibited three spots. Column chromatography (silica gel; dichloromethane–acetone, 9 : 1) gave first a 5 : 2 mixture (18 mg) of epimers (13) and (14). Recrystallization from methanol gave prisms, $\nu_{max.}$ 3400, 1740, 1697, and 1250 cm^{-1}, δ 5·25 (2/7H, d, *J* 9 Hz, 15-H), 5·10 (1H, d, *J* 9 Hz, 6-H), 4·82 (5/7H, d, *J* 4 Hz, 15-H), 4·33 and 3·96 (each 1H, AB-type, *J* 10 Hz, 20-H_2), 3·42 (1H, s, 7-OH), 2·17 and 2·05 (each 3H, s, 2 × OAc), 1·20 (d, *J* 7 Hz, 16β-Me), 1·00 and 0·90 (each 3H, s, 4-Me_2), and 0·80 (d, *J* 7 Hz, 16α-Me). Materials eluted later (12 and 16 mg) were not characterized.

Catalytic Hydrogenation of the 1-*Keto-analogue* (15) *of Trichokaurin.*—To a solution of compound (15) [10] (19 mg) in methanol (10 ml) was added platinum oxide (catalytic amount). The mixture was stirred for 12 h in an atmosphere of hydrogen, filtered, and evaporated. T.l.c. of the residue (20 mg) exhibited three spots. Column chromatography (silica gel; dichloromethane–acetone, 9 : 1) gave first a mixture (12 mg) of epimers (13) and (14) in a ratio of 5 : 2 (t.l.c. one spot), which gave prisms from methanol. The i.r. and n.m.r. spectra of the crystals were identical with those of the foregoing mixture of (13) and (14) obtained by catalytic hydrogenation of odonicin.

Reduction of Odonicin with Sodium Borohydride.—To a stirred solution of odonicin (11 mg) in methanol (5 ml) cooled in ice a solution of sodium borohydride (11 mg) in methanol was added slowly. After 30 min, neutralization with dil. hydrochloric acid, extraction with ethyl acetate, and washing with water, drying, and evaporation of the extract left a residue, which was separated by column chromatography (silica gel; dichloromethane–acetone, 95·5 : 0·5) to give a mixture (4·5 mg) of compounds (16) and (17) as a main product. Its n.m.r. spectrum revealed the following signals due to (16) [in addition to those due to (17) [13]]: δ 5·67 (t, *J* 2 Hz, 15-H), 5·57 (m, 2-H), 5·39 (dd, *J* 2 and 7 Hz, 3-H), 5·18 (d, *J* 8 Hz, 6-H), 5·03 and 4·91 (s, 17-H_2), 4·31 and 3·94 (AB-type, *J* 10 Hz, 20-H_2), 3·60 (s, 7-OH), 2·17 and 2·07 (s, 2 × OAc), and 1·18 and 0·95 (s, 4 Me). From integral values the mixture was found to consist of (16) and (17) in a ratio of *ca.* 2 : 3.

Jones Oxidation of the Mixture of Compounds (16) *and* (17).—To a solution of the foregoing mixture (4·5 mg) in acetone (treated with potassium permanganate) (2 ml), Jones reagent (1 drop) was added at 0°, and the mixture was stirred for 5 min. Neutralization with aqueous sodium carbonate solution and, after addition of water, extraction with dichloromethane and treatment of the extract as usual gave an oily product (4 mg). Its n.m.r. spectrum revealed the following signals attributed to the 1-keto-analogue (15) of trichokaurin [10] [in addition to those due to odonicin (11)]: δ 5·68 (t, *J* 2·5 Hz, 15-H), 5·16 (d, *J* 8 Hz, 6-H), 5·08 and 4·90 (m, 17-H_2) 4·18 and 4·00 (AB-type, *J* 10 Hz, 20 H_2), 2·24 and 2·10 (s 2 × OAc), and 0·98 and 0·92 (s, 4 Me_2). From integral values the mixture was estimated to consist of (11) and (15) in *ca.* 1 : 1 ratio.

Conversion of the Mixture of Compounds (16) *and* (17) *into Trihydroxykauranone* (21).—To a solution of the mixture (15 mg) in dry ether (1 ml) cooled in ice was added a suspension of lithium aluminium hydride (15 mg) in ether (1 ml). The mixture was stirred for 30 min with cooling. Ethyl acetate shaken with water was added to decompose the excess of lithium aluminium hydride; the solution was then washed with water and the organic layer was dried. Evaporation and column chromatography of the residue yielded a mixture (9·5 mg) of alcohols (18) and (19) (no carbonyl absorption in i.r.), which was dissolved in methanol (2 ml). Conc. hydrochloric acid (3 drops) was added and the mixture was stirred for 2 days at room temperature. After neutralization with aqueous sodium carbonate, the solvent was distilled off. The residue was extracted with ethyl acetate and the extract was treated as usual to afford a crude mixture (8 mg) of the rearranged products (20) and (21). This was dissolved in methanol (5 ml) and hydrogenated over platinum. Column chromatography (silica gel) and crystallization from methanol yielded homogeneous crystals (6 mg), m.p. 235—239°, $[\alpha]_D^{26}$ −59° (*c* 0·02 in $CHCl_3$), $\nu_{max.}$ 3250 and 1715 cm^{-1}, identical with an authentic sample of (21),[10] m.p. 235—239°, $[\alpha]_D^{26}$ −60° (*c* 0·02 in $CHCl_3$) (by m.p., mixed m.p., and i.r. spectrum).

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