

## Chemical Constituents of the Combretaceae. Part IV.<sup>1</sup> Phenanthrene Derivatives from the Heartwood of *Combretum hereroense*

By Roy M. Letcher\* and Llewellyn R. M. Nhamo, Department of Chemistry, University of Rhodesia, P.O. Box MP 167, Salisbury, Rhodesia

Two new compounds, shown to be 3,6-dihydroxy-2,4,7-trimethoxyphenanthrene and its 9,10-dihydro-derivative, have been isolated from the heartwood of *Combretum hereroense*.

WE now report on the heartwood extractives of *Combretum hereroense*<sup>2</sup> which contain six phenanthrenes or 9,10-dihydrophenanthrenes, three of which are new natural products. Of these, two have not been previously described. We confirm the structure of the third compound by synthesis.

Light petroleum extraction removed an oily material from the heartwood. The subsequent ether extract, which consisted entirely of phenolic material, was chromatographed on t.l.c. yielding gums from three of the bands. Acetylation followed by t.l.c. yielded amorphous acetates from bands A, B, and C. The designations (A—C) represent the order in which the phenols ran on the t.l.c. plates.

The acetate from band A was shown by mass and n.m.r. spectrometry to be a mixture of a phenanthrene (90%) and its dihydro-derivative (10%). Dehydrogenation of the amorphous solid gave only 2,7-diacetoxy-3,4,6-trimethoxyphenanthrene.<sup>1</sup> The n.m.r. spectrum of the amorphous acetate exhibited the same signals as that of the amorphous acetate from band C of *Combretum psidioides*.<sup>1</sup> Consequently, band A consists of 2,7-

dihydroxy-3,4,6-trimethoxyphenanthrene and its 9,10-dihydro-derivative.

The acetate from band B was shown by mass and n.m.r. spectrometry to be a mixture of phenol (B<sub>1</sub>) acetate (20%) and its dihydro-derivative phenol (B<sub>2</sub>) acetate (80%). Catalytic reduction of the amorphous solid gave the crystalline acetate of phenol (B<sub>2</sub>) (C<sub>21</sub>H<sub>22</sub>O<sub>7</sub>), with spectroscopic characteristics of a 9,10-dihydrophenanthrene. The n.m.r. spectrum of phenol (B<sub>2</sub>) acetate showed signals for three methoxy- and two acetoxy-groups, a singlet for four benzylic protons, and three aromatic protons, all singlets. Hydrolysis of phenol (B<sub>2</sub>) acetate yielded the crystalline phenol, which on methylation gave 9,10-dihydro-2,3,4,6,7-pentamethoxyphenanthrene,<sup>3</sup> thus establishing the oxygenation pattern of phenols (B<sub>1</sub>) and (B<sub>2</sub>). Deuteriation of phenol (B<sub>2</sub>) followed by acetylation gave a monodeuteriated species (mass spectrometry) whose n.m.r. spectrum showed that only the low-field proton at  $\tau$  2.10 (*viz.* H-5) had exchanged with deuterium.<sup>3</sup>

<sup>2</sup> A. W. Exell, *Kirkia* (Journal of the Government Herbarium, Salisbury, Rhodesia), 1970, 7 (II), 199.

<sup>3</sup> R. M. Letcher and L. R. M. Nhamo, *J. Chem. Soc. (C)*, 1971, 3070.

<sup>1</sup> Part III, R. M. Letcher and L. R. M. Nhamo, *J.C.S. Perkin I*, 1972, 2941.

Consequently phenol ( $B_2$ ) is 9,10-dihydro-3,6-dihydroxy-2,4,7-trimethoxyphenanthrene and phenol ( $B_1$ ) is 3,6-dihydroxy-2,4,7-trimethoxyphenanthrene. This was confirmed by a synthesis (employing an oxidative photochemical cyclisation)<sup>4</sup> of 3,6-diacetoxy-2,4,7-trimethoxyphenanthrene which proved to be identical with phenol ( $B_1$ ) acetate obtained by dehydrogenating the amorphous acetate from band B.

The acetate from band C, shown by mass and n.m.r. spectrometry to be a mixture of a tetra- (85%) and a penta-substituted phenanthrene (15%), separated into two bands on t.l.c. plates. The upper band yielded phenol (C) acetate, identical with a compound which Erdtman *et al.*<sup>5</sup> had prepared by acetylating the partial demethylation product of 2,4,6,7-tetramethoxyphenanthrene, and to which they ascribed the structure 6,7-diacetoxy-2,4-dimethoxyphenanthrene. As no rigorous structural proof for this compound has been reported, we have now synthesised 2,4-dimethoxy-6,7-methylenedioxyphenanthrene *via* an oxidative photochemical cyclisation of 3,5-dimethoxy-3',4'-methylene-dioxystilbene, and shown it to be identical with the methylenedioxy-derivative of phenol (C), thus confirming the structure proposed by Erdtman *et al.*<sup>5</sup> From a comparison with the original n.m.r. spectrum of 6,7-diacetoxy-2,4-dimethoxyphenanthrene, we noted an error in the published<sup>5</sup> n.m.r. spectrum which we now correctly report.

The acetate from the lower band of the t.l.c. separation of the acetates from band C was 6,7-diacetoxy-2,3,4-trimethoxyphenanthrene.<sup>3,4</sup>

#### EXPERIMENTAL

Irradiations were carried out in absolute ethanol containing 0.005% iodine, using a 1 l Hanovia reactor with a medium pressure mercury lamp submerged in the solution in quartz apparatus. The reaction was monitored by u.v. spectroscopy.<sup>4</sup> Other general experimental details are described in Parts I<sup>3</sup> and II.<sup>4</sup>

*Extraction of the Heartwood.*—By the procedure we have described,<sup>3</sup> the brown heartwood (360 g) from *Combretum hereroense* yielded an oily light petroleum extract (3.4 g) and a brown solid (5.0 g) from the ether extract.

*Isolation of the Phenolic Constituents.*—The ether extract (1 g) was chromatographed as previously described<sup>3</sup> in 5% methanol-chloroform and yielded a red gum from each band. A (50 mg), B (30 mg), and C (60 mg) had  $R_F$  0.67, 0.52, and 0.28, respectively. These crude phenolic products (which exhibited no carbonyl absorption in the i.r. spectrum) were acetylated and purified as previously described,<sup>3</sup> yielding amorphous acetates from band A (25 mg), band B (10 mg), and from band C (20 mg). The amorphous acetates from band A had m.p. 162—174°,  $m/e$  386, 384, 344, 342, 302, and 300 (base peak). Dehydrogenation gave prisms, m.p. 179—181°, identical (mixed m.p., i.r., and n.m.r. spectra) with 2,7-diacetoxy-3,4,6-trimethoxyphenanthrene.<sup>1</sup>

3,6-Dihydroxy-2,4,7-trimethoxyphenanthrene [*Phenol* ( $B_1$ )].

<sup>4</sup> R. M. Letcher, L. R. M. Nhamo, and I. T. Gumiro, *J.C.S. Perkin I*, 1972, 206.

—The amorphous acetate from band B, m.p. 175—190°,  $m/e$  386, 384, 344, 342, 302, and 300 (base peak) was dehydrogenated to give 3,6-diacetoxy-2,4,7-trimethoxyphenanthrene as prisms, m.p. 191—193° (from methanol) identical (mixed m.p., i.r., and n.m.r. spectra) with the synthetic product (see later). Acidic hydrolysis gave 3,6-dihydroxy-2,4,7-trimethoxyphenanthrene as a gum,  $\nu_{\max}$  (film) 3500, 2930, 1620, 1520, and 1490  $\text{cm}^{-1}$ ,  $\lambda_{\max}$  258 ( $\log \epsilon$  4.95), 282.5 (4.58), 290sh (4.43), and 313 nm (4.16),  $\tau$  1.12 (1H, s), 2.62 (2H, s), 2.92 (1H, s), 3.06 (1H, s), 4.10br (2H, disappears on shaking with  $D_2O$ ), 6.04 (6H, s), and 6.10 (3H, s),  $m/e$  300 (base peak), and 285 (Found:  $M^+$ , 300.1001.  $C_{17}H_{16}O_5$  requires  $M$ , 300.0998). Methylation gave 2,3,4,6,7-penta-methoxyphenanthrene.<sup>3</sup>

9,10-Dihydro-3,6-dihydroxy-2,4,7-trimethoxyphenanthrene [*Phenol* ( $B_2$ )].—Hydrogenation of the amorphous acetate in glacial acetic acid gave 3,6-diacetoxy-9,10-dihydro-2,4,7-trimethoxyphenanthrene as plates, m.p. 198—200° (from methanol),  $\nu_{\max}$  2930, 1755, 1610, and 1500  $\text{cm}^{-1}$ ,  $\lambda_{\max}$  284 ( $\log \epsilon$  4.37), 295sh (4.25), 306sh nm (4.06),  $\tau$  2.10 (1H, s), 3.25 (1H, s), 3.43 (1H, s), 6.20 (6H, s), 6.40 (3H, s), 7.26 (4H, s), 7.65 (3H, s), and 7.70 (3H, s),  $m/e$  386, 344, and 302 (base peak) (Found: C, 65.2; H, 5.8.  $C_{21}H_{22}O_7$  requires C, 65.3; H, 5.7%). Acidic hydrolysis gave needles of 9,10-dihydro-3,6-dihydroxy-2,4,7-trimethoxyphenanthrene, m.p. 134—135° (from light petroleum),  $\nu_{\max}$  3360, 2930, 1620, 1610, and 1510  $\text{cm}^{-1}$ ,  $\lambda_{\max}$  260 ( $\log \epsilon$  4.05), 283 (4.15), and 318 nm (4.12),  $\tau$  2.18 (1H, s), 3.36 (1H, s), 3.52 (1H, s), 4.5br (2H, disappears on shaking with  $D_2O$ ), 6.14 (6H, s), 6.31 (3H, s), and 7.33 (4H, s),  $m/e$  302 (base peak), and 287 (Found:  $M^+$ , 302.1147.  $C_{17}H_{18}O_5$  requires  $M$ , 302.1154). Methylation gave 9,10-dihydro-2,3,4,6,7-penta-methoxyphenanthrene.<sup>3</sup>

6,7-Dihydroxy-2,4-dimethoxyphenanthrene [*Phenol* (C)].—The amorphous acetate from band C, m.p. 121—136°,  $m/e$  384, 354, 342, 312, 300, and 270 (base peak), separated into two bands on t.l.c. plates. The upper band gave 6,7-diacetoxy-2,4-dimethoxyphenanthrene as prisms, m.p. 146—147° (from methanol) (lit.<sup>5</sup> 145—146°),  $\tau$  0.75 (1H, s), 2.46 (1H, s), 2.50 (2H, s), 3.22 (1H, d,  $J$  2 Hz), 3.34 (1H, d,  $J$  2 Hz), 6.00 (3H, s), 6.12 (3H, s), 7.66 (3H, s), and 7.69 (3H, s), identical (mixed m.p., i.r., and n.m.r. spectra) with an authentic specimen. Acidic hydrolysis gave 6,7-dihydroxy-2,4-dimethoxyphenanthrene as needles, m.p. 213—214° (from methanol-chloroform),  $\nu_{\max}$  3380, 2940, 1615, 1590, 1550, and 1510  $\text{cm}^{-1}$ ,  $\lambda_{\max}$  261.5 ( $\log \epsilon$  4.87), 284 (4.13), 290sh (4.01), and 307 nm (3.91),  $\tau$  ( $CD_3OD$ ) 1.10 (1H, s), 2.63 (2H, s), 2.92 (1H, s), 3.17 (1H, d,  $J$  2 Hz), 3.31 (1H, d,  $J$  2 Hz), 6.00 (3H, s), and 6.15 (3H, s),  $m/e$  270 (base peak), and 255 (Found: C, 70.8; H, 5.3.  $C_{16}H_{14}O_4$  requires C, 71.1; H, 5.2%). Methylenation with di-iodomethane and anhydrous potassium carbonate in acetone gave 2,4-dimethoxy-6,7-methylenedioxyphenanthrene as prisms, m.p. 207—208° (from methanol-chloroform) identical (mixed m.p., i.r., and n.m.r. spectra) with the synthetic product (see later).

The lower band from the t.l.c. separation of the acetates from band C gave prisms, m.p. 121—123°, identical (mixed m.p., i.r., and n.m.r. spectra) with 6,7-diacetoxy-2,3,4-trimethoxyphenanthrene.<sup>3,4</sup>

*Synthesis of 3,6-Diacetoxy-2,4,7-trimethoxyphenanthrene.*—A mixture of 4-hydroxy-3-methoxybenzaldehyde (0.35 g), 4-hydroxy-3,5-dimethoxyphenylacetic acid<sup>1</sup> (0.5 g), acetic

<sup>5</sup> H. Erdtman and A. Ronlan, *Acta Chem. Scand.*, 1969, **23**, 249.

anhydride (0.5 ml), and triethylamine (0.25 ml) was heated at 90° for 12 h. The solution was evaporated under reduced pressure leaving a gum, which after decarboxylation was irradiated in ethanol yielding 3,6-diacetoxy-2,4,7-trimethoxyphenanthrene (45 mg) as prisms, m.p. 191—193° (from methanol),  $\nu_{\max}$  2930, 1760, 1620, 1510, and 1485  $\text{cm}^{-1}$ ,  $\lambda_{\max}$  258 (log  $\epsilon$  4.91), 280 (4.27), 292 (4.18), and 301 nm (3.92),  $\tau$  1.05 (1H, s), 2.54 (2H, s), 2.84 (1H, s), 3.01 (1H, s), 6.10 (6H, s), 6.15 (3H, s), 7.59 (3H, s), and 7.64 (3H, s), *m/e* 384, 342, and 300 (base peak) (Found: C, 65.5; H, 5.2.  $\text{C}_{21}\text{H}_{20}\text{O}_7$  requires C, 65.6; H, 5.2%).

*Synthesis of 2,4-Dimethoxy-6,7-methylenedioxyphenanthrene.*—A Perkin condensation (as above) of 3,4-methylenedioxybenzaldehyde and 3,5-dimethoxyphenylacetic acid gave  $\alpha$ -(3,5-dimethoxyphenyl)-3,4-methylenedioxy-cinnamic acid as needles, m.p. 230—232° (from acetic acid-water),  $\nu_{\max}$  2930, 2600, 1680, 1600, 1515, and 1500  $\text{cm}^{-1}$ , *m/e* 328 (base peak), 284, and 283 (Found: C, 65.8; H, 4.9.  $\text{C}_{18}\text{H}_{16}\text{O}_6$  requires C, 65.85; H, 4.9%). Decarboxylation followed by irradiation in ethanol yielded

2,4-dimethoxy-6,7-methylenedioxyphenanthrene as prisms, m.p. 207—208° (from methanol-chloroform),  $\nu_{\max}$  2900, 1615, 1540, 1510, and 1475  $\text{cm}^{-1}$ ,  $\lambda_{\max}$  259 (log  $\epsilon$  4.93), 283 (4.15), 291 (4.06), and 306 nm (3.78),  $\tau$  1.05 (1H, s), 2.53 (2H, s), 2.88 (1H, s), 3.22 (1H, d, *J* 2 Hz), 3.35 (1H, d, *J* 2 Hz), 4.00 (2H, s), 5.98 (3H, s), and 6.13 (3H, s), *m/e* 282 (base peak), 267, 239, 237, 224, and 141 (Found: C, 71.4; H, 4.9.  $\text{C}_{17}\text{H}_{14}\text{O}_4$  requires C, 72.3; H, 5.0%).

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