A New Amide from *Zanthoxylum armatum*†

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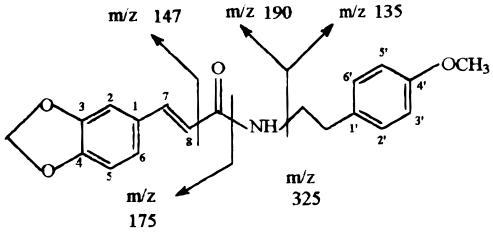
A new amide designated as armatamide **(1)**—along with two lignans, asarinin and fargesin, α- and *β*-amyrins, lupeol, and *β*-sitosterol-*β*-D-glucoside—has been isolated from the bark of *Zanthoxylum armatum*. The structure of the new compound was deduced by spectral and chemical analysis as N-(4′-methoxyphenyl ethyl)-3, 4-methylenedioxy cinnamoyl amide.

Zanthoxylum armatum DC [syn. *Z. alatum* Roxb.] (Rutaceae) is extensively used in the Indian system of medicines as a carminative, stomachic, and anthelmintic. The bark is pungent, and sticks prepared from it are used for preventing toothache. The fruits and seeds are employed as an aromatic tonic in fever, dyspepsia, and expelling roundworms.[1] Previous phytochemical examinations of *Z. armatum* have afforded four lignans and an alkaloid,[2] in addition to other secondary metabolites.[3] Here, we describe the isolation and characterization of a new amide, armatamide **(1)**, along with six previously reported compounds. The known compounds were identified as α- and *β*-amyrins, lupeol, and *β*-sitosterol *β*-D-glucoside from the hexane extract and two lignans, asarinin and fargesin, from the chloroform extract. The identities of the known compounds were confirmed with the help of published spectral data and mixture melting points.[4,5]

Armatamide **(1)**, a white crystalline compound, was determined to have a molecular formula of $C_{19}H_{19}NO_4$ on the basis of its molecular ion peak at *m/z* 325 (M^+) in the EIMS. UV absorption peaks were observed for a highly unsaturated system that, on alkali addition, remained unaltered, thus confirming the absence of phenolic functions.[6,7] In the ^{1}HNMR spectrum, characteristic signals for a methylenedioxy as a sharp singlet at *δ* 6.00, and a trans pair of doublets at *δ* 6.16 (J = 15.5 Hz) and 7.50 (J = 15.5 Hz) and an aromatic methoxy group (*δ* 3.80, singlet) were observed. A triplet at *δ* 2.78, (J = 6.9 Hz) and a quartet at *δ* 3.58 (J = 6.9 Hz) were assigned for two methylenes attached to an amide moiety.[8] The ^{13}C NMR also corroborated the proposed structure. Diagnostic signals were readily observed and assigned as δ_C 163.60 (*C*=O), 55.45 (−OCH_3), 101.36 (O−CH_2−O), 140.91, 129.79 (HC=CH) 35.07, 41.09 (CH_2CH_2NH). The structure assigned as *N*-(4′-methoxyphenyl ethyl)-3,4-methylenedioxy cinnamoyl amide was confirmed by an unambiguous synthesis by the union of *p*-methoxyphenylethylamine and 3,4-methylene dioxycinnamoyl chloride.

This is the first report of the presence of a *trans*-cinnamoylamide in *Z. armatum*. The isolation of these type of amides in *Zanthoxylum* species is of chemotaxonomic importance, as structurally related alkaloids have been reported earlier from *Zanthoxylum rubescens* and *Zanthoxylum thomense*.[9−12]



Experimental Section

General Experimental Procedures. Melting points were determined with a Mettler digital instrument FP80 and are uncorrected. The UV spectra were recorded on a Hitachi model 150-20. The IR spectra were taken on a Perkin−Elmer 399 instrument (KBr pellets). NMR spectra were recorded on a Bruker AC-200 P instrument at 200 MHz for ^{1}H and 50 MHz for ^{13}C, using TMS as internal standard. The MS were obtained on a JEOL JMS-D300 mass spectrophotometer with a JMA-2000 data processing unit.

TLC was performed on Si gel-G and were visualized with iodine vapors and/or alcoholic H_2SO_4 acid followed by heating at 110 °C. Si gel (60−120 mesh) was used for column chromatography.

Plant Material. The bark of *Z. armatum* was collected from Palampur in Himachal Pradesh (alt. 1400 m) in 1992. The plant material was identified, and a voucher specimen (no. 10989) was deposited in the Herbarium of the Regional Research Laboratory, Canal Road, Jammu Tawi −180 001, India.

Extraction and Isolation. Dried, powdered bark (4 kg) of plant was exhaustively extracted with MeOH for 72 h at room temperature. The solvent was evaporated under vaccum to give 220 g of MeOH extract, 60 g of which was redissolved in MeOH−H_2O (1:1) and partitioned with *n*-hexane and then $CHCl_3$. The solvents were removed in vacuo. The hexane extract (6.0 g) on repeated column chromatographic separation led to the isolation of α- and *β*-amyrin, lupeol, and *β*-sitosterol-*β*-D-glucoside. From the $CHCl_3$ extract, asarinin, fargesin (lignans), and armatamide (**1**) were isolated.

Armatamide (*N*-(4′-methoxyphenyl ethyl)-3, 4-methylenedioxy cinnamoyl amide) (1): white crystals; mp −159.4 °C, R_f 0.7 (1% MeOH in $CHCl_3$ with 5 drops of diethylamine) IR(KBr) υ_{max} 3309, 1666−1668, 1623, 1617, 1586, 1447, 933 cm^{-1}; UV λ_{max} (MeOH) 202, 226, 288, and 320 nm; EIMS *m/z* 325 $[M]^+$ (31), 190 $[M - C_9H_{11}O]^+$ (51), 175 $[M - C_9H_{12}ON]^+$ (100, 148 $[M - C_9H_8O_2]^+$ (11), 145 (25), 134 $[M - C_{10}H_8O_3N - H]^+$ (92), 121 $[M - C_{11}H_{10}O_3N]^+$ (30), 117 (18), 89 (35), 77 (7), 63 (10).

^{1}H NMR ($CDCl_3$) *δ* 2.78 (2H, t, J = 6.9 Hz, H-11), 3.58 (2H, q, J = 6.9 Hz, H-10), 3.80 (3H, s, H-12), 6.00 (2H, s, H-13), 6.16 (1H, d, J = 15.5 Hz, H-8), 7.50 (1H, d, J = 15.5 Hz, H-7), 6.80−7.06 (2H, m, H-aromatic), 6.70−6.92 (4H, m, H-aromatic); ^{13}C NMR ($CDCl_3$) *δ* 35.08 (C-11), 41.04 (C-10), 55.45 (C-

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12), 101.36 (C-13), 106.58 (C-3′), 107.87 (C-2′)*, 108.18 (C-2)*, 109.01 (C-5′), 114.28 (C-5), 119.58 (C-6′), 124.27 (C-6), 126.36 (C-1′), 129.79 (C-8), 130.81 (C-1), 140.91 (C-7), 146.96 (C-4′), 148.96 (C-3), 151.74 (C-4), 163.60 (C-9), assignments bearing an asterisk may be interchanged.

Synthesis of *N*-(4′-methoxyphenyl ethyl)-3, 4-methylenedioxy cinnamoyl amide (1). 3,4-Methylenedioxy cinnamic acid (3.84 g, 0.02 mol) was refluxed with redistilled thionyl chloride (1.8 mL., 0.025 mol) for 30 min to yield 3,4-methylenedioxy cinnamoyl chloride in 62% yield. 4-Methoxy-*β*-nitrostyrene (12.5 g) dissolved in 100 mL HOAc containg 5% HCl was hydrogenated in the presence of 10% Pd-charcoal (1%) for 1 h. After usual workup procedure, it yielded *p*-methoxyphenylethylamine (8.9 g, 71%). *p*-Methoxyphenylethylamine (0.75 g, 0.005 mol) was taken in a mixture of dry C_6H_6 and pyridine (1 mL each) and stirred with 3,4-methylenedioxy cinnamoyl chloride (1.05 g, 0.005 mol) for two h. The solvent was removed in vacuo. The gummy mass (1.63 g) thus obtained was purified with hexane and EtOAc to furnish the compound **1** (210 mg). The product prepared exhibited spectral and analytical data identical to the natural product.

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