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PIGMENTS OF *GNOMONIA ERYTHROSTOMA*—IV[1]

THE SYNTHESIS OF 5,8-DIBENZYLOXY-3-HYDROXY-6-METHOXY-1,4-NAPHTHOQUINONE

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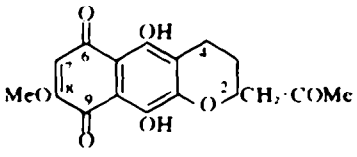
Abstract—The synthesis of the title compound (29), and some limitations of the benzyl group for the protection of phenolic hydroxy-groups, are reported.

The structure of deoxyerythrostominone (1) has been established[1,2] and the methyl ether (2) of its deoxy-derivative (3) has been synthesised from 5 - chloro - 7 - oxo - octanoyl chloride and methyl 3,5-dimethoxyphenylacetate.[1] The dibenzyloxy-ester (4) appeared to be suitable for use in the synthesis of deoxyerythrostominone, since benzyl ethers have been reported[3] to be stable to organometallic reagents, to basic conditions, and to oxidations in weak acid. However, during the synthesis of the ester (4) important limitations of the benzyl protecting group were discovered and are outlined below.

2,5 - Dihydroxy - 3 - methoxybromobenzene, prepared in 84% yield from bromovanillin[4] by a modification of the method of Dorn *et al.*[4] was converted into its dibenzyl ether (5). To introduce the acetic acid side-chain, the bromo-ether (5) was treated with ethyl lithium to form the aryl lithium reagent (cf. Ref. 5) which was then reacted with ethylene oxide. The required alcohol (6) was obtained, but only in low yield. The major product was an ether and its NMR spectrum showed that it possessed three aromatic protons in a 1,2,4-substitution pattern [τ 3.73 (1H, dd, J 8.5 and 2.5 Hz, 5-H), 3.43 (1H, d, J 2.5 Hz, 3-H), and 3.37 (1H, d, J 8.5 Hz, 6-H)], that one of the benzylic methylenes was still present (τ 5.06), but that the other had lost a proton and now gave rise to a triplet (τ 5.1, J 6.5 Hz). The spectrum also revealed the presence of an Et group [τ 9.03 (3H, t, J 6.5 Hz) and 8.04 (2H, m)] and gave no indication that the compound was a mixture. The ether has therefore been assigned structure (18) or (21). In a similar reaction the bromo-ether (5) was treated with ethyl lithium followed by formaldehyde. The alcohol (7) was obtained, but only in poor yield and the major product was again the ether (18 or 21). A third product from this reaction was shown by its NMR spectrum (Experimental) to be the oily alcohol (19 or 22) in which one of the benzyl groups had been ethylated. This alcohol was characterised as its chloride (20 or 23) and appeared to be a single compound. Aryl lithium compounds can exchange[6] their metal atoms for hydrogens by either intra- or inter-molecular processes. An intramolecular interchange would be expected to take place via a cyclic



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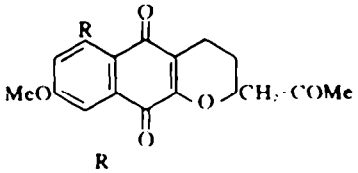
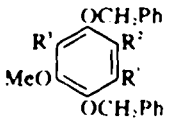
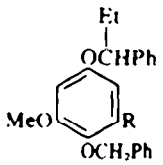


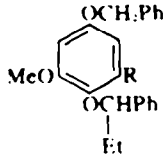
2: OMe
3: OH



	R'	R²	R'
4	CH_2CO_2Me	H	H
5	Br	H	H
6	CH_2CH_2OH	H	H
7	CH_2OH	H	H
8	Li	H	H
9	$CH_2O{\cdot}COH$	H	H
10	Br	$PhCH_2$	H
11	Br	H	$PhCH_2$
12	CH_2OH	$PHCH_2$	H
13	CH_2OH	H	$PhCH_2$
14	CH_2Cl	H	H
26	CH_2CN	H	H
15	CH_2CO_2H	H	H
17	CH_2CO_2Me	COMe	H



	R
18	H
19	CH_2OH
20	CH_2Cl



	R
21	H
22	CH_2OH
23	CH_2Cl

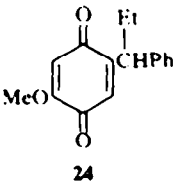
transition state[7] involving the lithium atom and the *o*-benzyloxy group and would therefore account for the apparent selectivity of the alkylation, i.e. the ether would have structure **21**. However such a mechanism does not explain the formation of the ethylated alcohol (**19** or **22**), which presumably arises by reaction of the aryl lithium (**8**) with formaldehyde. In this case metalation of the benzyl group probably occurs either directly with ethyl lithium or intermolecularly with a second molecule of the aryl lithium (**8**), and the structure of the product is less predictable. In agreement with structure (**28** or **21**) for the ether, it gave dihydro - 4 - methoxydalbergione (**24**)[8] on treatment with trifluoroacetic acid.

As a result of the poor yields obtained with the aryl lithium (**8**), the bromo-ether (**5**) was converted into its Grignard derivative and treated with formaldehyde. The yield of the required alcohol (**7**) was poor using ether as solvent, but was greatly improved in tetrahydrofuran. A major by-product was readily identified as the formate (**9**) [ν_{max} 1722 cm^{-1}; τ 1.96 (1H, s)] and on alkaline hydrolysis it afforded the alcohol (**7**). Two minor products were isolated, the less polar had the formula, $C_{28}H_{25}BrO_5$, indicating that metal–halogen interchange had not occurred, and it showed no CO or OH bands in its IR spectrum. However, its NMR spectrum, which contained the expected benzyloxy and methyl signals, showed only one aromatic proton (τ 3.42, s) and revealed the presence of a third benzyl group directly attached to the ring of the bromobenzene (τ 5.77, 2H, s, $ArCH_2Ph$). Hence this product must have structure **10** or **11**, and the former is preferred because OMe groups are known[9] to direct condensations preferentially to the *p*-position. Furthermore the fact that the bromine had not been displaced during the reaction is consistent with steric hindrance to the formation of the Grignard reagent, as expected for structure **10** but not **11**.

The NMR spectrum of the other minor product, $C_{29}H_{28}O_4$, showed that it also contained a third benzyl group and an extra 2-proton singlet at τ 5.48 which was assigned to the methylene group of a benzyl alcohol. The presence of the OH group was confirmed by its IR spectrum (ν_{max} 3590 cm^{-1}) and the alcohol therefore has structure **12** or **13**. The presence of the third benzyl group in these two minor products indicates that a small amount of benzyl group migration takes place during the Grignard reaction.

The benzyl alcohol (**7**) was converted into the required methyl phenylacetate (**4**) by the standard sequence **14** → **15** → **16** → **4**. The benzyl groups were readily removed from **4** and **16** by hydrogenolysis.

An attempt to oxidise the alcohol (**6**) to the corresponding acid (**16**) with Jones reagent gave benzoic acid as the only identifiable product and suggested that the protecting groups were lost very easily. Moreover it is known[10] that benzyl ethers can cleave under Friedel Crafts conditions. However, in a model reaction acetylation of the ester (**4**) with acetic anhydride, using perchloric acid as the catalyst,[1,11] gave the expected product (**17**) [IR and NMR spectra (Experimental)] together with some benzyl acetate. Two minor products were also isolated. The first was shown to be both an aryl acetate and an aryl ketone (ν_{max} 1770 and 1670 cm^{-1}), whilst its NMR spectrum showed signals corresponding to only one benzyl group and was consistent with either structure **25** or **26**. The former was preferred since the chemical shift (τ 6.34) of the methylene group in the ester side-chain occurred at higher field than that (τ 6.20) in the ester (**17**), thus suggesting a change in its environment. The IR spectrum of the other minor product indicated the presence of aryl acetate and aliphatic ester CO groups (ν_{max} 1765 and 1740 cm^{-1}) and the absence of a keto group. Its NMR spectrum (Experimental) showed that of the two benzyl groups, one was directly attached to the aromatic ring. Hence the compound has either structure **27** or **28**. The structure of the keto-ester (**17**) was confirmed by cyclisation and aerial oxidation in ethanolic base,[1,11] which gave the dibenzyloxy-quinone (**29**), together with a small amount of another quinone, $C_{20}H_{16}O_6$. The NMR spectrum of the latter showed that it contained an OEt group [τ 8.54 (3H, t) and 6.19 (2H, q)], and only one benzyl group, and that it was probably a mixture of the isomers (**30** and **31**).



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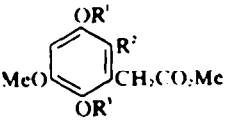
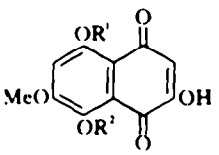


	R'	R²	R³
25	$PhCH_2$	COMe	COMe
26	COMe	COMe	$PhCH_2$
27	$PhCH_2$	$PhCH_2$	COMe
28	COMe	$PhCH_2$	$PhCH_2$



	R'	R²
29	$PhCH_2$	$PhCH_2$
30	Et	$PhCH_2$
31	$PhCH_2$	Et

EXPERIMENTAL

Details of chromatographic materials and conditions used for the determination of physical data, etc. have been reported.[1,2]

2,5 - *Dihydroxy* - 3 - *methoxybromobenzene*. A modification of the method of Dorn, *et al.*[4] was used. 5-Bromovanillin[4] (46 g) was suspended in 1N KOH (200 ml) under N_2 and 5% H_2O_2 (150 ml) was added dropwise with stirring whilst the temp. was kept below 40°. When the addition was complete, stirring was continued for 20 hr at room temp. 2,5 - Dihydroxy - 3 - methoxybromobenzene (37.4 g) was collected by filtration and was used without purification in the next reaction. Crystallisation from benzene gave needles, m.p. 138–140° (lit.,[4] 141°).

2,5 - *Dibenzoyloxy* - 3 - *methoxybromobenzene* (**5**). The above hydroquinone (20 g), benzyl chloride (28 g), and freshly powdered K_2CO_3 (20 g) were added to dry MeOH (75 ml) and the mixture was refluxed for 16 hr under N_2. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (45 × 6 cm). Elution with light petroleum–EtOAc (99:4) gave 2,5 - *dibenzyloxy* - 3 - *methoxybromobenzene* (**5**) which crystallised from EtOAc–light petroleum as white needles (20.4 g), m.p. 65–66° (Found: C, 62.85; H, 4.7; Br, 19.8. $C_{21}H_{19}BrO_3$ requires: C, 63.2; H, 4.8; Br, 20.05%), ν_{max} 1600 and 1570 cm^{-1}; τ 6.21 (3H, s, 3-OMe), 5.05 (2H, s, OCH_2Ph), 5.01 (2H, s, OCH_2Ph), 3.48 (1H, d, *J* 2.5 Hz, 4- or 6-H), 3.26 (1H, d, *J* 2.5 Hz, 6- or 4-H) and 2.61 (10H, m, 2 X $C_6H_5CH_2$).

2 - (2',5' - *Dibenzyloxy* - 3' - *methoxy*) - *phenylethanol* (**6**). The bromobenzene **5** (6.4 g), in dry ether (10 ml), was added to an EtLi soln [prepared from EtBr (2.94 g) and Li wire (380 mg) in dry ether at −30°] and the temp was reduced to −50°. Liquid ethylene oxide (0.7 ml) was then added quickly and the temp. was allowed to rise

to room temp. during 1 hr. Water (30 ml) was poured onto the mixture and the product was recovered in ether and was chromatographed on silica gel (40 × 4 cm). Elution with light petroleum–EtOAc (19:1) gave **18** or **21** which crystallised from EtOAc–light petroleum as rods, m.p. 56–57° (Found: C, 79.15; H, 6.9. $C_{23}H_{24}O_4$ requires: C, 79.3; H, 6.9%).

Further elution with light petroleum–EtOAc (4:1) gave 2 - (2',5' - *dibenzyloxy* - 3' - *methoxy*) - *phenylethanol* (**6**) as an oil (Found: *m/e* 364.1670. $C_{23}H_{24}O_4$ requires: *M*, 364.1675), ν_{max} 3400 and 1605 cm^{-1}; τ 7.19 (2H, t, *J* 6.5 Hz, $ArCH_2$), 6.2 (2H, t, *J* 6.5 Hz, CH_2OH), 6.12 (3H, s, OMe), 4.97 (2H, s, $PhCH_2O$), 4.91 (2H, s, $PhCH_2O$), 3.49 (1H, d, *J* 2.5 Hz, 4- or 5-H), 3.37 (1H, d, J 2.5 Hz, 5- or 4-H), and 2.48 (10H, m, 2 X $C_6H_5CH_2$).

Oxidation of **6** with an excess of Jones reagent for 30 min at room temp. gave benzoic acid as the only identifiable product.

Preparation of 2,5 - *dibenzyloxy* - 3 - *methoxybenzyl alcohol* (**7**) *from* 2,5 - *dibenzyloxy* - 3 - *methoxybromobenzene*

(a) via *The aryllithium derivative*. Paraformaldehyde (3 g) was heated to 200° and the formaldehyde vapour was passed in a stream of dry O_2-free N_2 over a vigorously stirred mixture of the bromobenzene (25.6 g) and EtLi [from EtBr (12 g) and Li wire (1.52 g)] in ether (100 ml) at −30° during 45 min. The mixture was allowed to reach room temp. and was filtered. Ice (10 g) and NH_4Cl (3.5 g) were then added and the product was recovered in ether and chromatographed on silica gel (50 × 7 cm). Elution with EtOAc–light petroleum (1:19) gave **18** or **21** which crystallised from EtOAc–light petroleum (8.7 g), m.p. 56–57° identical (TLC, UV and NMR spectra) with the sample prepared above.

Further elution with EtOAc–light petroleum (1:4) afforded 2,5 - *dibenzyloxy* - 3 - *methoxybenzyl alcohol* (**7**) which crystallised from light petroleum as needles (1.7 g), m.p. 78–79° (Found: C, 75.8; H, 6.3. $C_{23}H_{24}O_4$ requires: C, 75.4; H, 6.3%), ν_{max} 3500 and 1600 cm^{-1}; τ 6.18 (3H, s, 3-OMe), 5.53 (2H, s, $ArCH_2OH$), 5.03 (2H, s, OCH_2Ph), 5.01 (2H, s, OCH_2Ph), 3.48 (2H, s, 4- and 6-H) and 2.63 (10H, m, 2 X $C_6H_5CH_2$).

The mother liquors from the alcohol were chromatographed on silica gel (30 × 2.5 cm). Elution with EtOAc–light petroleum (3:17) afforded first the benzyl alcohol (0.5 g) and then an oil (3.4 g), shown by its NMR spectrum to be either **19** or **22**. τ 9.05 (3H, t, *J* 7.5 Hz, CH_3CH_2), 8.14 (2H, m, $MeCH_2CH$), 6.23 (3H, s, OMe), 5.59 (2H, s, $ArCH_2OH$), 5.06 (2H, s, $PhCH_2O$), 5.03 (1H, t, *J* 6.5 Hz, $EtCHPh$), 3.61 (1H, d, *J* 3.0 Hz, 4- or 5-H), 3.53 (1H, d, *J* 3.0 Hz, 5- or 4-H) and 2.64 (10H, m, 2 X $C_6H_5CH_2$).

(b) via *The Grignard reagent in ether*. The bromobenzene (4.0 g) and EtBr (2.2 g) in ether were added dropwise to Mg (0.85 g) in ether (5 ml). The mixture was refluxed for 1 hr, cooled and decanted from the excess of Mg. Formaldehyde was passed over the stirred mixture, as in (a) and the latter was then treated with a sat NH_4Cl aq (50 ml). The product was recovered in ether and chromatographed on silica gel (30 × 3 cm). Elution with EtOAc–light petroleum (1:24) gave starting material (1.13 g). Elution with EtOAc–light petroleum (3:17) afforded crystals (420 mg), m.p. 78–79°, of **7**, identical (TLC, IR, and NMR spectra) with the sample prepared in (a).

(c) via *The Grignard reagent in tetrahydrofuran*. EtBr (2.2 g) and the bromobenzene (4.0 g) in THF (15 ml) were added dropwise with stirring to Mg (0.85 g) in THF (10 ml). The mixture was refluxed for 30 min, cooled, and treated with formaldehyde in the usual manner. The product was isolated as in (b) and chromatographed on silica gel (40 × 4 cm). Elution with EtOAc–light petroleum (7:93) afforded 2,5 - *dibenzyloxy* - 3 - *methoxybenzyl formate* (**9**) as an oil (Found: C, 73.5; H, 6.0. $C_{24}H_{24}O_5$ requires: C, 73.0; H, 5.9%), ν_{max} 1723 and 1605 cm^{-1}; τ 6.17 (3H, s, 3-OMe), 5.01 (2H, s, OCH_2Ph), 5.00 (2H, s, OCH_2Ph), 4.88 (2H, s, $HCOOCH_2Ar$), 3.48 (1H, d, *J* 2.5 Hz, 4- or 6-H), 3.41 (1H, d, *J* 2.5 Hz, 6- or 4-H), 2.62 (10H, m, 2 X $C_6H_5CH_2$) and 1.96 (1H, s, HCO_2R).

Further elution with EtOAc–light petroleum (3:17) gave **7** (1.61 g), m.p. 78–79°.

Hydrolysis of crude fractions containing 2,5 - dibenzyloxyanisole and the formate (NMR spectrum) with 25% KOH soln under reflux for 1 hr gave 2,5-*dibenzyloxyanisole* which crystallised from EtOAc–light petroleum as needles (40 mg), m.p. 72–73° (Found: C, 78.8; H, 6.35. $C_{21}H_{20}O_3$ requires: C, 78.7; H, 6.3%), and the benzyl alcohol **7** (240 mg).

During repetitions of the above reaction on a large scale the crude product was refluxed in 25% KOH soln for 5 hr before being chromatographed on silica gel. In this way yields of 75% were recorded for **7**.

The large scale preparation also produced two minor products. The first was eluted with EtOAc–light petroleum (1:9) and it is believed to be 6 - *benzyl* - 2,5 - *dibenzyloxy* - 3 - *methoxybromobenzene* (**10**) which crystallised from ether as rhombs, m.p. 129–130° (Found: C, 68.9; H, 5.2; Br, 16.6. $C_{28}H_{25}BrO_3$ requires: C, 68.7; H, 5.1; Br, 16.4%), τ 6.20 (3H, s, OMe), 5.77 (2H, s, $ArCH_2Ph$), 5.0 (4H, s, 2 X OCH_2Ph), 3.42 (1H, s, 4-H), 2.79 (5H, s, $C_6H_5CH_2$), 2.70 (5H, s, $C_6H_5CH_2$), and 2.58 (5H, m, $C_6H_5CH_2$).

The second compound was eluted with EtOAc–light petroleum (3:17) and crystallised from chloroform–light petroleum as rhombs, m.p. 96–98°, of **12** or its 4-benzyl isomer **13** (Found: C, 79.1; H, 6.4% *m/e* 440.1984. $C_{30}H_{28}O_4$ requires: C, 79.1; H, 6.4%; *M*, 440.1987), τ 6.19 (3H, s, OMe), 5.90 (2H, s, $ArCH_2Ph$), 5.48 (2H, s, $ArCH_2OH$), 5.03 (2H, s, OCH_2Ph), 5.0 (2H, s, OCH_2Ph), 3.42 (1H, s, 4- or 6-H), 2.88 (5H, m, $C_6H_5CH_2$), 2.74 (5H, m, $C_6H_5CH_2$), and 2.66 (5H, m, $C_6H_5CH_2$).

The reaction of the ether (**18** *or* **21**) *with trifluoroacetic acid*. The ether (500 mg) in TFA (15 ml) was left at room temp. for 18 hr the solvent was removed *in vacuo*, and the residue was dissolved in $CHCl_3$ and extracted with 2N NaOH. Evaporation of the extract *in vacuo* gave **25** (250 mg) which crystallised from chloroform–light petroleum as yellow needles, m.p. 145–147° (lit.,[9] 146–147°) (Found: C, 74.95; H, 6.35; *m/e* 256. Calc. for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3%; *M*, 256).

Conversion of the alcohol (**19** *or* **22**) *to the chloride* (**20** *or* **23**). The alcohol **20** or **23** (1.51 g) in ether (2.5 ml) was treated with $SOCl_2$ (1.5 ml) for 20 min and then evaporated *in vacuo*. The residue was chromatographed on silica gel and eluted with EtOAc–light petroleum (1:49) to give **21** or **24** which crystallised from EtOAc–light petroleum as prisms, m.p. 84–85° (Found: C, 72.55; H, 6.3; Cl, 9.05. $C_{24}H_{23}ClO_3$ requires: C, 72.7; H, 6.3; Cl, 9.0%), τ 9.02 (3H, t, *J* 7 Hz, CH_3CH_2), 8.07 (2H, *m*, CH_3CH_2CH), 6.25 (3H, s, OMe), 5.57 (2H, s, $ArCH_2Cl$), 5.03 (2H, s, $PhCH_2O$), 5.03 (1H, t, J 6.5 Hz, $EtCHPh$), and 3.55 (2H, s, 2 X ArH).

2,5 - *Dibenzyloxy* - 3 - *methoxybenzyl chloride* (**14**). $SOCl_2$ (1.5 ml) was added dropwise during 40 min to a stirred suspension of 2,5 - dibenzyloxy - 3 - methoxybenzyl alcohol (1.0 g) in ether (2.5 ml). After 20 min further stirring the soln was evaporated *in vacuo* and the residue was chromatographed on silica gel (40 × 1 cm). Elution with EtOAc–light petroleum (1:49) gave 2,5 - *dibenzyloxy* - 3 - *methoxybenzyl chloride* (**14**) which crystallised from EtOAc–light petroleum as needles (780 mg), m.p. 93–95° (Found: C, 71.4; H, 5.8; Cl, 9.95. $C_{22}H_{21}ClO_3$ requires: C, 71.6; H, 5.7; Cl, 9.6%).

2,5 - *Dibenzyloxy* - 3 - *methoxybenzonitrile* (**15**). KCN (2.0 g) was stirred for 5 min in DMSO (100 ml), the above benzyl chloride (7.0 g) was added, and stirring was continued for 17 hr at room temp. The mixture was poured into water and the product was recovered by continuous extraction with light petroleum-diethyl ether. Evaporation of the solvents *in vacuo* gave 2,5 - *dibenzyloxy* - 3 - *methoxybenzonitrile* (**15**) which crystallised from EtOAc light petroleum as needles (6.5 g), m.p. 89–91° (Found: C, 76.7; H, 5.9; N, 4.15. $C_{23}H_{21}NO_3$ requires: C, 76.9; H, 5.9; N, 3.9%).

2,5 - *Dibenzyloxy* - 3 - *methoxyphenylacetic acid* (**16**). KOH (140 mg) and the benzonitrile (360 mg) in ethylene glycol (7 ml) and water (1.5 ml) were heated under reflux for 16 hr. The soln was acidified with 2N H_2SO_4 and extracted with ether, and the extract was evaporated *in vacuo*. Crystallisation from chloroform-light petroleum afforded 2,5 - *dibenzyloxy* - 3 - *methoxyphenylacetic acid* **16** (260 mg) m.p. 139–141° (Found: C, 73.1; H, 5.75. $C_{23}H_{22}O_5$ requires: C, 73.0; H, 5.9%).

Its *methyl ester* (**4**), prepared with diazomethane, was a pale yellow oil which distilled at 180° (bath)/0.015 mm Hg (Found: C, 73.1; H, 5.85; *m/e* 392. $C_{24}H_{24}O_5$ requires: C, 73.45; H, 6.2%; M,

392), ν_{max} (film) 1735 and 1605 cm^{-1}; τ 6.44 (2H, s, $ArCH_2CO$), 6.40 (3H, s, OMe), 6.19 (3H, s, OMe), 5.04 (2H, s, $PhCH_2O$), 5.0 (2H, s, $PhCH_2O$), 3.57 (1H, d, J 2 Hz, ArH), 3.46 (1H, d, J 2 Hz, ArH) and 2.60 (10H, m, 2 X $C_6H_5CH_2$).

Hydrogenolysis of the ester (300 mg) in EtOH (25 ml) in the presence of 5% Pd-C (150 mg), and recovery under N_2 gave a gum which crystallised from chloroform–light petroleum as cubes of *methyl 2,5 - dihydroxy - 3 - methoxy - phenylacetate* (150 mg), m.p. 97–99° (Found: C, 56.4; H, 3.35; *m/e* 212. $C_{10}H_{12}O_5$ requires: C, 56.6; H, 5.7%; M, 212).

Then the hydroquinone was kept overnight in solution in $CHCl_3$ substantial oxidation to the quinone occurred (70% by NMR).

Its *diacetate* crystallised from EtOAc–light petroleum as cubes, m.p. 85–87° (Found: C, 56.3; H, 5.4; *m/e* 296. $C_{14}H_{16}O_7$ requires: C, 56.75; H, 5.4% M, 296), ν_{max} 1760, 1720, 1623 and 1600 cm^{-1}; τ 7.74 (3H, s, $MeCO_2$), 7.70 (3H, s, $MeCO_2$), 6.47 (2H, s, $ArCH_2CO$), 6.33 (3H, s, OMe), 6.20 (3H, s, OMe) and 3.28 (2H, s, 4-H and 6-H).

Hydrogenolysis of 2,5 - dibenzyloxy - 3 - methoxyphenylacetic acid (**16**). The dibenzyloxy-acid (400 mg) in EtOH (30 ml) was hydrogenated over 5% Pd-C (200 mg) until uptake of H_2 ceased (1 h). Recovery under N_2 and crystallisation from EtOAc–light petroleum gave *2,5 - dihydroxy - 3 - methoxy - phenylacetic acid* as needles, m.p. 165–170° dec. (Found: *m/e* 198.0524. $C_9H_{10}O_5$ requires: M, 198.0528), ν_{max} 3440, 3340, 1685, 1675, 1630 and 1620 cm^{-1}; τ (in d_6-acetone) 6.46 (2H, s, $ArCH_2CO$), 6.22 (3H, s, OMe), 3.66 (1H, d, J 2.5 Hz, 4- or 6-H) and 3.57 (1H, d, J 2.5 Hz, 6- or 4-H).

With dicyclohexylcarbodiimide in MeCN it afforded *2,5 - dihydroxy - 3 - methoxyphenylacetic acid γ-lactone* which crystallised from chloroform–light petroleum as cubes (655 mg), m.p. 188–191° (Found: C, 60.0; H, 4.45; *m/e* 180. $C_9H_8O_4$ requires: C, 60.0; H, 4.5% M, 180), ν_{max} 3380 and 1780 cm^{-1}; τ 6.27 (2H, s, $ArCH_2CO$), 6.15 (3H, s, OMe) and 3.52 (2H, s, 2 X ArH).

Condensation of methyl 2,5 - dibenzyloxy - 3 - methoxyphenylacetate (**4**) *with acetic anhydride*. The arylacetic ester (1.0 g) in AcOH (5 ml) and Ac_2O (1.4 g) was treated with 70% $HClO_4$ (5 drops) and the soln was stirred at room temp. for 15 min and then water was added. Recovery in ether afforded an oil which was chromatographed on silica gel (45 × 2.5 cm). Elution with light petroleum–EtOAc (99:1) afforded benzyl acetate (93 mg), elution with light petroleum-EtOAc (19:1) gave starting ester (97 mg). Elution with light petroleum-ethyl acetate (9:1) gave *methyl 6 - acetyl - 2,5 - dibenzyloxy - 3 - methoxyphenylacetate* (**17**) which crystallised from ether as needles (247 mg), m.p. 91–92° (Found: C, 71.95; H, 6.2; *m/e* 434. $C_{26}H_{26}O_6$ requires: C, 71.9; H, 6.0%; M, 434), ν_{max} 1737, 1664, and 1598 cm^{-1}; τ 7.50 (3H, s, ArCOMe), 6.37 (3H, s, OMe), 6.20 (2H, s, $ArCH_2CO$), 6.13 (3H, s, 3-OMe), 5.08 (2H, s, OCH_2Ph), 4.90 (2H, s, OCH_2Ph), 3.43 (1H, s, 4-H) and 2.59 (10H, s, 2 X $C_6H_5CH_2$).

Continued elution with light petroleum–EtOAc (9:1) gave **27** or its isomer (**28**) as a gum (95 mg) (Found: *m/e* 434.1729. $C_{26}H_{26}O_6$ requires: M, 434.1720), τ 7.72 (3H, s, $MeCO_2$), 6.45 (5H, s, $ArCH_2CO_2Me$), 6.21 (3H, s, OMe), 5.88 (2H, s, $ArCH_2Ph$), 4.96 (2H, s, $PhCH_2O$), 3.37 (1H, s, ArH), 2.83 (5H, s, $C_6H_5CH_2$) and 2.70 (5H, s, $C_6H_5CH_2$).

Elution with light petroleum–EtOAc (4:1) afforded *methyl 2 - acetoxy - 6 - acetyl - 5 - benzyloxy - 3 - methoxyphenylacetate* (**25**) which crystallised from EtOAc–light petroleum as cubes (123 mg), m.p. 96–98° (Found: C, 65.35; H, 5.7; *m/e* 386.1359. $C_{21}H_{22}O_7$ requires: C, 65.3; H, 5.7; M, 386.1365), ν_{max} 1770, 1740 and 1670 cm^{-1}; τ 7.72 (3H, s, OCOMe), 7.50 (3H, s, ArCOMe) 6.34 (5H, s, $ArCH_2CO_2Me$), 6.20 (3H, s, OMe), 4.89 (2H, s, OCH_2Ph), 3.44 (1H, s, 4-H) and 2.61 (5H, s, $C_6H_5CH_2$).

Cyclisation of methyl 6 - acetyl - 2,5 - dibenzyloxy - 3 - methoxyphenylacetate (**17**). The keto-ester (100 mg) in dry EtOH (3 ml) was added dropwise to a boiling soln of Na (25 mg) in EtOH (2 ml), and refluxed for 18 min. The soln was cooled, aerated for 1 hr and evaporated *in vacuo*. The residue was dissolved in water, neutralised with 2N HCl, and the product was recovered in $CHCl_3$ and purified by PLC. Development with chloroform–methanol-formic acid (95:3:2) and recovery of the major band with Me_2CO gave *5,8 - dibenzyloxy - 3 - hydroxy - 6 - methoxy - 1,4 - naphthoquinone* (**29**) which crystallised from ether as orange rods (45 mg), m.p. 130–134° (Found: C, 71.9; H, 4.75; *m/e* 416. $C_{25}H_{20}O_6$ requires: C, 72.1; H, 4.8%; M, 416), ν_{max} ($CHBr_3$) 3380, 1660, 1640, 1583 and 1557 cm^{-1}; λ_{max} 266, 294, 378 sh and 426 nm (ϵ 17,100, 9160, 2870 and 3290); τ 6.18 (3H, s, OMe), 4.98 (2H, s, $PhCH_2O$), 4.74 (2H, s, $PhCH_2O$), 3.79 (1H, s, 2-H), 3.18 (1H, s, 7-H) and 2.5 (10H, m, 2 X $C_6H_5CH_2$).

Recovery of a minor slower-running band with Me_2CO, followed by crystallisation from ether, gave orange needles (2 mg), m.p. 131–135°, believed to be a mixture of **30** and **31**. (Found: *m/e* 354.1116. Calc. for $C_{20}H_{18}O_6$: M 354.1103), ν_{max} ($CHBr_3$) 3380, 1660, 1640, 1582 and 1556 cm^{-1}; λ_{max} 266, 295, 378 sh, and 422 nm (ϵ 15,200, 8900, 2850 and 3100); τ 8.54 (3H, t, CH_2CH_2), 6.19 (2H, q, CH_2CH_2O), 6.15 (3H, s, OMe), 4.77 (2H, s, OCH_2Ph), 3.81 (1H, s, 2-H), 3.20 (1H, s, 7-H) and 2.66 (5H, m, $C_6H_5CH_2$).

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