Photochemical Reactions. Part I. A New Route to Tetradehydropodophyllotoxin, Taiwanin E, and Related Compounds

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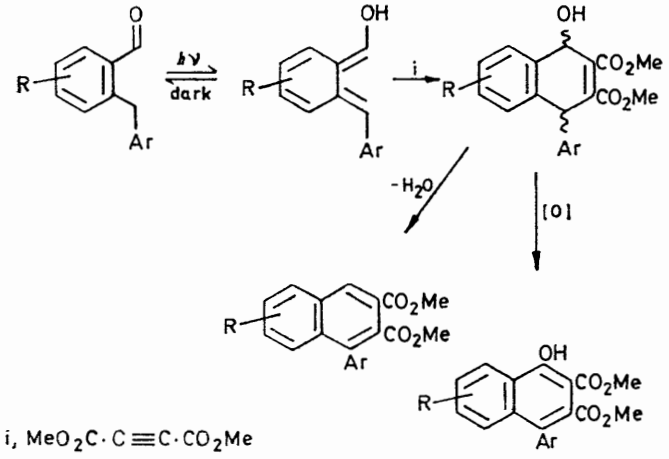
Irradiation of *ortho*-substituted aromatic aldehydes generates reactive intermediates which can be trapped with dienophiles. Dehydration of the trapped products allows formation of substituted naphthalenes, whereas mild oxidation affords the corresponding naphthols. In this way the lignans tetradehydropodophyllotoxin, taiwanins E and C, and justicidin E have been prepared.

PHOTOENOLISATION is one of the most efficient and most studied photochemical reactions.[1] Both *ortho*-alkyl-substituted aromatic carbonyl compounds[2] and conjugated, aliphatic derivatives[3] can undergo this process, thus generating reactive dienol intermediates (*e.g.* as in Scheme 1). These intermediates generally revert to

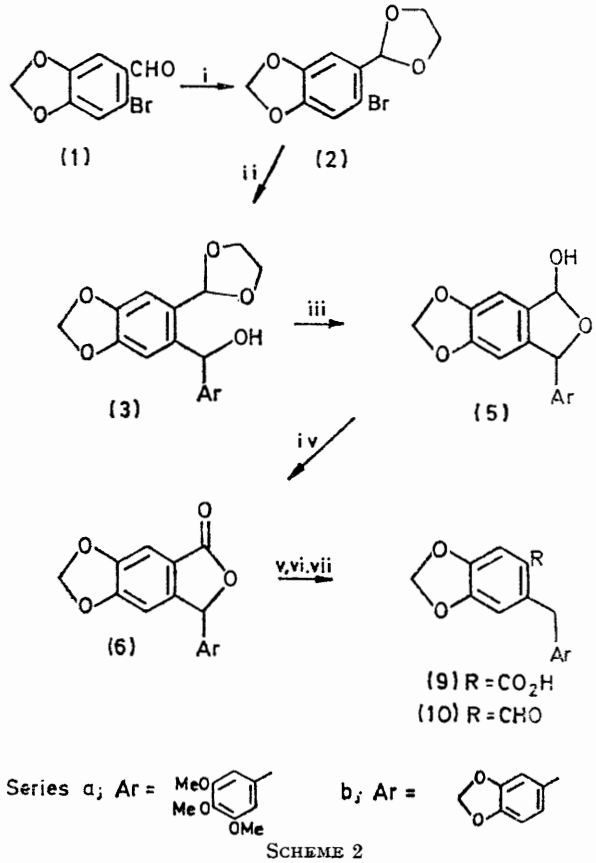


SCHEME 1

starting materials in the dark; tests for their transient existence include trapping with deuteriated solvents, reaction with oxygen, and cycloaddition reactions with dienophiles. Exchange of hydrogen for deuterium appears to be convincing evidence for the transient existence of dienols in the photochemical reaction;[4] however it could be argued that both trapping with oxygen and cycloaddition reactions do not involve ground-state dienols, but diradical intermediates. Recent studies on the cycloaddition reaction, using model substrates, suggest that the process is stereospecific, a finding consistent with the trapping of true dienol species.[5]

Hitherto the cycloadducts formed from photogenerated dienols have not been used in the synthesis of natural products. It was considered that the reaction would be of value as a further route to the aryl-naphthalene group of lignans.[6] In order to develop a synthesis of such compounds bearing a phenolic function at position 4 (Scheme 1), the photolysis of appropriately substituted aldehydes was investigated. The photochemistry of aromatic aldehydes has shown to be similar to that of aromatic ketones.[7]

Initially, a general route to the *ortho*-(substituted benzyl)benzaldehydes was devised (Scheme 2). Because



SCHEME 2

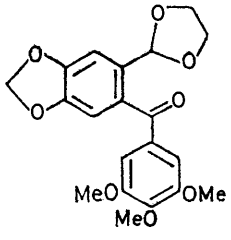
Reagents: i, $HO \cdot CH_2 \cdot CH_2 \cdot OH$–$H^+$; ii, Mg then ArCHO; iii, H_3O^+; iv, CrO_3; v, H_2–Pd; vi, $LiAlH_4$; on Et ester; vii, MnO_2

direct benzylation of, for example, piperonal with benzylic halides failed, the known monobromide (1)[8] was prepared. The aldehyde group was then protected by formation of its ethylene acetal, which was necessary

[1] P. J. Wagner and G. S. Hammond, *Adv. Photochem.*, 1968, **5**, 21.
[2] N. C. Yang and C. Rivas, *J. Amer. Chem. Soc.*, 1961, **83**, 2213.
[3] N. C. Yang and M. J. Jorgenson, *Tetrahedron Letters*, 1964, 1203.
[4] W. A. Henderson and E. F. Ullman, *J. Amer. Chem. Soc.*, 1965, **87**, 5424.
[5] F. Nerdel and W. Brodowski, *Chem. Ber.*, 1968, **101**, 1398.
[6] K. Weinges and R. Spänig, 'Oxidative Coupling of Phenols,' eds. W. I. Taylor and A. R. Battersby, Dekker, New York, 1967, ch. 7.
[7] J. S. Bradshaw, R. D. Knudsen, and W. W. Parish, *J.C.S. Chem. Comm.*, 1972, 1321.
[8] A. M. B. Orr, R. Robinson, and M. M. Williams, *J. Chem. Soc.*, 1917, 3202.

in order to be able to attempt coupling reactions with its Grignard derivative. Both benzylation of the Grignard derivative of the acetal (2), with 3,4,5-trimethoxybenzyl chloride under the conditions reported by Vinguello *et al.*,[9] and benzylation with hexamethylphosphoric triamide according to the method of Stork,[10] failed to effect the desired unsymmetrical coupling. The Grignard reagent was therefore added to 3,4,5-trimethoxybenzaldehyde to give the alcohol (3a), characterised as its manganese dioxide oxidation product, the ketone (4). Hydrolysis of the acetal (3a) gave the hemiacetal (5a), which was oxidised to the phthalide (6a) with chromic acid in acetone.[11]

Attempted selective hydrogenolysis of the alcohol (3a) or of the derived isobenzofuran (5a) produced the phthalan (7); the ketone (4) similarly gave the fully reduced system (8). In contrast, selective hydrogenolysis of the diphenylcarbinol group was possible in the case of the phthalide (6a), with palladised charcoal as



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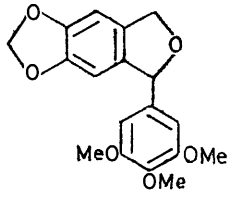

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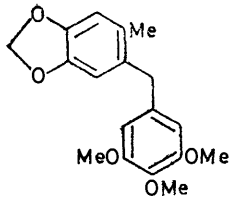
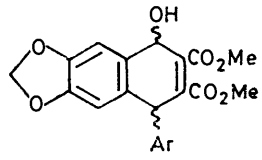


(8)

catalyst,[12] and gave the acid (9a), itself readily converted into the required aldehyde (10a). The overall yield of these steps was 32%.

The *ortho*-benzyl aldehyde (10a) was irradiated in the presence of dimethyl acetylenedicarboxylate, known to be capable of trapping dienols,[2,13] with tetrahydrofuran as solvent. Rapid disappearance of the starting material occurred when a medium-pressure mercury light source and a quartz reaction vessel were used. In order to avoid precipitation of photoproducts dilute solutions (0·01—0·02M) were preferred. The unstable, crude product obtained by careful evaporation of the solvent, showed both alcohol and ester bands in its i.r. spectrum but the aldehyde band of the starting material was absent. Attempts to isolate the initial photoproduct (11a), *e.g.* by t.l.c., caused extensive decomposition, the products including the naphthalene (12a). In contrast, dehydration of the alcohol (11a), by refluxing solutions of the initial irradiation products in the presence of a trace of toluene-*p*-sulphonic acid for 30 min, produced the naphthalene (12a) in a much cleaner reaction.



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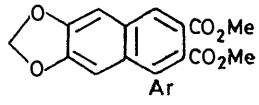

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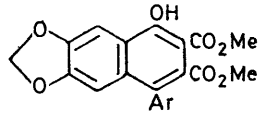

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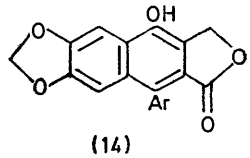

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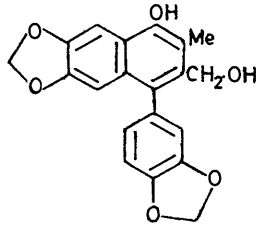

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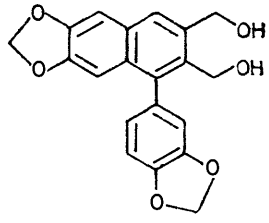

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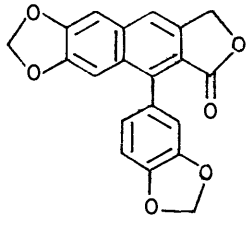

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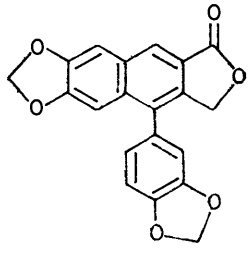

(18)

Alternatively, oxidation of the photoproducts with activated manganese dioxide[14] afforded the naphthol (13a).

The conditions for the photochemical reaction were critical. In a control reaction, photolysis of the aldehyde in the absence of the acetylenic ester also led to its rapid disappearance. This was attributed to the participation of competing reactions, such as intermolecular hydrogen abstraction, since a precipitate formed which showed hydroxy-bands in its i.r. spectrum.

[9] F. A. Vinguello, S. G. Ono, and J. Sheridan, *J. Org. Chem.*, 1961, **26**, 3203.
[10] G. Stork, P. A. Grieco, and M. Gregson, *Tetrahedron Letters*, 1969, 1393.
[11] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.
[12] S. Mitsui and T. Kamaishi, *Nippon Kagaku Zasshi*, 1961, 1382 (*Chem. Abs.*, 1962, **57**, 16453f).
[13] N. D. Heindel and M. Pfau, *Tetrahedron Letters*, 1968, 3579.
[14] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1952, 1094.

Another competing process was the polymerisation of the acetylenic ester: a non-polar fraction typical of such low molecular weight polymers was also formed in the trapping reaction. A brief examination of the effect of solvent on the reaction showed that acetone and benzene were detrimental. In the example under examination, the use of a Pyrex reaction vessel considerably slowed the rate of cycloaddition and lower yields of the desired products were obtained.

Transformation of the two ester functions into the corresponding lactone group typical of the aryl-naphthalene lignans was achieved by reduction. With sodium borohydride in methanol the naphthol (13a) was smoothly reduced to give a good yield of tetradehydropodophyllotoxin (14a).[15] Reduction of simple esters by sodium borohydride is unusual, although activated esters can be reduced.[16] In the present case initial complexation of the reagent with the adjacent phenol group helps direct reduction of the desired ester group—none of the isomeric phthalide was obtained. That complexation of the reducing agent with the phenolic group occurs was substantiated by the nature of the initial reduction product, which appeared to be a borate complex and which required exposure to dilute acid to effect its hydrolysis. Use of lithium aluminium hydride, even at low temperatures, always caused over-reduction with formation [from (13b)] of the methylnaphthol (15).

The photocyclisation reaction was also repeated in the bismethylenedioxy-series (series b). The starting aldehyde was again prepared by the general route (Scheme 1), in overall 40% yield from piperonal. Irradiation with dimethyl acetylenedicarboxylate, followed by either dehydration or oxidation gave the naphthalene (12b) and the naphthol (13b), respectively. The former (12b) has previously been prepared by Stevenson *et al.*,[17] using a method originally devised by Baddar.[18]

Reduction of the ester groups of the naphthalene (12b) gave the diol (16), which was oxidised with silver carbonate on Celite [19] to produce a mixture of the two lactones taiwanin C (17) [20] and justicidin E (18).[21] In accord with previous work,[17] the major isomer from this oxidation was justicidin E.

Reduction of the naphthol (13b) with sodium borohydride in methanol again proceeded stereoselectively to give the lactone (14b), identical with an authentic sample of taiwanin E.[20]

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. I.r. spectra were recorded on a Unicam SP 200 spectrophotometer and u.v. spectra with a Unicam SP 800 instrument for ethanolic solutions. ^{1}H N.m.r. spectra were recorded on either a Varian A60 or a T60 instrument, generally for solutions in deuteriochloroform containing tetramethylsilane as internal reference. Solvents were distilled and dried before use. Anhydrous sodium sulphate was used to dry extracts. T.l.c. was carried out on silica gel GF_{254}, normally with benzene–ethyl acetate as eluant.

6-Bromopiperonal Ethylene Acetal (2).—Piperonal was brominated [8] to afford 6-bromopiperonal, m.p. 127—129° (lit.,[8] 129°). The bromide (10 g) and ethylene glycol (4·0 g) were heated in refluxing benzene (100 ml) containing a trace of toluene-*p*-sulphonic acid, under a Dean–Stark head. After 8 h the mixture was cooled, washed with saturated sodium hydrogen carbonate solution and water, dried, and evaporated to afford crystals of the acetal (11·9 g, 96%), m.p. 68—69°, τ 3·00br (2H, s, aromatic), 4·04 (2H, s, O·CH_2·O), 4·14 (1H, s, acetal), and 6·0 (4H, s, O·CH_2·CH_2·O).

α-[2-(1,3-Dioxolan-2-yl)-4,5-methylenedioxyphenyl]-3,4,5-trimethoxybenzyl Alcohol (3a).—The Grignard reagent from 6-bromopiperonal ethylene acetal (2) (2·0 g) was prepared in dry tetrahydrofuran (15 ml) under nitrogen by the entrainment procedure,[22] with 1,2-dibromoethane (1·4 g, 1 equiv.) and dry magnesium turnings (0·36 g, 2 equiv.) at 50°. To the Grignard reagent was added, at room temperature, 3,4,5-trimethoxybenzaldehyde (1·1 g, 0·75 equiv.) in dry tetrahydrofuran (10 ml). The mixture was stirred for 12 h, and ether (20 ml) and saturated aqueous ammonium chloride were added. Separation of the aqueous phase followed by re-extraction with ether, and washing of the ethereal extracts with water, drying, and evaporation gave an oil (1·9 g). A small portion was purified by preparative t.l.c. to give, as a viscous oil, the *acetal*, $\nu_{max.}$ 3450 cm^{-1}, τ 3·03—3·46 (4H, aromatic), 4·12br (4H, s, O·CH_2·O and benzylic protons), 5·96—6·00 (4H, m, O·CH_2·CH_2·O), 6·13 (3H, s, MeO), 6·25 (6H, s, 2 × MeO), and 7·2br (1H, s, exchanged with D_2O), characterised as the ketone (4a).

1,3-Dihydro-5,6-methylenedioxy-3-(3,4,5-trimethoxyphenyl)-isobenzofuran-1-ol (5a).—The carbinol (3a) (1·8 g) was dissolved in benzene (60 ml) and stirred vigorously with dilute sulphuric acid (100 ml) for 3 h. The precipitate was collected, washed with saturated aqueous sodium hydrogen carbonate and then water, and dried. Crystallisation from benzene–ethanol afforded needles of the *isobenzofuran* (1·47 g, 75% from trimethoxybenzaldehyde), m.p. 129—135°, $\nu_{max.}$ (Nujol) 3300 cm^{-1}, $\lambda_{max.}$ 283sh, 290 (ε 5400), and 295sh nm, τ 3·13 and 3·30 (2H, singlets, aromatic protons), 3·47 (2H, s, aromatic protons), 4·00 and 4·07 (4H, benzylic and O·CH_2·O), and 6·17 (9H, s, 3 × MeO) (Found: C, 62·4; H, 5·2. $C_{18}H_{18}O_7$ requires C, 62·4; H, 5·2%).

5,6-Methylenedioxy-3-(3,4,5-trimethoxyphenyl)phthalide (6a).—The isobenzofuran (5a) (2·0 g) in acetone (100 ml) was stirred rapidly while a solution of sodium dichromate dihydrate (4·0 g) in 0·5N-sulphuric acid (200 ml) was added. After 10 min benzene (100 ml) was added and the mixture was stirred until the precipitated solid had redissolved. The organic phase was separated and the aqueous phase re-extracted with benzene (3 × 100 ml); the organic extract was washed with saturated sodium hydrogen carbonate solution and water, dried, and evaporated. The residue crystallised from benzene–ethanol to yield needles

[15] W. T. Gensler and F. Johnson, *J. Amer. Chem. Soc.*, 1955, **77**, 3674; H. Kofod and C. Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1296.
[16] S. Takahashi and L. A. Cohen, *J. Org. Chem.*, 1970, **35**, 1505.
[17] E. Block and R. Stevenson, *J. Org. Chem.*, 1971, **36**, 3450.
[18] F. G. Baddar and L. S. El-Assal, *J. Chem. Soc.*, 1951, 1844; F. G. Baddar, L. S. El-Assar, and N. A. Doss, *ibid.*, 1959, 1027.
[19] V. Balogy, M. Fetizon, and M. Golfier, *Angew. Chem. Internat. Edn.*, 1969, **8**, 444.
[20] Y.-T. Lin, T.-B. Lo, K. T. Wang, and B. Weinstein, *Tetrahedron Letters*, 1967, 849.
[21] K. Wada and K. Munakata, *Tetrahedron Letters*, 1970, 2017.
[22] D. E. Pearson, J. F. Baxter, and K. N. Carter, *Org. Synth.*, 1955, Coll. Vol., **3**, p. 154.

of the phthalide (1·3 g, 65%), m.p. 217—223° (lit.,[23] m.p. 218°), $\nu_{max.}$ (Nujol) 1760 cm^{-1}, $\lambda_{max.}$ 302 nm (ε 6750), τ 2·60 (1H, s, aromatic), 3·15 (1H, s, aromatic), 3·37 (2H, s, aromatic), 3·67 (1H, s, benzylic), 3·73 (2H, s, O·CH_2·O), and 6·02 (9H, 3 × MeO) (Found: C, 62·8; H, 4·9. Calc. for $C_{18}H_{16}O_7$: C, 62·8; H, 4·7%).

6-(3,4,5-*Trimethoxybenzyl*)*piperonylic Acid* (9a).—The phthalide (6a) (4·0 g) in acetic acid (300 ml) was hydrogenolysed over 5% palladium–charcoal (1·0 g) at atmospheric pressure and 80°. Filtration, evaporation, and crystallisation of the residue from benzene gave the *acid* (2·8 g, 70%), m.p. 165—168°, $\nu_{max.}$ (Nujol) 1680 cm^{-1}, $\lambda_{max.}$ 259 and 299 nm (ε 6500 and 4200), τ 2·58 (1H, s, aromatic), 3·31 (1H, s, aromatic), 3·55 (2H, s, aromatic), 3·98 (2H, s, O·CH_2·O), 5·70 (2H, s, benzylic H), and 6·25 (9H, 3 × MeO). The *ethyl ester*, m.p. 98—99°, obtained by a Fischer–Speier esterification (82%), had $\nu_{max.}$ 1710 cm^{-1}, $\lambda_{max.}$ 263 and 300 nm (ε 7400 and 5000), τ 2·53 (1H, s, aromatic), 3·33 (1H, s, aromatic), 3·56 (2H, s, aromatic), 3·99 (2H, s, O·CH_2·O), 5·68 (2H, q, *J* 6 Hz, CH_2·CH_3), 5·71 (2H, s, benzylic), 6·16 (9H, 3 × MeO), and 8·67 (3H, t, *J* 6 Hz, CH_3·CH_2) (Found: C, 64·3; H, 5·7. $C_{20}H_{22}O_7$ requires C, 64·2; H, 5·9%).

6-(3,4,5-*Trimethoxybenzyl*)*piperonal* (10a).—The ethyl ester of the acid (9a) (0·75 g), in dry ether (25 ml), was added slowly to a suspension of lithium aluminium hydride (0·1 g) in ether (25 ml) at room temperature. After 1 h a saturated solution of sodium potassium tartrate was added; the mixture was stirred for a further 1 h, then extracted to give 6-(3,4,5-trimethoxybenzyl)piperonyl alcohol (0·6 g, 90%), m.p. 89—90° (from EtOH), $\nu_{max.}$ (Nujol) 3400 cm^{-1}, $\lambda_{max.}$ 285 nm (ε 4400), τ 3·00 (1H, s, aromatic), 3·25 (1H, s, aromatic), 3·53 (2H, s, aromatic), 3·98 (2H, s, O·CH_2·O), 5·33 (2H, s, benzylic), 6·00 (2H, s, benzylic), and 6·08—6·10 (9H, 3 × MeO).

The foregoing alcohol (0·5 g) was heated with manganese dioxide (1·0 g) in refluxing benzene for 4 h. The mixture was filtered, the solids were washed with acetone, and the combined filtrates were evaporated to give the *aldehyde* (0·42 g, 84%), m.p. 124—125° (from EtOH), $\nu_{max.}$ 1680 cm^{-1}, $\lambda_{max.}$ 280 and 322 nm (ε 8100 and 7600), τ −0·25 (1H, s, aldehyde), 2·60 (1H, s, aromatic), 3·23 (1H, s, aromatic), 3·58 (2H, s, aromatic), 3·82 (2H, s, O·CH_2·O), 5·67 (2H, s, benzylic), and 6·20 (9H, s, 3 × MeO) (Found: C, 65·5; H, 5·6. $C_{18}H_{18}O_6$ requires C, 64·45; H, 5·5%).

Reduction of the Alcohol (3a).—The alcohol (1·0 g) in ethyl acetate (20 ml) was hydrogenolysed over 10% palladium–charcoal (25 mg) at room temperature and atmospheric pressure. When uptake ceased (12 h) the mixture was filtered through Celite and the filtrate evaporated to afford crystals of 5,6-*methylenedioxy*-1,3-*dihydro*-1-(3,4,5-*trimethoxyphenyl*)*isobenzofuran* (7) (0·8 g, 90%), m.p. 116—117° (from EtOH), $\lambda_{max.}$ 294 nm (ε 6300), τ 3·22, 3·33, and 3·46 (1H, 2H, and 1H, singlets, aromatic), 4·07 (3H, s, O·CH_2·O and benzylic), 4·85br (2H, s, benzylic), and 6·20 (9H, 3 × MeO) (Found: C, 65·6; H, 5·6. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·5%).

Hydrogenation of the alcohol (5a) afforded the same isobenzofuran (7). The product was stable to further treatment with palladium–charcoal and hydrogen, even up to 60°, although the hydrocarbon (8) began to form under more vigorous conditions.

6-(3,4,5-*Trimethoxybenzoyl*)*piperonal Ethylene Acetal* (4).—The alcohol (3a) (1·8 g) was oxidised with manganese dioxide (5 g) in refluxing benzene (100 ml) for 2 h. Filtration through Celite, followed by evaporation of the solvent, gave the *acetal* (0·9 g), m.p. 117—118° (from MeOH), $\nu_{max.}$ (Nujol) 1660 cm^{-1}, $\lambda_{max.}$ 294 nm (ε 12,500) (Found: C, 61·9; H, 5·3. $C_{20}H_{20}O_8$ requires C, 61·8; H, 5·2%).

Reduction of the Ketone (4).—(a) *In ethanol.* The ketone (0·05 g) in ethanol (7 ml) was reduced over 10% palladium–charcoal (20 mg) and platinum oxide monohydrate (10 mg) at atmospheric temperature and pressure for 9 h. Filtration, evaporation, and crystallisation of the residue from ethanol gave 4,5-*methylenedioxy*-2-(3,4,5-*trimethoxybenzyl*)*toluene* (8) (0·045 g, 100%), m.p. 108—109°, $\lambda_{max.}$ 292 nm (ε 5000), τ 3·33, 3·43, and 3·66 (1H, 1H, and 2H, s, aromatic), 4·12 (2H, s, O·CH_2·O), 6·16 and 6·22 (11H, two singlets, 3 × MeO and benzylic), and 7·82 (3H, s, aromatic Me) (Found: C, 68·4; H, 6·6. $C_{18}H_{20}O_5$ requires C, 68·4; H, 6·4%).

(b) *In ethyl acetate.* The ketone (0·10 g) in ethyl acetate (10 ml) was reduced over 10% palladium–charcoal (40 mg) for 24 h at atmospheric temperature and pressure to give, on work-up, a mixture of two compounds, the isobenzofuran (7) (35 mg, 40%) and the hydrocarbon (8) (35 mg, 40%), which were separated by preparative t.l.c. and identified by comparison with authentic samples.

6-(3,4-*Methylenedioxybenzyl*)*piperonal* (10b).—This was prepared like the trimethoxybenzyl analogue (10a). The physical and spectral properties recorded for the intermediates were as follows: 5,6-*methylenedioxy*-3-(3,4-*methylenedioxyphenyl*)*phthalide* (6b) (44% from piperonal), m.p. 146—147° (from MeOH), $\nu_{max.}$ (Nujol) 1760 cm^{-1}, $\lambda_{max.}$ 223, 245, 261, 293, and 308 nm (ε 29,000, 8000, 6300, 8500, and 5700), τ 2·70 (1H, s, aromatic), 3·10—3·34 (4H, m, aromatic), 3·77 (1H, s, benzylic), 3·80 (2H, s, O·CH_2·O), and 3·97 (2H, s, O·CH_2·O) (Found: C, 64·0; H, 3·6. $C_{16}H_{10}O_6$ requires C, 64·4; H, 3·4%); 6-(3,4-*methylenedioxybenzyl*)*piperonylic acid* (9b) (95%), m.p. 190—194° (from benzene), $\nu_{max.}$ (Nujol) 3400—2500 and 1680 cm^{-1}, $\lambda_{max.}$ 243, 258, and 260 nm (ε 8900, 6600, and 8900), τ 2·70 and 3·30—3·37 (5H, aromatic), 4·00 (2H, s, O·CH_2·O), 4·12 (2H, s, O·CH_2·O), and 5·77 (2H, s, benzylic) (Found: C, 64·1; H, 4·2. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%); 6-(3,4-*methylenedioxybenzyl*)*piperonyl alcohol*, obtained by reduction of the corresponding ethyl ester (m.p. 79°), needles, m.p. 109—110° (from EtOH), $\nu_{max.}$ (Nujol) 3400 cm^{-1}, $\lambda_{max.}$ 239 and 290 nm (ε 8700 and 8100), τ 3·25, 3·50, and 3·54 (5H, aromatic), 4·20 (2H, s, O·CH_2·O), 4·24 (2H, s, O·CH_2·O), 5·50br (2H, s, CH_2·OH), 6·20 (2H, s, benzylic), and 8·40 (1H, s, exchanged with D_2O) (Found: C, 67·1; H, 4·9. $C_{16}H_{14}O_5$ requires C, 67·2; H, 4·9%); 6-(3,4-*methylenedioxybenzyl*)*piperonal* (10b) (95% from the acid), m.p. 120—121° (from EtOH), $\nu_{max.}$ (Nujol) 1680 cm^{-1}, $\lambda_{max.}$ 283 and 321 nm (ε 8900 and 5700), τ −0·09 (1H, s, aldehyde), 2·67, 3·67, and 3·40 (5H, aromatic), 3·98 (2H, s, O·CH_2·O), 4·10 (2H, s, O·CH_2·O), and 5·75 (2H, s, benzylic) (Found: C, 67·5; H, 4·4. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%).

Irradiation of the Aldehydes (10).—A solution of the aldehyde (0·5% w/v) in dry tetrahydrofuran containing 1 mol. equiv. of dimethyl acetylenedicarboxylate was irradiated in a silica apparatus with a medium-pressure mercury lamp (450 W, Hanovia Reading Reactor) at room temperature while oxygen-free nitrogen was bubbled through the solution. Disappearance of the starting material was generally complete in 50—60 min (t.l.c.). Spectral examination of the crude reaction mixture showed

[23] E. Späth, F. Wesselly, and E. Nadler, *Ber.*, 1933, **66***B*, 125.

that it probably contained dihydronaphthols. The reaction mixtures were worked up in the following manner.

Oxidation. The crude product from the irradiation of the trimethoxy-compound (10a) (0·2 g) and the acetylenic ester (0·1 g) in tetrahydrofuran (40 ml) was heated to reflux with manganese dioxide (1 g) for 2 h. The solution was filtered, the inorganic solids were washed well with solvent, and the filtrate was evaporated to dryness. The residue was crystallised from ethanol to give *dimethyl 1-hydroxy-6,7-methylenedioxy-4-(3,4,5-trimethoxyphenyl)-naphthalene-2,3-dicarboxylate* (13a) (0·058 g, 20%), m.p. 242—244°, $\nu_{max.}$ (Nujol) 1730 and 1660 cm^{-1}, $\lambda_{max.}$ 238, 255sh, 261sh, 270, 275, 303, 315, 347, and 351 nm (ε 25,000, 16,000, 20,000, 40,000, 40,000, 7900, 6300, 2500, and 2500), τ −2·1 (1H, s, exchanged with D_2O), 3·28, 3·32, and 3·58 (1H, 1H, and 2H, aromatics), 4·02 (2H, s, O·CH_2·O), 6·11 (6H, s, 2 × MeO), 6·26 (6H, s, 2 × MeO), and 6·50 (3H, s, MeO) (Found: C, 61·35; H, 4·85. $C_{24}H_{22}O_{10}$ requires C, 61·3; H, 4·7%).

In a similar manner the crude product from the photolysis of the aldehyde (10) (0·28 g) and the acetylenic ester (0·17 g) in tetrahydrofuran (50 ml) gave, by oxidation with manganese dioxide (3·0 g), *dimethyl 1-hydroxy-6,7-methylenedioxy-4-(3,4-methylenedioxyphenyl)naphthalene-2,3-dicarboxylate* (13b) (0·12 g, 28%), m.p. 189—192° (from EtOH), $\nu_{max.}$ 3600—2700, 1730, and 1660 cm^{-1}, $\lambda_{max.}$ 239, 270, 276, 300, 314, 347, and 356 nm (ε 21,000, 39,000, 40,000, 13,000, 8700, 3100, and 3100), τ 2·40 (1H, s, aromatic), 3·0—3·4 (4H, m, aromatic), 3·90 (2H, s, O·CH_2·O), 4·00 (2H, s, O·CH_2·O), 6·10 (3H, s, MeO), and 6·50 (3H, s, MeO) (Found: C, 62·6; H, 3·85. $C_{22}H_{16}O_9$ requires C, 62·3; H, 3·8%).

Dehydration.—The crude photo-products were dehydrated by refluxing the solutions obtained after irradiation, in the presence of a trace of toluene-*p*-sulphonic acid (*ca.* 2 mg), for 30 min. Evaporation followed by preparative t.l.c. afforded one major component. From the former reaction mixture was obtained *dimethyl 6,7-methylenedioxy-1-(3,4,5-trimethoxyphenyl)naphthalene-2,3-dicarboxylate* (12a) (20%), m.p. 215—217° (from EtOH), $\nu_{max.}$ (Nujol) 1715 cm^{-1}, $\lambda_{max.}$ 255, 261, 292, 305, and 345 nm (ε 40,000, 40,000, 7900, 7900, and 1300), τ 1·68 (1H, s, aromatic), 2·85 (1H, s, aromatic), 3·15 (1H, s, aromatic), 3·55 (2H, s, aromatic), 4·03 (2H, s, O·CH_2·O), 6·15 (6H, s, 2 × MeO), 6·26 (6H, s, 2 × MeO), and 6·43 (3H, s, MeO) (Found: C, 63·5; H, 4·9. $C_{24}H_{22}O_9$ requires C, 63·4; H, 4·85%).

From the latter series was obtained dimethyl 6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)naphthalene-2,3-dicarboxylate (12b) (30%), m.p. 215—218° (from EtOH) (lit.,[17] 216°), $\nu_{max.}$ 1725 cm^{-1}.

Tetradehydropodophyllotoxin {*4-Hydroxy-6,7-methylenedioxy-9-(3,4,5-trimethoxyphenyl)naphtho*[c]*furan-1*(3H)*-one*} (14a).—The ester (13a) (0·047 g) in methanol (5 ml) was treated with portions of sodium borohydride (3 × 0·5 g) at room temperature over 5 h. 2N-Hydrochloric acid was then added until the pH reached 2—3, and the mixture was stirred for a further 30 min and then extracted with ether. The extract was evaporated to give, as a crystalline residue, tetradehydropodophyllotoxin (0·028 g, 67%), m.p. 263—265° (lit.,[15] 286—288° *), $\nu_{max.}$ (Nujol) 3600—3200 and 1760 cm^{-1}, $\lambda_{max.}$ 226, 263, 269sh, 312sh, 323, and 355 nm (ε 30,000, 37,000, 8000, 9500, and 5000), τ [$(CD_3)_2CO$] 2·43 (1H, s, aromatic), 3·09 (1H, s, aromatic), 3·50 (2H, s, aromatic), 3·94 (2H, s, O·CH_2·O), 4·71 (2H, s, ArCH_2), and 6·27 (9H, s, 3 × MeO) (Found: C, 64·3; H, 4·5. Calc. for $C_{22}H_{18}O_8$: C, 64·4; H, 4·4%).

Taiwanin E (14b).—In a similar manner the ester (13b) (0·06 g) was reduced to give the phthalide (0·03 g, 60%), m.p. 292° (with sublimation), $\nu_{max.}$ (Nujol) 3200 and 1720 cm^{-1}, identical with an authentic sample.†

6,7-Methylenedioxy-1-(3,4-methylenedioxy)naphthalene-2,3-dimethanol (16).—The ester (12b) (0·03 g) in 1 : 1 ether–tetrahydrofuran (7 ml) was added slowly to a suspension of lithium aluminium hydride (0·06 g) in dry ether (5 ml) at room temperature under dry nitrogen. The mixture was stirred for 30 min and a saturated aqueous solution of ammonium chloride was then added. The mixture was stirred for a further 10 min and then extracted into ether, to give, after the normal work-up, the diol (0·028 g, 100%), m.p. 183—185° (lit.,[24] 185—187°), $\nu_{max.}$ (Nujol) 3400 cm^{-1}, τ 2·60—3·40 (5H, m, aromatic), 3·97 (2H, s, O·CH_2·O), 4·03 (2H, s, O·CH_2·O), 5·17 (2H, s, CH_2·OH), 5·41 (2H, s, CH_2·OH), and 6·77br (2H, s, exchanged by D_2O).

Justicidin E and Taiwanin C.—The diol (16) (0·028 g) was dissolved in dry benzene (25 ml) and heated to reflux while stirring with silver carbonate on Celite [19] (0·70 g) under a Dean–Stark head for 40 min. The hot solution was filtered and the inorganic material was washed with more warm benzene. The filtrate was evaporated to give a crystalline residue (0·028 g, 100%) which was separated by multiple-elution t.l.c.‡ Examination of the original product indicated a ratio of 85 : 15 of justicidin E to taiwanin C. The separated lignans were identified by spectral comparison with reported data for the natural products and, in the case of taiwanin C, direct comparison. Justicidin E (18) (10 mg) had m.p. 270—271° (lit.,[21] 270—271°), M^+ 348·0636 (Calc. for $C_{20}H_{12}O_6$: *M*, 348·0634). This was the least polar isomer (silica gel G; ethyl acetate–light petroleum–acetic anhydride, 100 : 100 : 1). Taiwanin C (17) (2 mg) had M^+ 348·0629 (Calc. for $C_{20}H_{12}O_6$: *M*, 348·0634).

3-Hydroxymethyl-2-methyl-4-(3,4-methylenedioxyphenyl)-6,7-methylenedioxy-1-naphthol (15).—The diester (13b) (0·120 g) in dry tetrahydrofuran (10 ml) was added to a stirred suspension of lithium aluminium hydride (0·25 g) in tetrahydrofuran (10 ml) at room temperature. The mixture was then heated to reflux for 2 h, cooled, and worked up in the normal manner. The *naphthol* (0·095 g, 95%) had m.p. 183—184° (from EtOH), $\nu_{max.}$ (Nujol) 3200—3600 cm^{-1}, τ [$(CD_3)_2CO$] 2·4 (1H, s, aromatic), 2·9—3·4 (4H, m, aromatic), 3·85 (2H, s, O·CH_2·O), 3·90 (2H, s, O·CH_2·O), 5·43br (2H, s, CH_2·OH), and 7·40 (3H, s, Me) (Found: C, 68·0; H, 4·7. $C_{20}H_{16}O_6$ requires C, 68·2; H, 4·55%). The same product was obtained by carrying out the reduction at 10°.

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* The m.p. depends on the rate of heating. In an evacuated, sealed tube our material had m.p. 280—285°.

† An authentic sample was prepared according to the method reported in ref. 20. We thank Dr. K.-T. Wang for a sample of natural Taiwanin A.

‡ As reported by Professor Stevenson,[17] the lactones were extremely difficult to separate by t.l.c., a problem compounded by the insolubility of the compounds in common organic solvents.

[24] T. Gilchrist, R. Hodges, and A. L. Porte, *J. Chem. Soc.*, 1962, 1770.