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A CINNAMOYL PYRROLIDINE AMIDE FROM *PIPER PEEPULOIDES*

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Key Word Index—*Piper peepuloides*; Piperaceae; leaves; amides; terpenoids.

Abstract—Analysis of a petrol extract of the leaves of *Piper peepuloides* resulted in the isolation of a new cinnamoyl pyrrolidine amide characterized as *Z*-pyrrolidine-1-3-(6-methoxy-1,3-benzodioxol-5-yl)-1-oxo-2-propenyl along with peepuloidin, 2-methoxy-4,5-methylenedioxy-*Z*-cinnamoyl piperidide, β-sitosterol and β-sitosterol glucoside.

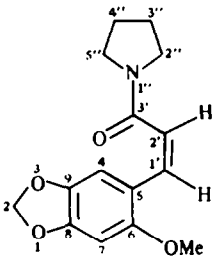
INTRODUCTION

In continuation of our work on the chemistry of various *Piper* species, we wish to report a new cinnamoyl pyrrolidine amide, namely *Z*-pyrrolidine-1,3-(6-methoxy-1,3-benzodioxol-5-yl)-1-oxo-2-propenyl besides other known amides and terpenoids isolated from a petrol extract of *P. peepuloides*. Such amides with *cis*-geometry at C-1′,2′ are quite rare in nature, although, prior to this report, a new cinnamoyl piperdide amide with a *cis* double bond at C-1′,2′ has been reported by Dhar *et al.* [1] from the same plant. Incidentally there is no report of a *trans* isomer of cinnamoyl pyrrolidine amide from a natural sources although it has been synthesized [2].

RESULTS AND DISCUSSION

The petrol extract of *P. peepuloides* on CC over silica gel gave two known amides characterized as peepuloidin [3] and 2-methoxy-4,5-methylenedioxy-*Z*-cinnamoyl piperdide. However, careful examination of the fractions containing peepuloidin, on TLC and under UV light revealed the presence of two distinguishable UV fluorescent compounds with very close R_f values. Repeated CC of these fractions over silica gel afforded peepuloidin in addition to a very minor compound **1** at slightly lower R_f. Compound **1** on repeated crystallization from ethyl acetate–petrol furnished white needles, mp 118°. It analysed for $C_{15}H_{17}O_4N$ ($[M]^+$ *m/z* 275). The UV spectrum displayed bands at 336 and 274 nm indicating the presence of an α,β-unsaturated system in the molecule. The IR spectrum exhibited bands at 1650 (α,β-unsaturated amide carbonyl), 1260, 1040 and 930 cm^{-1} (methylene dioxy grouping). However, the IR showed no peaks corresponding to an NH group, indicating that nitrogen could be in the form of a tertiary amide.

Compound **1** on catalytic hydrogenation over Pd–C furnished a dihydro derivative, which analysed for $C_{15}H_{19}O_4N$, absorbing one mole of hydrogen, thereby indicating the presence of only one double bond in the molecule. Its ^1H NMR spectrum ($CDCl_3$, 90 MHz) displayed a characteristic pair of AB doublets (J = 12.6 Hz) each integrating for one proton at δ5.86 and δ6.88 assigned to protons at the α and β positions of an α,β-unsaturated carbonyl system. Comparison of the chemical shifts and J values of these protons with the piperdide derivative of the present compound suggested that the double bond was *cis*. Two triplets at δ3.24 and 3.46 (each integrating for two protons) due to the methylenes adjacent to the nitrogen gave a further clue to the *cis*-geometry at the double bond due to restricted rotation of the >N–C=O group, making the two methylenes non-equivalent. A multiplet (4H) at δ1.82 was due to the two other methylenes of the pyrrolidine ring. A singlet (2H) at δ5.86 and another singlet (3H) at δ3.88, were due to the



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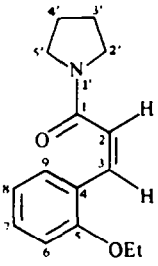

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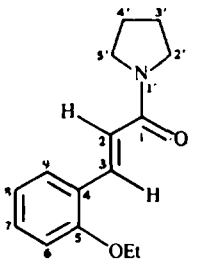

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methylenedioxy and aromatic methoxyl groups, respectively. Two sharp singlets, each of 1H, at δ6.46 and 7.4 were due to two aromatic protons *para* to each other. The chemical shifts of these protons indicated the placement of the methoxyl function at C-6 and the methylenedioxy group at C-8 and C-9. The mass spectrum in addition to the $[M]^+$ at m/z 275 showed a prominent peak at m/z 205 $[M-C_4H_8N]^+$ due to the loss of a pyrrolidine moiety. All other mass fragments in the mass spectrum and the ^{13}C NMR spectrum were consistent with the proposed structure **1** for the amide.

The structure **1** was further confirmed by synthesis, following the procedure of Dhar *et al.* [1] using pyrrolidine instead of piperdine in the last step. The synthesized product showed identical NMR and a superimposable IR with that of **1**. In order to confirm the various ^{13}C NMR assignments two novel model amides were prepared. Coumarin was converted into 1-oxo-3-(5-ethoxy phenyl)-2*Z*-propenyl-1-pyrrolidine (**2**, mp 86°) and 1-oxo-3-(5-ethoxy phenyl)-2*E*-propenyl-1-pyrrolidine (**3**, mp 120°).

EXPERIMENTAL

Air dried, finely powdered leaves (500 g) of *P. peepuloides* were extracted exhaustively with petrol (60–80°) (3 × 2 l.). The petrol extracts upon concn under vacuum afforded a residue (100 g). The residue (10 g) on CC over silica gel (600 g) was eluted successively with *n*-hexane–EtOAc mixtures of increasing polarity. Fractions obtained with *n*-hexane–EtOAc (9:1, 4:1, 7:3 and 3:7) furnished β-sitosterol (mp 138°), its glucoside (mp 268°), 2-methoxy-4,5-methylenedioxy-*Z*-cinnamoyl piperidide (mp 98°) and peepuloidin (mp 149°), respectively. Compound **1** was obtained from *n*-hexane–EtOAc (3:7) eluates as white needles (100 mg) R_f = 0.6 (C_6H_6–EtOAc, 6:4), mp 118°. Found: C, 65.42; H, 6.20; N, 5.05. Required C, 65.44; H, 6.22; N, 5.08%. EIMS (probe) 70 eV, m/z (rel. int.): 275 $[M]^+$ (20), 246 (35), 244 (80), 205 (80), 175 (30), 162 (20) and 28 (100). ^{13}C NMR ($CDCl_3$, 90 MHz) 24.0 (*t*, C-3″), 30.0 (*t*, C-4″), 46.0 (*t*, C-2″), 47.0 (*t*, C-5″), 57.0 (*q*, Ar–OMe), 95.0 (*d*, C-7), 101.5 (*t*, C-2), 109.0 (*d*, C-2′), 117.0 (*s*, C-5), 122.0 (*d*, C-4), 129.5 (*d*, C-1′), 141.0 (*s*, C-9), 147.5 (*s*, C-8), 153.0 (*s*, C-6) and 165.5 (C=O).

^1H NMR ($CDCl_3$) of dihydroderivative: δ6.64 (1H, *s*, H-4), 6.44 (1H, *s*, H-7), 5.84 (2H, *s*, H-2), 3.68 (3H, *s*, Ar–OMe), 3.40 (4H, *m*, H-2″, H-5″), 2.82 (2H, *m*, H-1′), 2.26 (2H, *m*, H-2′), 1.82 (4H, *m*, H-3″, H-4″). ^1H NMR (CCl_4) of 1-oxo-3-(5-ethoxy phenyl)-2-*Z*-propenyl 1-pyrrolidine: δ7.5 (1H, *d*, H-3, J = 12 Hz), 7.2 (4H, *m*, H-6, 7, 8, 9), 5.8 (1H, *d*, H-2, J = 12 Hz), 4.1 (2H, *q*, Ar–O<u>CH$_2$</u>Me), 3.4 (2H, *t*, H-2′), 3.1 (2H, *t*, H-5′), 1.6 (4H, *m*, H-3′, 4′), 1.4 (3H, *t*, Ar–OCH$_2$<u>Me</u>), ^{13}C NMR ($CDCl_3$, 100 MHz): δ15.4 (*q*, C–OCH$_2$<u>Me</u>), 24.9 (*t*, C-4′), 26.7 (*t*, C-3′), 46.4 (*t*, C-5′), 47.6 (*t*, C-2′), 64.2 (*t*, C–O<u>C</u>H$_2$Me), 111.8 (*d*, C-2), 121.3 (*d*, C-6), 122.9 (*d*, C-8), 124.2 (*s*, C-4), 129.7 (*d*, C-3), 130.5 (*d*, C-9), 131.0 (*d*, C-7), 153.2 (*s*, C-5), 163.0 (C=O). ^1H NMR (CCl_4) of 1-oxo-3-(5-ethoxy phenyl) 2-*E*-propenyl-1-pyrrolidine: δ8.1 (1H, H-3, J = 16 Hz, 7.2 (4H, *m*, H-6, 7, 8, 9), 6.4 (1H, *d*, H-2), 4.1 (*q*, 2H, Ar–O<u>CH$_2$</u>Me), 3.6 (*m*, 4H, H-2′, 5′), 2.0 (*m*, 4H, H-3′, 4′), 1.4 (3H, *t*, Ar–OCH$_2$<u>Me</u>). ^{13}C NMR ($CDCl_3$, 200 MHz). δ14.8 (*q*, Ar–OCH$_2$<u>Me</u>), 24.2 (*t*, C-3′), 26.1 (*t*, C-4′), 45.8 (*t*, C-2′), 46.4 (*t*, C-5′), 63.8 (*t*, Ar–O<u>C</u>H$_2$Me), 111.9 (*d*, C-2), 119.0 (*d*, C-6), 120.3 (*d*, C-8), 129.3 (*s*, C-4), 129.6 (*d*, C-9), 130.4 (*d*, C-7), 136.5 (*d*, C-3), 157.7 (*s*, C-5), 164.4 (C=O).

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