IR: 3500 m (COOH); 3300 F (NH); 1750 F, 1720 F, 1685 F (COOH, COOR). – RMN ^{1}H ($CDCl_3$); 10,7 et 9,3 (massifs, NH et COOH); 3,88, 3,80 et 3,77 (*s*, 3 CH_3O); 2,97 (2H, massif, CH_2-cycle); 2,40 (2H, massif, CH_2—COOH); 1,77 (4H, massif, CH_2—CH_2).

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221. Piperaceae Alkaloids: Part III. Synthesis of N-Isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,4,6-*trans*, *trans*, *trans*-trienoic Amide and N-Isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,8,10-*trans*, *trans*, *trans*-trienoic Amide (Piperstachine)[1]

by **Narayanan Viswanathan, Venkatachalam Balakrishnan** and **Balawant S. Joshi**

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Dedicated to Prof. T. R. Govindachari on the occasion of his 60th birthday

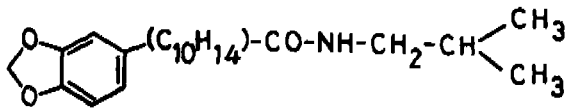
(25. VIII. 75)

Summary. N-Isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,4,6-*trans*,*trans*,*trans*-trienoic amide (II) and N-isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,8,10-*trans*, *trans*, *trans*-trienoic amide (III), two of the three possible structures of the alkaloid piperstachine, have been synthesized. Compound (III) has been found to be identical with piperstachine. The ^{1}H- and ^{13}C-NMR. spectra of the compound (II) are discussed.

The alkaloid piperstachine [2], $C_{22}H_{29}NO_3$, isolated from *Piper trichostachyon* C.DC. (family *Piperaceae*), was found mainly from spectral characteristics to be an

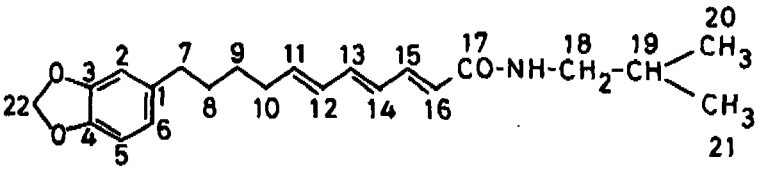
[1] Contribution No. 403 from *Ciba-Geigy* Research Centre; ^{13}C-NMR.-Spectroscopy, Part 9. For Part 8 see [1].

N-isobutyl amide with the partial structure I wherein the $C_{10}H_{14}$ aliphatic unit contains three olefinic *trans* double bonds and four contiguous methylene groups. From an examination of its ^{1}H-NMR. spectrum measured in the presence of the shift reagent Pr(fod)$_3$ [tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)

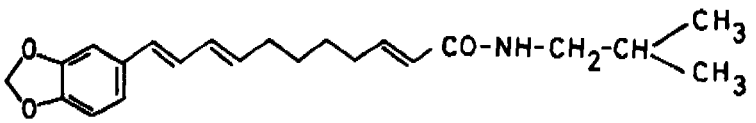


I

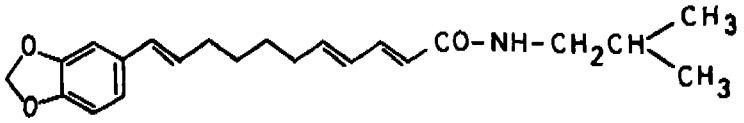
praseodymium], one of the three double bonds was shown to be *trans* and α,β- to the amide carbonyl group. The presence of a *trans*-diene system in piperstachine was indicated by the ready formation of an adduct with maleic anhydride. These data led to three possible structures II, III and IV, for the alkaloid:



II



III

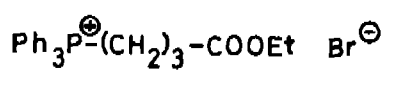


IV

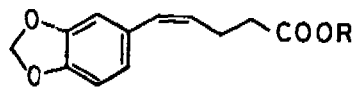
We wish to report here the synthesis of compounds II and III and the identity of the latter with piperstachine.

Wittig reaction of piperonal with the ylid from carbethoxypropyltriphenylphosphonium bromide (V) yielded the ester VIa presumably having the *cis* double bond [3] [4]. Catalytic hydrogenation of VIa gave, with some difficulty due to trace amounts of a catalyst poison in VIa, the saturated ester VIIa. It was found more convenient to proceed through the acid VIb which was smoothly reduced to VIIb. Esterification of the latter gave VIIa. Reduction of VIIa with lithium aluminium hydride yielded the alcohol VIIc which was oxidized by *Collins* reagent [5] to the aldehyde VIId. *Wittig* condensation of VIId with the phosphonium bromide VIII obtained from methyl ω-bromo-*trans*, *trans*-sorbate [6] gave the *trans*, *trans*,

trans-triene ester IXa using sodium methoxide in dimethyl formamide/methanol, phenyl lithium in tetrahydrofuran or sodium methylsulfinylmethide in dimethyl sulfoxide. The newly generated C(11)–C(12) double bond has to be *trans* since the reaction involves the condensation of a resonance-stabilised phosphorane [3] [4]. The triene ester IXa was hydrolysed to the acid IXb which was converted to the amide (II).

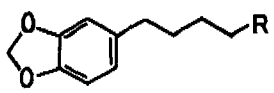


V



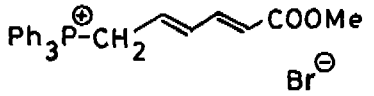
VI

a: R = Et
b: R = H

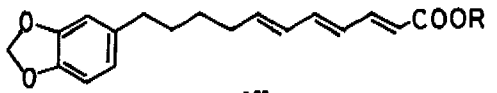


VII

a: R = COOEt
b: R = COOH
c: R = CH_2OH
d: R = CHO



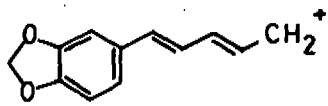
VIII



IX

a: R = Me
b: R = H

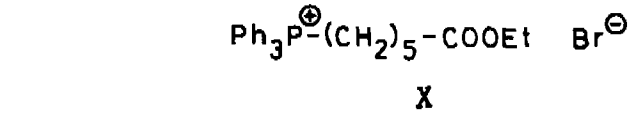
The synthetic amide II, m.p. 146–148°, is different from piperstachine in its mixed melting point, UV., IR., NMR. spectra and mass spectral fragmentation. Its UV. spectrum shows a single maximum at 295 nm (log ε 4.70) as expected for a conjugated triene amide [7]. Piperstachine in contrast has λ_{max} 216, 283, 293 and 315 nm (log ε 4.54, 4.34, 4.39 and 4.26). A significant difference in the mass spectra of the two compounds is the occurrence of an ion at *m/e* 187 in the spectrum of the natural product. This ion assigned to fragment (a) suggests structure III for piperstachine which has been confirmed by synthesis. Amide II exhibits an intense peak at *m/e* 135, due to methylenedioxytropylium ion, presumably due to rearrangement [8].



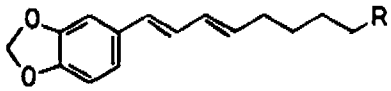
(a) m/e 187

Condensation of 3,4-methylenedioxy-*trans*-cinnamaldehyde with the ylid from carbethoxypentyl-triphenylphosphonium bromide (X) in dimethyl formamide yielded a mixture of the *trans, trans* XIa and the *trans, cis* XIIa diene esters in the ratio of 4:6. The mixture gave an adduct (XIIIa) with maleic anhydride in a yield of about 40% in agreement with the expectation that only XIa but not XIIa would react

with the anhydride [9]. Previous workers have reported that the *Wittig* condensation of *trans*-α,β-unsaturated aldehydes with non-stabilised phosphoranes yield only the *trans*, *cis*-dienes [10]. Alkaline hydrolysis of the mixture of esters XIa and XIIa gave the acids XIb and XIIb which were separated by utilising the differential solubilities of their potassium salts in ethanol. The acid XIb gave the adduct XIIIb with maleic anhydride whereas the acid XIIb failed to react. The acid XIb was converted to the methyl ester XIc which was reduced with lithium aluminium hydride to the alcohol XId. The acid XIIb similarly gave the ester XIIc which was reduced to the alcohol XIId. Oxidation of XId by the *Pfitzner-Moffat* procedure [11] furnished the aldehyde XIe. Oxidation of XId by *Collins* reagent [5] or CrO_3/3,5-dimethylpyrazole complex [12] was unsatisfactory and resulted in the formation of piperonal and 3,4-methylenedioxycinnamaldehyde in addition to

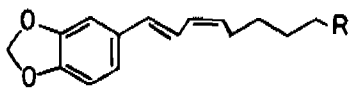


X



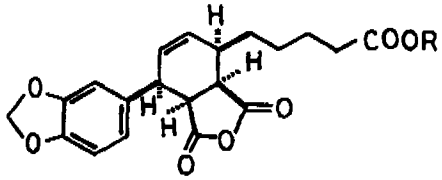
XI

a : R = COOEt
b : R = COOH
c : R = COOMe
d : R = CH_2OH
e : R = CHO



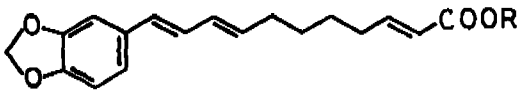
XII

a : R = COOEt
b : R = COOH
c : R = COOMe
d : R = CH_2OH



XIII

a : R = Et
b : R = H



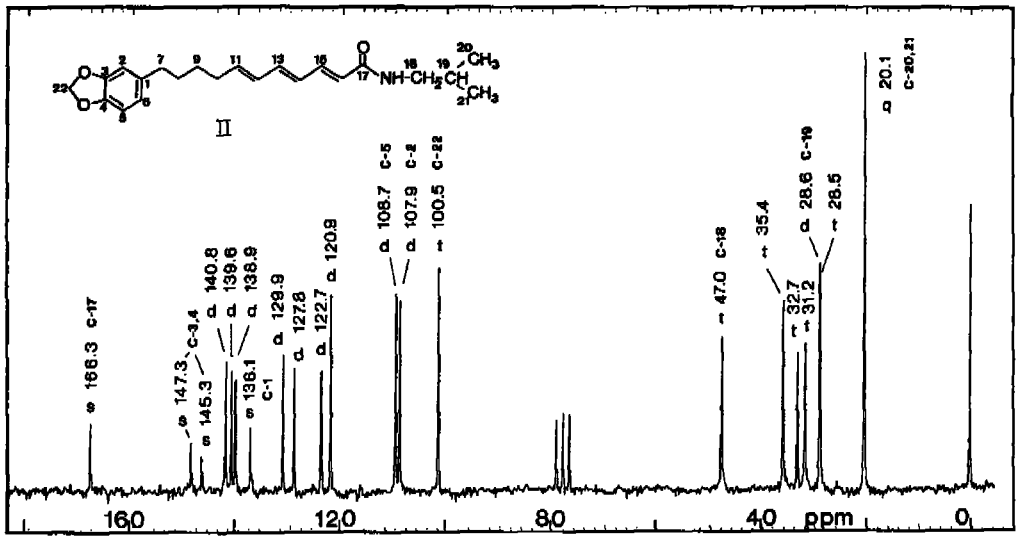
XIV

a : R = Me
b : R = H

the aldehyde XIe. *Wittig* reaction of the aldehyde XIe with carbomethoxymethylenetriphenylphosphorane yielded the triene-ester XIVa. This was hydrolysed to the acid XIVb and then converted to the amide III which proved to be identical in all respects with naturally occurring piperstachine.

In the ^{1}H-NMR. spectra, whereas piperstachine III shows the allylic CH_2 groups as a four-proton multiplet at 2.1–2.2 ppm, in compound II, the allylic CH_2 yields an apparent quartet at 2.15 and the benzylic CH_2 a broad triplet at 2.54 ppm. In the natural product III a significant shift effect on the vinyl protons upon addition of $Pr(fod)_3$ is not observable (except for H–C(16), α to the amide carbonyl group), whereas in compound II the pattern in the 5.8–7.4 ppm region changes considerably. H–C(16) is shifted from 5.85 to 5.20 ppm and is seen clearly as a doublet (J = 15 Hz, due to the *trans*-coupling with H–C(15)) after deuteration to remove the NH which occurs also near 5.2 ppm in the $Pr(fod)_3$ – shifted spectrum. Before addition of $Pr(fod)_3$, H–C(15) (β to the amide carbonyl group) of compound (II) appears as a doublet of doublets at 7.24 ppm with J = 10.5 and 15 Hz, due to coupling with H–C(14) and H–C(16) respectively. Addition of the shift reagent moves it upfield and causes it to overlap with the rest of the vinylic and aromatic hydrogen atoms.

The proton decoupled ^{13}C-NMR. spectrum of II (figure) exhibits 21 lines with the lowest-frequency signal corresponding to twice the intensity of the other proton-bearing carbon atoms. Furthermore, the off-resonance decoupled spectrum reveals the presence of four singlets, ten doublets, six triplets and one quartet. A comparison of this spectrum with that of the natural product (III) [2] shows characteristic differences in both the olefinic and aliphatic regions. Of structural significance are the high-frequency shift of C(1) and the low-frequency shift of C(15) in going from III to II. Assignments of further signals in the spectrum of II are given in the figure.



^{13}C-NMR. spectrum of II in $CDCl_3$ (proton noise-decoupled)

We wish to thank Professor *T.R. Govindachari* for his interest in the work and Dr. *S. Selvavinayakam* and his colleagues for the analytical data. Part of this work was supported by the *Swiss National Research Foundation.*

Experimental Part

UV. and IR. spectra were determined on *Beckman* model DK-2A and *Perkin-Elmer* model 421 spectrophotometers. Mass spectra were recorded on an *Atlas Varian* Mat CH-7 spectrometer using direct inlet system. ^{13}C-NMR. spectra were measured on an XL-100-15 spectrometer at 25.2 MHz in the pulsed mode, ^{1}H-NMR. spectra on a *Varian* A-60 instrument with double resonance on an HA-100 instrument. Chemical shifts δ are given in ppm, coupling constants in Hz. Deuteriochloroform as a solvent and tetramethylsilane as an internal reference were used for ^{13}C-NMR. spectra. To obtain the praseodymium-shifted proton spectrum, 5 mg of the shift reagent Pr(fod)$_3$ were dissolved together with 30 mg of the compound in 0.3 ml of $CDCl_3$.

A. Synthesis of N-isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,4,6-*trans*, *trans*, *trans*-trienoic amide (II). – *Ethyl 5-(3,4-methylenedioxyphenyl)-cis-4-pentenoate* (*VIa*). A solution of Ph_3P (26.2 g) and ethyl γ-bromobutyrate (19.5 g) in DMF (50 ml) was heated at 90–100° for 16 h, cooled and added to a stirred solution of sodium (2.3 g) in EtOH (100 ml) in N_2-atmosphere at 20–25°. After stirring for 5 min, piperonal (15 g) was added and the solution stirred overnight at room temperature. The solution was evaporated *in vacuo*, the residue extracted with ether/hexane 1:1 and the gummy residue discarded. The ether/hexane extract was evaporated and the oily residue chromatographed over silica. Elution with hexane/benzene gave the ester (VIa) (9.4 g), b.p. 147–150°/1 Torr.-IR. (ν_{max}^{neat}): 1730, 965 cm^{-1}. – ^{1}H-NMR. (CCl_4): 5.2–7.3 (5H, complex, aromatic and vinylic H); 5.8 (2H, *s*, $-O\cdot CH_2\cdot O-$); 4.05 (2H, *q*, $J = 7$, $-O\cdot CH_2\cdot CH_3$); 2.35 (4H, br. *s*, $CH_2\cdot C=C$, CH_2COOEt); 1.15 (3H, *t*, $J = 7$, OCH_2CH_3).

$C_{14}H_{16}O_4$ (248.3) Calc. C 67.7 H 6.5% Found C 67.9 H 6.7%

5-(3,4-Methylenedioxyphenyl)-cis-4-pentenoic acid (*VIb*). The above ester (10 g) was refluxed for 2 h with KOH (10 g) in MeOH (90 ml) and water (10 ml). The solution was evaporated *in vacuo*, diluted with water and extracted with ether. The aqueous solution was acidified (HCl) and extracted with ether to yield the acid (8.5 g), m.p. 130° (from CH_2Cl_2/hexane).

$C_{12}H_{12}O_4$ (220.2) Calc. C 65.4 H 5.5% Found C 65.4 H 5.7%

5-(3,4-Methylenedioxyphenyl)-valeric acid (*VIIb*). A solution of the above acid (8 g) in a mixture of EtOAc (100 ml) and EtOH (10 ml) was reduced with H_2 at 1 atm. pressure in presence of PtO_2 (0.5 g) to yield VIIb (7.5 g), m.p. 90–91° (from EtOAc/hexane).

$C_{12}H_{14}O_4$ (222.2) Calc. C 64.9 H 6.4% Found C 64.8 H 6.6%

Ethyl 5-(3,4-methylenedioxyphenyl)-valerate (*VIIa*). a) A solution of the acid VIIb (23 g) in EtOH (250 ml) was refluxed with conc. H_2SO_4 (6 ml) for 8 h, evaporated *in vacuo*, poured on ice and extracted with ether to yield the ester (22 g), b.p. 155°/1 Torr. – IR. (ν_{max}^{neat}): 1730 cm^{-1}. ^{1}H-NMR. (CCl_4): 6.3–6.8 (3H, aromatic H); 5.8 (2H, *s*, $-O\cdot CH_2\cdot O-$); 4.02 (2H, *q*, $J = 7$, OCH_2—CH_3), 2.45 (2H, *t*, $J = 6$, Ar—CH_2); 2.2 (2H, *t*, $J = 6$, CH_2–COOEt); 1.6 (4H, *m*); 1.2 (3H, *t*, $J = 7$, OCH_2—CH_3).

$C_{14}H_{18}O_4$ (250.3) Calc. C 67.2 H 7.3% Found C 67.6 H 7.6%

(b) A solution of the ester VIa (9.4 g) in EtOAc (100 ml) was reduced with H_2 at 1 atm. pressure in presence of PtO_2 (0.7 g) to yield the dihydroester VIIa (8 g) identical with the above product.

5-(3,4-Methylenedioxyphenyl)-pentan-1-ol (*VIIc*). A solution of the ester VIIa (8.5 g) in dry ether (50 ml) was added to $LiAlH_4$ (2.5 g) in ether (100 ml). The solution was refluxed for 3 h and then decomposed to yield VIIc (7 g), b.p. 135–138°/1 Torr. – IR. (ν_{max}^{neat}): 3350 cm^{-1}.

$C_{12}H_{16}O_3$ (208.3) Calc. C 69.2 H 7.7% Found C 69.5 H 7.9%

5-(3,4-Methylenedioxyphenyl)-valeraldehyde (*VIId*). Chromic anhydride (32 g) was added slowly during 1/2 h to pyridine (240 ml) with stirring at 0–5° and the suspension stirred for 1 h more. Excess hexane was added, the solid filtered and dried *in vacuo*. This complex was added to a solution of the alcohol VIIc (8 g) in CH_2Cl_2 (1 l). The solution was stirred for 45 min at 25°, filtered and the solid washed with CH_2Cl_2. The filtrate was washed successively with 5% aq.

NaOH, 5% aq. HCl, 5% aq. $NaHCO_3$ and aq. NaCl, dried (Na_2SO_4) and evaporated. The residue obtained was chromatographed over silica. Elution with hexane/C_6H_6 1:1 yielded the aldehyde (4.7 g). A small sample was sublimed at 160° (bath temp.) at 1 Torr. – IR. (ν_{max}^{neat}): 2730, 1730 cm^{-1}. – ^1H-NMR. (CCl_4): 9.7 (1H, *t*, $J = 1.5$, CHO); 6.3–6.7 (3H, aromatic H); 5.85 (2H, *s*, $O \cdot CH_2 \cdot O$–); 2.2–2.7 (4H, *m*); 1.55 (4H, br.).

$C_{12}H_{14}O_3$ (206.2) Calc. C 69.9 H 6.8% Found C 69.4 H 6.8%

*5-Methoxycarbonyl-2,4-*trans,trans-*pentadienyl triphenylphosphonium bromide* (*VIII*). A solution of methyl ω-bromosorbate [6] (21 g) and Ph_3P (27 g) in C_6H_6 (150 ml) was allowed to stand at 30° overnight. The precipitate obtained was filtered off, washed with C_6H_6 and used as such (38 g), m.p. 187° (dec.).

*Methyl 11-(3,4-methylenedioxyphenyl)-undeca-2,4,6-*trans,trans,trans-*trienoate* (*IXa*). a) *Using NaOMe;* A solution of the phosphonium bromide VIII (4.9 g) in DMF (30 ml) was added to a solution of sodium (260 mg) in MeOH (20 ml) in N_2 atmosphere with stirring. After stirring for 5 min at 25°, the aldehyde VIId (2.4 g) was added. The solution was stirred overnight at 25°, evaporated *in vacuo* and the residue extracted with ether/hexane 1:1. The insoluble gum was discarded. The ether/hexane phase was evaporated and the residue chromatographed over silica in hexane/C_6H_6 1:1 to yield the ester IXa (1.3 g), m.p. 63–65° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 297 nm (log ε 4.56). – IR. (ν_{max}^{KBr}): 1700, 1620 cm^{-1}. – ^1H-NMR. ($CDCl_3$): 5.6–7.9 (9H, complex, aromatic and vinylic H); 5.83 (2H, *s*, $-O \cdot CH_2 \cdot O$–); 3.7 (3H, *s*, OMe); 2.5 (2H, *t*, $J = 7$, Ar—CH_2); 2.15 (2H, *m*, HC=CH—CH_2); 1.5 (br., 4H). – MS.: M^+, *m/e* 314.

$C_{19}H_{22}O_4$ (314.4) Calc. C 72.6 H 7.1% Found C 72.6 H 7.4%

b) *Using PhLi:* Bromobenzene (1.57 g) was refluxed under stirring with Li (170 mg) in ether (30 ml) in N_2 atmosphere for 2 h, cooled to 25° and treated with the phosphonium bromide VIII (4.7 g) in THF (20 ml). The dark red solution was stirred for 2 h at 25° and the aldehyde VIId (2.1 g) added. The solution was refluxed for 6 h, left overnight at room temperature and filtered. The filtrate was evaporated and the residue chromatographed over silica gel to yield the ester IXa, m.p. 63–65° (1.1 g), identical with the above product.

c) *Using $MeSOCH_2^{\ominus}Na^{\oplus}$:* NaH (0.6 g of 50% oil-dispersion) was rinsed with dry hexane. DMSO (15 ml) was added and the solution heated at 70–75° with stirring for 45 min under N_2 till the evolution of H_2 had stopped. The dark solution was cooled to 20–25° and the bromide VIII (4.7 g) in DMSO (5 ml) added. The deep red solution was stirred at 25° for 45 min and the aldehyde VIId (2.1 g) added. The solution was stirred overnight at room temperature and decomposed with $NaHSO_4$ aq. Extraction with ether gave the ester IXa (0.8 g), m.p. 63–65°, identical with the earlier product.

*11-(3,4-Methylenedioxyphenyl)-undeca-2,4,6-*trans, trans, trans-*trienoic acid* (*IXb*). The ester IXa (1.2 g) was refluxed for 45 min with KOH (0.8 g) in MeOH (8 ml) and water (2 ml). Working-up as usual yielded the acid (0.8 g), m.p. 125–127° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 295 nm (log ε 4.53). – ^1H-NMR. ($CDCl_3$ + $(CD_3)_2SO$): 5.5–7.5 (11H, complex); 2.55 (2H, *t*, $J = 7$); 2.15 (2H, *m*); 1.5 (4H, *m*). – MS.: M^+, *m/e* 300.

$C_{18}H_{20}O_4$ (300.3) Calc. C 72.0 H 6.7% Found C 72.1 H 6.9%

*N-Isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,4,6-*trans, trans, trans-*trienoic amide* (*II*). A solution of the above acid (1.6 g) in C_6H_6 (45 ml) was cooled to 5°, stirred in N_2 atmosphere and treated with NEt_3 (1.5 ml). After stirring for 10 min ethyl chloroformate (1.1 ml) was added and the solution stirred for 2 h at 0–10°. Isobutylamine (2.5 ml) was added and the solution stirred for 2 h at 25° and finally at 45° for 15 min. The solution was cooled, washed successively with HCl aq., Na_2CO_3 aq. and water, dried and evaporated to yield the amide (0.7 g), m.p. 146–148° (from CH_2Cl_2/ether). – UV. (λ_{max}^{EtOH}): 295 nm (log ε 4.70). – IR. (ν_{max}^{Kbr}): 3280, 1640, 1610 cm^{-1}. – ^1H-NMR. ($CDCl_3$): 7.24 (*d*×*d*, $J = 10.5, 15$, H—C(15)); 5.6–6.8 (9H, complex); 5.88 (2H, *s*, $-O \cdot CH_2 \cdot O-$); 3.15 (2H, *t*, $J = 7$, N—CH_2); 2.54 (2H, *t*, $J = 7$, Ar—CH_2); 2.15 (2H, *m*,

H_2C—C(11)); 1.2–1.9 (5H, complex); 0.92 (6H, *d*, $J = 7$). MS.: *m/e* 355 (M^+, 30%), 240 (10), 220 (16), 152 (40), 135 (100).

$C_{22}H_{29}NO_3$ (355.5) Calc. C 74.3 H 8.2% Found C 74.7 H 8.5%

B. Synthesis of N-isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,8,10-*trans*, *trans*, *trans*-trienoic amide (piperstachine) (III). – *Ethyl 9-(3,4-methylenedioxyphenyl)-6,8-nonadienoate (XIa + XIIa).* A solution of Ph_3P (44 g) and ethyl ε-bromocaproate [13] (38 g) in DMF (70 ml) was heated at 90–95° for 20 h, cooled and added to a stirred solution of sodium (4 g) in EtOH (150 ml) in N_2 atmosphere at 20–25°. After 5 min 3,4-methylenedioxycinnamaldehyde [14] (25 g) was added and the solution stirred overnight at room temperature. Working-up as usual gave after chromatography over alumina in hexane/C_6H_6 9:1 a mixture of the esters XIa and XIIa, in the approximate ratio of 4:6, as a pale yellow liquid (25 g). A sample sublimed at 240°/0.2 Torr had: UV. (λ_{max}^{EtOH}): 222, 283, 293, 317 nm (log ε 4.32, 4.35, 4.36, 4.25); IR. (ν_{max}^{neat}): 1735, 1680, 1660, 1040, 990, 930 cm^{-1}; MS.: M^+, *m/e* 302.

$C_{18}H_{22}O_4$ (302.4) Calc. C 71.5 H 7.3% Found C 71.8 H 7.6%

Reaction of the mixed esters with maleic anhydride. The above ester (0.3 g) in C_6H_6 (3 ml) was heated at 80° for 16 h with maleic anhydride (0.1 g). The solution was concentrated and hexane added to yield the adduct XIIIa (150 mg), m.p. 95° (from CH_2Cl_2/hexane). – IR. (ν_{max}^{nujol}): 1850, 1785, 1730 cm^{-1}. – UV. (λ_{max}^{EtOH}): 235, 286 nm (log ε 3.67, 3.66).

$C_{22}H_{24}O_7$ (400.4) Calc. C 66.0 H 6.0% Found C 66.1 H 6.1%

9-(3,4-Methylenedioxyphenyl)-6,8-nonadienoic acids (XIb and XIIb). The mixture of esters XIa and XIIa (10 g) obtained in the *Wittig* reaction was refluxed with KOH (10 g) in EtOH (90 ml) and water (10 ml) for 1½ h. The solution was cooled in ice, filtered and the solid washed with cold EtOH. The solid potassium salt was dissolved in water, acidified and extracted with ether to yield XIb (3.6 g), m.p. 110–112° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 222, 283, 293, 317 nm (log ε 4.35, 4.42, 4.43, 4.30). – IR. (ν_{max}^{KBr}): 1705 cm^{-1}. – MS.: *m/e* 274 (M^+, 45%), 187 (66), 173 (100), 157 (68), 148 (15), 143 (34), 135 (25), 129 (58), 128 (42), 115 (26).

$C_{16}H_{18}O_4$ (274.3) Calc. C 70.1 H 6.6% Found C 70.3 H 6.9%

The alkaline alcoholic filtrate was concentrated *in vacuo*, diluted with water, acidified and extracted with ether to yield XIIb (4.6 g), m.p. 53–55° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 222, 284, 293, 317 nm (log ε 4.32, 4.35, 4.37, 4.28). – IR. (ν_{max}^{KBr}): 1708 cm^{-1}. – MS.: *m/e* 274 (M^+, 42%), 187 (56), 173 (100), 157 (72), 148 (15), 143 (35), 135 (32), 129 (68), 128 (44), 115 (28).

$C_{16}H_{18}O_4$ (274.3) Calc. C 70.1 H 6.6% Found C 69.7 H 6.8%

Reaction of the acids XIb and XIIb with maleic anhydride. The acid XIb (100 mg) in C_6H_6 (3 ml) was heated at 80° for 12 h with maleic anhydride (270 mg) to yield the adduct XIIIb (300 mg), m.p. 185° (from CH_2Cl_2). – UV. (λ_{max}^{EtOH}): 234, 286 nm (log ε 3.66, 3.65). – IR. (ν_{max}^{nujol}): 1850, 1790, 1720 cm^{-1}.

$C_{20}H_{20}O_7$ (372.4) Calc. C 64.5 H 5.4% Found C 64.7 H 5.7%

The acid XIIb under similar conditions did not yield any adduct.

Methyl 9-(3,4-methylenedioxyphenyl)-6,8-nonadienoate (XIc and XIIc). a) A solution of the acid XIb (3 g) in MeOH (5 ml) and ether (50 ml) was treated with excess ethereal diazomethane to yield the ester XIc (2.8 g) m.p. 42° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 222, 283, 293, 316 nm (log ε 4.32, 4.38, 4.39, 4.26). – IR. ($\nu_{max}^{CH_2Cl_2}$): 1735 cm^{-1}.

$C_{17}H_{20}O_4$ (288.3) Calc. C 70.8 H 7.0% Found C 70.7 H 7.3%

b) The acid XIIb (3 g), on similar treatment, gave the ester XIIc (2.9 g) as a viscous oil, sublimed at 180–190°/0.7 Torr. – UV. (λ_{max}^{EtOH}): 222, 285, 293, 317 nm (log ε 4.30, 4.29, 4.31, 4.23). – IR. (ν_{max}^{neat}): 1715 cm^{-1}.

$C_{17}H_{20}O_4$ (288.3) Calc. C 70.8 H 7.0% Found C 71.1 H 7.2%

9-(3,4-Methylenedioxyphenyl)-6,8-nonadien-1-ol (XId and XIId). a) A solution of the ester XIc (7.8 g) in dry ether (100 ml) was added to $LiAlH_4$ (2 g) in ether (100 ml) and the mixture stirred at 30° for 3 h. Decomposition with water yielded the alcohol XId (7.1 g), m.p. 64° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 283, 293, 316 nm (log ε 4.41, 4.42, 4.29). – IR. ($\nu_{max}^{CH_2Cl_2}$): 3630, 1600, 1040, 990, 935 cm^{-1}. – MS.: *m/e* 260 (M^+, 38%), 187 (56), 173 (58), 157 (62), 148 (30), 143 (25), 135 (45), 129 (100), 128 (74), 127 (36), 115 (50). ^{1}H-NMR. ($CDCl_3$): 5.5–7.0 (5H, complex *m*); 5.88 (2H, *s*, —O · CH_2 · O—); 3.6 (2H, *t*, *J* ≈ 6); 2.15 (2H, *m*); 1.8 (1H, *s*, OH); 1.45 (6H, br.).

$C_{16}H_{20}O_3$ (260.3) Calc. C 73.8 H 7.7% Found C 74.0 H 8.0%

b) The ester XIIc (2.8 g), on reduction as above, yielded the alcohol XIId (2.5 g), m.p. 37° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 221, 284, 293, 318 nm (log ε 4.31, 4.34, 4.35, 4.27). MS.: M^+, *m/e* 260.

$C_{16}H_{20}O_3$ (260.3) Calc. C 73.8 H 7.7% Found C 73.5 H 8.0%

*9-(3,4-Methylenedioxyphenyl)-6,8-*trans,trans*-nonadien-1-al (XIe).* a) *Collins oxidation* [5]: *Collins* reagent (from 2 g CrO_3) was added portionwise to a solution of the alcohol XId (1 g) in CH_2Cl_2 (75 ml) at 15–20°. After stirring at 25° for 45 min the solution was filtered and worked-up as usual. Chromatography of the product over silica in C_6H_6 gave the aldehyde XIe (200 mg). A sample sublimed at 210°/0.5 Torr had: UV. (λ_{max}^{EtOH}): 225, 283, 293, 315 nm (log ε 4.26, 4.22, 4.23, 4.18); IR. ($\nu_{max}^{CH_2Cl_2}$): 2730, 1730 cm^{-1}; ^{1}H-NMR. ($CDCl_3$): 9.75 (1H, *t*, *J* ≈ 1.5, CHO); 5.5–7.0 (7H, complex *m*); 5.9 (2H, *s*, —O · CH_2 · O—); 2.0–2.5 (4H, *m*); 1.55 (4H, br.); MS.: *m/e* 258 (M^+, 10%), 230 (4), 187 (12), 173 (6), 157 (12), 150 (80), 149 (100), 135 (12), 129 (16), 128 (14), 121 (56).

$C_{16}H_{18}O_3$ (258.3) Calc. C 74.4 H 7.0% Found C 73.9 H 6.8%

Subsequent elution of the column with C_6H_6 and C_6H_6/CH_2Cl_2 1:1 gave piperonal (100 mg) and 3,4-methylenedioxycinnamaldehyde (100 mg) both identified by direct comparison with authentic samples.

b) *Oxidation using CrO_3-3,5-dimethylpyrazole complex* [12]. 3,5-Dimethylpyrazole (5.8 g) was added to a suspension of CrO_3 (6 g) in CH_2Cl_2 (200 ml) and the mixture stirred under N_2 for 15 min. To the resulting dark red solution was added a solution of the alcohol XId (5.5 g) in CH_2Cl_2 (20 ml). The solution was stirred at 20° for 1/2 h, diluted with excess ether and filtered. The filtrate was evaporated *in vacuo* and the residue chromatographed as above to yield the aldehyde XIe (0.5 g) in addition to piperonal and 3,4-methylenedioxycinnamaldehyde.

c) Pfitzner-Moffat *oxidation* [11]. A solution of the alcohol XId (7.2 g) in a mixture of DMSO (75 ml) and C_6H_6 (100 ml) was treated with pyridine (2.1 ml) and trifluoracetic acid (1.5 ml). Dicyclohexyl carbodiimide (16.8 g) was then added and the resulting solution stirred at 25° for 5 h and then left overnight at room temperature. A solution of oxalic acid (9 g) in MeOH (30 ml) was added. After stirring for 1/2 h the precipitated urea was filtered and the filtrate washed with $NaHCO_3$ aq. and H_2O, dried and evaporated. The residue was filtered through a short column of silica in C_6H_6 to yield the aldehyde XIe (6 g).

*Methyl11-(3,4-methylenedioxyphenyl)-undeca-2,8,10-*trans,trans,trans*-trienoate (XIVa).* A solution of the aldehyde XIe (6.5 g) in C_6H_6 (120 ml) was refluxed with carbomethoxymethylidenetriphenylphosphorane [15] (8 g) for 1 1/2 h, the solvent evaporated *in vacuo* and the residue chromatographed over silica in hexane. Elution with hexane/CH_2Cl_2 9:1 gave the ester XIVa (6 g), m.p. 40–41° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 217, 283, 293, 318 nm (log ε 4.41, 4.31, 4.32, 4.20). – IR. (ν_{max}^{KBr}): 1725, 1660, 980 cm^{-1}. ^{1}H-NMR. (CCl_4): 5.5–7.3 (9H, complex *m*); 5.9 (2H, *s*, —O · CH_2 · O—); 3.65 (3H, *s*, $COOCH_3$); 2.15 (4H, br.); 1.45 (4H, br.). – MS.: *m/e* 314 (M^+, 32%), 277 (5), 255 (11), 254 (21), 240 (8), 232 (22), 206 (10), 187 (34), 173 (48), 157 (50), 148 (50), 143 (22), 135 (100), 131 (32), 129 (66), 128 (55), 127 (25), 115 (38).

$C_{19}H_{22}O_4$ (314.4) Calc. C 72.6 H 7.1% Found C 72.7 H 7.3%

11-(3,4-Methylenedioxyphenyl)-undeca-2,8,10-trans,trans,trans-*trienoic acid* (*XIVb*). The above ester (2.4 g) was refluxed for $1^1/_2$ h with KOH (1.6 g) in MeOH (20 ml) and water (5 ml) to yield the acid XIVb (1.5 g), m.p. 120° (from ether/hexane). – UV. (λ_{max}^{EtOH}): 214, 282, 293, 316 nm (log ε 4.45, 4.39, 4.40, 4.28). – IR. (ν_{max}^{KBr}): 1690, 1660 cm^{-1}. – MS.: *m/e* 300 (M^+, 65%), 277 (4), 255 (6), 254 (6), 240 (4), 218 (26), 187 (58), 173 (100), 157 (56), 148 (50), 143 (40), 135 (80), 129 (65), 128 (50), 127 (25), 115 (88).

$C_{18}H_{20}O_4$ (300.3) Calc. C 72.0 H 6.7% Found C 71.7 H 7.0%

N-Isobutyl-11-(3,4-methylenedioxyphenyl)-undeca-2,8,10-trans,trans,trans-*trienoic amide* (*III*). A solution of the above acid (0.7 g) in C_6H_6 (20 ml) was heated at 60° with oxalyl chloride (1.6 ml) for $^1/_2$ h. The solution was evaporated *in vacuo* and the residual acid chloride in C_6H_6 (20 ml) treated with isobutylamine (2.5 ml). The solution was left overnight at room temperature, washed with HCl aq., Na_2CO_3 aq. and water, dried and evaporated to yield the amide (0.3 g), m.p. 153° (from CH_2Cl_2/hexane). – UV. (λ_{max}^{EtOH}): 283, 293, 315 nm (log ε 4.40, 4.41, 4.28). – IR. (ν_{max}^{KBr}): 3300, 1662, 1620, 1260, 985, 930 cm^{-1}. – MS.: M^+, *m/e* 355. Mixed m.p., UV., IR., NMR. and mass spectra identical with naturally occurring piperstachine.

$C_{22}H_{29}NO_3$ (355.5) Calc. C 74.3 H 8.2 N 3.9% Found C 74.6 H 8.5 N 4.2%

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