Pyrrolylpolyenes. Part 2.[1] Stereochemistry of Wallemia A and Synthesis of its (*E*)-Isomer and Other Models

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By X-ray analysis of (*E*)-2-methyl-3-(pyrrol-2-yl)prop-2-enal (9) the Z-configuration of the trisubstituted double bond in wallemia A (1) has been established. The *E*-isomer (10) has been synthesised, together with two lower vinylogues (8) and (16). The synthesis of other pyrrolylpolyenes is also reported.

In Part 1 [1] we reported the elucidation (apart from the stereochemistry about the acyclic trisubstituted double bond) of the structure (1) of the pigment wallemia A from the fungus *Wallemia sebi* (Fr.) v. Arx. We also described the synthesis of a number of model compounds and established on the basis of n.m.r. chemical shifts that all the compounds derived from a 2-methyl-3-(pyrrol-2-yl)prop-2-enal had the stereochemistry about the trisubstituted double bond opposite to that of the natural material. The *E*-configuration of the enal (9) has now been established unambiguously by X-ray crystallographic analysis (see Experimental section). We accordingly assign the 10Z-configuration to wallemia A, and the *E*-configuration to the synthetic compounds derived from (9). In this paper we also report the synthesis of a series of model compounds and analogues of wallemia A, including its 10*E*-isomer (10).

Bestmann [2] has reported the synthesis of the phosphorane (24), which will undergo Wittig condensation with aldehydes to yield enol ethers of conjugated β-diketones. The latter compounds can be hydrolysed to give the free β-diketones. In a preliminary experiment we established that 2-formylpyrrole, a comparatively unreactive aldehyde, condenses with the phosphorane (24) to give the enol ether (18). In order to introduce the isopropyl function at the end of the side chain the phosphorane (25) is required. This compound was prepared from 2,2-diethoxyethenyltriphenylphosphonium tetrafluoroborate [3] (26) by treatment with sodamide in liquid ammonia and then with methylbutanone. Condensation of the phosphorane (25) thus formed with 2-formylpyrrole yielded the enol ether (19). Hydrolysis with dilute sulphuric acid gave a small sample of a compound which, from its mass spectrometric fragmentation and its electronic spectrum, corresponds to the enolic β-diketone (20). Condensation of the same phosphorane (25) with the enal (9) furnished the enol ether (11).

Extensions of this route to the higher polyenes in the series require the development of syntheses of pyrrolyl-polyene aldehydes. We had already shown [1] that reduction of model pyrrolylpolyene esters with lithium aluminium hydride would give highly unstable allylic alcohols. Reduction of the Z-series dienoate [1] (2) followed by immediate oxidation of the crude product (3) with manganese dioxide gave the dienal (4) together with an isomeric aldehyde † but only in poor yield. Reduction of the dienoate [1] (2) with sodium dihydridobis-(2-methoxyethoxy)aluminate failed to give the aldehyde (4).

Reduction of nitriles with di-isobutylaluminium hydride ‡ can be used in the synthesis of aldehydes. A Horner condensation between 2-formylpyrrole and diethyl cyanomethylphosphonate [4] (27) yielded both *E*- and Z-pyrrolylpropenonitriles, (21) and (23), respectively. Reduction of the *E*-isomer (21) with di-isobutylaluminium hydride gave, after acidic work-up, the *E*-aldehyde (22), which had spectroscopic properties identical with those previously reported [1] for this compound.

Methylation of diethyl cyanomethylphosphonate [4] (27) gave (28). A Horner reaction between this compound and 2-formylpyrrole yielded both *E*- and Z-nitriles, (12) and (5), respectively. We have also prepared the *E*-pyrrolylpentadienonitrile (13) in good yield by a Horner condensation between diethyl cyanomethylphosphonate [4] (27) and the *E*-aldehyde [1] (9). Di-isobutylaluminium hydride reduction of the *E*-nitrile (12) produced the known [1] *E*-aldehyde (9) in reasonable yield after mild acidic treatment. However, the corresponding reduction of the Z-nitrile failed to yield the desired Z-aldehyde (6), a synthetic intermediate required for the natural stereochemical series: the product of mild acidic treatment was not an aldehyde; more severe acidic conditions resulted in the production, in low yield, of the stereoisomeric aldehyde (9) only. The desired Z-aldehyde was eventually synthesised by a route derived from work by Nagata *et al.*,[5] who had used phosphonates in which the aldehyde group had been protected by condensation with cyclohexylamine, *e.g.* (29). The methylated phosphonate (30) underwent a Horner condensation with 2-formylpyrrole. Treatment

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† The compound reported [1] as (2) was later found to contain a small amount of an isomeric dienoate ester having the methyl group α to the carbonyl group. The quoted [1] n.m.r. spectrum for the aldehyde (9) should have given the chemical shift of the methyl protons as δ 2.05.

‡ We thank May and Baker, Dagenham, for the use of this reagent.

[1] Part 1, Y. Badar, W. J. S. Lockley, T. P. Toube, B. C. L. Weedon, and L. R. G. Valadon, *J.C.S. Perkin I*, 1973, 1416.

[2] H. J. Bestmann and R. W. Saalfrank, *Angew. Chem. Internat. Edn.*, 1970, **9**, 367.

[3] H. J. Bestmann, R. W. Saalfrank, and J. P. Snyder, *Angew. Chem. Internat. Edn.*, 1969, **8**, 216; H. J. Bestmann, personal communication.

[4] E. C. Ladd, U.S.P. 2,632,019/1953.

[5] W. Nagata and Y. Hayase, *J. Chem. Soc. (C)*, 1969, 460.

of the product (7) with aqueous oxalic acid removed the protecting group and gave the elusive Z-aldehyde (6) in low yield.

The higher vinylogue (14) of the aldehyde in the E-series was produced in a similar fashion by the Nagata procedure.[5] A Horner condensation between the

shown that aldol condensations involving conjugated polyene aldehydes proceed normally, whereas condensation with conjugated polyene esters under appropriate conditions leads to β-diketones.[7]

Treatment of the Z-dienoate[1] (2) with methylbutanone in the presence of lithium amide produced the

(1) R = (structure with OH and O)

(2) R = CO₂Me → $R = CO_2Me$

(3) R = CH₂OH → $R = CH_2OH$

(4) R = CHO

(5) R = CN

(6) R = CHO

(7) R = CH=NH—(cyclohexyl)

(8) R = (structure with OH and O)

(9) R = CHO

(10) R = (structure with OH and O)

(11) R = (structure with OEt and O)

(12) R = CN

(13) R = CN

(14) R = CHO

(15) R = CO₂Me → $R = CO_2Me$

(16) R = (structure with OH and O)

(17) R = CO₂Me → $R = CO_2Me$

(18) R = (structure with OEt and O)

(19) R = (structure with OEt and O)

(20) R = (structure with OH and O)

(21) R = CN

(22) R = CHO

(23)

$Ph_3\overset{+}{P}-\overset{-}{C}H-C=CH-COR$ with OEt

(24) R = Me
(25) R = CHMe₂ → $R = CHMe_2$

$Ph_3\overset{+}{P}CH=C(OEt)_2$
BF_4^-

(26)

$(EtO)_2\overset{+}{P}-CH-CN$ with −O and R

(27) R = H
(28) R = Me

$(EtO)_2\overset{+}{P}-CR=CH-NH-(cyclohexyl)$ with −O

(29) R = H
(30) R = Me

E-aldehyde[1] (9) and the protected aldehyde phosphonate (29) yielded a crude product which, after hydrolysis with aqueous oxalic acid, gave the desired aldehyde (14).

In view of the difficulties encountered in preparing the required pyrrolylpolyene aldehydes, attention was directed to other methods of synthesising compounds related to wallemia A. The condensation of enolate anions, derived from ketones, with derivatives of αβ-unsaturated carboxylic acids might be expected to lead to products of Michael addition rather than to β-diketones. However, work in these laboratories[6] has

crystalline lower vinylogue (8) of wallemia A in reasonable yield. An analogous reaction using the E-dienoate[1] (15), derived from the aldehyde (9), yielded the isomeric β-diketone (16) in similar yield. The Z-isomer (8) is in the same stereochemical series as the natural pigment. The n.m.r. spectra of (16) and (8) show differences consistent with those of the esters from which they were prepared. In particular (16) has the signal for the methyl group on the double bond at δ 2.06, whereas the corresponding signal for (8) is at δ 1.94, the same chemical shift as the corresponding protons in wallemia A.[1] In addition, the proton on the carbon atom between the oxygen functions resonates at δ 5.77 in (8) (cf. δ 5.79 in wallemia A), but at δ 5.55 in (16). Further-

[6] R. D. G. Cooper, L. M. Jackman, and B. C. L. Weedon, Proc. Chem. Soc., 1962, 215; L. Cholnoky, J. Szabolcs, R. D. G. Cooper, and B. C. L. Weedon, Tetrahedron Letters, 1963, 1257.

[7] A. Chopra, Ph.D. Thesis, University of London, 1976.

more, the *E*-isomer (16) shows an AB system (*J* 15 Hz) at δ 5.92 and 7.39 for the protons on the disubstituted olefinic bond, in this respect resembling the ester (15) and nitrile (13) [but neither (2) nor wallemia A (1), presumably because in these latter compounds the chemical shifts of the relevant protons cause the signals to be hidden by those of other hydrogen atoms in the molecule].

Treatment of the 6*E*-trienoate ester [1] (17) with methylbutanone under the same conditions yielded (10), the 10*E*-isomer of wallemia A, in about 50% yield as a solid, m.p. 152°. It resembled its lower vinylogue (16) in having a methyl signal in its n.m.r. spectrum at δ 2.08, a singlet at δ 5.51, and an AB system (*J* 15 Hz) at δ 5.90 and 7.34, and in these respects differed from wallemia A.

We have previously reported [1] a shift to lower wavelengths of 15 nm in the position of the absorption maximum of a methanolic solution of wallemia A when treated with base. In our studies on the synthetic compounds (8), (10), and (16), we have observed that careful addition of base to solutions of these compounds causes a shift to lower wavelength of 15 nm; the new maximum remains at the same wavelength over a small increase in pH and then shifts again by a further 10—12 nm. The same result was obtained using a sample of the natural pigment.

Syntheses designed to produce the full chromophore in the natural *Z*-series are being pursued.

EXPERIMENTAL

Where appropriate, operations were carried out under nitrogen. Solvents were redistilled before use. Light petroleum refers to that fraction with b.p. 60—80 °C except where stated otherwise. M.p.s were determined on a Reichert heated-stage microscope. Silica gel for t.l.c. was Kieselgel H unless otherwise indicated. Electronic spectra were recorded on a Unicam SP 800 instrument and i.r. spectra on a Perkin-Elmer 257 or 225 spectrometer. N.m.r. spectra at 60 or 100 MHz were determined on a Varian A60 or HA 100 spectrometer using solutions in deuteriochloroform. Mass spectra were determined on an A.E.I. MS902 spectrometer; high resolution measurements were made relative to heptacosafluorotributylamine as reference.

4-*Ethoxy*-6-(*pyrrol*-2-*yl*)*hexa*-3,5-*dien*-2-*one* (18).—2-Ethoxy-4-oxopent-2-enylidenetriphenylphosphorane [2] (24) (40 mg) and 2-formylpyrrole (10 mg) were heated in a sealed tube at 120 °C for 50 min. The product was extracted with ether and the extract purified by t.l.c. (silica gel HF; 5% ether in light petroleum) to yield the yellow *enol ether* (18) (7 mg), m.p. 95—97°; $\lambda_{max.}$ (ether) 370 nm; δ (100 MHz) 1.40 (3 H, t), 2.18 (3 H, 6), 5.41 (1 H, s), 6.21 (1 H, m), 6.40 (1 H, m), 6.84 (1 H, m), 7.21 (1 H, d, *J* 16 Hz), and 7.7 (1 H, d, *J* 16 Hz); *m/e* 205.110 ($M^{+\cdot}$, $C_{12}H_{15}NO_2$ requires 205.110), 190, 162, and 132 (100%).

2-*Ethoxy*-5-*methyl*-4-*oxohex*-2-*enylidenetriphenylphosphorane* (25).—Sodium (300 mg) and iron(III) nitrate (a few crystals) were added to dry liquid ammonia (40 cm³) which had been redistilled from sodium. Dried, powdered 2,2-diethoxyethenyltriphenylphosphonium tetrafluoroborate [3] (26) (4.5 g) was added and the mixture stirred. The ammonia was evaporated off and the residue dissolved

by boiling for 10 min with dry benzene (50 cm³). The solution was filtered and 3-methylbutan-2-one (5 cm³) added slowly to the filtrate. The mixture was stored for 24 h at 20 °C and evaporated to yield the phosphorane as a brownish substance that could not be crystallised.

5-*Ethoxy*-2-*methyl*-7-(*pyrrol*-2-*yl*)*hepta*-4,6-*dien*-3-*one* (19).—The phosphorane (25) (*ca.* 250 mg) and 2-formylpyrrole (50 mg) were heated together in a sealed tube at 130—135 °C for 1 h. The product was extracted with ether and the extracts were purified by t.l.c. (silica gel HF; 20% ether in light petroleum) to yield the *enol ether* (19) (24 mg); $\lambda_{max.}$ (ether) 370 nm; δ (100 MHz) 1.09 (6 H, d), 1.4 (3 H, t), 3.95 (2 H, q), 5.42 (1 H, s), 6.20 (1 H, m), 6.38 (1 H, m), 6.81 (1 H, m), 7.21 (1 H, d, *J* 16 Hz), and 7.71 (1 H, d, *J* 16 Hz); *m/e* 233.141 ($M^{+\cdot}$, $C_{14}H_{19}NO_2$ requires 233.142), 190, and 162.

5-*Hydroxy*-2-*methyl*-7-(*pyrrol*-2-*yl*)*hepta*-4,6-*dien*-3-*one* (20).—The enol ether (19) (20 mg) was stirred in sulphuric acid (5 ml; 10% solution in water) at 25 °C for 15 min and the mixture extracted with ether. The extract was washed, dried (MgSO₄), and evaporated. The residue was purified by t.l.c. (silica gel HF; 15% acetone in light petroleum) to yield a small quantity of the *enol ketone* (20), $\lambda_{max.}$ (ether) 386 nm; *m/e* 205 ($M^{+\cdot}$), 162, and 134.

(4*Z*)-4-*Methyl*-5-(*pyrrol*-2-*yl*)*penta*-2,4-*dienal* (4).—Methyl (4*Z*)-4-methyl-5-(pyrrol-2-yl)penta-2,4-dienoate [1] (2) in dry tetrahydrofuran was treated with lithium aluminium hydride. The crude alcohol (3), $\lambda_{max.}$ (ether) 314 nm,[1] was oxidised by active manganese dioxide to yield, after t.l.c., the *aldehyde* (4); $\lambda_{max.}$ (ether) 365 nm; δ (100 MHz) 1.90 (s), 6.06—7.04 (m), 7.5 (dd, *J* 10 and 2 Hz), and 9.5 (d, *J* 10 Hz); *m/e* 161.084 ($M^{+\cdot}$, $C_{10}H_{11}NO$ requires 161.084).

(*E*)- *and* (*Z*)-3-(*Pyrrol*-2-*yl*)*prop*-2-*enonitrile* (21) *and* (23).—To a stirred suspension of sodium hydride (60%; 180 mg, 4.5 mmol) in dry dimethylformamide (10 cm³) was added a solution of diethyl cyanomethylphosphonate [4] (796.5 mg, 4.5 mmol) (27) in dry dimethylformamide (5 cm³). The solution was stirred until evolution of gas had ceased, and 2-formylpyrrole (285 mg, 3 mmol) in dry dimethylformamide (5 cm³) was then added dropwise. The mixture was stirred at 120—130 °C for 2.5 h, cooled to room temperature, poured into water, and extracted with ether. The ethereal solution was washed with saturated aqueous sodium chloride, dried (Na₂SO₄), and evaporated to yield an oil. Column chromatography (silica gel; benzene) gave (i) the *trans-nitrile* (21) (188 mg), m.p. 71—73°; $\lambda_{max.}$ (ether) 318 nm; $\nu_{max.}$ (film) 2 250, 1 610, and 960 cm⁻¹; δ (CDCl₃; 100 MHz) 5.33 (1 H, d, *J* 16 Hz), 6.29 (1 H, m), 6.54 (1 H, m), 6.90 (1 H, m), and 7.17 (1 H, d, *J* 16 Hz) (Found: $M^{+\cdot}$, 118.053. $C_7H_6N_2$ requires *M*, 118.053), and (ii) a small amount of the *cis-nitrile* (23) as an oil, $\lambda_{max.}$ (ether) 322 nm, δ (CDCl₃; 100 MHz) 4.86 (1 H, d, *J* 12 Hz), 6.18 (1 H, m), 6.43 (1 H, m), 6.85 (1 H, d, *J* 12 Hz), and 6.92 (1 H, m) (Found: $M^{+\cdot}$, 118.053).

(*E*)-3-(*Pyrrol*-2-*yl*)*prop*-2-*enal* (22).—The *trans*-nitrile (21) (46.9 mg) in dry ether (10 cm³) was treated below 10 °C with di-isobutylaluminium hydride (200 mg) in dry toluene (2 cm³). The mixture was stirred at room temperature for 1 h and then carefully poured into 2N-acetic acid at 0 °C. Solid sodium hydrogen carbonate was added until the solution was alkaline and the mixture was then extracted with ether. The ethereal solution was washed with saturated sodium chloride, dried (Na₂SO₄), and evaporated to yield a brown oil which was purified (t.l.c., silica gel; 3% acetone in benzene) to give the *E*-aldehyde (22) (21 mg,

45%), identical (n.m.r., mass, and u.v. spectra) with an authentic sample.[1]

(E)- *and* (Z)-2-*Methyl*-3-(*pyrrol*-2-*yl*)*prop*-2-*enonitrile*, (12) *and* (5).—A solution of diethyl cyanomethylphosphonate[4] (27) (3.54 g) in dry dimethylformamide (20 cm³) was added to sodium hydride (60%; 800 mg) suspended in dry dimethylformamide (15 cm³), and the mixture stirred for 1 h. To the clear solution was added, dropwise and with cooling, iodomethane (2.84 g) dissolved in dry dimethylformamide (15 cm³). The mixture was stirred at 25 °C for 1 h, a few drops of iodomethane were added, and the mixture was heated to 50 °C for 1 h, then cooled. Sodium hydride (60%; 800 mg) was added, and the mixture was stirred for 1 h. 2-Formylpyrrole (800 mg) in dry dimethylformamide (15 cm³) was added and the solution heated at 110 °C for 2.5 h, cooled, and poured into water (0 °C). The resulting solution was extracted with benzene and the organic phase washed with saturated aqueous sodium chloride, dried (Na_2SO_4) and evaporated to give an oil. T.l.c. (silica gel; 3% acetone in benzene) yielded (i) the E-*nitrile* (12) (595 mg), m.p. 80—82°; $\lambda_{max.}$ (ethanol) 319 nm; $\nu_{max.}$ (chloroform) 3 434, 3 314, 2 214, 1 624, and 972 cm⁻¹; δ ($CDCl_3$; 100 MHz) 2.11 (3 H, d, J 2 Hz), 6.32 (1 H, m), 6.49 (1 H, m), 6.92 (1 H, m), 7.01br (1 H, s), and 8.80br (1 H) (Found: $M^{+\cdot}$, 132.069. $C_8H_8N_2$ requires M, 132.069); and (ii) the Z-*nitrile* (5) (389 mg), m.p. 84—86°; $\lambda_{max.}$ (ethanol) 328 nm; $\nu_{max.}$ (chloroform) 3 422, 2 182, and 1 630 cm⁻¹; δ ($CDCl_3$; 100 MHz) 1.99 (3 H, d, J 2 Hz), 6.21 (1 H, m), 6.43 (1 H, m), 6.70 (1 H, m), 6.86 (1 H, m), and 9.40br (1 H) (Found: $M^{+\cdot}$, 132.068).

(E)-2-*Methyl*-3-(*pyrrol*-2-*yl*)*prop*-2-*enal* (9).—A solution of the E-nitrile (12) (78 mg) in dry ether (15 cm³) was treated below 10 °C with di-isobutylaluminium hydride (350 mg) in dry toluene (5 cm³), added dropwise. The mixture was stirred for 1.5 h and then poured into aqueous acetic acid (2N) at 0 °C. Sodium hydrogen carbonate was added until the solution was basic and the mixture was then extracted with ether. The ethereal solution was washed with saturated aqueous sodium chloride, dried (Na_2SO_4), and evaporated. The crude product was purified (t.l.c.) to yield the E-aldehyde (9) (44 mg, 56%), identical with an authentic sample (t.l.c., n.m.r., and u.v.).[1]

The same conditions produced from the Z-nitrile (5) (92 mg) an oil which was not the corresponding Z-aldehyde (6). Treatment of this product with acetic acid (2N for 1.5 h) and work-up of the resulting brown solution gave after t.l.c. the E-aldehyde (9) (18 mg, 21%) only.

Crystal Structure Analysis of the Pyrrolenal (9).—*Crystal data.* C_8H_9NO, $M = 135.17$. Monoclinic, $a = 11.75(1)$, $b = 11.97(1)$, $c = 10.92(1)$ Å, $\beta = 106.44(5)°$; $U = 1 472.8$ Å³, $D_m = 1.21$, $Z = 8$, $D_c = 1.22$ g cm⁻³. Space group $C2/c$. Cu-K_α radiation, $\mu = 5.75$ cm⁻¹.

Oscillation and Weissenberg photographs were used for preliminary determination of all dimensions. Accurate values were calculated from diffractometer measurement of 2θ and ϕ values for axial reflections. Intensities were measured on a General Electric XRD6 manual diffractometer in a manner described previously.[8] 1 114 Independent reflections within the range $5 < 2\theta < 120°$ were measured, of which only 621 satisfied the condition $I > 3\sigma(I)$. The structure was solved by application of the centrosymmetric direct methods routine in the SHELX[9] program and refined by full matrix least squares. Hydrogen

* For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

atom positions were determined experimentally. Refinement with all non-hydrogen atoms assigned anisotropic and all hydrogen atoms isotropic temperature factors terminated at an R value of 0.074 (weighted $R = 0.071$). The weighting scheme used was $\omega = 1/[\sigma(F) + 0.0002F]$ with $\sigma(F)$ derived from the $\sigma(I)$ from counting statistics. The final atomic co-ordinates are given in the Table; temperature
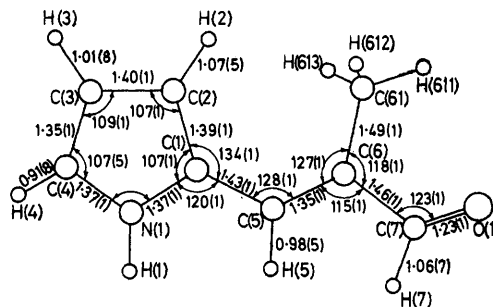
Bond lengths (Å) and angles (°) in structure (9)

factor parameters and lists of F_o and F_c are available as Supplementary Publication No. SUP 22033 (6 pp.).* Bond lengths and angles are given in the Figure.

(Z)-2-*Methyl*-3-(*pyrrol*-2-*yl*)*prop*-2-*enal* (6).—To a stirred suspension of sodium hydride (60%; 400 mg) in dry bis-(2-methoxyethyl) ether (3 cm³) was added dropwise a solution of diethyl 2-(cyclohexylamino)ethenylphosphonate[5]

Fractional atomic co-ordinates (e.s.d.s in parentheses)

Atom	x/a	y/b	z/c
C(1)	−0.100 8(6)	0.276 2(5)	0.091 4(6)
C(2)	−0.051 3(7)	0.341 2(6)	0.014 4(7)
C(3)	0.014 0(7)	0.269 7(6)	−0.041 3(8)
C(9)	0.010 0(7)	0.165 3(7)	0.005 4(8)
C(5)	−0.176 5(6)	0.299 8(5)	0.170 5(6)
C(6)	−0.214 8(6)	0.400 2(5)	0.199 3(6)
C(7)	−0.293 5(8)	0.396 1(7)	0.281 0(7)
C(61)	−0.183 8(11)	0.511 0(6)	0.156 8(11)
N(1)	−0.061 1(5)	0.169 5(5)	0.085 1(5)
O(1)	−0.337 9(5)	0.480 2(4)	0.314 1(5)
H(1)	−0.090 (6)	0.106 (7)	0.111 (6)
H(2)	−0.061 (5)	0.430 (5)	0.002 (5)
H(3)	0.072 (6)	0.302 (6)	−0.085 (7)
H(4)	0.038 (7)	0.097 (6)	−0.071 (7)
H(5)	−0.202 (5)	0.233 (4)	0.208 (5)
H(7)	−0.311 (6)	0.315 (6)	0.309 (6)
H(611)	−0.205 (9)	0.586 (9)	0.205 (9)
H(612)	−0.230 (6)	0.527 (6)	0.072 (7)
H(613)	−0.099 (7)	0.512 (6)	0.171 (7)

(30) (2.7 g) in dry bis-(2-methoxyethyl) ether (20 cm³). The mixture was stirred at 25 °C for 30 min. 2-Formylpyrrole (190 mg) in dry bis-(2-methoxyethyl) ether (2 cm³) was then added to the suspension. The mixture was stirred at 170—180 °C for 48 h and poured into ice; the aqueous solution was saturated with sodium chloride, and extracted with ether. The extract was washed with aqueous sodium chloride and extracted with aqueous tartaric acid (20%). The acidic layer was basified at 0 °C with solid potassium carbonate and extracted with ether. The ethereal extract, after the usual work-up, yielded the crude enamine as an oil. A solution of this enamine in benzene (20 cm³) was shaken with aqueous oxalic acid (1%; 40 cm³) for 6 h. The benzene layer was removed, the aqueous phase saturated with sodium chloride and

[8] R. Bonnett, M. B. Hursthouse, and S. Neidle, *J.C.S. Perkin II*, 1972, 902.
[9] The SHELX Crystal Structure Calculation System, G. M. Sheldrick, University of Cambridge.

extracted with benzene, and the extracts combined and worked up to yield a crude oil (144 mg). T.l.c. (silica gel; 3% acetone in benzene) yielded the Z-aldehyde (6) as an oil (6 mg), $\lambda_{max.}$ (ethanol) 348 nm; δ (CDCl₃; 100 MHz) 2.04 (3 H, s), 6.30 (1 H, m), 6.72 (1 H, m), 6.92 (1 H, m), 7.08 (1 H, s), and 9.47 (1 H, s). It was less polar on t.l.c. than its *trans*-isomer.

(4E)-4-*Methyl*-5-(*pyrrol*-2-*yl*)*penta*-2,4-*dienal* (14).—A solution of diethyl 2-(cyclohexylamino)ethenylphosphonate [5] (29) (786 mg) in dry bis-(2-methoxyethyl) ether (8 cm³) was added slowly to a suspension of sodium hydride (60%, 120 mg) in dry bis-(2-methoxyethyl) ether (3 cm³) and the mixture stirred for 30 min. A solution of 2-methyl-3-(pyrrol-2-yl)prop-2-enal [1] (9) (115 mg) in dry bis-(2-methoxyethyl) ether (8 cm³) was added, and the mixture was stirred at room temperature for 30 min, then heated at 130 °C for 2.5 h and poured onto ice. The resulting aqueous layer was saturated with sodium chloride and the products were extracted into ether. The ethereal solution was washed with aqueous sodium chloride and extracted with cold aqueous tartaric acid (20%). The acidic layer was basified at 0 °C with solid potassium carbonate and extracted with ether, and the ethereal extract worked up in the usual way to yield a crude enamine. This compound was dissolved in benzene (5 cm³) and hydrolysed by shaking with aqueous oxalic acid (1%; 15 cm³) at room temperature for 8 h. The benzene layer was then separated, the aqueous phase was saturated with sodium chloride and extracted with benzene, and the combined benzene extracts were worked up in the usual way to yield an oil. The crude product was taken up in ether, and the solution washed well with water, dried (Na₂SO₄), and evaporated to give an oil which on purification (t.l.c., silica gel; 3% acetone in benzene) gave the *aldehyde* (14) as a red solid (20 mg), $\lambda_{max.}$ (ethanol) 389 nm; $\nu_{max.}$ (chloroform) 3 500, 3 350, 2 850, 2 740, 1 660, 1 595, and 970 cm⁻¹; δ (CDCl₃; 100 MHz) 2.12 (3 H, s), 6.19 (1 H, dd, *J* 16 and 8 Hz), 6.35 (1 H, m), 6.56 (1 H, m), 6.68 (1 H, s), 6.94 (1 H, m), 7.20 (1 H, d, *J* 16 Hz), and 9.59 (1 H, d, *J* 8 Hz) (Found: $M^{+\cdot}$, 161.084. C₁₀H₁₁NO requires *M*, 161.084).

(4E)-4-*Methyl*-5-(*pyrrol*-2-*yl*)*penta*-2,4-*dienonitrile* (13).— To a suspension of sodium hydride (60%; 18 mg, 0.45 mmol) in dry dimethylformamide (2 cm³) was added diethyl cyanomethylphosphonate [4] (27) (78.6 mg, 0.45 mmol) in dry dimethylformamide (1 cm³). When the reaction had subsided 2-methyl-3-(pyrrol-2-yl)prop-2-enal (9) (40 mg, 0.3 mmol) in dry dimethylformamide (2 ml) was added. The mixture was stirred at 120 °C for 3 h and then poured into ice–water. Extraction with benzene and ether followed by drying (Na₂SO₄) and evaporation of the organic phase yielded a brown oil which was purified (t.l.c. on silica gel; 3% acetone in benzene) to give the E-*nitrile* (13) (17 mg), m.p. 70—73°; $\lambda_{max.}$ (ether) 356 nm; $\nu_{max.}$ (chloroform) 3 500, 3 350, 2 250, 1 590, and 970 cm⁻¹; δ (CDCl₃; 100 MHz) 2.04 (3 H, s), 5.23 (1 H, d, *J* 16 Hz), 6.32 (1 H, m), 6.55 (1 H, m), 6.90 (1 H, m), 7.10 (1 H, d, *J* 16 Hz), and 8.64br (1 H) (Found: $M^{+\cdot}$, 158.085. C₁₀H₁₀N₂ requires *M*, 158.084).

(8Z)-5-*Hydroxy*-2,8-*dimethyl*-9-(*pyrrol*-2-*yl*)*nona*-4,6,8-*trien*-3-*one* (8).—To methyl (4Z)-4-methyl-5-(pyrrol-2-yl)-penta-2,4-dienoate [1] (2) (90 mg) and an excess of 3-methyl-butan-2-one (*ca.* 1 cm³) was added an excess of lithium amide (*ca.* 700 mg). The mixture was heated under reflux for 4 days, cooled, and cautiously quenched with water containing a little hydrochloric acid. The solution was extracted with ether, and the ethereal layer dried (MgSO₄) and evaporated to yield a gum. T.l.c. (silica gel; 20% acetone in light petroleum) produced the β-*diketone* (8) (70 mg, 60%), m.p. 79—80° (from ether–cyclohexanone); $\lambda_{max.}$ (ethanol) 411 nm; δ (CDCl₃; 100 MHz) 1.16 (6 H, d, *J* 7 Hz), 1.94 (3 H, s), 2.54 (1 H, m, *J* 7 Hz), 5.77 (1 H, s), 6.2 (1 H, m), 6.4 (1 H, m), 6.6—6.8 (2 H, m), 6.8 (1 H, m), 7.2 (1 H, m), 8.8br (1 H), and 15.74br (1 H); *m/e* 245.141 (50%, $M^{+\cdot}$, C₁₅H₁₉NO₂ requires 245.142) and 80 (100%).

(8E)-5-*Hydroxy*-2,8-*dimethyl*-9-(*pyrrol*-2-*yl*)*nona*-4,6,8-*trien*-3-*one* (16).—To methyl (4E)-4-methyl-5-(pyrrol-2-yl)-penta-2,4-dienoate [1] (15) (75 mg) and 3-methylbutan-2-one (*ca.* 1 cm³) in dry tetrahydrofuran (50 cm³) was added an excess of lithium amide (*ca.* 1 g), and the mixture heated under reflux for 28 h and then cooled. Water containing a little hydrochloric acid was cautiously added and the solution extracted with ether (50 cm³). The ethereal layer was dried (MgSO₄) and evaporated to yield a gum, which after t.l.c. (silica gel; 20% acetone in light petroleum) gave the β-*diketone* (16) (56 mg, 58%), m.p. 139—140°, $\lambda_{max.}$ (ethanol) 412 nm; δ (CDCl₃; 100 MHz) 1.14 (6 H, d, *J* 7 Hz), 2.06 (3 H, s), 2.51 (1 H, m, *J* 7 Hz), 5.55 (1 H, s), 5.92 (1 H, d, *J* 15 Hz), 6.2—7.0 (4 H, m), 7.39 (1 H, d, *J* 15 Hz), 8.6br (1 H), and 15.5br (1 H, exchanges with D₂O) (Found: $M^{+\cdot}$, 245.141. C₁₅H₁₉NO₂ requires *M*, 245.142).

(10E)-5-*Hydroxy*-2,10-*dimethyl*-11-(*pyrrol*-2-*yl*)*undeca*-4,6,8,10-*tetraen*-3-*one* (E-*Isomer of Wallemia A*) (10).—To methyl (6E)-6-methyl-7-(pyrrol-2-yl)hepta-2,4,6-trienoate [1] (17) (38 mg) and an excess of 3-methylbutan-2-one (*ca.* 1 cm³) in dry tetrahydrofuran (50 cm³) was added an excess of lithium amide (*ca.* 500 mg), and the mixture heated under reflux for 28 h and then cooled. The reaction was cautiously quenched with water containing a little hydrochloric acid and the solution extracted with ether (50 cm³). The ethereal solution was dried (MgSO₄) and evaporated to yield a gum which after t.l.c. (silica gel; 20% acetone in light petroleum) gave the E-*isomer of wallemia A* (10) (23 mg, 49%), m.p. 152° (from ether), $\lambda_{max.}$ (ethanol) 432 nm; δ (CDCl₃; 100 MHz) 1.14 (6 H, d, *J* 7 Hz), 2.08 (3 H, s), 2.52 (1 H, m, *J* 7 Hz), 5.51 (1 H, s), 5.90 (1 H, d, *J* 15 Hz), 6.1—6.9 (*ca.* 6 H, m), 7.34 (1 H, dd, *J* 15 and 10 Hz), 8.4br (1 H), and 15.4br (1 H), $M^{+\cdot}$ 271.