A PIPERIDINE ALKALOID FROM *EXCOECHARIA AGALLOCHA*

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**Key Word Index** Excoi'charia agallocha; Euphorbiaceae; 2,4-dimethoxy-3-\(\psi,\psi\)-dimethylallyl-trans-cinnamoyl-piperidine; 2',4',6',4-tetramethoxychalcone.

**Abstract**—Isolation of a new piperidine alkaloid and 2',4',6',4-tetramethoxychalcone from *Excocharia agallocha* is reported. The structure 2,4-dimethoxy-3-\(\psi,\psi\)-dimethylallyl-trans-cinnamoyl-piperidine assigned to the alkaloid was confirmed through synthesis.

*Excocharia agallocha* L. (Euphorbiaceae) is native to Goa [1] and is used there as fish poison when the more potent *Holitianum anitiattianum* (Anacardiaceae) is not available. Work-up of its stemwood afforded a crystalline compound and an oil. The \(^1\)H NMR spectrum of the crystalline compound agrees with that of 2',4',6',4-tetramethoxychalcone and this identification was confirmed through comparison with the permethylation product of the corresponding tetrahydroxychalcone.

The oil could not be induced to crystallize but was homogeneous on TLC. It gives a positive test with the Dragendorff reagent, shows an amide carbonyl band in the IR spectrum at 1650 cm\(^{-1}\) and UV maxima at the same values as in cinnamates [2]. These structural features are confirmed by the \(^1\)H NMR spectrum which has singlets of two methoxyls at \(\delta 3.62\) and \(3.72\), doublets of two aromatic protons at \(6.55\) and \(7.20\) \((J = 9\) Hz\) and trans [3] olefinic protons at \(6.70\) and \(7.62\) \((J = 16\) Hz\), the one at higher field overlapping with the doublet of the aromatic proton. The remaining position in the benzene ring is occupied by a 3,3-dimethylallyl side chain of which only the methine triplet at \(\delta 5.04\) is clearly visible. The signals of the methylenes and gem-dimethyl groups at higher field are distorted by broad 4H and 6H signals at \(\delta 3.40-3.50\) and 1.40-1.65. These chemical shifts are the same as reported for the ring methylenes in cinnamoylpiperidines [4].

With regard to location of substituents only those structures are possible for the alkaloid which allow for two protons in ortho relationship and the choice is narrowed to 1 and 2 by the fact that the doublet of one aromatic proton appears at a value which is possible only if it is ortho and para to two methoxyls [5]. The ortho relationship of one methoxyl to a proton is easily established through benzene induced shift [6]. The spectrum in the presence of benzene is helpful further in resolving neatly the signals of the \(\psi,\psi\)-dimethylallyl side chain and the piperidine ring methylenes.

Biogenetic considerations strongly favoured 1 and this structure was confirmed through synthesis. Methylative ring opening of osthol (3) according to the procedure of Divakar and Rao [7], gave 2,4-dimethoxy-3-\(\psi,\psi\)-dimethylallyl-trans-cinnamic acid (4) which was converted to the corresponding chloride, 5, the reaction of which with piperidine yielded a compound identical in all respects with the natural sample (Scheme 1). Cinnamoylpiperidines have been encountered so far only in the genus *Piper* (Piperaceae). Isolation of 1 from a member of the Euphorbiaceae is, therefore, of some interest.

**Scheme 1.**
EXPERIMENTAL

Extraction and isolation. Air-dried stemwood (4 kg) of E. andicola identified by Dr. Peerzada S. H. Khan, Scientist, National Botanical Research Institute, Lucknow was extracted with petrol in a Soxhlet and the residue (40 g) obtained on evaporation of the extract was chromatographed over Si gel. Elution with petrol and CHCl3 removed the fatty material and the column was then run with CHCl3 and CHCl3-MeOH (95:5).

2.4-Dimethoxy-3-pal-dimethylallyl-trans-cinnamoylpiperideine (1). The impure oil obtained from the CHCl3 eluate was further purified through repeated chromatography to give TLC pure material (40 mg). [M] " m/z 343. C21H22NO8; 1H NMR (60 MHz, CDCl3): δ 7.62 (1H, d, J = 16 Hz, Ar CH = CH CO ), 7.20 (1H, d, J = 9 Hz, Ar-H), 6.70 (1H, d, J = 16 Hz, Ar-CH = CH-CO ), 6.55 (1H, d, J = 9 Hz, Ar-H), 5.04 (2H, m, -CH2-CH=). 3.62 and 3.72 (3H each, 3X-OMe), 3.40 3.60 [4H, br s, N(CH3)2], 3.25 (2H, d, Ar-CH=CH=), 1.68 (3H, s, =C-Me), 1.40-1.65 (9H, br s, =C-Me and - (CH2)3 ). 1H NMR (90 MHz, CDCl3, 8 drops of CD3OD): 7.66 (1H, d, J = 16 Hz, Ar-CH = CH CO ), 7.16 (1H, d, J = 9 Hz, Ar-H), 6.68 (1H, d, J = 16 Hz, Ar CH = CH-CO ), 6.38 (1H, d, J = 9 Hz, Ar-H), 5.04 (1H, m, -CH2-CH=), 3.58 (6H, s, 2X-OMe), 3.15-3.50 [6H, m, -N-(CH2)2 and Ar-CH=CH=], 1.55 and 1.66 (3H each s, 2X = C Me), 1.30-1.50 (6H, br s, (CH2)3 ).

2.4-Dimethoxy-3-pal-dimethylallyl-trans-cinnamoyl chloride (5). The trans-cinnamic acid, 0.1 (100 mg), in dry CH2Cl2 (10 ml) was refluxed with SOCl2 (2 ml) in presence of traces of pyridine for 1 hr. Evaporation of the solvent under red. press. gave a viscous mass which was used for the next step.

REFERENCES

STILBENES OF GNETUM ULA

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Abstract—Gnetin, a new stilbene isolated from Gnetum ula is assigned the structure 3,4-methylenedioxy-4'-methoxy-trans-stilbene, 1b, on the basis of spectroscopic data and synthesis. The structure 3,3',4-trihydroxy-2-methoxy-trans-stilbene, 1a, earlier assigned to a trihydroxymonomethoxy stilbene is now revised to 3,4,5-trihydroxy-3'-methoxy-trans-stilbene, 1b.

INTRODUCTION

We have earlier reported [1, 2] the isolation of two stilbenes, together with bergenin, 2-hydroxy-4-benzoyloxy acetophenone and bis-2(2,2',4,4'-tetrahydroxy)-acetophenone. These were identified as 3,3'-4-trihydroxy-2-methoxy-trans-stilbene (1a) and 2,3,5,6-tetrahydroxy-trans-stilbene (gnetol, 2). A third stilbene, gnetin, has now been obtained in small amounts from the combined benzene eluates of several columns and identified as 3,4-methylenedioxy-4'-methoxy-trans-stilbene (3). The structure of the stilbene must therefore be revised to 1b. 3,3',4-Trimethoxy-trans-stilbene (1e) was also synthesised as a model compound and since it is not known it has been revised to 1b.

RESULTS AND DISCUSSION

The presence of methylenedioxy and OMe groups in gnetin was evident from 2 and 3H singlets at 5.93 and 3.80, respectively, in its 1H NMR spectrum. While the pattern of multiplets of the aromatic protons definitely located the OMe group it left open the possibility of fusion of the methylenedioxy group to C-2 and C-3 of the stilbene nucleus. Confirmation of 3 was obtained by synthesis through condensation [3] of piperonal with para-methoxyphenylacetic acid.

The structure of the methoxy stilbene reported earlier was based on the presence of a fragment at m/z 107 (100%), in the mass spectrum of the dihydro derivative and two ortho coupled doublets in the 1H NMR spectrum. The mono substitution of one benzene ring and the presence of substituents on three contiguous carbon atoms in the other therefore did not seem open to doubt. The 360 MHz spectrum of gnetol obtained later made it possible to assign resonances of all the aromatic protons in gnetol (2) and the assignments being then checked through benzene induced shifts. Comparison of 1H NMR spectra of the two compounds made structure 1a doubtful for the methoxy stilbene. 2,3,3',4-Tetramethoxy-trans-stilbene (1e) was therefore synthesised and comparison revealed it to be different from the permethyl derivative of the natural compound. A similar comparison with synthetic 3,3',4,5-tetramethoxy-trans-stilbene (1d) then showed that the trihydroxymonomethoxy stilbene had identical substitution. The only explanation of the parent peak at m/z 107 is that it arises through loss of formaldehyde. Also notable is that one of the ortho coupled doublets changes to a doublet doublet at 270 MHz. The green ferric colour suggested that the OMe group is located in the ring having a resorcinol type substitution and this was confirmed through formation of the diphenylmethylenedioxy derivative on reaction with dichloro diphenylmethane [4].

The structure of the stilbene must therefore be revised to 1b. 3,3',4-Trimethoxy-trans-stilbene (1e) was also synthesised as a model compound and since it is not known it has been revised to 1b.

EXPERIMENTAL

Isolation of gnetin (3). Deseeded stem-wood of G. ula (5 kg) was cut into small pieces and extracted in a Soxhlet with MeCO. The residue obtained after removal of solvent under red. pres. was taken up in H2O and exhaustively extracted with EtOAc in a liquid liquid extractor. The EtOAc sol fraction (25 g) was chromatographed and elution with C6H6 gave a viscous mass which was repeatedly fractionated on silica gel to give 3 (100 mg), a light yellow plates from CHCl3, petrol, mp 121-122; MS [M]+ m/z 254 (C17H12O3), Mmax (Nujol) 1600, 1500, 1255, 1180, 1030, 936, 930 cm-1; δmax (MeOH) 205, 302, 330 nm; 1H NMR (CCl4, 60 MHz) 7.40 (2H, d, J = 9 Hz, Ar H-2',6'), 6.97 (2H, s, Ar H-2, 5, 6), 6.14 (2H, s, Ar H-3, 4), 6.00 (2H, s, O CH2 C=O), 6.93 (2H, s, Ar H-3, 4), 6.87 (2H, s, Ar H-2, 5, 6), 5.93 (2H, s, O CH2 C=O), 3.80 (3H, s, OMe), MS m/z 254 (100), 239 (23.5), 181 (17.7), 153 (15.6), 121 (11.5).

Dihydrognetin (3) (50 mg) in MeOH (20 ml) was hydrogenated over Pd/C (10%, 50 mg) for 4 hr to give a colourless oil (40 mg). Mmax (Nujol) 1600, 1500, 1245, 1040 cm-1; 1H NMR (CDCl3, 60 MHz) 6.50 (7H, m, ArCH), 5.80 (2H, s, O CH2 C=O), 3.73 (3H, s, OMe), 2.80 (4H, s, Ph (CH2)2). Synthesis of 3. Piperonal (1.5 g), p-methoxyphenylacetic acid (1.66 g) and piperidine (0.25 g) were heated at 160-170° for 15 hr. The reaction mixture was cooled, dissolved in CH2Cl2 and filtered. The filtrate was first extracted with dil HCl to remove piperidine and then extracted with 5% NaOH (3 x 20 ml) to isolate the corresponding stilbene-β-carboxylic acid 4. The CH2Cl2 layer was washed several times with H2O and evaporated to yield a gum (2.3 g) which was chromatographed on silica gel to give 3 (250 mg) identical with the natural sample (mp 113, IR 14XH NMR)
The NaOH extract was neutralised with dil HCl and ppted solid was collected and crystallised from MeOH to give colourless needles of 4 (500 mg), mp 252°C; MS [M]^+ m/z 298 (C17H12O4); v(Nujol) 1660, 1610, 1505, 1420, 1375, 1350, 1290, 1240, 1180, 1100, 1030, 920 cm\(^{-1}\); \(^1\)H NMR (CDCl3, 60 MHz) 10.7 (1H, brs, COOH), 6.70, 7.50 (8H, m, ArH and CH=CH(=)), 5.95 (2H, s, O CH\(_2\) O ), 3.85 (3H, s, OMe); MS m/z: 298 (100), 280 (90), 265 (50), 195 (46), 152 (70), 148 (65), 126 (45), 120 (55).

Decarboxylation of 4, 4 (100 mg) was refluxed with quinoline (10 ml) and CuCO\(_3\) (5) (100 mg) for 2 hr. The cooled reaction mixture was dissolved in Et\(_2\)O and extracted with dil HCl until free from quinoline. The solid obtained after usual work up of the Et\(_2\)O layer was crystallised from CHCl\(_3\)-petrol to give plates of 3 (50 mg), identical with the material obtained from plant.

3,4,5-Trihydroxy-3-methoxy-trans-stilbene (1b). Isolation according to the procedure in ref [1]. \(^1\)H NMR (DMSO-d\(_6\), 270 MHz) 9.50 (3H, brs, exchangeable on addition of D\(_2\)O, 3 × -OH), 7.16 (1H, d, J = 2 Hz, ArH-5), 6.96 (1H, dd, J = 8, 2 Hz, ArH-6), 6.90 (2H, dd, J = 17 Hz, CH=CH(=)), 7.67 (1H, d, J = 8 Hz, ArH-3), 6.40 (2H, d, J = 2 Hz, ArH-2, 6), 6.12 (1H, br s, ArH-4), 3.82 (3H, s, OMe); \(^1\)H NMR (DMSO-d\(_6\), CDCl3, 270 MHz) 9.40 (3H, brs, exchangeable on addition of D\(_2\)O, 3 × -OH), 7.20 (1H, d, J = 2 Hz, ArH-5), 6.99 (1H, dd, J = 8, 2 Hz, ArH-6), 6.90 (2H, dd, J = 17 Hz, CH=CH(=)), 7.67 (1H, d, J = 8 Hz, ArH-3), 6.40 (2H, d, J = 2 Hz, ArH-2, 6), 6.12 (1H, br s, ArH-4), 3.82 (3H, s, OMe). 3,4,5-Trihydroxy-3-methoxy-trans-stilbene (1b). Isolation according to the procedure in ref [1]. \(^1\)H NMR (DMSO-d\(_6\), 270 MHz) 9.50 (3H, brs, exchangeable on addition of D\(_2\)O, 3 × -OH), 7.16 (1H, d, J = 2 Hz, ArH-5), 6.96 (1H, dd, J = 8, 2 Hz, ArH-6), 6.90 (2H, dd, J = 17 Hz, CH=CH(=)), 7.67 (1H, d, J = 8 Hz, ArH-3), 6.40 (2H, d, J = 2 Hz, ArH-2, 6), 6.12 (1H, br s, ArH-4), 3.82 (3H, s, OMe).

2,3,4-Tetramethoxystilbene (1c). A mixture of 2,3,4-trimethoxybenzaldehyde (1.96 g), m-methoxyphenylacetic acid (1.66 g) and piperidine (0.25 ml) was heated at 160 - 170°C for 20 hr. The reaction mixture was dissolved in CH\(_2\)Cl\(_2\) and worked up as before to give a gum (1.5 g). Chromatographic separation of this material on silica gel gave 1c as a colourless oil (300 mg), MS [M]^+ m/z 300 (C\(_{17}\)H\(_{14}\)O\(_4\)); \(^1\)H NMR (CDCl3, 60 MHz) 6.5-7.5 (9H, m, ArH and CH=CH(=)), 3.60, 3.90 and 4.0 (3H each, 3 × OCH\(_3\)).

Synthesis of 3,3',4-Tetramethoxy-trans-stilbene (1e). Condensation of 3,4-dimethoxybenzaldehyde (1.66 g) and 3-methoxyphenylacetic acid (1.66 g) as above gave 1e (300 mg) along with the corresponding stilbene-beta-carboxylic acid 1f (700 mg) from the NaOH extract. 1e: colourless oil; MS [M]^+ m/z 314 (C\(_{17}\)H\(_{14}\)O\(_4\)); \(^1\)H NMR (CDCl3, 60 MHz) 6.5-7.5 (9H, m, ArH and CH=CH(=)), 3.60, 3.90 and 4.0 (3H each, 3 × OCH\(_3\)). 1f: Colourless needles from MeOH, mp 200-201°C; MS [M]^+ m/z 314 (C\(_{17}\)H\(_{14}\)O\(_4\)); \(^1\)H NMR (CDCl3, 60 MHz) 6.5-7.5 (9H, m, ArH and CH=CH(=)), 3.60, 3.90 and 3.95 (3H each, 3 × OMe).

Synthesis of 3,3',4-Tetramethoxy-trans-stilbene (1f). Condensation of 3,4-dimethoxybenzaldehyde with 3,5-dimethoxyphenylacetic acid (1 mmol each) in presence of piperidine (0.25 ml) at 160 - 170°C for 20 hr gave 1f (300 mg) in the neutral and 1g (600 mg) in the alkaline fraction. 1f: colourless oil; MS [M]^+ m/z 330 (C\(_{17}\)H\(_{16}\)O\(_6\)); \(^1\)H NMR (CDCl3, 60 MHz) 6.5-7.0 (9H, m, ArH and CH=CH(=)), 3.85 (3H, s, OMe), 3.80 (9H,
THREE 3-BENZYL-4-CHROMANONES FROM MUSCARI COMOSUM

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Key Word Index M. comosum; Liliaceae; bulbs; 3-benzyl-4-chromanones; homoisoflavonones; 5,8-dihydroxy-3-(4'-hydroxybenzyl)-6,7-dimethoxy-4-chromanon; 5,7-dihydroxy-3-(3'-hydroxy-4'-methoxybenzyl)-4-chromanon; 5,7-dihydroxy-3-(4'-hydroxybenzyl)-4-chromanon.

Abstract—Three novel 3-benzyl-4-chromanones have been isolated from the bulbs of Muscari comosum.

INTRODUCTION

We recently [1] described the structural elucidation of three components of the homoisoflavonone fraction extracted from the bulbs of Muscari comosum. In the present paper we report the spectral data which now allow us to assign structures 1, 2 and 3 to a further three homoisoflavonones from the same source, named muscomin, 3'-hydroxy-3,9-dihydroeucomin and 4'-demethyl-3,9-dihydroeucomin, respectively. It is noteworthy that 1 and 2, as compared to known 3-benzyl-4-chromanones [2], possess new oxygenation patterns. Compound 1 bears oxygen functions at both positions 6 and 8 of ring A in addition to the normally oxygenated functions 5 and 7, and compound 2 bears a hydroxyl group at the 3' position like scillascillins, although it does not possess the 3'-spirocyclobutene ring which is characteristic of these compounds.

RESULTS AND DISCUSSION

Compound 1 possesses the molecular formula C_{18}H_{18}O_{7} (high-resolution mass spectrum). In the $^1$H NMR spectrum the signals of the protons of rings B and C were clearly seen (Table I). The remaining resonances were those of three hydroxyl and two methoxyl groups. The appearance of the hydroxytriplyium fragment (m/z 107) in the mass spectrum indicated that one hydroxyl group was at the 4' position. It was assigned the $\delta^{9.31}$ 'H NMR signal because an NOE was measured between this and the 3',5' signals. The UV absorption at...