# The Structure of Tingenone, a Quinonoid Triterpene Related to Pristimerin

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Tingenone, an unusual new quinonoid triterpene related to celastrol and pristimerin, has been isolated from various plants of the Celastraceae and Hippocrateaceae families. It has been shown to be 20-decarboxy-21-oxocelastrol by chemical and spectroscopic methods.

We have previously reported [1-4] the isolation, from various plants of the Celastraceae and Hippocrateaceae families, of a bright red pigment with antitumour activity, named maitenin.† Maitenin was shown to be a quinonoid triterpene related to pristimerin (1) and celastrol (2), found previously in other Celastraceae,[6-8] and a partial structure (3) was proposed.[3] Subsequently maitenin, m.p. 228—229°, was found to be identical [9] with tingenone, m.p. 182—183°, an orange pigment from *Euonymus tingens*, to which an incorrect structure had been previously assigned.[10] The difference in m.p., despite identical spectroscopic properties, was attributed to retention of solvent, and the problem posed by this observation was overcome by the preparation of two derivatives (a leucodiacetate and a toluene-*p*-thiol adduct) from each pigment; the products were identical on the basis of spectroscopic parameters, m.p., and mixed m.p.

We now report chemical studies which establish that the ketone group in structure (3) is at C-21. Reduction of tingenone with sodium borohydride, followed by acetylation, yielded tri-*O*-acetyltingenol (4) [3] and di-*O*-acetyltingenol (5), with the former in larger amount. This may be explained in terms of the formation of two epimeric alcohols of which only one is easily acetylated. Di-*O*-acetyltingenol, $C_{32}H_{44}O_5$ ($M^+$ 508) shows hydroxy-absorption in the i.r.; the n.m.r. spectrum includes only two acetyl signals, and a one-proton signal ($\rangle CH\cdot OH$) at δ 3·85 (displaced to δ 5 in the spectrum of the triacetate).

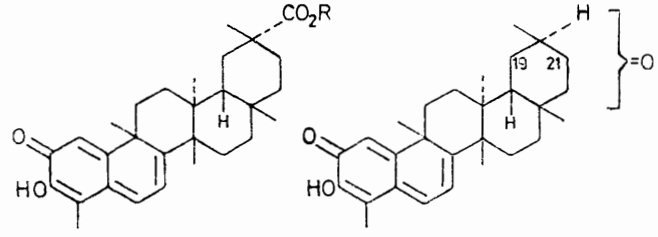
Catalytic hydrogenation of tingenone over 10% platinised charcoal, followed by acetylation, afforded the ketone (6), $C_{32}H_{42}O_5$ ($M^+$ 506; $\nu_{CO}$ 1695 $cm^{-1}$) and a small amount of tri-*O*-acetyltingenol. The mass spectra of the tingenols and the ketone (6) support the suggested structures. In the upper mass range stepwise losses of a methyl radical and of two fragments of 42 m.u. are observed, as well as loss of 60 m.u. from tri-*O*-acetyltingenol, loss of 18 m.u. from di-*O*-acetyltingenol, and combinations of these. Cleavage occurs principally through ring C, and intense ions at *m/e* 271, 229, and 187 and at *m/e* 285, 243, and 201 are attributed to the benzotropylium ion (7) (R = H and Me, respectively). An ion

† The name Maitenin should not be confused with Maytenin, an alkaloid from *Maytenus chuchuhuasca*.[5]

[1] O. Gonçalves de Lima, I. Leôncio d'Albuquerque, J. Sidney de Barros Coêlho, D. Gimino Martins, A. Lins Lacerda, and Gessé M. Maciel, *Rec. Inst. Antibiot. Recife*, 1969, **9**, 17.
[2] O. Gonçalves de Lima, J. Sidney de Barros Coêlho, E. Weigert, I. Leôncio d'Albuquerque, Dardano de Andrade Lima, and M. Alves de Moraes e Souza, *Rev. Inst. Antibiot. Recife*, 1971, **11**, 35.
[3] F. Delle Monache, G. B. Marini Bettòlo, O. Gonçalves de Lima, I. Leôncio d'Albuquerque, and J. Sidney de Barros Coêlho, *Gazzetta*, 1972, **102**, 317.
[4] F. Delle Monache, J. Francisco De Méllo, G. B. Marini Bettòlo, O. Gonçalves de Lima, and I. Leôncio d'Albuquerque, *Gazzetta*, 1972, **102**, 636.
[5] G. Englert, K. Klinga, Raymond-Hamet, E. Schlittler, and W. Vetter, *Helv. Chim. Acta*, 1972, **56**, 474.
[6] A. W. Johnson, P. F. Juby, T. J. King, and S. W. Tam, *J. Chem. Soc.*, 1963, 2883.
[7] K. Nakanishi, Y. Takahashi, and H. Budzikiewicz, *J. Org. Chem.*, 1965, **30**, 1729.
[8] P. J. Ham and D. A. Whiting *J.C.S. Perkin I*, 1972, 330.
[9] F. Delle Monache, G. B. Marini Bettòlo, P. M. Brown, M. Moir, and R. H. Thomson, *Gazzetta*, in the press.
[10] V. Krishnamoorthy, J. D. Ramanathan, and T. R. Seshadri, *Tetrahedron Letters*, 1962, 1047.

at *m/e* 207 from the ketone (6) may be formally attributed to rings D and E, formed by cleavage through ring C from the ion at $M - 15$, as evidenced by the presence of a metastable peak at *m/e* 86·5; in the spectra of di-*O*-acetyl- and tri-*O*-acetyl-tingenol the corresponding ion appears at *m/e* 191 (parent ions at $M - 15 - 18$ and $M - 15 - 60$, respectively).

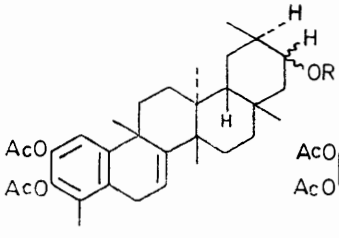
In order to establish the position of the hydroxy-group in di-*O*-acetyltingenol (5), and consequently of the keto-group in tingenone, we made several attempts to dehydrate this derivative. All attempts failed owing to the great instability, under strongly acidic conditions, of the starting material and of tingenone derivatives in general. This also applies to pristimerin,[6,7] which rearranges in boiling methanol containing a little 2N-sulphuric acid to give[11] isopristimerin III (8). We decided therefore to use such an acid-catalysed rearrangement product for structural studies.



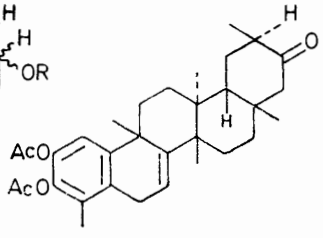
(1) R = Me
(2) R = H



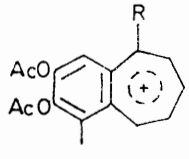
(3)



(4) R = Ac
(5) R = H

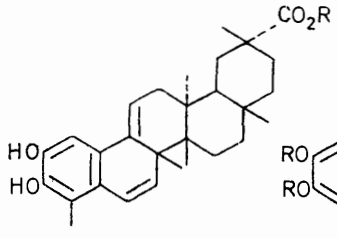


(6)

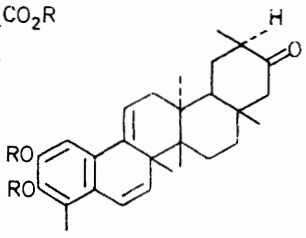


(7)

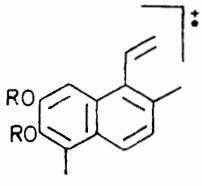
Tingenone, under the same conditions, yields a rearranged product which we have named isotingenone III (9). This substance was characterised by formation of its diacetyl ($C_{32}H_{40}O_5$; $M^+$ 504) (10), and dimethyl (11) derivatives. Both derivatives show u.v. absorption in accord with a divinylbenzene system, and a carbonyl band at 1700 $cm^{-1}$ in the i.r. spectrum. Their n.m.r. spectra are also consistent with the assigned structures, and include signals from one aromatic and three vinyl protons, two of the latter forming an AB quartet (*J* 10 Hz). The mass spectral breakdown pattern of isotingenone III derivatives follows essentially two paths: (*a*) formal retro-Diels–Alder fragmentation of ring C to give the



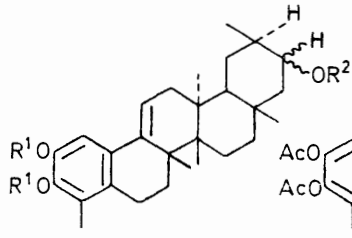
(8)



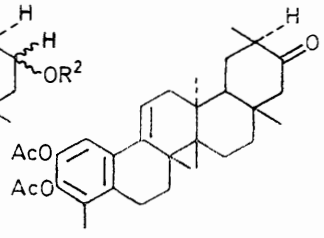
(9) R = H
(10) R = Ac
(11) R = Me



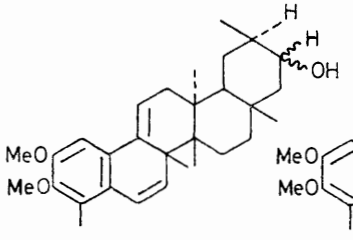
(12)



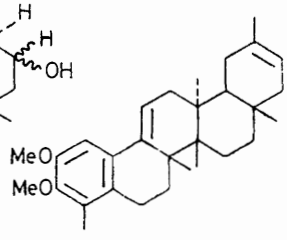
(13) $R^1 = R^2 = Ac$
(15) $R^1 = Ac, R^2 = H$
(17) $R^1 = Me, R^2 = H$



(14)



(16)



(18)

cation (12) (*m/e* 242 for the dimethyl ether and 298 for the diacetate), and (*b*) loss of the bis-allylic methyl group to give the ion at $M - 15$ followed by cleavage of ring D to yield the ion at $M - 15 - 164$; both pathways are supported by observation of metastable peaks.

Catalytic hydrogenation of di-*O*-acetylisotingenone III gave a mixture showing both hydroxy- and keto-bands in the i.r. spectrum; chromatographic separation was possible only after acetylation. The least polar product ($C_{34}H_{46}O_6$; $M^+$ 550) showed neither hydroxylic nor ketonic absorption, but both aromatic (1780 $cm^{-1}$) and aliphatic (1740 $cm^{-1}$) ester groups were present. The

[11] P. K. Grant, A. W. Johnson, P. F. Juby, and T. J. King, *J. Chem. Soc.*, 1960, 549.

n.m.r. spectrum provided evidence for the presence of one aromatic and one vinyl proton, and one secondary and four tertiary aliphatic methyl groups. Furthermore, four methyl signals in the range δ 2—2·30 were assigned to an aromatic methyl and three acetoxy-groups. A one-proton resonance at δ 5 was attributed to >C*H*·OAc. On the basis of these findings structure (13) (tri-*O*-acetyldihydroisotingenol III) was attributed to this product.

The product of lower $R_F$ value ($C_{32}H_{46}O_5$; $M^+$ 506) shows ketonic absorption at 1702 $cm^{-1}$ and is assigned structure (14). It is evident that the 9(11)-double bond is resistant to reduction, whereas the keto-group is partially reduced, so that a mixture of the hydroxy-derivative (15) and the ketone (14) is obtained.

To avoid partial reduction of the ketonic group during catalytic hydrogenation we first reduced the ketone function with sodium borohydride. Thus di-*O*-methylisotingenone III (11) gave di-*O*-methylisotingenol III (16) ($C_{30}H_{42}O_3$; $M^+$ 450) ($\nu_{OH}$ observed but no $\nu_{CO}$), and this on catalytic hydrogenation gave di-*O*-methyldihydroisotingenol III (17) ($C_{30}H_{44}O_3$; $M^+$ 452).

Dehydration of compound (17) with boron trifluoride–ether complex gave a compound ($C_{30}H_{42}O_2$; $M^+$ 434), which can be formulated as (18) or the $\Delta^{19}$-isomer on the basis of its spectroscopic properties. There is no hydroxy-band in the i.r. spectrum and no secondary methyl signal in the n.m.r. spectrum. On the other hand signals for a new vinyl proton and a vinylic methyl group appear at δ 5·27 (1H) and 1·7 (3H), respectively. On the basis of these findings the keto-group of tingenone can be assigned to C-21 or C-19. Position 19 is excluded by the following considerations: (i) tingenone and all its derivatives containing a keto-group in ring E (see Experimental section) show a one-proton signal at δ 2·9 (d, *J* 14 Hz) which can be attributed to an equatorial proton of a methylene group α to the ketonic function; (ii) this signal is absent from the spectra of all derivatives of tingenone in which the keto-group in ring E has been reduced to a hydroxy-group, and it is also absent from the spectra of pristimerin [12] and isopristimerin III,[6] which contain no keto-group in ring E. The carbonyl group must therefore be at C-21, and tingenone can thus be considered as 20-decarboxy-20-oxocelastrol. Biogentically it may originate from celastrol (2) by oxidation at C-21 followed by decarboxylation of the β-keto-acid.

## EXPERIMENTAL

*Purification of Tingenone.*—Crude tingenone (500 mg) (single spot on t.l.c.) was purified on a silica gel column with chloroform as eluant to give pure *tingenone* (450 mg) and still impure hydroxytingenone (30 mg; $M^+$ 436). The m.p. of tingenone is considerably influenced by the solvent used for crystallisation, as previously noted.[2] Values varying between 147 and 229° were found, the appropriate solvent peaks being observed in the n.m.r. spectra. On the other hand analytical data were in accord with the molecular formula (Found: C, 80·05; H, 8·7; O, 11·2. $C_{28}H_{36}O_3$ requires C, 79·95; H, 8·65; O, 11·4%), $\lambda_{max.}$ ($CHCl_3$) 422, 345sh, 262sh, and 250 nm (log ε 4·19, 3·22, 3·89, and 3·98), c.d. $\lambda_{max.}$ 257 (Δε −10·24), 265 (−11·65), 373 (+9·62), and 450 (−5·05) nm, $\nu_{max.}$ ($CHCl_3$) 3400, 1720, 1660, and 1610 $cm^{-1}$, $\nu_{max.}$ (KBr) 3300, 1700, and 1590 $cm^{-1}$, δ (100 MHz; $CDCl_3$) 7·2 (1H, s, disappearing on adding $D_2O$), 7·03 (1H, dd, *J* 1·5 and 7 Hz), 6·55 (1H, d, *J* 1·5 Hz), 6·37 (1H, d, *J* 7 Hz), 2·8br (d, *J* 14 Hz), 2·2 (3H, s), 1·5 (3H, s), 1·35 (3H, s), and 1·03—0·98 (9H, 3 × $CH_3$), δ [60 MHz; $CDCl_3$–$C_6H_6$ (1 : 1)] aliphatic methyl peaks at 1·38 (3H, s), 1·17 (3H, s), 1·01 (3H, d, *J* 6 Hz), 0·91 (3H, s), and 0·77 (3H, s), *m/e* 420 (64%), 406 (16), 391 (7), 378 (5), 363 (3), 267 (8), 253 (15), 241 (28), 239 (11), 227 (20), 219 (26), 215 (17), 203 (35), 202 (100), 201 (88), 200 (57), 187 (15), 172 (14), and 163 (30).

Treatment of tingenone with pyridine–acetic anhydride gave mono-*O*-acetyltingenone as needles, m.p. 185—186° (from chloroform–cyclohexane) (Found: C, 78·05; H, 8·2. $C_{30}H_{38}O_4$ requires C, 77·9; H, 8·3%), $\lambda_{max.}$ ($CHCl_3$) 245, 267, and 275 nm (log ε 2·95, 2·74, and 2·70), $\nu_{max.}$ (KBr) 1770 and 1710 $cm^{-1}$, δ (100 MHz; $CDCl_3$) 7·13 (1H, s), 6·09 (1H, d, *J* 6·5 Hz), 4·93 (1H, d, *J* 6·5 Hz), 2·95 (1H, d, *J* 14 Hz), 2·32 (3H, s), 2·27 (3H, s), 1·61 (3H, s), 1·35 (3H, s), 0·99 (3H, s), and 0·96 (3H, d, *J* 5·5 Hz).

Tingenone (300 mg) in acetic anhydride (10 ml) was refluxed for 4 h with zinc powder (2 g) and sodium acetate (2 g). The mixture was filtered into ice–water. The precipitate was collected and purified on a silica gel column, with chloroform as eluant. Pure tingenone leucodiacetate was obtained as leaflets (from methylene dichloride), m.p. 230—233°, identical (t.l.c., i.r. and n.m.r. spectra, and mixed m.p.) with the compound described in the preceding paper.

To tingenone (300 mg) in methanol (10 ml) was added a solution of toluene-*p*-thiol (100 mg) in methanol (10 ml). After 30 min the solution was evaporated *in vacuo* and the residue treated with acetic anhydride (4 ml) and pyridine (1 ml) overnight. Chromatographic purification and precipitation from acetone–water gave an amorphous pale yellow solid, m.p. 122—125°, identical (t.l.c., i.r. and n.m.r. spectra, mixed m.p.) with the adduct described in the preceding paper.

*Sodium Borohydride Reduction and Acetylation of Tingenone.*—Tingenone (300 mg) in methanol (10 ml) was treated with sodium borohydride in excess. After 2 h the excess of reagent was decomposed with acetic acid and the solution was evaporated. The product was dissolved in chloroform and washed with water. Evaporation afforded crude tingenol, which was acetylated with acetic anhydride (2 ml) and pyridine (2 ml) overnight at room temperature. Standard work-up yielded a product (320 mg) showing two spots on t.l.c. Separation on a silica gel column in methylene chloride gave tri-*O*-acetyltingenol (240 mg) and di-*O*-acetyltingenol (50 mg). *Tri-O-acetyltingenol* (4) formed micro-crystals (from methanol–water), m.p. 118—120° (Found: C, 74·05; H, 8·45. $C_{34}H_{46}O_6$ requires C, 74·15; H, 8·4%), $\lambda_{max.}$ ($CHCl_3$) 240 (log ε 3·14) 266 (2·89), and 276 nm (2·88), $\nu_{max.}$ (KBr) 1780 and 1740 $cm^{-1}$, δ (100 MHz; $CDCl_3$), 7·0 (1H, s), 5·75 (1H, dd, *J* 5·5 and 2·5 Hz), 5·0br (1H, q, $W_{\frac{1}{2}}$ 8 Hz, C*H*·OAc), 3·2 (2H, octet, *J* 5·5 and 2·5, $J_{gem}$ 20 Hz), 2·32, 2·28, 2·10, and 2·06 (each 3H, s, 3 × $CH_3$·$CO_2$ and $ArCH_3$), 1·40, 1·28, 1·21, and 0·90 (each 3H, s, $CH_3$), and 0·88 (3H, d, *J* 6 Hz), *m/e* 550 (16%), 535 (60), 508 (12), 493 (51), 475 (100), 451 (28), 433 (60), 391 (20), 285 (40), 279 (28), 271 (48), 243 (27), 229 (85), 201 (40), 191 (56), and 187 (76).

*Di-O-acetyltingenol* (5) formed needles (from ether–

[12] O. Gonçalves de Lima, I. Leôncio d'Albuquerque, J. Sidney de Barros Coêlho, and Gessé M. Maciel, *Rev. Inst. Antibiot.*, 1969, **9**, 3.

hexane), m.p. 214—215°, $\nu_{max.}$ (KBr), 3600 and 1780 $cm^{-1}$, δ (100 MHz; $CDCl_3$) 7·02 (1H, s), 5·75 (1H, dd, *J* 2·4 and 5·5 Hz), 3·85br (1H, s, $W_{\frac{1}{2}}$ 8 Hz), 3·2 (2H, octet, *J* 2·4 and 5·5, $J_{gem}$ 20 Hz), 2·31, 2·27, and 2·07 (each 3H, s, 2 × $CH_3{\cdot}CO_2$ and $ArCH_3$), 1·38, 1·28, 1·25, and 0·84 (each 3H, s), and 0·9 (3H, d, *J* 6 Hz), *m/e* 508 (20%), 493 (90), 475 (95), 466 (10), 451 (50), 433 (80), 409 (40), 391 (15), 285 (40), 271 (70), 243 (40), 229 (90), 201 (45), 191 (65), and 187 (100).

*Catalytic Hydrogenation and Acetylation of Tingenone.*—Tingenone (250 mg) in acetic acid (5 ml) was hydrogenated over platinised charcoal (10%; 150 mg). After absorption of 1 mol. equiv. of hydrogen, the solution was filtered and evaporated to dryness under reduced pressure. The residue was acetylated with acetic anhydride (2 ml) in pyridine (2 ml) overnight at room temperature. Standard work-up followed by purification on a silica gel column in methylene chloride afforded tri-*O*-acetyltingenol (50 mg), identical (m.p. and mixed m.p. 118—120°) with an authentic specimen, and *di*-O-*acetyldihydrotingenone* (6) (185 mg), m.p. 208—209° (from methanol–water) (Found: C, 79·95; H, 8·25. $C_{32}H_{42}O_5$ requires C, 75·85; H, 8·35%), $\lambda_{max.}$ (EtOH) 266 (log ε 3·13) and 274 nm (3·11), $\nu_{max.}$ (KBr) 1780 and 1695 $cm^{-1}$, δ (60 MHz; $CDCl_3$) 6·95 (1H, s), 5·75br (1H, dd), 3·2 (2H, m), 2·9 (1H, d, *J* 13·5 Hz), 2·30, 2·24, and 2·05 (each 3H, s), 1·37, 1·27, 1·0, and 0·97 (each 3H, s), and 0·97 (3H, d, *J* 6 Hz), *m/e* 506 (5%), 491 (45), 473 (3), 464 (3), 449 (17), 431 (33), 407 (15), 389 (3), 285 (13), 271 (35), 243 (27), 229 (8), 207 (10), 201 (27), and 187 (100).

*Di*-O-*acetyl*- (10) *and Di*-O-*methyl*- (11) *isotingenone III.*—Tingenone (300 mg) in methanol (45 ml) containing 2N-sulphuric acid (0·8 ml) was boiled under reflux for 20 min. The colour of the solution changed from dark red to light yellow. The methanol was evaporated off under reduced pressure at room temperature and the residue was diluted with ice–water and extracted with chloroform. The organic phase was washed with water, dried ($Na_2SO_4$), and evaporated. The residue of crude isotingenone III (9) (300 mg) was treated with acetic anhydride to give the *diacetate* (10), m.p. 207—210° (from hexane–methylene chloride) (Found: C, 76·05; H, 8·05; O, 15·8%. $C_{32}H_{40}O_5$ requires C, 76·15; H, 8·0; O, 15·85%), $\lambda_{max.}$ (EtOH) 250 and 290 nm (log ε 4·90 and 4·04), $\nu_{max.}$ ($CHCl_3$) 1770 and 1700 $cm^{-1}$, δ (60 MHz; $CDCl_3$) 6·97 (1H, s), 6·43 (2H, q, *J* 10 Hz), 5·63 (1H, dd, *J* 2·2 and 6 Hz), 2·95 (1H, d, *J* 14 Hz), 2·30, 2·35, and 2·1 (each 3H, s), 1·28, 1·07, 1·03, and 0·95 (each 3H, s), and 0·99 (3H, d, *J* 5·5 Hz), *m/e* 504 (37%), 489 (35), 462 (17), 447 (23), 420 (15), 405 (10), 325 (41), 298 (36), 283 (70), 269 (19), 265 (15), 256 (100), 241 (60), 223 (26), 214 (85), 201 (34), and 165 (17).

*Di*-O-*methylisotingenone III* (11) was obtained from crude isotingenone III (9) by refluxing for 4 h in acetone with dimethyl sulphate and potassium carbonate; the product had m.p. 173—176° (from methanol) (Found: C, 80·45; H, 8·75. $C_{30}H_{40}O_3$ requires C, 80·3; H, 9·0%), $\nu_{max.}$ ($CHCl_3$) 1702 $cm^{-1}$, δ (60 MHz; $CDCl_3$) 6·75 (1H, s), 6·3 (2H, q, *J* 10 Hz), 5·63br (1H, m), 3·90 and 3·78 (each 3H, s), 3·0 (1H, d, *J* 15 Hz), 2·22 (3H, s), 1·33 (3H, s), and 1·08—0·97 (12H, $CH_3$), δ (60 MHz; $C_6H_6$), aliphatic methyls at 1·19 (s), 1·13 (s), 1·02 (d, *J* 6 Hz), 0·88 (s), and 0·82 (s), *m/e* 448 (66%), 433 (72), 281 (20), 269 (100), 255 (45), 242 (72), 229 (20), 215 (13), 211 (38), and 165 (7).

*Catalytic Hydrogenation of Di*-O-*acetylisotingenone III* (10).—Di-*O*-acetylisotingenone III (280 mg) in ethanol (10 ml) was hydrogenated over platinum [from platinum dioxide (100 mg)]. After absorption of 1—1·5 mol. equiv. of hydrogen, the solution was filtered and evaporated under reduced pressure. The residue (280 mg) showed two spots on t.l.c., close together. Silica gel chromatography in chloroform gave di-*O*-acetyldihydroisotingenone III (14) (20 mg) and the original mixture (250 mg). After acetylation of the latter with pyridine–acetic anhydride, followed by chromatographic separation, on a silica gel column (in methylene chloride) tri-*O*-acetyldihydroisotingenol III (13) (200 mg) and di-*O*-acetyldihydroisotingenone III (14) (35 mg) were obtained pure. *Tri*-O-*acetyldihydroisotingenol III* (13) formed leaflets (from methanol–methylene chloride), m.p. 249—252° (Found: C, 74·2; H, 8·4. $C_{34}H_{46}O_6$ requires C, 74·15; H, 8·4%), $\nu_{max.}$ ($CHCl_3$) 1780 and 1740 $cm^{-1}$, δ (60 MHz; $CDCl_3$) 7·08 (1H, s), 5·83br (1H, m), 5·0br (1H, s, C*H*·OAc), 2·30 and 2·25 (each 3H, s) and 2·03 (6H, s), *m/e* 550 (35%), 508 (100), 490 (5), 466 (70), 448 (8), and 406 (10). *Di*-O-*acetyldihydroisotingenone III* (14) formed leaflets (from methylene chloride), m.p. 202—204°, $\nu_{max.}$ 1775 and 1700 $cm^{-1}$, *m/e* 506 (100%), 464 (90), and 422 (33).

*Reduction of Di*-O-*methylisotingenone III* (11) *with Sodium Borohydride.*—Di-*O*-methylisotingenone III (250 mg) in methanol (15 ml) was stirred and treated with an excess of sodium borohydride. After 2 h the excess of reagent was decomposed with acetic acid and the solution was evaporated. The residue in chloroform was washed with water and then evaporated. Purification by chromatography on a silica gel column in methylene chloride gave di-*O*-methylisotingenol III (16) as needles (210 mg), m.p. 202—205° (from methanol), $\nu_{max.}$ ($CHCl_3$) 3650 $cm^{-1}$ (no carbonyl band), δ (60 MHz; $CDCl_3$) 6·75 (1H, s), 6·37 (2H, q, *J* 10 Hz), 5·63br (1H, m), 3·87 and 3·75 (each 3H, s), 3·8br (1H, m), and 2·2 (3H, s), *m/e* 450 (47%), 435 (35), 433 (10), 432 (8), 417 (7), 295 (10), 281 (20), 269 (100), 267 (12), 255 (35), 242 (83), 229 (23), 215 (16), and 211 (33).

*Catalytic Reduction of Di*-O-*methylisotingenol III* (16).—Di-*O*-methylisotingenol III (200 mg) in ethanol (10 ml) was hydrogenated over platinum [from platinum dioxide (100 mg)]. After absorption of 1 mol. equiv. of hydrogen, the solution was filtered and evaporated under reduced pressure to give *di*-O-*methyldihydroisotingenol III* (17) (200 mg) as needles, m.p. 251—254° (from methanol) (200 mg) (Found: C, 79·75; H, 9·7. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%), $\nu_{max.}$ 3650 $cm^{-1}$, δ (60 MHz; $CDCl_3$) 6·7 (1H, s) and 5·65br (1H, m), *m/e* 452 (100%), 434 (27), 419 (4), 297 (7), 283 (12) 271 (15), 257 (8), 244 (25), 230 (14), 217 (24), 213 (12), 205 (12), 203 (8), 191 (10), and 165 (10).

*Dehydration of Di*-O-*methyldihydroisotingenol III* (17).—Di-*O*-methyldihydroisotingenol III (17) (180 mg) in acetic acid (10 ml) was treated with boron trifluoride–ether complex (0·7 ml) and left for 15 h. The mixture was diluted with water (30 ml) and extracted with chloroform. The organic layer was washed successively with water, saturated sodium hydrogen carbonate solution, and water. After drying ($Na_2SO_4$) the solvent was evaporated off to give an oily residue (150 mg) which was purified on a silica gel column in benzene to give the product as an oil (107 mg) which crystallised from hexane; m.p. 177—179° (from hexane) (Found: C, 82·85; H, 9·75; O, 7·4%. Calc. for $C_{30}H_{42}O_2$: C, 82·9; H, 9·75; O, 7·35%), $\nu_{OH}$ absent, δ (100 MHz; $CDCl_3$) 6·8 (1H, s), 5·76br (1H, m), 5·27br (1H, m), 3·83 and 3·74 (each 3H, s), 2·15 (3H, s), 1·7br (3H, s), and 1·27, 1·08, 1·0, and 0·9 (each 3H, s), *m/e* 434 (100%), 419 (4), 311 (5), 297 (20), 283 (5), 271 (6), 257 (10), 256 (16), 244 (7), 232 (5), 230 (5), 217 (8), 205 (5), 191 (5), and 165 (5).

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