Tetrahedron Vol. 25, pp. 4409 to 4414 Pergamon Press 1969 Printed in Great Britain

DALBERGIA SPECIES—VII[1]

THE ISOLATION AND STRUCTURE OF MELANOXIN[2] A NEW DIHYDROBENZOFURAN FROM *DALBERGIA MELANOXYLON* GUILL. AND PERR. (LEGUMINOSEAE)

B. J. DONNELLY, D. M. X. DONNELLY, A. M. O'SULLIVAN and J. P. PRENDERGAST

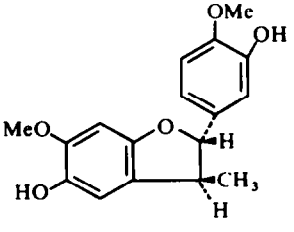
Department of Chemistry, University College, Belfield, Dublin 4, Ireland

(*Received in the UK* 8 *May* 1969; *Accepted for publication* 19 *May* 1969)

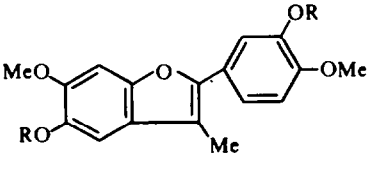
Abstract—The isolation and structure of (−)-melanoxin a new 2,3-dihydrobenzofuran is described Spectroscopic methods established structure I for melanoxin and confirmation was obtained by synthesis of O-diethyldehydromelanoxin (II, R = Et). Ozonolysis of (−)-melanoxin yielded (−)-(2*S*,3*R*)-3-methylmalic acid (III), whilst hydrogenolysis and subsequent ozonolysis gave (+)-(*R*)-methyl-succinic acid (IV). These experiments show (−)-melanoxin to have a (2*S*,3*S*)-configuration. The known (*S*)-4′-hydroxy-4-methoxydalbergione (V) melannein (VI) and 2,5-dimethoxyquinone were also isolated from *Dalbergia melanoxylon*.

EXTRACTION of the heartwood of *Dalbergia melanoxylon* Guill. and Perr. (African Blackwood, Senegal Ebony, Mozambique Ebony) (Leguminoseae) has led to the isolation of *S*-4′-hydroxy-4-methoxydalbergione (V),[3] 6-hydroxy-4-(3-hydroxy-4-methoxy-dalbergione (V),[3] 6-hydroxy-4-(3-hydroxy-4-methoxyphenyl)-7-methoxy-coumarin (melannein) (VI),[1] 2,5-dimethoxybenzoquinone[4] and a new optically active compound $C_{17}H_{18}O_5$ (I) for which the name melanoxin is suggested.

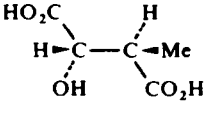
(*S*)-4′-Hydroxy-4-methoxydalbergione[3] was identified by consideration of its IR spectrum, ORD curve[5] and formation of a triacetate. The latter compound was found to be identical with an authentic specimen.



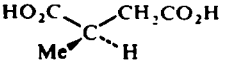
I



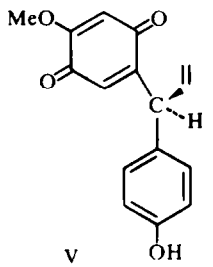
II: R = Me, Et



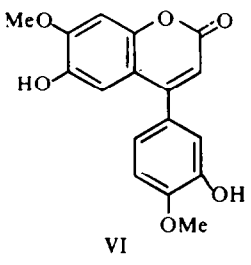
III



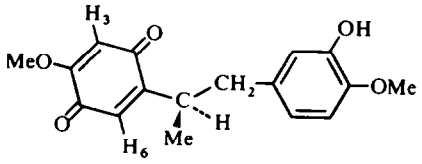
IV



V



VI



VII

Reductive acetylation of the 2,5-dimethoxybenzoquinone yielded a diacetate undepressed on admixture with an authentic sample of 2,5-dimethoxyquinol diacetate.[6] The 2,5-bisbutylaminobenzoquinone[7] derivative was also prepared. The possibility that 2,5-dimethoxybenzoquinone was an artifact arising during extraction seemed unlikely as the solvent (MeOH) was acid free. However all attempts to isolate the 2,5-dimethoxybenzoquinone from the second batch of heartwood were unsuccessful. The heartwood samples vary considerably. An independent investigator,[8] studying the petroleum ether extract of *D. melanoxylon* has found quinones to be present but not melanoxin.

The optically active compound $C_{17}H_{18}O_5$ showed strong OH absorptions in both IR and NMR spectra (ν_{max} 3378 cm^{-1}; τ 4·78 and 4·38 singlets). The assignment of the signals for the OH groups in the NMR spectrum were confirmed by D_2O exchange and were characterized by formation of a diacetate (ν_{max} 1755 cm^{-1}) and of an O-dimethyl ether.

Consideration of the PMR spectra of (−)-melanoxin and its derivatives indicated the presence of a 2,3-dihydrobenzofuran skeleton, with a Me and an aryl substituent on the heterocyclic ring. The protons of this ring when coupled with the Me group, analysed as an AMX_3 system [τ_A 4·98 (d, 1H), τ_M 6·4–6·86 (m, 1H), τ_X 8·65 (d, 3H); J_{AM} = 8·5 Hz, and J_{MX} = 7·0 Hz (>CH—CH—CH_3)]. A broad singlet at τ 3·61 was assigned to the C_7 aromatic proton *para*-related to the C-4 proton. The signal for the C_4 proton overlapped with an aromatic proton multiplet.

Unequivocal proof for the assignment of an OH at position-5 and a OMe group at position-6 was obtained by isolation of 1-(3-hydroxy-4-methoxyphenyl)-2-(4-methoxy-2,5-benzoquinonyl)propane (VII) [τ 4·1 s and τ 3·59 d (J_{6H,H_A} 0·9 Hz) for the C_3—H and C_6—H of the benzoquinonyl ring respectively] as a product of hydrogenolysis of (−)-melanoxin. This oxygenation pattern for Ring A is present in the co-occurring 6-hydroxy-4-(3-hydroxy-4-methoxyphenyl)-7-methoxycoumarin (VI) and in other naturally occurring neoflavanoids. The aromatic protons in ring B of melanoxin paralleled closely the pattern observed in the NMR spectrum of melannein.

Dehydrogenation of (−)-melanoxin with Pd–C in dry decalin gave dehydromelanoxin. The UV spectrum of dehydromelanoxin [λ_{max} 213, 287, and 325 nm (log ε 4·47, 4·54, 4·28)] supports the assignment of a 1,2-diarylpropanoid skeleton.

5,6-Dimethoxy-2-(3,4-dimethoxyphenyl)-3-methylbenzofuran was synthesized by reaction of the Na salt of 3,4-dimethoxyphenol with 1-bromo-1-(3,4-dimethoxyphenyl)prop-2-one[9] and was found to be identical with O-dimethyldehydromelanoxin. The placement of the second OH group at position 3′ was confirmed by identification of O-diethyldehydromelanoxin with 5-ethoxy-2-(3-ethoxy-4-methoxyphenyl)-6-methoxy-3-methylbenzofuran (II, R = Et).

The magnitude of the vicinal coupling of C_2 and C_3 protons does not unequivocally define the relative stereochemistry of dihydrobenzofurans,[10] however, the τ value of 8·6 for the Me protons on C_3 of (−)-melanoxin suggests a *trans*-arrangement. The C_3—Me protons in a *cis*-3-methyl-2-phenyl-2,3-dihydrobenzofuran would be shielded and register a signal at 9·2 τ.

The relative stereochemistry of (−)-melanoxin was determined by the ozonolysis of the natural product and the isolation of (−)-*erythro*-3-methylmalic acid. The di-*p*-bromophenacyl ester of (−)-*erythro*-3-methylmalic acid was compared with the diester of its antipode (+)-*erythro*-3-methylmalic acid. The racemate, (±)-*erythro*-3-methylmalic acid di-*p*-bromophenacyl ester, prepared by crystallization of equimolar quantities of (+) and (−)-enantiomers was identical with an authentic sample.[10]

Ozonolysis of (+)-1-(3-hydroxy-4-methoxyphenyl)-2-(4-methoxy-2,5-benzoquinonyl)propane (VII) and subsequent decomposition of the ozonide with H_2O_2 gave (+)-(*R*)-methylsuccinic acid (IV). Thus an (*R*)-configuration may be assigned to compound VII. The assignment of a (2*S*,3*S*) configuration for melanoxin is based on a knowledge of the absolute stereochemistry of (+)-1-(3-hydroxy-4-methoxyphenyl)-2-(4-methoxy-2,5-benzoquinonyl)propane (VII) and of a *trans* arrangement of the substituents in the 2/3 positions of the dihydrobenzofuran.

As a consequence, the absolute stereochemistry of the *erythro*-3-methylmalic acids is known. (−)-*Erythro*-3-methylmalic acid has a (2*S*,3*R*) configuration.

A second dihydrobenzofuran 2*R*,3*R*-(+)-obtusafuran has been recently isolated from the heartwood of *D. obtusa* Lecomte (sym. *D. retusa*).[12]

EXPERIMENTAL

PMR spectra were obtained with a Varian HR-60A Spectrometer in $CDCl_3$ using TMS as internal standard. The IR spectra were measured on a Grubb Parsons Spectrometer usually as KBr pellets and UV spectra were determined on a Bausch and Lomb Spectronic 505. M.ps were taken on a Kofler block and are uncorrected. Analytical and preparative TLC plates were prepared with Kieselgel G (Merck). The microanalyses were determined by Mrs. E. M. Carey of this department. Rotations were determined on a Perkin–Elmer Model 141 Polarimeter.

Extraction of Dalbergia melanoxylon Guill. et Perr. *heartwood*

Isolation of melanoxin (I), *S-4′-hydroxy-4-methoxydalbergione*[3] (V), *melannein*[2] (VI) *and* 2,5-*dimethoxybenzoquinone*.[4] Shavings of the heartwood (1·67 kg) were exhaustively extracted with ligroin and the extract, after concentration and addition of Et_2O, gave a grey amorphous solid (15 g), which on repeated crystallization from ligroin afforded hydrated melanoxin in needles, m.p. 54–74°. This material was dried at 78°/10^{-2} mm when it crystallized from ligroin in needles, m.p. 107–108°, $[\alpha]_D^{22}$ −49° (acetone). (Found: C, 67·2; H, 6·1; OMe 20·3 $C_{17}H_{18}O_5$ requires: C, 67·5; H, 6·0; OMe, 20·5%); λ_{max} (EtOH) 207 nm (log ε 4·53), 233 nm (log ε 4·08) infl., 291 nm (log ε 3·73), 3·05 nm (log ε 3·8); ν_{max} 3378 cm^{-1} (OH).

The heartwood shavings were subjected to further exhaustive extraction with EtOH and evaporation of

the solvent yielded a brown oil (490 g), which was subsequently extracted with benzene. An aliquot (10 g) of the benzene extract (350 g) in $CHCl_3$ was fractionated chromatographically using a silica gel column (500 g). Elution with $CHCl_3$ gave *S*-4′-hydroxy-4-methoxydalbergione (60 mg), m.p. 143–146° (dec); the derivative *S*-4′-acetoxy-4-methoxydalbergione quinol diacetate had a m.p. 126–127·5°. A further fraction from the column gave melannein (110 mg), which crystallized from EtOH in yellow rhombs, m.p. 220·5–222°; the derivative O-dimethylmelannein had a m.p. 220–221°.

A second batch of heartwood shavings (1·8 kg) previously extracted with ligroin, was exhaustively extracted with MeOH (Merck). Evaporation of the solvent afforded an oil (520 g), which was re-extracted with benzene. Addition of Et_2O to the residual oil (91 g; from C_6H_6 extract) caused precipitation of a brown solid (fraction I). Concentration of the filtrate gave two further solids (fractions II and III) and total evaporation of the Et_2O filtrate afforded an oil (fraction IV).

Fraction I. Crystallized from EtOAc in yellow leaflets of 2,5-dimethoxybenzoquinone (530 mg), m.p. 298° (dec); ν_{max} ($CHCl_3$) 1667 cm^{-1} (CO). NMR spectrum ($CHCl_3$ + TFA) τ 6·05 singlet (2 × OMe); τ 3·9 singlet (2 × —CO—C<u>H</u>=C—); the derivatives 2,5-dimethoxyquinol diacetate had m.p. 183–184°[6] and 2,5-bisbutylamino-p-benzoquinone had m.p. 162–163°.[7] *Fraction II.* Crystallized from ligroin in needles of melanoxin hydrate. *Fractions III and IV.* These yielded melannein (120 mg), m.p. 220·5–222°.

Dehydromelanoxin. Pd-C (10%; 20 mg) was added to a soln of (−)-melanoxin (250 mg) in dry decalin (5 ml) and the mixture refluxed for 6 hr. Chloroform was then added. Evaporation of the filtrate gave a brown oil which was purified by preparative TLC (silica gel HF) 6 times developed with $C_6H_6/CHCl_3$ (1 : 1). Elution with $CHCl_3$ of the blue fluorescent spot silica gel gave a solid (10 mg) which crystallized from EtOH in pale yellow needles, m.p. 171–172°. λ_{max} (MeOH) 213, 287 and 325 nm (log ε 4·47, 4·04, 4·28); PMR spectrum τ 7·6 singlet (C<u>H</u>$_3$); τ 6·1 singlet (2 × OMe); τ 4·78 and 4·35 singlets (2 × O<u>H</u>).

O-*Diacetylmelanoxin.* A mixture of melanoxin (100 mg), anhyd pyridine (1 ml) and Ac_2O (2 ml) was kept at room temp for 12 hr. Dilution of the mixture with ice-water (50 ml) gave O-*diacetylmelanoxin* which crystallized from EtOH in needles (60 mg), m.p. 111–113°, $[\alpha]_D^{22°}$ −15·5° (acetone). (Found: C, 65·4; H, 5·7. $C_{21}H_{22}O_7$ requires: C, 65·4; H, 5·7%); ν_{max} 1755 cm^{-1} (CO); λ_{max} (MeOH) 210 nm (log ε 4·24), 225 nm (log ε 4·14), 2·93 nm (log ε 3·71); PMR spectrum; τ_A 4·89, d (1H), τ_M 6·39–6·87, m (1H) τ_X 8·64, d (3H), AMX_3 system, J_{AM} 8·5 Hz, J_{MX} 7·0 Hz [$\rangle$CH—CH—Me]; τ 6·12 and 6·14, s's (2 × OMe); τ 7·12, s (2 × O·CO·Me); τ 3·45, s (C_7-proton); τ 3·17–2·75, m (4 × aromatic protons).

O-*Dimethylmelanoxin.* A mixture of melanoxin (200 mg), Me_2SO_4 (0·3 ml), anhyd K_2CO_3 (2 g) and dry acetone (10 ml) was refluxed for 48 hr. The K salts were removed and washed with hot acetone. Evaporation of the combined filtrate gave a residue which was taken up in Et_2O, washed with 10% NaOH aq, water and dried. Evaporation of the ethereal soln afforded O-*dimethylmelanoxin* which crystallized from EtOH as plates, m.p. 74–75°; $[\alpha]_D^{22°}$ +41° (acetone). (Found: C, 69·1; H, 6·7. $C_{19}H_{22}O_5$ requires: C, 69·1; H, 6·6%); PMR spectrum: τ_A 4·89, d (1H), τ_M 6·29–6·84, m (1H); τ_X 8·6, d (3H), AMX_3 system J_{AM} 9·0 Hz, J_{MX} 7·0 Hz. [$\rangle$CH—CH—Me]; τ 6·12, and 6·1, s (4 × OMe); τ 3·43, s (C_7-proton); τ 3·22–2·8, m (4 × aromatic).

O-*Dimethyldehydromelanoxin* (II R = Me). Pd–C (10%; 10 mg) was added to a soln of O-dimethylmelanoxin (160 mg) in dry decalin (5 ml) and the mixture was refluxed for 24 hr. Chloroform was then added. Evaporation of the filtrate gave a solid which crystallized from EtOH in needles of O-*dimethyldehydromelanoxin* (50 mg), m.p. 148–149°. (Found: C, 69·6; H, 6·1; OMe, 38·4. $C_{19}H_{20}O_5$ requires: C, 69·5; H, 6·1; OMe, 37·8%); λ_{max} (MeOH) 286 nm (log ε 4·18), 3·24 nm (log ε 4·49); PMR spectrum τ 7·6, s (C<u>H</u>$_3$); τ 6·08, s (4 × OMe); τ 3·16–2·57, m (aromatic).

O-*Diethyldehydromelanoxin* (II R = Et). Ethylation (Et_2SO_4-anhyd K_2CO_3–acetone method) of (−)-melanoxin afforded O-diethylmelanoxin which was crystallized from EtOH in plates, m.p. 74·5–76·5°. Dehydrogenation (method as for O-dimethylmelanoxin above) of the foregoing ether gave the *dehydro derivative* which crystallized from EtOH as plates, m.p. 136·5–138·5°. (Found: C, 70·7; H, 7·1. $C_{21}H_{24}O_5$ requires: C, 70·8; H, 6·8%); λ_{max} (MeOH) 221 nm (log ε 4·3), 285 nm (log ε 4·17), 324 nm (log ε 4·5).

1-*Bromo*-1-(3,4-*dimethoxyphenyl*)*propan*-2-*one.* Bromine (8·1 g) was added dropwise during 90 min to a stirred soln of 1-(3,4-dimethoxyphenyl)propan-2-one[12] (9 g) and benzoyl peroxide (0·1 g) in $CHCl_3$ (100 ml) at < 10°. The reaction mixture was stirred at 22° for 2 hr. The $CHCl_3$ soln was washed with 10% $NaHCO_3$ aq, water and dried (Na_2SO_4). Evaporation gave a brown oil which gradually solidified on trituration with light petroleum (b.p. 40–60°). Fractional crystallization from light petroleum (b.p. 40–60°)-Et_2O afforded two compounds (a) 1-bromo-1-(3,4-dimethoxyphenyl)propan-2-one[9] (2·1 g) as plates, m.p. 82–84°, and (b) 1-(2-*bromo*-4,5-*dimethoxyphenyl*)-3-*bromopropan*-2-*one* (3 g) as needles, m.p. 107–108°. (Found: C, 37·5;

H, 3·6; OMe 17·8; Br, 45·5. $C_{11}H_{12}Br_2O_3$ requires: C, 37·5; H, 3·4; OMe, 17·6; Br, 45·4%); ν_{max} 1718 cm^{-1} (CO); PMR spectrum, τ 6·17, s (2 × OMe); τ 6·05 and 6·02, s's (—C<u>H</u>$_2$—CO·C<u>H</u>$_2$Br); τ 3·25, s (C_6-aromatic proton); τ 2·96, s (C_3-aromatic proton).

5,6-Dimethoxy-2-(3,4-dimethoxyphenyl)-3-methylbenzofuran (II, R = Me). A mixture of 3,4-dimethoxyphenol (1·08 g), dry THF (50 ml) and Na (161 mg) was stirred and refluxed for 12 hr. At 0° 1-bromo-1-(3,4-dimethoxyphenyl)propan-2-one (1·82 g) in dry THF (50 ml) was added slowly and the reaction mixture was refluxed for 3·5 hr. The NaBr was removed and washed with Et_2O. The combined filtrates were washed with 10% NaOH aq, water and dried ($MgSO_4$). The oil obtained on evaporation of the solvent was treated with conc H_2SO_4 (0·175 ml) at 0° for 15 min and poured onto ice. The aqueous mixture was extracted with Et_2O, which in turn was washed with 10% NaOH aq, water and dried. Evaporation and crystallization from EtOH afforded a mixture which was resolved by preparative TLC with $CHCl_3$–C_6H_6 (1:1) as solvent. The 5,6-dimethoxy-2-(3,4-dimethoxyphenyl)-3-methylbenzofuran, obtained by evaporation of the eluant, crystallized from EtOH as needles, m.p. 148–149°, mixed m.p. with natural O-dimethyldehydromelanoxin 148–149°.

1-Bromo-1-(3-ethoxy-4-methoxyphenyl)propan-2-one. Bromination (method as for 1-bromo-1-(3,4-dimethoxyphenyl)propan-2-one above) of 1-(3-ethoxy-4-methoxyphenyl)propan-2-one[13] gave a mixture of two compounds. Fractional crystallization from light petroleum (b.p. 40–60°)–Et_2O afforded (a) *1-bromo-1-(3-ethoxy-4-methoxyphenyl)propan-2-one* (30%) as needles, m.p. 84–85°. (Found: C, 50·2; H, 5·4; Br, 27·9 $C_{12}H_{15}O_3Br$ requires: C, 50·2; H, 5·3; Br, 27·9%); ν_{max} 1724 cm^{-1} (CO); PMR spectrum τ 7·69, s (CH_3); τ 8·53, t and 5·87 q (J = 7·0 Hz) (OEt); τ 6·1, s (OMe); τ 4·6, s (—C<u>H</u>Br); 3·29–2·89, m (3 aromatic protons); (b) *1-(2-Bromo-5-ethoxy-4-methoxyphenyl)-3-bromopropan-2-one* (10%) as needles m.p. 114–115°. (Found: C, 39·8; H, 3·8; Br, 43·9. $C_{12}H_{14}O_3Br_2$ requires: C, 39·3; H, 3·9; Br, 43·7%). ν_{max} 1720 cm^{-1} (CO); PMR spectrum τ 8·55, t, τ 5·91, q (J = 7·0 Hz) (OEt); τ 6·12, s (OMe); τ 6·01 and 5·97, s's (C<u>H</u>$_2$·CO·C<u>H</u>$_2$Br); τ 2·94, s (C_3-aromatic proton); τ 3·21, s (C_6 aromatic proton).

5-Ethoxy-2-(3-ethoxy-4-methoxyphenyl)-6-methoxy-3-methylbenzofuran (II R = Et). Condensation [method as for II (R = Me) above] of the Na salt of 4-ethoxy-3-methoxyphenol and 1-bromo-1-(3-ethoxy-4-methoxyphenyl)propan-2-one gave 5-ethoxy-2-(3-ethoxy-4-methoxyphenyl)-6-methoxy-3-methylbenzofuran which was crystallized from EtOH as laths, m.p. 139·5–140·5°, mixed m.p. with natural O-diethyldehydromelanoxin (II R = Et) showed no depression.

Ozonolysis of melanoxin. Melanoxin (500 mg) in HOAc (30 ml) was treated with ozone at room temp for 10 hr. The ozonide was decomposed with H_2O_2 (1 ml; 30%). After 12 hr Pd–C was added and the mixture heated gently and then filtered. The residue, obtained by evaporation of the filtrate, was dissolved in water and $NaHCO_3$ was added. Continuous Et_2O extraction (24 hr) removed the neutral components. The aqueous phase was adjusted to pH 3·6, saturated with NaCl and an acidic component was removed on prolonged ether extraction. The 3-methylmalic acid obtained by evaporation of the dried ethereal soln, was dissolved in water and titrated with 10% NaOH aq (phenolphthalein). *p*-Bromophenacyl bromide (425 mg) in aqueous EtOH was added to the salt (147 mg) and the mixture was refluxed for 2 hr. The (−)-erythro-3-*methylmalic acid di-p-bromophenacyl ester* was crystallized from EtOH in plates (25 mg), m.p. 203–203·5° $[\alpha]_D^{22°}$ −8·1° (DMSO). (+)-*Erythro*-3-methylmalic acid[11] (20 mg) was converted to its di-*p*-bromophenacyl ester (method as for the (−)-*erythro*-3-methylmalic acid above). The *diester* crystallized from EtOH in plates (40 mg), m.p. 202–203° $[\alpha]_D^{22°}$ +7·9° (DMSO). Crystallization from EtOH with an equimolecular quantity of (−)-erythro-3-*methylmalic acid di-p-bromophenacyl ester* gave a racemate 186°; mixed m.p. with an authentic sample of the racemate showed no depression.

Hydrogenolysis of melanoxin. Melanoxin (350 mg) in AcOH (10 ml) was hydrogenated at room temp and atm press with a 10% Pd/C catalyst (800 mg) during 5 hr. The soln yielded the quinol, which was easily oxidized when oxygen was bubbled through a CH_2Cl_2 soln of the quinol in contact with saturated K_2CO_3 aq. The yellow CH_2Cl_2 soln. yielded (R)-1-(3-*hydroxy-4-methoxyphenyl*)-2-(4-*methoxy*-2,5-*benzoquinonyl*)-*propane* (VII), which crystallized from Et_2O–MeOH as needles m.p. 158–158·5; $[\alpha]_D^{22}$ + 39·1 ($CHCl_3$). (Found: C, 67·2; H, 6·1: $C_{17}H_{18}O_5$ requires: C, 67·2; H, 6·0%); PMR spectrum τ 8·92, d, J = 6·5 Hz (—C<u>H</u>$_3$); τ 6·5–7·75, m (CH_3—C<u>H</u>—C<u>H</u>$_2$—); τ 6·19 and 6·15, s's (2 × OMe); τ 4·41, s (OH); τ 4·1, s (C_3—H of quinone); τ 3·59, d, J = 0·9 Hz, (C_6-proton of quinone ring).

1-(3-Acetoxy-4-methoxyphenyl)-2-(2,5-diacetoxy-4-methoxyphenyl)propane. A $CHCl_3$ soln of (*R*)-1-(3-hydroxy-4-methoxyphenyl)-2-(4-methoxy-2,5-benzoquinonyl)propane (40 mg) was reduced with aqueous sodium dithionite (5%, 10 ml) and the $CHCl_3$ layer added quickly to a mixture of Ac_2O (3 ml) and pyridine (3 ml). The $CHCl_3$ was then removed under N_2 and after 12 hr at room temp, water (20 ml) was added;

extraction with Et_2O yielded a solid (35 mg) and crystallization from di-isopropyl ether gave the *quinol triacetate* as plates, m.p. 148–149·5°, $[\alpha]_D^{22}$ −19·7° ($CHCl_3$). (Found: C, 64·6; H, 6·2. $C_{23}H_{26}O_7$ requires: C, 64·2; H, 6·1%).

(−)-*Methyisuccinic acid di-p-bromophenacyl ester.* Compound VII was treated with O_3 in AcOH at room temp for 10 hr. The method of decomposition of the ozonides, isolation of the (+)-(*R*)-methylsuccinic acid and derivative formation was similar to that described for 3-methylmalic acid above. (−)-(*R*)-Methylsuccinic acid di-p-bromophenacyl ester crystallized for MeOH in needles, m.p. 131–133° $[\alpha]_D^{22}$ −24·7° ($CHCl_3$). (Found: C, 46·9; H, 3·4. $C_{21}H_{18}O_6Br_2$ requires: C, 46·4; H, 3·4%). An authentic sample of (+)-(*R*)-methylsuccinic acid $[\alpha]_D^{22}$ +13·5° (H_2O) was prepared by resolution of (±)-methylsuccinic acid with strychnine.[14]

Acknowledgement—The authors thank Professor E. M. Philbin for her constant interest, the Director, An Foras Taluntais, for the award of a research scholarship (to A.M. O'S.); the Minister of Education, Republic of Ireland, for award of a maintenance grant (to J.P.P.). They are indebted to Dr. R. Laidlaw, Forest Products Research Laboratory, Princes Risborough, for a gift of *Dalbergia melanoxylon*; Professor Yoshiharu Izumi for the sample of (+)-erythro-3-methylmalic acid and Dr. Gunhild Aulin-Erdtman for samples of the *p*-bromophenacyl esters of racemic *erythro-* and *threo*-3-methylmalic acids; Professor Klyne and Dr. P. M. Scopes for the ORD curves; Professor D. Ollis for a sample of (*S*)-4′-hydroxy-4-methoxydalbergione.

REFERENCES

[1] For part VI, see B. J. Donnelly, D. M. X. Donnelly and A. M. O'Sullivan, *Tetrahedron* **24**, 2617 (1968).
[2] B. J. Donnelly, D. M. X. Donnelly, A. M. O'Sullivan and J. P. Prendergast, *Lecture at 5th International Symposium on The Chemistry of Natural Products.* London, July (1968).
[3] W. B. Eyton, W. D. Ollis, I. O. Sutherland, L. M. Jackman, O. R. Gottlieb and M. Taveira Magalhaes, *Proc. Chem. Soc.* 301 (1962).
[4] J. D. Bu'Lock, *J. Chem. Soc.* 575 (1955).
[5] D. M. X. Donnelly, B. J. Nangle, P. B. Hulbert, W. Klyne and R. J. Swan, *Ibid.* (C) 2450 (1967).
[6] H. Davidge, A. G. Davies, J. Kenyon and R. F. Mason, *Ibid.* 4569 (1958).
[7] D. Buckley, H. B. Henbest and P. Slade, *Ibid.* 4891 (1957).
[8] Björn M. Hausen, pers. comm.
[9] A. M. Eastham, H. E. Fisher, M. Kulka and H. Hibbert, *J. Am. Chem. Soc.* **66**, 26 (1944).
[10] G. Aulin-Erdtman, Y. Tomita and S. Forsén, *Acta Chem. Scand.* **17**, 535 (1963); C. H. Ludwig, B. J. Nist and J. L. McCarthy, *J. Am. Chem. Soc.* **86**, 1186 (1964); C. A. Anirudhan, D. W. Mathieson, and W. B. Whalley, *J. Chem. Soc.* (C), 634 (1966); L. H. Zalkow and M. Ghosal, *Chem. Comm.* 922 (1967); E. C. Hayward, D. S. Tarbell, and L. D. Colebrook, *J. Org. Chem.* **33**, 399 (1968).
[11] S. Tatsumi, M. Imaida and Y. Izumi, *Bull. Chem. Soc. Japan* **39**, 1818 (1966).
[12] M. Gregson, W. D. Ollis, B. T. Redman and I. O. Sutherland, *Chem. Comm.* 1394 (1968).
[13] I. A. Pearl and D. L. Beyer, *J. Org. Chem.* **16**, 223 (1951).
[14] Ladenberg, *Ber. Dtsch. Chem. Ges.* **28**, 1170 (1895).