and the molar ratio was 1:0.85. L-*erythro*-2-amino-3-hydroxy-hex-4-ynoic acid. Mp >135° (decomp.) (lit. [3], 140–54° (decomp.)). Found: C, 50.08; H, 6.38; N, 9.57. Calc. for $C_6H_9NO_3$ C, 50.35; H, 6.34; N, 9.79%, $[\alpha]_D^{22}$ −20.0 (H_2O; c = 1.61) (lit. [3], $[\alpha]_D^{28}$ −24° (H_2O; c = 1.151) L-glutamic acid. Mp >197° (decomp.) Found: C, 40.54; H, 6.21; N, 9.49%. $[\alpha]_D^{22}$ +10.3° (H_2O; c = 1.19).

Dansylation [7, 8]. Samples were dissolved in 0.5 M $NaHCO_3$ to give a final concn of 10 mM of each. To 0.1 ml of this soln, 0.1 ml dansyl chloride soln (5.5 mg in 2 ml cold Me_2CO) was added. The tubes were covered with Parafilm and the reaction mixture was allowed to stand for 1 hr at 37°. The reaction was stopped by adding 20 μl HCO_2H (85%) and the mixture diluted ×20 with H_2O. In the case of the peptides half vol. (0.1 ml) of the reaction mixture was hydrolysed in N H_2SO_4 (1 ml) for 4 hr at 100°. To an aliquot (0.1 ml), EtOAc (0.2 ml) was added and shaken. The upper layer was analysed by TLC on polyamide (5 × 5 cm) with the solvents, 1.5% HCO_2H in H_2O, C_6H_6–HOAc (9:1) and EtOAc–HOAc–MeOH (20:1:1). The chromatogram, dried by air, was examined under UV light (365 and 254 nm).

Chromatographic data. R_{Ala}-values of γ-L-glutamyl-L-2-amino-hex-4-ynoic acid on cellulose using solvents (a) and (b) were 1.58 and 1.1 respectively and those of its hydroxylated form 0.9 and 0.73, respectively.

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A NEW AMIDE FROM *PIPER OFFICINARUM*

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Key Word Index—*Piper officinarum*; Piperaceae; *N-iso*butyl eicosa-*trans*-2-*trans*-4-*cis*-8-trienamide.

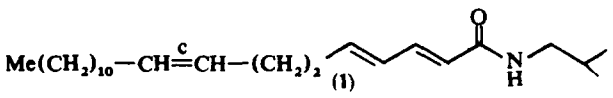
During investigations of the constituents of the fruits of *Piper officinarum*, we have reported previously the presence of 3 new compounds namely, Me piperate [1], *N-iso*butyl-trideca-13-(3,4, methylenedioxyphenyl)-2,14, 12-trienamide [2] and *N-iso*butyl docosa-*trans*-2-*trans*-4-*cis*-10-trienamide [3] (filfiline). We now wish to report the structure of another new *iso*butylamide from the same source.

The petrol extract of the fruits, on repeated column chromatography over neutral Al_2O_3 and repeated recrystallization, gave a white waxy crystalline compound mp 67–67.5°. The compound analysed for $C_{24}H_{43}NO$ (found C, 79.82; H, 12.34; N, 3.61; calc. for $C_{24}H_{43}NO$: C, 80.2; H, 12.08 and N, 3.59%). The UV spectrum (MeOH) λ_{max} 259 nm, indicated the presence of a conjugated system related to sorbamide [4, 5]. IR (KBr) showed characteristic bands for —NH, (3300, 3080 cm^{-1}), —C=O (1625 cm^{-1}), —C=C_1 (1660 cm^{-1}), —C=C_2 (1620 cm^{-1}), —(CH=CH)$_2$ (997 cm^{-1}) and no peak in the region 960–965 cm^{-1}; indicating the presence of a *trans*-2-*trans*-4-dienamide system [4, 5]. The 100 MHz PMR ($CDCl_3$) spectrum showed a doublet at 0.9 δ (9H, J = 6 Hz) which has been assigned to —C(CH_3)$_2$ and terminal —CH_3 protons, a broad singlet at 1.28 due to methylene groups (18H), a multiplet between 1.8 and 2.22 (6H) is attributed to allylic protons, a triplet centred at 3.13 accounts for two protons (N—CH_2—C—), typical for *iso*butylamides, which is replaced by a doublet after D_2O exchange.

The PMR also showed a triplet at 5.33 due to two *cis* protons (—CH=CH—), a doublet at 5.78 (J = 16 Hz) is attributed to one α-olefinic proton adjacent to a carbonyl group. The multiplet between 5.65 to 6.24 accounts for two (γ, δ) olefinic protons and a broad multiplet at 7.2 is attributed to one (β) olefinic proton.

Because of the conjugated nature of the carbonyl with two double bonds, as shown by the IR and UV spectra of the compound, it appears that one of the double bonds (isolated) is located elsewhere in the chain. The appearance of a triplet at 5.33 (2H) in the PMR spectrum indicated the presence of identical olefinic protons of an isolated double bond and were thus assigned as *cis*. The $KMnO_4$ oxidation of the compound to dodecanoic acid showed the exact location of this *cis* isolated double bond in the molecule.

MS of the compound with fragments at *m/e* 361, (M^+), 333, 289, 261, 254, 236, 223, 208, 192, 180, 156, 152, 121, 115, 96, 95 and 81 supported its structure 1 as the *iso*-butylamide of eicosa -2,4,8-trienoic acid.



(1)

EXPERIMENTAL

Isolation. The powdered fruits of *P. officinarum* Cas. DC (1.5 kg) were exhaustively extracted with petrol 60–80°. The resultant viscous liquid was adsorbed on a column of neutral Al_2O_3 (Brockmann). Elution with petrol gave a crude yellowish brown liquid which on repeated column chromatography over neutral Al_2O_3 gave a yellowish-white waxy compound, mp 60–62°. Repeated crystallization from petrol furnished a pure white waxy crystalline compound, mp 67–67.5°.

Hydrogenation. The compound (500 mg) in MeOH (375 ml) was hydrogenated over 10% Pd/C catalyst (200 mg) at room temp. and pres. Absorption of H_2 was complete after 1.5 hr during which 3 mol of H_2 was absorbed. The catalyst was filtered, the filtrate evapd under red. pres. to yield a viscous residue which on chromatography over neutral Al_2O_3 yielded a pale yellow crystalline solid, mp 58–60°. Repeated crystallization from petrol–EtOAc furnished a pure (TLC) white crystalline compound $C_{24}H_{49}NO$ (350 mg), mp 72–73°, M^+ 367, (R_f, 0.42, C_6H_6–EtOAc, 1:1).

Hydrolysis of hexahydro derivative. The satd amide (150 mg) was hydrolysed with 10% HCl in EtOH in a sealed tube at 100° for 90 hr. The contents were concd under red. pres., H_2O added and extracted with Et_2O. The aq. portion was concd and the residue after several crystallizations from petrol–EtOAc gave shining colourless plates of *iso*butylamine HCl. mp 170–171° (undepressed with authentic sample). The Et_2O extract was extracted with 5% aq. KOH and the aq. portion acidified and extracted with Et_2O. The Et_2O extract upon removal of the solvent gave a waxy residue. Several crystallizations of the residue from MeOH furnished a white waxy solid, mp 75–76° which was identified as eicosanoic acid by GLC of its Me ester.

Oxidation. $KMnO_4$ (*ca* 1 g) was added in small portions during 30 min to the compound (200 mg) suspended in H_2O (25 ml) and Me_2CO (5 ml) at 50°. The contents were refluxed for 15 min at 100° when the soln became colourless. MnO_2 was removed by filtration and washed with hot H_2O. The filtrate was acidified and steam distilled. *Ca* 200 ml of the distillate was collected and extracted with Et_2O which on evaporation yielded a waxy crystalline compound (35 mg), mp 43.5°, M^+ 200 which was identified as dodecanoic acid by GLC (Me ester) and MS.

Synthesis of hexahydro derivative. Eicosanoic acid (500 mg) in dry C_6H_6 on treatment with freshly dist. $SOCl_2$ (2.5 ml) gave the corresponding acid chloride. *Iso*butylamine (1.5 ml) dissolved in dry C_6H_6 was added slowly with stirring at 0–5° to the acid chloride in dry C_6H_6. Removal of solvent under red. pres. gave a thick liquid which on chromatography over neutral Al_2O_3 and crystallization from petrol–EtOAc afforded the *iso*butylamide of eicosanoic acid as a white crystalline compound mp 71–73°, identical with the hydrogenated product (TLC, mmp IR and PMR).

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SYNTHESIS OF WISANINE, A NEW PIPERINE AMIDE FROM *PIPER GUINEENSE*

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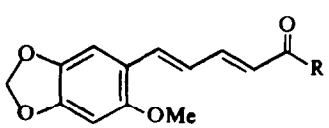
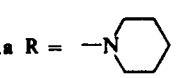
Key Word Index—*Piper guineense*; wisanine; piperine amide.

Wisanine is a new piperine-type amide isolated recently together with the (α,β)-dihydro analogue from seed and roots of the W. African black pepper *Piper guineense*. Structure **1a** has been proposed for the amide [1, 2]. In connection with our contemporaneous synthetic studies amongst piperine alkaloids from other species of *Piper*, we now record a synthesis of wisanine.



1a R = 

1b R = -OEt
1c R = -OH

Condensation between 2-methoxypiperonal [3] and 3-ethoxycarbonylbut-2-enyltriphenylphosphorane led first to the *trans,trans*-diene ester (**1b**) (70%), yellow needles, mp 64–66° (benzene) λ_{max} (EtOH) 238, 271, 309, 370 nm, ν_{max} (KBr) 1700, 1620, 1610 cm^{-1}, τ 2.0–4.2 m (6H), 4.1 (2H), 5.8 *q* (*J* 7, 2H), 6.25 (3H), 8.7*t* (*J* 7, 3H) (Found: C, 65.3; H, 6.1. $C_{15}H_{16}O_5$ requires: C, 65.2; H, 5.8%) which was then saponified to the corresponding acid (**1c**) (67%), yellow microcrystals, mp 220–223° (benzene) (naturally derived acid shows mp 221–224°), λ_{max} (EtOH) (log ε) 244 (4.06), 261 (4.02), 269 (4.02), 300 (4.0), 368 (4.13) nm, λ_{max} (KBr) 1690, 1620, 1608 cm^{-1} τ (CD_6CO) 2.0–4.0m (6H), 4.1 (2H), 6.0 (3H) (Found: C 62.7; H, 4.8. $C_{13}H_{12}O_5$ requires: C, 62.9; H, 4.8%).