Phytochemistry, Vol. 21, No. 6, pp. 1321–1323, 1982.
Printed in Great Britain.

0031-9422/82/061321-03$03.00/0

A NEW ALKAMIDE FROM *PIPER SYLVATICUM*

AVIJIT BANERJI and SUDHIR CHANDRA PAL

Pure Chemistry Department, University of Calcutta, Calcutta 700009, India

(*Received* 13 *October* 1981)

Key Word Index—*Piper sylvaticum*; Piperaceae; seeds; sylvamide; N-isobutyl-4, 5-dihydroxy-2(E)-decenamide.

Abstract—Sylvamide, a new amide derivative, has been isolated from the petrol extract of the seeds of *Piper sylvaticum* (Roxb.). From spectral and chemical studies its structure has been elucidated as N-isobutyl-4, 5-dihydroxy-2(E)-decenamide.

INTRODUCTION

In continuation of our work on *Piper* species [1] we have isolated two new lignans and a new amide from *Piper sylvaticum*. The present communication describes the isolation and characterisation of the amide.

RESULTS AND DISCUSSION

Air-dried seeds of the plant were extracted with petrol in a Soxhlet apparatus. The concentrated extract was chromatographed over silica gel when sylvamide migrated out in the 5% methanolic chloroform eluates.

The compound, $C_{23}H_{27}NO_3$ (M^+ 257.1973) was crystallised from petrol–acetone as colourless shining plates, mp 143–44°, $[\alpha]_D^{21} - 2°$ (ethanol). The UV (λ_{max}^{EtOH} 214 nm; log ϵ 4.15) and IR (ν_{max}^{KBr} 1632 and 1670 cm^{-1}) absorption spectra of the compound indicated the presence of an α, β-unsaturated amide carbonyl system. A very strong IR absorption band at 980 cm^{-1} further suggested the associated double bond to be *trans*-disubstituted. The presence of -NH- and/or -OH group(s) was revealed by IR absorption at 3290 cm^{-1}(broad).

The presence of the *trans*-disubstituted secondary amide moiety, -CH=CH-CONH-, was confirmed by the 270 MHz ^1H NMR spectrum (d_6 - acetone) which exhibited signals for the olefinic protons at δ6.17 (1H, *dd*, $J_1 = 15$ Hz and $J_2 = 1.6$ Hz) and δ6.85 (1H, *dd*, $J_1 = 15$ Hz and $J_2 = 4.8$ Hz), and the amide proton at δ7.23 (1H, broad *s*, disappeared on D_2O shaking). A study of the 270 MHz ^1H NMR spectrum (d_6-acetone) which exhibited signals for the olefinic protons at δ6.17 (1H, *dd*, formation regarding the structure:

(a) Presence of an N - isobutyl group: δ0.90 (6H, *d*, $J = 6$ Hz), δ3.08 (2H, *t*, $J \simeq 6.4$ Hz, collapsing to *d*, $J = 6.9$ Hz after deuteration), and δ1.8 (1H, 9-line *m*, $J \simeq 6.6$ Hz).

(b) Only one proton was present at the α - position (allylic). This was evident from the splitting patterns of the olefinic protons.

(c) The allylic methine bore an oxygen substituent, as the allylic proton appeared at the low-field value of δ4.0. Irradiation at this position resulted in the disappearance of the small coupling constants of the olefinic protons and vice-versa.

(d) Besides the amide proton, two protons at δ3.71 (1H, *d*, $J = 5.5$ Hz) and δ4.10 (superimposed with the allylic proton signal) were exchangeable on D_2O shaking. These would correspond to two hydroxyl groups in the molecule.

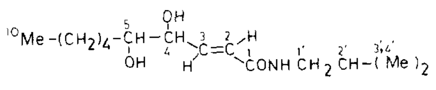
The partial structure, **2**, could be proposed for the compound from the analyses made so far. The nature of the C_6H_{12} alkyl moiety and the position of the non-allylic hydroxyl group in it was determined from a study of its ^{13}C–NMR spectra (NDC and SFORD).

The noise-decoupled ^{13}C–NMR spectrum (d_6-DMSO) displayed 13 signals (see Table 1) altogether; the two Me groups of the isobutyl group appeared at the same position at δ20.17. The signals for the carbons of the settled structural part were easily assigned. The signals to be accounted for by the 6 carbons of the unidentified part were δ13.96 (*q*), 22.19 (*t*), 31.54 (*t*), 25.00 (*t*), 32.65 (*t*), 73.55 or 73.87 (*d*). The absence of any upfield methine or quaternary carbon indicated that the alkyl chain was unbranched. Further the presence of a third methyl group (δ13.96) as well as the absence of any signal for primary carbinol carbon precluded the possibility that this hydroxyl group was attached at the end of this unbranched alkyl chain. Hence, 5 alternative structures were possible depending on the position of the second hydroxyl group at any of the 5 available positions, 5–9. We decided to compare the ^{13}C-chemical shifts of sylvamide with those of model compound, **3**, lacking the two hydroxyl groups. We synthesised the latter, a new compound, by the sequence of reactions outlined in Scheme 1.

The ^{13}C–NMR spectral assignments of the synthetic amide (Table 1) were made on the basis of the SFORD spectrum and calculations based on the Lindeman-Adam's rule [2]. From these values, the chemical shifts of the remaining 6 carbons, 5–10, of the natural amide were calculated by introducing the necessary corrections [2] for various positions of the second hydroxyl group. The best fit of values (Table 1) was obtained for the 4, 5-dihydroxy structure **1**.

The significant fragments in the mass spectrum (Scheme 2) supported the structure. In particular, the formation of the base peak at *m/z* 157.1107 ($C_8H_{15}O_2N$) by a McLafferty rearrangement involving the non-allylic hydroxyl group confirmed the position of the latter at the C–4 position.

Conclusive evidence in support of the assigned



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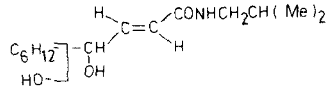

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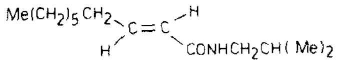

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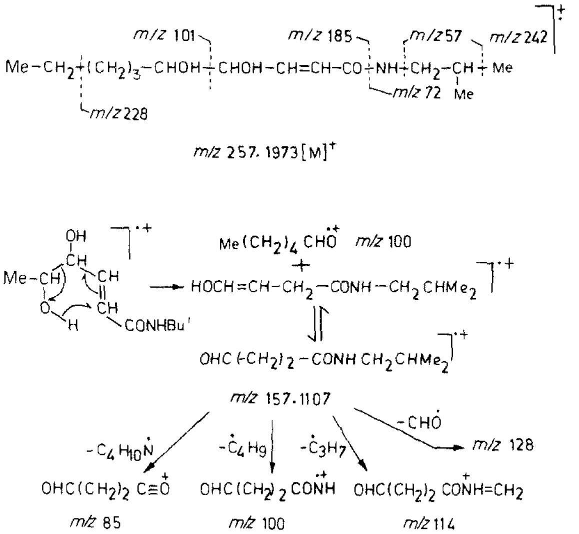
Scheme 1. Synthesis of N-isobutyl-2(E)-decenamide, 3.

$$CH_3(CH_2)_8CO_2H \xrightarrow[PCl_3(trace)]{Br_2} CH_3(CH_2)_7CHBrCO_2H \xrightarrow[Bu^tOH]{Bu^tO^-K^+}$$

$$CH_3(CH_2)_6CH=CHCO_2H + CH_3(CH_2)_5CH=CHCH_2CO_2H \xrightarrow[EtOH]{H_2SO_4}$$

$$CH_3(CH_2)_6CH=CHCO_2H \xrightarrow[C_6H_6]{(COCl)_2} CH_3(CH_2)_6CH=CHCOCl \xrightarrow[ether]{Bu^iNH_2}$$

$$CH_3(CH_2)_6CH=CHCONHBu^i$$



Scheme 2. Mass spectral fragmentation pattern of sylvamide.

Table 1. Assignments of ^{13}C NMR signals of sylvamide, 1, and model compound, 3

	Chemical shift values (δ in ppm) of			
	Model compound		Sylvamide	
Carbons	Calculated	Observed	Calculated	Observed
10	13.86	13.39	13.39	13.96
9	22.65	22.01	22.01	22.19
8	32.40	31.46[b]	31.46	31.54
7	29.71	27.97	22.97	25.00
6	29.96	28.61[a]	31.61	32.65
5	29.96	27.97[a]	76.97	75.55[c]
4	—	31.17[b]	80.17	73.87[c]
3	—	142.93	—	143.25
2	—	123.83	—	123.90
1	—	166.15	—	165.18
1′	—	46.45	—	46.20
2′	—	28.54	—	28.17
3′,4′	—	19.64	—	20.17

a,b,c = Values may be interchangeable.

structure 1 containing a *vic*-glycol system at C–4 and C–5 was obtained by a degradative experiment. Sylvamide was oxidised by lead tetra-acetate in acetic acid–ether at room temperature. One of the components of the product mixture was found to be identical with *n*-hexanal by GC-analysis as would be expected.

EXPERIMENTAL

Mps are uncorr. UV spectrum was recorded in aldehyde-free EtOH and IR spectra in KBr discs or nujol mull. ^1H NMR spectra were recorded at 270 and 80 MHz in d_6-acetone and $CDCl_3$ using TMS as int. standard. ^{13}C NMR spectra were recorded at 20 MHz in d_6-DMSO and $CDCl_3$.

Analytical samples were routinely dried over P_2O_5 *in vacuo* at room temp. Na_2SO_4 was normally used for drying organic solvents and extracts. Si gel was used for column chromatography and Si gel G for TLC. Unless otherwise stated, spots were detected with I_2 vapor.

Plant material. Seeds of *P. sylvaticum* Roxb. were collected in West Bengal. A voucher specimen (N.P.S–S) has been preserved in our laboratory.

Isolation of sylvamide. Air-dried powdered seeds (2 kg) were extracted with petrol (bp 60–80°) (8 l.) in a Soxhlet apparatus for 48 hr. The extract was concd and chromatographed. MeOH–$CHCl_3$ (1:19) eluates afforded sylvamide, as colourless shining plates (yield 100 mg, 0.005%), $C_{14}H_{27}NO_3$, mp 143–144° (acetone–petrol), $[\alpha]_D^{21} - 2°$ (EtOH), R_f (TLC) 0.50 (EtOAc). λ_{max}^{EtOH} nm (log ϵ): 214 (4.15), 272 (2.65). ν_{max}^{KBr} cm^{-1}: 3290 (*br*, –OH and –NH), 1670 (*m*, $>C=C<$), 1632 (*s*, –N–C=O), 1081 and 1040 (–C–O–), 980 (*trans* double bond). ^1H NMR (270 MHz): δ(d_6-acetone), 0.88 (3H, *t*, $J \simeq 6.5$ Hz, C_{10}–H) partially overlapped with $C_{3',4'}$–H; 0.90 (6 H, *d*, $J \simeq$ 6.5 Hz, $C_{3',4'}$–H); 1.21 – 1.45 (6H, *m*, simplified on irr. at ~1.55, $C_{7,8,9}$–H); 1.48 – 1.62 (2H, *m*, C_6–H); 1.78 (1H, 9-line *m*, $J \simeq 6.6$ Hz, $C_{2'}$–H); 3.08 (2H, *t*, $J \simeq 6.4$ Hz, changed to *d* after D_2O shaking, $C_{1'}$–H); 3.46–3.56 (1H, *m*, simplified on D_2O shaking or irr. at ~1.55 or at ~4.10, C_5–H), 3.71 (1H, *d*, $J = 5.5$ Hz, disappeared on deuteration, C_5–OH); *ca.* 4.10 (2H, *m*, area diminished to 1H after deuteration, simplified on irr. at 6.85, C_4–H and C_4–OH); 6.17 (1H, *dd*, $J = 15$ and 1.6 Hz, collapsed to *d*, $J \simeq 1.6$ Hz on irr. at 6.85 and collapsed to *d*, $J = 15$ Hz, on irr. at ~ 4.10, C_2–H); 6.85 (1H, *d* of *d*, $J = 15$ and 4.8 Hz, collapsed to *d*, $J = 15$ Hz, on irr. at ~ 4.10, C_3–H); 7.23 (1H, *br s*, disappeared on D_2O shaking –NH–). MS, *m/z* (% rel. int.): 257.1973, M^+ (10) (calc. for $C_{14}H_{27}NO_3$ 257.1990), 242 (0.5), 229 (0.7), 228 (0.6, 223 (0.5), 224 (0.5), 185 (4), 171 (1.5), 167 (1.2), 158 (20), 157.1107 (100) (calc. for $C_8H_{15}NO_2$, 157.1103), 128 (9), 114 (5), 105 (10), 101 (9), 110 (7), 85 (35), 84 (30), 74 (12), 57 (45), 58 (20), 55 (30) 43 (16), 41 (35), ^{13}C–NMR (see Table 1).

2-*Bromodecanoic acid.* Freshly dist. decanoic acid (17.2g, 0.1 ml) and PCl_3 (0.5 ml) were heated in a flask fitted with a $CaCl_2$ guard tube at 90–95°. To this, dry Br_2 (5.7 ml, 0.11 mol) was added with stirring. After 2 hr an additional 5 ml Br_2 was added. Heating and stirring were continued for a further 5 hr. Cooled CCl_4 (70 ml) was added and the mixture shaken with 2×75 ml H_2O. The organic layer was filtered through dry Na_2SO_4, and excess Br_2 and solvent distilled off at 100° under red. pres. (H_2O-aspirator).

$\Delta^{2,3}$ *Decenoic acid.* The residue of bromo acid, pale yellow in colour, was slowly added at room temp. to a soln of $BuO^- K^+$ (prepd from 9.8 gK and 250 ml dry BuOH). The thick suspension was heated under gentle reflux for 3 hr. After cooling the mixture was diluted to ~1 l. with H_2O, and then acidified to congo red with 5N H_2SO_4. The soln was extracted with petrol and fractionally distilled at red. pres. after removal of the solvent. The distillate (a mixture of $\Delta^{2,3}$ and $\Delta^{3,4}$ acids) at 175–85°/20–22 mm was dissolved in EtOH (100 ml) containing 1 ml conc. H_2SO_4 and kept for 4 hr at room temp. The soln was diluted to 500 ml with H_2O and extracted with petrol. The extract was washed successively with H_2O, $NaHCO_3$ soln and H_2O and then dried. The solvent was removed and the residue on distillation under red. pres. gave $\Delta^{2,3}$ decenoic acid at 165–68°/20 mm (yield 3.7 g, 22% from decanoic acid).

N–isobutyl-2(E)-decenamide. $\Delta^{2,3}$ Decenoic acid (2.5 g, 0.015 mol) in dry benzene (20 ml) was treated with $(COCl)_2$ (2.5 ml, 0.003 mol) at room temp. After 30 min, the mixture was refluxed for another 30 min. The solvent and excess of $(COCl)_2$ was removed on a rotary evaporator. The residue was taken up in dry ether (20 ml) to which was added with stirring at 10° a soln of iso-$BuNH_2$ (4 ml, 0.04 mol) in ether (10 ml). After 1 hr 50 ml H_2O was added. The ether layer was sepd, washed successively with 1N H_2SO_4 soln, aq. $NaHCO_3$ soln and H_2O and then dried. After evapn of solvent, the residue was chromatographed over Si gel yielding the amide, mp 38°, from benzene eluate. Yield 2.2 g (66%). Found: C, 74.74: H, 11.92; N, 6.30 (calc. for $C_{14}H_{27}ON$: C, 74.67; H, 12.00; N, 6.20). ν_{max}^{Nujol} cm^{-1}: 1670 (*m*, $>C=C<$), 1630 (*s*, $-\overset{|}{N}-\overset{|}{C}=O$). ^1H–NMR (80 MHz); δ ($CDCl_3$) 6.72 (1H, *t* of *d*, $J = 15$ and 7 Hz, C_3–H), 5.67 (1H, *d* with fine splitting, $J = 15$ and 1.5 Hz, C_2–H), 3.05 (2 H, *t*, $J \simeq 6.5$ Hz, $C_{1'}$–H), *ca* 2.12 (2 H, *m*, C_4–H), *ca* 1.70 (1 H, *m*, $C_{2'}$–H), 1.05–1.50 (10 H, *br* signal, C_{5-9}–H), 0.85 (6 H, *d*, $J = 6.5$ Hz, $C_{3',4'}$–H), 0.80 (3 H, *t*, $J = 6.5$ Hz, C_{10}–H). ^{13}C–NMR (see Table 1).

Oxidation of sylvamide by Pb(*IV*) *acetate.* Sylvamide (13 mg: 0.05 mmol) in ether (20 ml) and HOAc (5 ml) was treated with Pb(IV) acetate (20 mg; 0.05 mmol) in HOAc (5 ml). The mixture was stirred at room temp. for 15 min. The mixture was diluted with H_2O and then neutralised with aq. $NaHCO_3$. The upper ethereal layer was removed, dried, concd and then analysed by GC. The extract was thereafter mixed with an authentic sample of *n*-hexanol and analysed separately. The peak having R_t 6.2 min (on a 10% SE column) was intensified. (Detector: dual FID, column temp. 70° (isothermal) detector temp. 140°, injector temp. 80°, N_2 flow rate 45 ml/min.).

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