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A PIPERIDINE ALKALOID FROM *EXCOECHARIA AGALLOCHA*

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Key Word Index—*Excoecharia agallocha*; Euphorbiaceae; 2,4-dimethoxy-3-ψ,ψ-dimethylallyl-*trans*-cinnamoylpiperidide; 2′,4′,6′,4-tetramethoxychalcone.

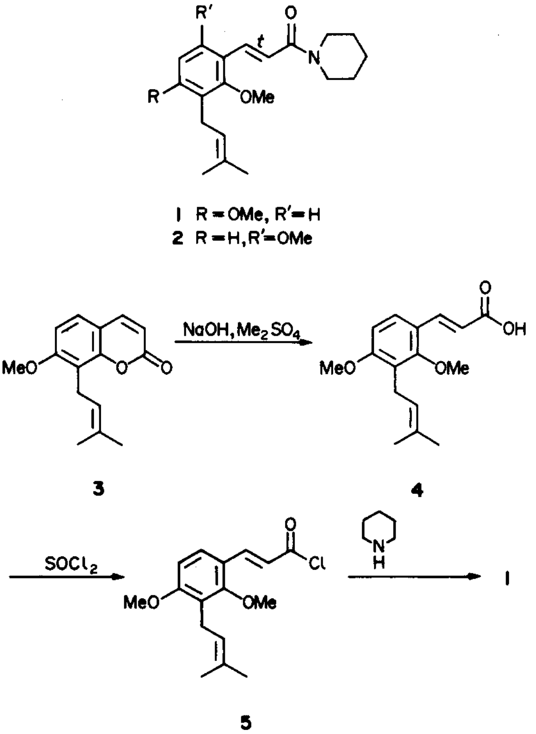
Abstract—Isolation of a new piperidine alkaloid and 2′,4′,6′,4-tetramethoxychalcone from *Excoecharia agallocha* is reported. The structure 2,4-dimethoxy-3-ψ,ψ-dimethylallyl-*trans*-cinnamoylpiperidide assigned to the alkaloid was confirmed through synthesis.

Excoecharia agallocha L. (Euphorbiaceae) is native to Goa [1] and is used there as fish poison when the more potent *Holigarna arnottiana* (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 δ 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 δ 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 δ 3.40–3.60 and 1.40–1.65. These chemical shifts are the same as reported for the ring methylenes in cinnamoylpiperidides [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 a benzene induced shift [6]. The spectrum in the presence of benzene is helpful further in resolving neatly the signals of the ψ,ψ-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-ψ,ψ-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). Cinnamoylpiperidides 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. agallocha* (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 C_6H_6 removed the fatty material and the column was then run with $CHCl_3$ and $CHCl_3$–MeOH (95:5).

2,4-*Dimethoxy*-3-*ψ*,*ψ*-*dimethylallyl*-trans-*cinnamoylpiperidide* (**1**). The impure oil obtained from the $CHCl_3$ eluate was further purified through repeated chromatography to give TLC pure material (400 mg), $[M]^{+\cdot}$ *m/z* 343, $C_{21}H_{29}NO_3$; IR ν_{max}^{KBr} cm^{-1}: 1650, 1600, 1498, 1425, 1290, 1280, 1215, 1100, 1015 and 780; UV λ_{max}^{MeOH} nm: 235, 285, 350; ^{1}H NMR (60 MHz, $CDCl_3$): δ 7.62 (1H, *d*, $J = 16$ Hz, Ar–C$\underline{H}$=CH–CO–), 7.20 (1H, *d*, $J = 9$ Hz, ArH-6), 6.70 (1H, *d*, $J = 16$ Hz, Ar–CH=C$\underline{H}$–CO–), 6.55 (1H, *d*, $J = 9$ Hz, ArH-5), 5.04 (1H, *m*, –CH_2–C$\underline{H}$=), 3.62 and 3.72 (3H each *s*, 2X-OMe), 3.40–3.60 [4H, *br s*, –N–($C\underline{H}_2$–)$_2$], 3.25 (2H, *d*, Ar–$C\underline{H}_2$–CH=), 1.68 (3H, *s*, =C–Me), 1.40–1.65 [9H, *br s*, =C–Me and –$(CH_2)_3$–]. ^{1}H NMR (90 MHz, $CDCl_3$ + 8 drops of C_6D_6): δ 7.66 (1H, *d*, $J = 16$ Hz, Ar–C$\underline{H}$=CH–CO–), 7.16 (1H, *d*, $J = 9$ Hz, ArH-6), 6.68 (1H, *d*, $J = 16$ Hz, Ar–CH=C$\underline{H}$–CO–), 6.38 (1H, *d*, $J = 9$ Hz, ArH-5), 5.04 (1H, *m*, –CH_2–C$\underline{H}$=), 3.58 (6H, *s*, 2X –OMe), 3.15–3.50 [6H, *m*, –N–$(CH_2)_2$– and Ar–CH_2–CH=], 1.55 and 1.66 (3H each *s*, 2X =C–Me), 1.30–1.50 [6H, *br s*, –$(CH_2)_3$–].

2,4-*Dimethoxy*-3-*ψ*,*ψ*-*dimethylallyl*-trans-*cinnamic acid* (**4**). To osthol (**3**) (300 mg) in aq. NaOH (60 % 5 ml), Me_2SO_4 (5 ml) was added drop-wise with vigorous stirring. The mixture was kept on a water bath for 5 hr with occassional stirring, cooled and extracted with Et_2O to remove unreacted coumarin and excess Me_2SO_4. The aq. layer was then acidified with dilute HCl and extracted with Et_2O. Evaporation of Et_2O yielded an oil which was purified by CC on Si gel to give **4** as colourless oil (200 mg).

2,4-*Dimethoxy*-3-*ψ*,*ψ*-*dimethylallyl*-trans-*cinnamoyl chloride* (**5**). The *trans*-cinnamic acid, **4** (100 mg), in dry C_6H_6 (10 ml) was refluxed with $SOCl_2$ (2 ml) in presence of traces of pyridine for 1 hr. Evaporation of the solvent under red. pres. gave a viscous mass which was used for the next step.

2,4-*Dimethoxy*-3-*ψ*, *ψ*-*dimethylallyl*-trans-*cinnamoylpiperidide* (**1**). The acid chloride, **5**, in dry C_6H_6 (20 ml) and piperidine (1 ml) was refluxed on a water bath for 30 min. The reaction mixture was cooled and washed successively with dilute HCl until free from piperidine. The organic layer was washed several times with H_2O, dried and the solvent evaporated to yield a gum which was purified by CC to give a light yellow oil (50 mg) which was found to be identical with the natural sample (Co-TLC, IR).

2′,4′,6′,4-*Tetramethoxychalcone*. Crystallized from MeOH as pale yellow prisms (500 mg), mp 140°, $[M]^{+\cdot}$ *m/z* 328, $C_{19}H_{20}O_5$; ^{1}H NMR (100 MHz, $CDCl_3$): δ 7.34 (2H, *dd*, $J = 9, 2$ Hz, ArH-2, ArH-6), 7.15 (1H, *d*, $J = 16$ Hz, Ar–C$\underline{H}$=CH–CO–), 6.72 (2H, *dd*, $J = 9, 2$ Hz, ArH-3, ArH-5), 6.65 (1H, *d*, $J = 16$ Hz, Ar–CH=C$\underline{H}$–CO–), 6.02 (2H, *s*, ArH-3′, ArH-5′), 3.74 and 3.72 (3H each *s*, 2X –OMe), 3.66 (6H, *s*, 2X –OMe).

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