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SESQUITERPENOIDS OF *CINNAMOSMA FRAGRANS* BAILLON

STRUCTURE OF CINNAMOLIDE, CINNAMOSMOLIDE AND CINNAMODIAL

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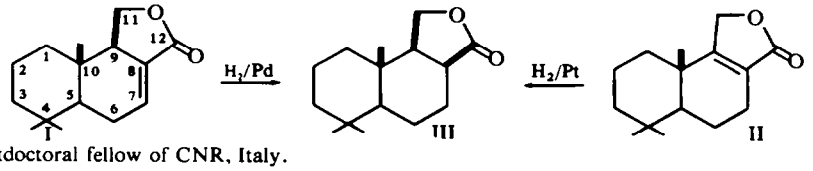
Abstract—The constitution and absolute stereochemistry of three new sesquiterpenoid lactons with drimane skeleton have been elucidated by correlating them to confertifolin.

CANELLACEAE is a small plant family consisting of only nine species grouped into four genera: of these, *Winterana* and *Cinnamodendron* are endemic to South America, *Warburgia* to West Africa and *Cinnamosma* to Madagascar. The genus *Cinnamosma* contains three known species *C. fragrans*, *C. macrocarpa* and *C. madagascariensis*; *C. fragrans* is a shrub widespread in the north-western regions of Madagascar and in particular near the Diego Suarez bay and along the Bemarivo basin.[1]

The crude acetone extract of the bark of *C. fragrans* has a distinct pepper-like taste and exhibits antifungal activity.† A preliminary examination of this extract with an LKB-9000 gas chromatograph-mass spectrometer indicated the presence of three major compounds, which we have named cinnamolide, cinnamosmolide and cinnamodial, and three other compounds, bemarivolide, bemadienolide and fragrolide. Trace quantities of other structurally related compounds, were also detected.

The structure determination and stereochemistry of the three major products is the subject of this publication.

Cinnamolide (I)[2] has the structure and the stereochemistry of drim-7-ene-12,11-olide. It is identical with the compound obtained by alkaline treatment of the naturally occurring polygodial[3] and it has been correlated with confertifolin (II) *via* its dihydro-derivative (III).[4]



I III II

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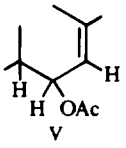
† The *in vitro* activity of cinnamolide has been tested against dermatophites: MIC has been evaluated for *Tricophyton rubrum* 1007 (20 μg/ml), *Tricophyton mentagrophytes* 6 (< 10 μg/ml) and *Microsporum gypseum* 350 (20 μg/ml).

Cinnamosmolide (IV). Elementary analysis and mass spectral data indicate the formula $C_{17}H_{24}O_5$. The NMR spectrum shows resonances indicative of three tertiary Me's (3H, s's at 1·03, 1·13 and 1·17 δ), an OAc (3H, s at 2·08 δ) and an OH group (1H, s at 3·63 δ which disappears on exchange with D_2O), and contains an AB pattern (2H, qu at 4·40 δ) characteristic of a $—CH_2—O—$ group. Other signals at 2·15 δ (1H, d, J_1 = 4·3 c/s), at 5·80 δ (1H, t, $J_1 = J_2$ = 4·3 c/s) and at 6·78 δ (1H, d, J_2 = 4·3 c/s) are assigned to the system shown in V, and this was confirmed by spin-decoupling experiments.



V

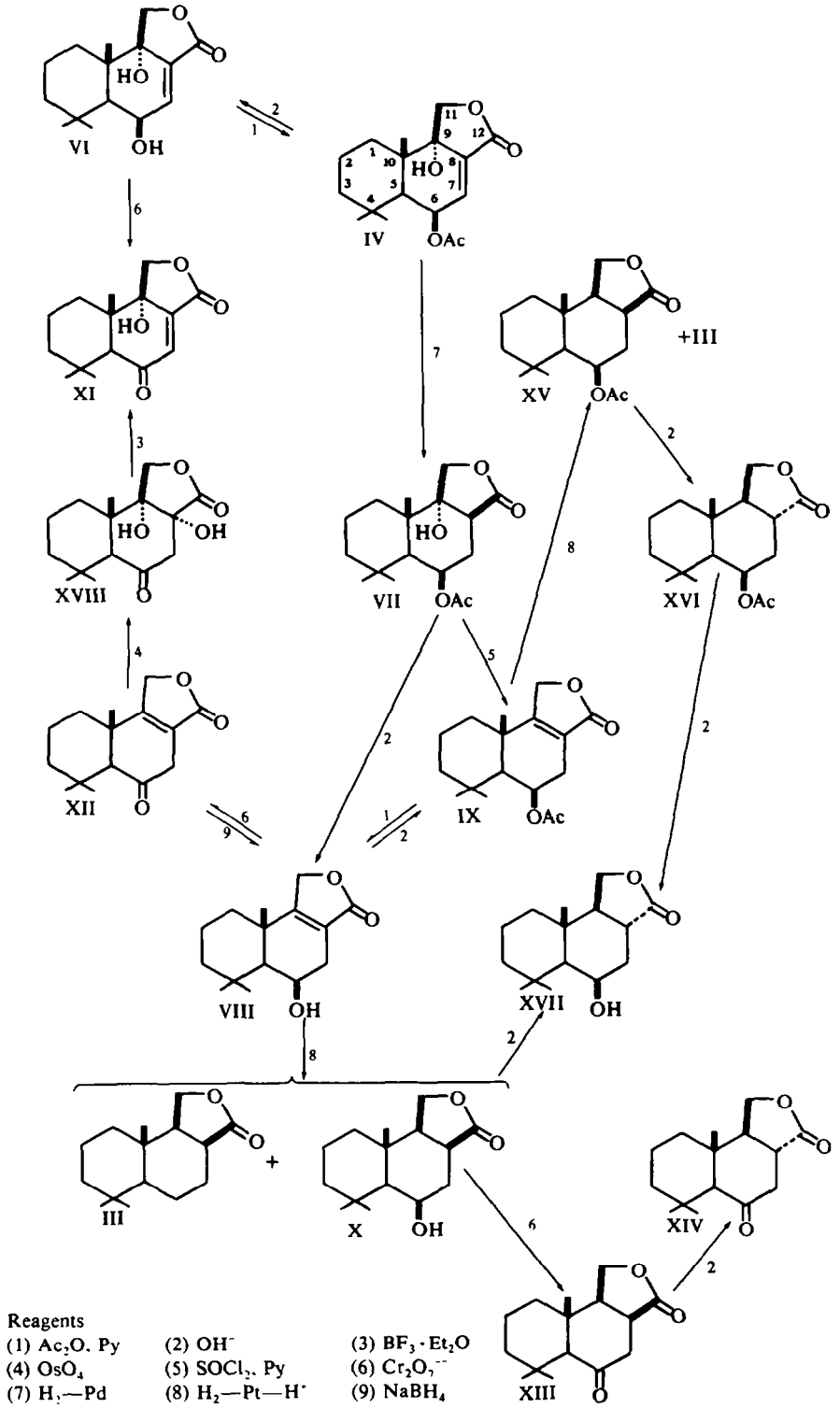
The IR spectrum of cinnamosmolide (IV) confirms the presence of an OH (3573, 3432 cm^{-1}), of an OAc group (1735, 1240 cm^{-1}) and shows absorptions at 1763, 1703 and 832 cm^{-1} attributed to an α,β-unsaturated-γ-lactone. An absorption max at 211 mμ in the UV of IV (isooctane) is abnormal for an α,β-unsaturated-γ-lactone (e.g. cinnamolide (I) exhibits a max at 224 mμ), but the stereochemistry of IV indicates that the strong 1,3-diaxial interactions present in the molecule prevent complete overlap of π-orbitals.

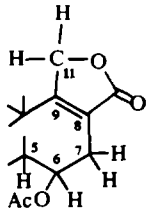
The tertiary nature of the OH group in IV is in keeping with its resistance to normal acetylation and oxidation with Jones reagent.

Alkaline hydrolysis of cinnamosmolide gives the diol VI in which the new OH is secondary. The NMR spectrum of VI shows that the signal for the C-6 proton, present at 5·80 δ in the spectrum of IV, has been shifted 1 ppm to higher fields. Acetylation of VI reforming IV, excludes the possibility of skeletal rearrangement or change in stereochemistry during hydrolysis.

Oxidation of the diol VI in a heterogeneous phase[5] affords a hydroxyketone (XI) with absorptions in its IR spectrum at 3640, 1762, 1676 and 1654 cm^{-1} and a max in its UV spectrum at 235 mμ; the NMR spectrum of XI shows a two protons quartet at 4·50 δ ($—CH_2—O—$) and three one proton singlets at 6·50 δ ($=C—H$), 3·02 δ ($—C(H)—C=O$) and 3·52 δ (—OH; exchangeable with D_2O). These results confirm that the OAc group in IV is on an allylic carbon as shown in the partial structure V.

Catalytic hydrogenation of IV with Pd/C in aprotic solvent yields dihydrocinnamosmolide (VII) which lacks a max in its UV spectrum whereas its IR spectrum shows an absorption at 1784 cm^{-1} of a saturated γ-lactone. Dehydration of this compound (VII) with thionyl chloride and pyridine affords a new α,β-unsaturated -γ-lactone (IX; 6β-acetoxyconfertifolin); its 100 Mc NMR spectrum includes a resonance pattern which, on the basis of double resonance studies, could be assigned to the system shown in XIX.[2] The C-5 proton gives rise to a doublet at 1·38 δ (J = 1·5 c/s), whereas the C-6 proton appears as a sextet (1 : 1 : 3 : 3 : 1 : 1) at 5·71 δ and is equally coupled (J = 3·5


VI
IV
XI
XV
+III
XVIII
VII
XVI
XII
IX
VIII
XVII
III
X
XIV
XIII
Reagents
(1) Ac2O. Py
(2) OH⁻
(3) BF3 · Et2O
(4) OsO4
(5) SOCl2. Py
(6) Cr2O7⁻⁻
(7) H2—Pd
(8) H2—Pt—H⁺
(9) NaBH4



XIX

c/s) to the two protons at C-7. These appear as a multiplet at 2·47 δ showing homoallylic coupling with the C-11 methylene (multiplet at 4·77 δ).

Alkaline hydrolysis of IX gives the alcohol (VIII; 6β-hydroxyconfertifolin) which on acetylation reforms IX; since VIII can also be obtained from dihydrocinnamosmolide (VII) by mild alkaline treatment, the tertiary OH in cinnamosmolide must be in β-position with respect to the lactonic CO.

Hydrogenation of VIII in the presence of Adams catalyst in acid solution affords the expected product of hydrogenation (X; 6β-hydroxy-*cis*-dihydroconfertifolin) together with a significant quantity of another compound which lacks OH groups and is identical with an authentic sample of *cis*-dihydroconfertifolin (III). This correlation proves that cinnamosmolide and cinnamolide, are drimane derivatives with the same absolute stereochemistry at C-5 and C-10 as confertifolin (II).

The catalytic reduction of VIII to III can be explained by assuming a hydrogenolysis of the secondary OH. Spectroscopic evidence available at this stage excludes the possibility that the OH in VIII is allylic to the double bond. Furthermore, oxidation of the alcohol (VIII) with Brown's reagent[5] gives a ketone (XII; 6-ketoconfertifolin) which lacks spectroscopic evidence for conjugation. Similar oxidation of X gives the ketone (XIII; 6-keto-*cis*-dihydroconfertifolin) which, on treatment with aqueous alkali does not decarboxylate, but isomerizes to the *trans*-lactone (XIV) as observed for *cis*-dihydroconfertifolin (III). In view of this evidence, the hydrogenolysis of the secondary OH in VIII must occur because of the intermediate migration of the double bond from C-8 to C-7.

The OAc group at C-6 in cinnamosmolide (IV) has been assigned the β-configuration. The NMR of IX, examined with the aid of double resonance studies, shows the C-6 proton coupled with that at C-5 (J = 1·5 c/s) and, furthermore, the C-6 proton is equally coupled with the two protons at C-7 (J = 3·5 c/s). These values are consistent for a *quasi*-equatorial configuration for the C-6 proton.

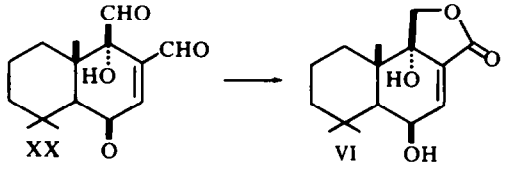
On treatment with dilute alkali, 6β-acetoxyconfertifolin (IX) is readily converted to 6β-hydroxyconfertifolin (VIII), whereas 6β-acetoxy-*cis*-dihydroconfertifolin (XV), under the same conditions, gives the epimeric 6β-acetoxy-*trans*-dihydroconfertifolin (XVI); the OAc group in XVI can be hydrolysed only under forcing conditions.

The hindered nature of the 6-OH is more evident in the chemical behaviour of the 6-hydroxy derivatives: the alcohol (VIII) reacts slowly with acetic anhydride and pyridine whereas 6β-hydroxy-*cis*-dihydroconfertifolin (X) is recovered unchanged after prolonged treatment under the same conditions, but is readily oxidized to the ketone (XIII) with Brown's reagent. Further proof of the β-configuration of the OAc at C-6 in cinnamosmolide was obtained by sodium borohydride reduction of the ketone (XII) to the alcohol (VIII), obviously by attack of the reagent from the less hindered α-side of the molecule.

Only the configuration of the tertiary OH at C-9 remained to be assigned. From biogenetic considerations an α-configuration was expected and chemical proof was obtained. Reaction of the ketone (XII) with OsO_4 gives the diol (XVIII). Since hydrogenation of the C-8 double bond in compounds of this type is known to add hydrogen in a completely stereospecific manner from the α-side of the molecule, it seemed certain that OsO_4, with greater steric requirements, would approach from the same side to give the α-diol and XVIII is formulated accordingly. On treatment with BF_3-etherate, the diol (XVIII) gives an α,β-unsaturated ketone identical with XI obtained from cinnamosmolide.

These results, together with the correlation of cinnamosmolide with confertifolin, the absolute stereochemistry of which is known,[4] confirm structure IV for cinnamosmolide.

Cinnamodial. On the basis of the new results and the correlation of cinnamodial with cinnamosmolide, the structure and the absolute stereochemistry of cinnamodial is as shown in XX.*



EXPERIMENTAL

M.ps are uncorrected and were determined in unsealed capillaries. IR spectra were measured in CHCl soln, unless otherwise specified, with a Perkin–Elmer mod 137 IR spectrophotometer; UV spectra were recorded in MeOH soln, unless otherwise specified, on a Perkin–Elmer mod 137 spectrophotometer; optical rotations were measured with a Perkin–Elmer mod 141 polarimeter for 1% soln in $CHCl_3$ at 20°. A Perkin–Elmer R-10 (60 Mc) instrument was used to record the NMR spectra; $CDCl_3$ was used as solvent and TMS was the internal standard. Gas-chromatography was performed with a Carlo Erba Fractovap GV gas-chromatograph. A mixture of silica gel G Merck and celite (1/1; v/v) was used for column chromatography. Solutions were dried over anhydrous Na_2SO_4.

Isolation of cinnamolide (I), *cinnamosmolide* (IV) *and cinnamodial* (XX). The bark (0·625 Kg) of *Cinnamosma fragrans* was extracted with acetone (3 times) at room temp. The combined extracts were concentrated *in vacuo*, diluted with water and extracted with ethyl ether. Evaporation of the solvent gave a residue (50 g) which was dissolved in benzene and absorbed on a silica gel–celite column (500 g). Fractions of 250 ml were collected using the following solvents as eluents: light petroleum (fr 1–3), light petroleum–benzene (1:1; fr 4–12), light petroleum–benzene (2:8; fr 13–20), benzene (fr 21–28), benzene-ethyl ether (9:1; fr 29–31), benzene-ethyl ether (8:2; fr 32–38) and ethyl ether (fr 39–46).

Fractions 6–11 (13·4 g) on crystallization from light petroleum gave *cinnamolide* (I, 0·82 g), m.p. 125–126°; $[\alpha]_D$ −29·4°; λ_{max} 224 mμ (log ε 3·94); ν_{max} 1755, 1688 cm^{-1}. NMR: 0·81 δ (3H, s, ≥C—Me), 0·93 δ (6H, s, ≥C—Me) for three tertiary methyls; 4·04 δ (1H, qu), 4·40 δ (1H, qu) for two protons at C-11; 6·86 δ (1H, qu, at C-7; $J_1 = 3$, $J_2 = 8$ c/s). (Found: C, 76·80; H, 9·40. Calc. for $C_{15}H_{22}O_2$: C, 76·88; H, 9·46%).

Fractions 20–30 (7·18 g) on crystallization from ethyl ether–light petroleum gave *cinnamodial* (XX; 2·1 g), m.p. 141–143°; $[\alpha]_D$ −421·5°; λ_{max} (isooctane) 219 mμ (log ε 4·07); ν_{max} 3470, 2860, 2740, 1740.

* Independently C. J. W. Brooks attributed the structure XX to a product isolated from *Warburgia ugandensis* (private communication); in fact mixed m.p., IR and NMR spectra confirmed the identity of this product and cinnamodial.

1726, 1690, 1655, 1240 cm^{-1}. NMR: 1·03 δ (3H, s), 1·17 δ (3H, s), 1·35 δ (3H, s) for three tertiary Me's; 2·13 δ (3H, s, C$\underline{H_3}$—COO—), 4·1 δ (1H, d, —O$\underline{H}$; J = 1·4 c/s), 9·5 δ (1H, s, —C$\underline{H}$O), 9·78 δ (1H, d, —C$\underline{H}$O; J = 1·4 c/s), 2·03 δ (1H, d at C-5; J = 4·8 c/s), 5·89 δ (1H, tr, at C-6; J_1 = J_2 = 4·8 c/s) and 7·0 δ (1H, d, at C-7; J = 4·8 c/s). (Found: C, 66·29; H, 7·60. Calc. for $C_{17}H_{24}O_5$: C, 66·21; H, 7·85%).

Fractions 35–38 (9·7 g) on crystallization from ethyl ether gave *cinnamosmolide* (IV; 1·2 g), m.p. 204°; $[\alpha]_D$ −332·4°. (Found: C, 66·32; H, 7·80. Calc. for $C_{17}H_{24}O_5$: C, 66·21; H, 7·85%).

Work-up of the appropriate fractions of the chromatography and of the mother liquors of crystallization, yielded additional 2·2 g of cinnamolide, 3·0 g of cinnamodial and 2·9 g of cinnamosmolide.

Hydrogenation of cinnamolide (I). Cinnamolide (350 mg) in AcOH (20 ml) was hydrogenated over PtO_2 (50 mg) until the absorption of H_2 ceased (30 min). The soln was filtered and evaporated to dryness. The residue was crystallized from light petroleum and sublimed (125°, 0·05 mm) to give *dihydrocinnamolide* (III; 335 mg), m.p. 134–135°, alone or on admixture with an authentic sample of *cis*-dihydroconfertifolin; $[\alpha]_D$ −4·95°. The NMR and IR spectra of the two compounds were superimposable. Alkaline treatment of III yielded *trans*-dihydroconfertifolin,[5] m.p. 119–120°; $[\alpha]_D$ −7·32°.

Alkaline hydrolysis of cinnamosmolide (IV). Cinnamosmolide (1·0 g) in 5% KOH aq (25 ml) was refluxed for 15 min. The soln was acidified with 1N HCl and the *diol* (VI; 0·82 g) recovered with CH_2Cl_2. It was crystallized from ethyl ether and then from AcOEt–light petroleum; m.p. 178–179°; $[\alpha]_D$ −24·3°; λ_{max} 208 mμ (log ε 3·91); ν_{max} 3637,3488, 1760, 1700 cm^{-1}. NMR: 4·75 δ (1H, m, at C-6), 7·03 (1H, d, at C-7; J = 4·3 c/s). (Found: C, 67·68; H, 8·36. Calc. for $C_{15}H_{22}O_4$: C, 67·64; H, 8·33%).

Acetylation of VI with Ac_2O–pyridine reformed cinnamosmolide (IV).

Oxidation of the diol (VI). The diol (50 mg) in ethyl ether (5 ml) was treated with Brown's reagent[5] (1 ml) and the mixture stirred at room temp for 30 min. The organic layer washed with water, dried, evaporated *in vacuo* and the residue chromatographed with CH_2Cl_2 as eluent, yielded the *hydroxyketone* (XI; 40 mg); m.p. 201–202° from AcOMe–isopropyl ether; $[\alpha]_D$ −62°; λ_{max} 235 mμ (log ε 4·04). (Found: C, 68·30; H, 7·59. Calc. for $C_{15}H_{20}O_4$: C, 68·16; H, 7·63%).

Hydrogenation of cinnamosmolide (IV). Cinnamosmolide (625 mg) in AcOEt (30 ml) was hydrogenated over 10% Pd/C (200 mg) until the absorption of H_2 ceased (10 min). The soln was filtered on celite and evaporated to dryness; crystallization of the residue from AcOEt–light petroleum yielded *dihydrocinnamosmolide* (VII; 600 mg), m.p. 150°; $[\alpha]_D$ −44·2°; ν_{max} 3590, 3477, 1784, 1734 cm^{-1}. NMR: 2·02 δ (3H, s, C$\underline{H_3}$—COO—), 3·28 δ (1H, s, —O$\underline{H}$), 2·8 δ (1H, qu, at C-8), 5·35 δ (1H, m, at C-6) and 3·92 and 4·48 δ (2H, d's at C-11). (Found: C, 65·85; H, 8·46. Calc. for $C_{17}H_{26}O_5$: C, 65·78; H, 8·44%).

Dehydration of dihydrocinnamosmolide (VII). Dihydrocinnamosmolide (480 mg) in pyridine (8 ml) was treated with $SOCl_2$ (1 ml) and left at room temp overnight. Work up as usual gave a crude product (450 mg) which after chromatography and crystallization from isopropyl ether yielded 6β-*acetoxyconfertifolin* (IX), m.p. 146°; $[\alpha]_D$ −13·7°; λ_{max} 216 mμ (log ε 4·15); ν_{max} 1765, 1730, 1685 cm^{-1}. (Found: C, 70·10; H, 8·28. Calc. for $C_{17}H_{24}O_4$: C, 69·83; H, 8·27%).

Hydrolysis of 6β-*acetoxyconfertifolin* (IX). 6β-acetoxyconfertifolin (400 mg) in 5% KOH–MeOH (20 ml) was left at room temp overnight. Recovery of the product as for VI and crystallization from AcOEt–light petroleum gave 6β-*hydroxyconfertifolin* (VIII; 300 mg), m.p. 191–201°; $[\alpha]_D$ +39·2°; λ_{max} 218 mμ (log ε 4·05); ν_{max} 3633, 3484, 1744, 1670 cm^{-1}. NMR: 2·45 δ (2H, m, at C-7) and 4·8 δ (2H, m, at C-11 and 1H at C-6). (Found: C, 72·2·; H, 8·87. Calc. for $C_{15}H_{22}O_3$: C, 71·97; H, 8·86%).

Alkaline treatment of dihydrocinnamosmolide (VII). Dihydrocinnamosmolide (100 mg) in 5% KOH aq (15 ml) was refluxed for 15 min. Work-up as for VI and crystallization from AcOEt–hexane gave a product (60 mg) identical in all respects with VIII.

Acetylation of 6β-*hydroxyconfertifolin* (VIII). 6β-hydroxyconfertifolin (50 mg) in pyridine (1 ml) and Ac_2O (0·5 ml) was left at room temp for 64 hr. Work-up as usual gave a product identical with IX.

Hydrogenation of 6β-*hydroxyconfertifolin* (VIII). 6β-hydroxyconfertifolin (100 mg) in AcOH (20 ml) was hydrogenated in the presence of PtO_2 (150 mg) until the absorption of H_2 ceased (3 hr). The soln was filtered, evaporated to dryness *in racuo* and the residue chromatographed on silica gel–celite (10 g) with CH_2Cl_2–hexane (3 : 7), ethyl ether as eluents. From the first fractions a product (15 mg) identical with III was obtained; evaporation of the ethyl ether eluate yielded 6β-*hydroxy*-cis-*dihydroconfertifolin* (X; 60 mg), m.p. 192–193° from AcOEt–hexane; $[\alpha]_D$ −15·6°; ν_{max} 3604, 3491, 1771 cm^{-1}; NMR: 4·3 δ (2H, m, at C-11) and 4·48 δ (1H, m, at C-6). (Found: C, 71·27; H, 9·62. Calc. for $C_{15}H_{24}O_3$: C, 71·39; H, 9·59%).

Oxidation of 6β-*hydroxyconfertifolin* (VIII). 6β-hydroxyconfertifolin (330 mg) in ethyl ether (50 ml) was treated with Brown's reagent[5] (10 ml) and the mixture stirred at room temp for 20 min. Work-up as for XI and crystallization from isopropyl ether gave 6-*ketoconfertifolin* (XII; 280 mg), m.p. 165–166°; $[\alpha]_D$ +149°; λ_{max} (isooctane) 211 mμ (log ε 3·96); ν_{max} 1755, 1723, 1675 cm^{-1}; NMR: 4·99 δ (2H, m, at C-11), 3·37 δ (2H, m, at C-7) and 2·66 δ (1H, s, at C-5).

Oxidation of 6β-*hydroxy*-cis-*dihydroconfertifolin* (X). 6β-hydroxy-*cis*-dihydroconfertifolin (50 mg) in ethyl ether (10 ml) was treated with Brown's reagent[5] and worked-up as for XI. Crystallization from isopropyl ether gave 6-*keto*-cis-*dihydroconfertifolin* (XIII; 35 mg), m.p. 165°; $[\alpha]_D$ +57°; ν_{max} 1778, 1708 cm^{-1}.

Isomerization of 6-*keto*-cis-*dihydroconfertifolin* (XIII). 6-keto-*cis*-dihydroconfertifolin (30 mg) in 5% KOH–MeOH (5 ml) was left at room temp for 24 hr. Work-up as for VI and crystallization from ethyl ether–light petroleum gave 6-*keto*-trans-*dihydroconfertifolin* (XIV; 26 mg), m.p. 149°; $[\alpha]_D$ +21·4°; ν_{max} 1778, 1715 cm^{-1}.

Hydrogenation of 6β-*acetoxyconfertifolin* (IX). 6β-acetoxyconfertifolin (500 mg) in AcOH (20 ml) was hydrogenated in the presence of PtO_2 (100 mg) for 18 hr. Work-up as usual and chromatography gave III and 6β-*acetoxy*-cis-*dihydroconfertifolin* (XV; 300 mg), m.p. 135–136° from isopropyl ether; $[\alpha]_D$ −24·3°; ν_{max} 1774, 1728 cm^{-1}.

Alkaline treatment of 6β-*acetoxy*-cis-*dihydroconfertifolin* (XV). 6β-acetoxy-*cis*-dihydroconfertifolin (250 mg) in 5% KOH–MeOH (20 ml) was heated at 60° for 10 min, allowed to cool, acidified with 1N HCl and extracted with ether. Work-up as usual and crystallization from AcOEt–light petroleum yielded 6β-*acetocy*-trans-*dihydroconfertifolin* (XVI; 200 mg), m.p. 173·5°; ν_{max} 1780, 1738 cm^{-1}.

Hydrolysis of 6β-*acetoxy*-trans-*dihydroconfertifolin* (XVI). 6β-acetoxy-*trans*-dihydroconfertifolin (100 mg) in 5% KOH–MeOH (10 ml) was refluxed for 24 hr. Work-up as usual and crystallization from AcOEt–hexane gave 6β-*hydroxy*-trans-*dihydroconfertifolin* (XVII; 55 mg), m.p. 214–215°; ν_{max} 3550, 3450, 1772 cm^{-1}.

Alkaline treatment of 6β-*hydroxy*-cis-*dihydroconfertifolin* (X). 6β-hydroxy-*cis*-dihydroconfertifolin (100 mg) in 5% KOH–MeOH (10 ml) was left at room temp for 16 hr. Work-up as usual gave a product identical with XVII.

Treatment of 6-*ketoconfertifolin* (XII) *with* $NaBH_4$. 6-ketoconfertifolin (180 mg) in MeOH (5 ml) was treated at room temp with $NaBH_4$ and stirred for 1 hr, acidified with AcOH and evaporated to dryness *in vacuo*. Chromatography and crystallization of the residue from isopropyl ether gave a product identical with VIII.

Treatment of 6-*ketoconfertifolin* (XII) *with* OsO_4. 6-ketoconfertifolin (350 mg) and OsO_4 (500 mg) in ethyl ether (35 ml) and pyridiue (0·5 ml) were left at room temp for 15 days. The soln was evaporated to dryness *in vacuo* and the residue dissolved in CH_2Cl_2, treated with H_2S, filtered, chromatographed with AcOEt–light petroleum (1 :1) as eluent and crystallized from AcOMe-isopropyl ether, gave the *diol* (XVIII; 350 mg), m.p. 183°; $[\alpha]_D$ +17·5° (EtOH; *c* 0·7); ν_{max} (nujol) 3440, 1760, 1700 cm^{-1}; NMR: 4·60 δ (2H, broad s, at C-11), 3·35 δ (2H, qu, at C-7) and 3·18 δ (1H, s, at C-5). (Found: C, 4·10; H, 7·79. Calc. for $C_{15}H_{22}O_5$: C, 63·81; H, 7·85%).

Treatment of the diol (XVIII) *with* BF_3. The diol (50 mg) and BF_3–etherate (2 ml) in anhyd ethyl ether (10 ml) were left at room temp for 24 hr. The soln washed with $NaHCO_3$ aq, dried and evaporated to dryness gave a residue which was crystallized from AcOMe–isopropyl ether; the product resulted identical with XI.

Alkaline treatment of cinnamodial (XX). Cinnamodial (200 mg) in 2N NaOH (5 ml) was heated at 100° for 1 hr. The soln was acidified with 1N HCl and extracted with CH_2Cl_2. Evaporation of the solvent left a brown oil which was purified by chromatography using mixtures of light petroleum–AcOEt of increasing polarity as eluents: the fractions eluted with light petroleum–AcOEt (7 :3) gave a solid product which, after crystallization from AcOEt–hexane, resulted identical with the diol (VI).

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