Synthesis of Some Pterocarpenes obtained from *Brya ebenus*

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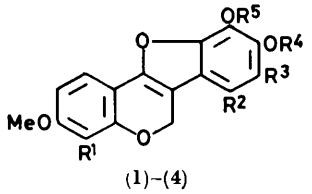
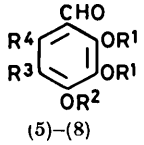
The syntheses of bryacarpenes-1, -2, and -4, [4,10-dihydroxy-3,8,9-trimethoxy- (1), 10-hydroxy-3,8,9-trimethoxy- (2), and 4-hydroxy-3,9,10-trimethoxy-6*H*-benzofuro[3,2-*c*][1]benzopyran (3)], (±)-bryaflavan [(±)-3',6,7-trihydroxy-2',4'-dimethoxyisoflavan (33)], 4-hydroxy-3,7-dimethoxy- (18) and 3,7-dimethoxy-6*H*-benzofuro[3,2-*c*][1]benzopyran-9,10-quinone (19) is described. The quinones are not identical with bryaquinone and deoxybryaquinone, for which structures (18) and (19) had been proposed previously. In the syntheses of the pterocarpenes the novel reduction of isoflavones to isoflavan-4-ones by di-isobutylaluminium hydride was used.

PTEROCARPENES are a restricted group of natural isoflavanoids represented, apart from the seven found in *Brya ebenus*,[1,2] only by 3,9-dihydroxypterocarpene obtained from infected *Tetragonolobus maritimus*,[3] its dimethyl ether obtained from *Swartzia madagascarensis*,[4] flemichapparin *B* from *Flemingia chappar*,[5] and leiocalycin from *Swartzia leiocalycina*.[6]

Since pterocarpenes are readily formed by acid-catalyzed ring-closure of isoflavan-4-ones, the recent development in our laboratory of a clean method for the reduction of isoflavones into isoflavanones [7] prompted us to tackle the synthesis of some of the pterocarpenes isolated from *Brya ebenus* by Ferreira *et al.*[1,2] [compounds (1)—(3), (18), and (19)].[8]



(1)–(4)

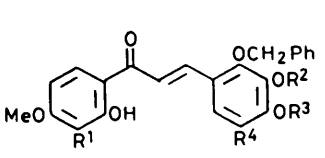


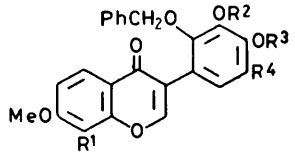
(5)–(8)

	R¹	R²	R³	R⁴	R⁵
(1)	OH	H	OMe	Me	H
(2)	H	H	OMe	Me	H
(3)	OH	H	H	Me	Me
(4)	OAc	OMe	H	Ac	Ac
(5)	H	Me	OMe	H	
(6)	Me	H	OH	H	
(7)	CH_2Ph	Me	OMe	H	
(8)	CH_2Ph	CH_2Ph	H	OMe	

The key intermediates, the isoflavones, were obtained by the oxidative rearrangement of 2'-hydroxy- or 2'-acetoxy-chalcones by thallium(III) nitrate (TTN) in methanol and subsequent ring-closure of the acetal-type product.[9]

The synthesis of bryacarpene-1 (1) required preparation of the unknown aldehyde (5). Reaction of 1,2-dihydroxy-3,4-dimethoxybenzene [10] with zinc cyanide and hydrogen chloride or with triethyl orthoformate and aluminium chloride gave, as the main product, the isomer (6) of compound (5). Reaction of the above catechol with 1,1',3,3'-tetraphenyl-2,2'-bi-imidazolidinylidene [11] gave, however, only the desired aldehyde (5), identified by its low field (δ 10.80) hydroxy-group signal which indicates chelation [in compound (6) δ_{OH} 5.00 and 6.20]. Also, when compound (5) was treated with a small amount of diazomethane a product with a positive ferric reaction was detected by t.l.c. Acetylation of compound (6) in turn resulted in a downfield shift (Δδ 0.18) of the signal of 6-H. Benzylation of the aldehyde (5) and condensation of the product (7) with 3-benzyloxy-2-hydroxy-4-methoxyacetophenone [12] gave the chalcone

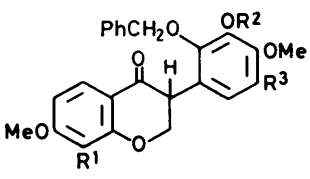


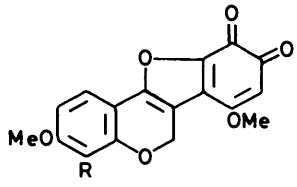


	R¹	R²	R³	R⁴	
(9)	OCH_2Ph	CH_2Ph	Me	OMe	(12)
(10)	H	CH_2Ph	Me	OMe	(13)
(11)	OCH_2Ph	Me	Me	H	(14)

(9), which was treated with TTN to give the isoflavone (12). The latter was reduced selectively with di-isobutylaluminium hydride in toluene at −60 °C [7] to give the isoflavanone (15). Debenzylation followed by acid-catalyzed ring-closure finally gave the pterocarpene (1), identical in every respect with bryacarpene-1.

An analogous sequence of reactions which involved the chalcone (10), the isoflavone (13), and the isoflavan-4-one (16) afforded bryacarpene-2 (2), while 2-benzyloxy-3,4-dimethoxybenzaldehyde [13] and 3-benzyloxy-2-hydroxy-4-methoxyacetophenone [(11)→(14)→(17)] provided bryacarpene-4 (3).

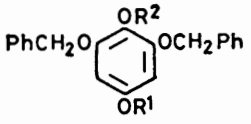




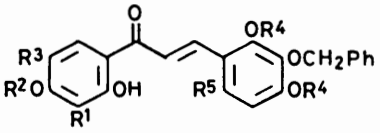
	R¹	R²	R³		
(15)	OCH_2Ph	CH_2Ph	OMe	(18)	R = OH
(16)	H	CH_2Ph	OMe	(19)	R = H
(17)	OCH_2Ph	Me	H		

Because they are both pterocarpenes and ortho-quinones, the synthesis of bryaquinone and of 4-deoxybryaquinone [proposed structures (18) and (19) respectively] was of interest. The aldehyde (8), the key intermediate for both compounds, was prepared as follows.

On treatment with 0.1M sodium methoxide the less hindered acetoxy-group of 2,5-diacetoxy-1,3-dibenzyloxybenzene [14] could be saponified selectively to give the monophenol (20). Methylation [to compound (21)], saponification [to compound (22)], benzylation [to compound (23)], and Vilsmeyer aldehyde synthesis in chlorobenzene afforded the required aldehyde (8) in 42% overall yield (five steps). The structure of compound (20) was indicated by the upfield shift of the aromatic protons by δ 0.38, as compared with the parent diacetate, and by the non-identity of the product obtained by debenzylation of compound (23) with the known 2,4,6-trihydroxyanisole.[15]



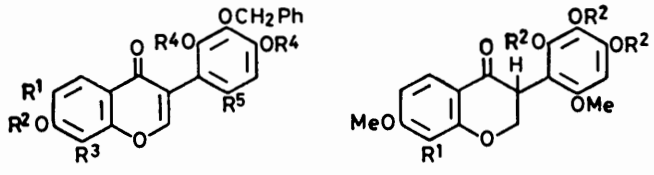
	R^1	R^2
(20)	H	Ac
(21)	Me	Ac
(22)	Me	H
(23)	Me	CH_2Ph



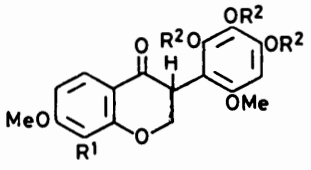
	R^1	R^2	R^3	R^4	R^5
(24)	OCH_2Ph	Me	H	CH_2Ph	OMe
(25)	H	Me	H	CH_2Ph	OMe
(26)	H	CH_2Ph	OCH_2Ph	Me	H

Condensation of the aldehyde (8) and 3-benzyloxy-2-hydroxy-4-methoxyacetophenone gave, *via* the chalcone (24), the non-crystalline isoflavone (27) which was characterized, after debenzylation and *in situ* acetylation, as the tetra-acetate.

Reduction of compound (27) gave the isoflavanone (30), which was debenzylated and cyclized in the absence of oxygen. The product was either *in situ* acetylated to give the leucoacetate (4) or oxidized in chloroform with Fetizon's reagent (silver carbonate-on-Celite) to give the quinone (18). The m.p. and ^1H n.m.r. spectrum of the leucoacetate (4) were different from those reported for bryaquinone leucoacetate,[2] as were the data of compound (18) and bryaquinone.



	R^1	R^2	R^3	R^4	R^5
(27)	H	Me	OCH_2Ph	CH_2Ph	OMe
(28)	H	Me	H	CH_2Ph	OMe
(29)	OCH_2Ph	CH_2Ph	H	Me	H



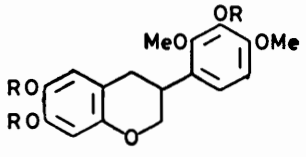
	R^1	R^2
(30)	OCH_2Ph	CH_2Ph
(31)	H	CH_2Ph
(32)	H	Ac

Also, the ^{13}C n.m.r. spectra of compound (4) and the leucoacetate of a sample of bryaquinone provided by Professor Thomson were similar but definitely not the same.

Through a similar series of intermediates [(25)→(28)→(31)], the isoflavanone acetate (32) was obtained, which was then transformed by hydrolysis, cyclization, and oxidation into the quinone (19). U.v., i.r., ^1H n.m.r., and mass spectra of compound (19) all differed distinctly from the corresponding spectra of 4-deoxybryaquinone.[2]

These results suggested that bryaquinone and 4-deoxybryaquinone, although most probably pterocarpene orthoquinones, are not the structures (18) and (19), respectively. A detailed analysis of the ^{13}C n.m.r. spectra of the leucoacetates suggests, but does not prove, that bryaquinone may have the same oxygenation pattern as bryacarpene-1.

Finally, (±)-bryaflavan (33) was synthesized by condensing 4,5-dibenzyloxy-2-hydroxyacetophenone [16] and 3-benzyloxy-2,4-dimethoxybenzaldehyde [17] to the chalcone (26), which was transformed into the isoflavone (29). Direct hydrogenation of compound (29) to give an isoflavan was unsuccessful; compound (29) had first to be converted into the corresponding isoflavone acetate which was then hydrogenated to yield the isoflavan acetate (34) and, after saponification, (±)-bryaflavan (33).



(33) R = H
(34) R = Ac

EXPERIMENTAL

^1H N.m.r. spectra were performed using a Perkin-Elmer R12 (60 MHz) and a JEOL FX-100 (100 MHz), and ^{13}C n.m.r. spectra using a JEOL FX-100 (25.2 MHz) spectrometer, both in [^2H]chloroform. Silica gel was used for column chromatography.

2,3-Dihydroxy-4,5-dimethoxybenzaldehyde (5).—1,2-Dihydroxy-3,4-dimethoxybenzene [10] (12.6 g) was dissolved in dimethylformamide (DMF) (112 ml), 1,1′,3,3′-tetraphenyl-2,2′-bi-imidazolidinylidene [18] (33 g) was added, and the mixture was refluxed for 10 min under argon. After evaporation under reduced pressure the residue was stirred for 1 h at 80 °C with hydrochloric acid (1 : 1, 400 ml). The solution was decanted from undissolved resinous material, kept in ice for a few hours, filtered, and the filtrate was extracted five times with ethyl acetate (100 and 4 × 50 ml). The extracts were washed with sodium hydrogen carbonate solution and evaporation gave the *aldehyde* (5) (5.2 g),

purified by chromatography, m.p. 76—78 °C; δ 3.80 and 3.98 (6 H, s, 2 × OMe), 5.9br (1 H, s, 3-OH), 6.52 (1 H, s, 6-H), 9.62 (1 H, s, CHO), 10.80 (1 H, s, 2-OH) (Found: C, 54.3; H, 5.15. $C_9H_{10}O_5$ requires C, 54.54; H, 5.09%).

4,5-*Dihydroxy*-2,3-*dimethoxybenzaldehyde* (6).—To a stirred solution of 1,2-dihydroxy-3,4-dimethoxybenzene [10] (0.85 g) in dry diethyl ether (25 ml), triethyl orthoformate (5.0 ml) and aluminium chloride (1.0 g) were added at 20 °C. The mixture was decomposed with ice and dilute hydrochloric acid. The diethyl ether layer was separated off, washed with water, and evaporated. The residue was chromatographed (eluant: benzene–ethyl acetate, 1 : 1) to give compound (5) (0.07 g), the starting material (0.20 g), and the aldehyde (6) (0.20 g) as an oil; δ (CD_3OD) 3.40 and 3.45 (6 H, s, 2 × OMe), 5.00 (1 H, s, OH), 6.20 (1 H, s, OH), 6.52 (1 H, s, 6-H), and 9.63 (1 H, s, CHO); δ($CDCl_3$) 7.30 (1 H, s, 6-H) and 10.22 (1 H, s, CHO).

4,5-Dihydroxy-2,3-dimethoxybenzaldehyde diacetate gave δ 2.35 and 2.40 (6 H, s, 2 × OAc), 3.95 and 4.06 (6 H, s, 2 × OMe), 7.48 (1 H, s, 6-H), and 10.20 (1 H, s, CHO).

2,3-*Dibenzyloxy*-4,5-*dimethoxybenzaldehyde* (7).—The aldehyde (5) (5.3 g), potassium iodide (1.0 g), potassium carbonate (10.0 g), and benzyl chloride (6.1 ml) were refluxed and stirred in acetone (80 ml) for 3 h. Evaporation, removal of the benzyl chloride by steam distillation, and chromatography on a short column (eluant: benzene–acetone, 8 : 1) gave the aldehyde (7) (6.0 g) as an *oil*; δ 3.70 and 3.88 (6 H, s, 2 × OMe), 5.02 (4 H, s, OCH_2), 7.00 (1 H, s, 6-H), 7.1—7.4 (10 H, m, Ph) (Found: M^+, 378.1459. $C_{23}H_{22}O_5$ requires M^+, 378.1461).

2,3,3′-*Tribenzyloxy*-2′-*hydroxy*-4,4′,5-*trimethoxychalcone* (9).—3-Benzyloxy-2-hydroxy-4-methoxyacetophenone (0.83 g) and the aldehyde (7) (1.3 g) were stirred in a mixture of ethanol (5 ml) and sodium hydroxide (25%, 3 ml) for 72 h. The usual work-up, and chromatography (eluant: hexane–ethyl acetate, 6 : 1) gave the chalcone (9) (0.65 g) as a *resin* (Found: C, 73.8; H, 5.6. $C_{39}H_{36}O_8$ requires C, 74.04; H, 5.73%); δ 3.87, 3.90, and 3.94 (9 H, s, 3 × OMe), 5.15br (6 H, s, 3 × OCH_2), 6.38 (1 H, d, *J* 8 Hz, 5′-H), 6.90 (1 H, s, 6-H), 7.2—7.7 (17 H, m, 3 × Ph, 6′-H, =C*H*Ar), and 8.05 (1 H, d, *J* 16 Hz, COCH=). Acetylation with pyridine–acetic anhydride gave the non-crystalline *acetate* in 90% yield; $\lambda_{max.}$ (liquid film) 1 775 nm (ester-CO) (Found: C, 72.6; H, 6.0. $C_{41}H_{38}O_9$ requires C, 72.98; H, 6.12%).

2′,3′,8-*Tribenzyloxy*-4′,5′,7-*trimethoxyisoflavone* (12).—The acetate of the chalcone (9) (0.93 g) was treated similarly to the chalcone used for the preparation of compound (28) (see later), except that cyclization was carried out by refluxing in 0.3M sodium methoxide for 10 min. The pure *isoflavone* (12) (0.40 g) crystallized directly after acidification, m.p. 105—106 °C; δ 3.86, 3.93, and 3.99 (9 H, s, 3 × OMe), 4.90 (2 H), and 5.14 (4 H) (s, 3 × OCH_2), 6.72 (1 H, s, 6′-H), 6.95—7.55 (16 H, m, 3 × Ph, 6-H), 7.85 (1 H, s, 2-H), and 8.01 (1 H, d, *J* 9.5 Hz, 5-H) (Found: C, 73.9; H, 5.6. $C_{39}H_{34}O_8$ requires C, 74.27; H, 5.43%).

2′,3′,8-*Tribenzyloxy*-4′,5′,7-*trimethoxyisoflavan*-4-*one* (15).—The isoflavone (12) (0.33 g) was reduced similarly to the isoflavone used for the preparation of compound (31) (see later) and the crude product was purified by layer chromatography to give the isoflavanone (15) as *prisms* (0.22 g) (from benzene–hexane), m.p. 102—103 °C; δ 3.78 (3 H) and 3.90 (6 H) (s, 3 × OMe), 4.36 (3 H, m, 3-CH_2, 3-H), 5.04 (2 H) and 5.10 (4 H) (s, 3 × OCH_2), 6.40 (1 H, s, 6′-H), 6.62 (1 H, d, *J* 8.5 Hz, 6-H), 7.2—7.5 (15 H, m, 3 × Ph), 7.68 (1 H, d, *J* 8.5 Hz, 5-H) (Found: C, 73.9; H, 5.8. $C_{39}H_{26}O_8$ requires C, 74.02; H, 5.73%).

4,10-*Dihydroxy*-3,8,9-*trimethoxy*-6H-*benzofuro*[3,2-c][1]-*benzopyran*, *Bryacarpene*-1 (1).—The isoflavone (15) (0.22 g) was debenzylated by catalytic hydrogenation in the usual way. The product was refluxed for 40 min in ethanol which contained 2 drops of concentrated hydrochloric acid. The product crystallised directly from the reaction mixture as plates (0.083 g), m.p. 202—204 °C (lit.,[1] m.p. 204—205 °C); δ 3.91, 3.92, and 3.95 (9 H, s, 3 × OMe), 5.50 and 5.92 (2 H, s, 2 × OH), 5.62 (2 H, s, OCH_2), 6.41 (1 H, s, 7-H), 6.56 (1 H, d, *J* 9 Hz, 2-H), and 7.14 (1 H, d, *J* 9 Hz, 1-H).

2,3-*Dibenzyloxy*-2′-*hydroxy*-4,4′,5-*trimethoxychalcone* (10).—The aldehyde (7) (0.76 g) was treated similarly to the aldehyde used in the preparation of compound (25) (see later) and the crude product was chromatographed (eluant: hexane–ethyl acetate, 6 : 1) to afford the chalcone (10) (0.83 g) as yellow *prisms*, m.p. 114—116 °C; δ 3.85, 3.91, and 3.94 (9 H, s, 3 × OMe), 5.04 and 5.14 (4 H, s, 2 × OCH_2), 6.2—6.5 (2 H, s, 3′-, 5′-H), 6.87 (1 H, s, 6-H), 7.1—7.7 (12 H, m, 2 × Ph, 6′-H, COCH=), 7.98 (1 H, d, *J* 15 Hz, COCH=C*H*), and 13.56 (1 H, s, OH) (Found: C, 73.1; H, 5.9. $C_{32}H_{30}O_7$ requires C, 72.99; H, 5.74%).

2′,3′-*Dibenzyloxy*-4′,5′,7-*trimethoxyisoflavone* (13).—*Compound* (13) was obtained from the chalcone (10) (0.52 g) as described for the preparation of compound (28) from the chalcone (25) (see later) and gave, after recrystallization from methanol, m.p. 141—142 °C (0.22 g); δ 3.86, 3.93, and 3.94 (9 H, s, 3 × OMe), 4.90 and 5.15 (4 H, s, 2 × OCH_2), 6.75 (1 H, s, 6′-H), 6.85 (1 H, d, *J* 2.5 Hz, 8-H), 7.00 (1 H, q, *J* 8.5 Hz and 2.5 Hz, 6-H), 7.1—7.6 (10 H, m, 2 × Ph), 7.81 (1 H, s, 2-H), and 8.19 (1 H, d, *J* 8.5 Hz, 5-H) (Found: C, 73.3; H, 6.1. $C_{32}H_{28}O_7$ requires C, 73.27; H, 6.15%).

2′,3′-*Dibenzyloxy*-4′,5′,7-*trimethoxyisoflavan*-4-*one* (16).—The isoflavone (13) (0.25 g) was reduced similarly to the isoflavone used to prepare compound (31) (see later) to give the isoflavanone (16) (0.13 g) as *needles* (from hexane), m.p. 120—121 °C; δ 3.79, 3.85, and 3.90 (9 H, 3 × OMe), 4.1—4.4 (3 H, m, 2-CH_2, 3-H), 5.04, and 5.11 (4 H, s, 2 × OCH_2), 6.43 (2 H, s, 6′,8-H), 6.59 (1 H, d, *J* 9 Hz, 6-H), 7.1—7.6 (10 H, m, 2 × Ph), and 7.88 (1 H, d, *J* 9 Hz, 5-H) (Found: C, 73.1; H, 5.8. $C_{32}H_{30}O_7$ requires C, 72.99; H, 5.74%).

10-*Hydroxy*-3,8,9-*trimethoxy*-6H-*benzofuro*[3,2-c][1]*benzopyran*, *Bryacarpene*-2 (2).—Hydrogenation and subsequent cyclization of the isoflavanone (16) (0.16 g), similar to that of the isoflavanone used to prepared compound (1), gave the benzopyran (2) as plates (from diethyl ether) (0.075 g), m.p. 188—189 °C (lit.,[1] m.p. 188—189 °C); δ 3.80, 3.90, and 3.94 (9 H, s, 3 × OMe), 5.54 (2 H, s, OCH_2), 5.9 (1 H, s, OH), 6.39 (1 H, s, 7-H), 6.50 (1 H, s, 4-H), 6.55 (1 H, d, *J* 9 Hz, 2-H), and 7.50 (1 H, d, *J* 9 Hz, 1-H).

2,3′-*Dibenzyloxy*-2′-*hydroxy*-3,4,4′-*trimethoxychalcone* (11).—3-Benzyloxy-2-hydroxy-4-methoxyacetophenone (2.25 g) and 2-benzyloxy-3,4-dimethoxybenzaldehyde [13] (2.25 g) were treated as for the reactants used to prepare compound (25) (see later) to yield, after recrystallization from ethyl acetate, the *chalcone* (11) (2.5 g), m.p. 117—119 °C; δ 3.85, 3.89, and 3.92 (9 H, s, 3 × OMe), 5.10 and 5.13 (4 H, s, 2 × OCH_2), 6.30 (1 H, d, *J* 8 Hz, 5-H), 6.72 (1 H, d, *J* 8 Hz, 5′-H), 7.2—7.6 (12 H, m, 6-, 6′-H, 2 × Ph), 7.6 and 8.00 (2 H, AB, *J* 16 Hz, $COCH_A{=}CH_B$), and 13.30 (1 H, s. OH) (Found: C, 73.1; H, 5.8. $C_{32}H_{30}O_7$ requires C, 72.99; H, 5.74%).

2′,8-*Dibenzyloxy*-3′,4′,7-*trimethoxyisoflavone* (14).—Compound (14) was obtained from the chalcone (11) (3.3 g) as described for the preparation of compound (28) from the

chalcone (25) (see later). Chromatography gave a *resin* (0.8 g) which crystallized from diethyl ether, m.p. 91—92 °C; δ 3.83, 3.85, and 3.89 (9 H, s, 3 × OMe), 4.95 and 5.07 (4 H, s, 2 × OCH_2), 6.5—7.4 (13 H, m, 5'-, 6-, 6'-H, 2 × Ph), 7.65 (1 H, s, 2-H), and 7.92 (1 H, d, *J* 9 Hz, 5-H) (Found: C, 73.4; H, 6.0. $C_{32}H_{28}O_7$ requires C, 73.27; H, 6.15%).

2',8-Dibenzyloxy-3',4',7-trimethoxyisoflavan-4-one (17).—The isoflavone (14) (0.70 g) was reduced similarly to the isoflavone (28) used to prepare compound (31) (see later), to give, after purification by layer chromatography, the isoflavanone (17) (0.43 g) as an oil; δ 3.84 (9 H, s, 3 × OMe), *ca.* 3.8 (1 H, overlapped, 3-H), 4.25 [2 H, multiplet centre (mc), 2-OCH_2], 4.95 and 5.03 (4 H, s, 2 × OCH_2), 6.4—6.7 (3 H, m, 5'-, 6-, 6'-H), 7.1—7.4 (10 H, m, 2 × Ph), and 7.6 (1 H, d, *J* 9 Hz, 5-H).

4-Hydroxy-3,9,10-trimethoxy-6H-benzofuro[3,2-c][1]benzopyran, Brycarpene-4 (3).—The isoflavanone (17) (0.20 g) was debenzylated and cyclized, as described in the preparation of compound (1) from the isoflavanone (15). Evaporation and crystallization from ethanol yielded the benzopyran (3) (0.7 g), m.p. 153—155 °C (lit.,[1] m.p. 154—155 °C); δ (60 MHz) 3.90 (6 H, s, 2 × OMe), 4.18 (3 H, s, OMe), 5.50 (2 H, s, OCH_2), *ca.* 5.5br (1 H, OH), 6.44 (1 H, d, *J* 9 Hz, 1-H), 6.89 (2 H, s, 7-, 8-H), and 6.97 (1 H, d, *J* 9 Hz, 2-H).

4-Acetoxy-3,5-dibenzyloxyphenol (20).—2,5-Diacetoxy-1,3-dibenzyloxybenzene [14] (18.0 g) was boiled in methanol (90 ml) and to the suspension was added 1M sodium methoxide (6 ml). Refluxing was continued for 20 min, the solution was acidified with acetic acid, and evaporated. The residue was triturated with water to give the *phenol* (20) (15.9 g), m.p. 133—135 °C (from C_6H_6); δ 2.20 (3 H, s, OAc), 4.85 (4 H, s, 2 × OCH_2), 6.04 (2 H, s, 4-, 6-H), and 7.28 (10 H, mc, 2 × Ph) (Found: C, 71.3; H, 5.3. $C_{22}H_{20}O_5$ requires C, 72.51; H, 5.55%).

2-Acetoxy-1,3-dibenzyloxy-5-methoxybenzene (21).—The phenol (20) (36.4 g), potassium carbonate (15.6 g), and dimethyl sulphate (10.5 ml) were refluxed in acetone (220 ml) for 6 h. Evaporation and trituration with water gave the *benzene* (21) (37.5 g), m.p. 125—127 °C (from methanol); δ 2.21 (3 H, s, OAc), 3.62 (3 H, s, OMe), 4.98 (4 H, s, 2 × OCH_2), 6.16 (2 H, s, 4-, 6-H), and 7.28 (10 H, mc, 2 × Ph) (Found: C, 75.45; H, 6.0. $C_{23}H_{22}O_5$ requires C, 75.39; H, 6.05%).

2,6-Dibenzyloxy-4-methoxyphenol (22).—The acetate (21) (15.3 g) was refluxed in 0.25M sodium methoxide (70 ml) for 20 min. Evaporation and trituration with water gave the *phenol* (22) (13.0 g), m.p. 56—58 °C (from methanol); δ 3.60 (3 H, s, OMe), 5.00 (4 H, s, 2 × OCH_2), 5.15 (1 H, s, OH), 6.14 (2 H, s, 4-, 6-H), and 7.30 (10 H, s, 2 × Ph) (Found: C, 74.65; H, 6.1. $C_{21}H_{20}O_4$ requires C, 74.98; H, 5.99%).

1,2,3-Tribenzyloxy-5-methoxybenzene (23).—The phenol (22) (33.6 g) was stirred at 120 °C with benzyl chloride (21.6 ml) and potassium carbonate (27.6 g) in DMF (100 ml) for 4.5 h. Addition of water precipitated the product which was recrystallized from methanol to yield the *benzene* (23) (29.0 g), m.p. 92—94 °C; δ 3.63 (3 H, s, OMe), 4.93, and 5.02 (6 H, s, 3 × OCH_2), 6.15 (2 H, s, 4-, 6-H), and 7.30 (15 H, mc, 3 × Ph) (Found: C, 78.55; H, 6.15. $C_{28}H_{26}O_4$ requires C, 78.85; H, 6.14%).

2,3,4-Tribenzyloxy-6-methoxybenzaldehyde (8).—The above ether (23) (29.0 g) was added to a mixture of phosphoric chloride (12.9 ml), *N*-methylformanilide (16.7 ml) and chlorobenzene (66 ml), and the mixture was stirred at 60 °C for 3 h. After the addition of sodium acetate (70 g) the mixture was distilled with steam for 1 h. The organic residue was separated off and crystallized from methanol to give the *aldehyde* (8) (19.0 g), m.p. 108—110 °C; δ 3.73 (3 H, s, OMe), 4.91 (2 H), 5.08 (4 H) (s, 3 × OCH_2), 6.18 (1 H, s, 5-H), and 7.2—7.4 (15 H, m, 3 × Ph) (Found: C, 76.75; H, 6.0. $C_{29}H_{26}O_5$ requires C, 76.63; H, 5.77%).

2,3,3',4-Tetrabenzyloxy-2'-hydroxy-4',6-dimethoxychalcone (24).—3-Benzyloxy-2-hydroxy-4-methoxyacetophenone (3.6 g) and the aldehyde (8) were treated similarly to the reactants used in the preparation of compound (25), and the resinous crude product was chromatographed (eluant: benzene–acetone, 8 : 1). Crystallization from diethyl ether gave yellow *prisms* (3.1 g), m.p. 88—90 °C; δ 3.80 (6 H, s, 2 × OMe), 4.9—5.02 (8 H, m, 4 × OCH_2), 6.15 (1 H, d, *J* 8 Hz, 5'-H), 6.25 (1 H, s, 5-H), 7.0—7.5 (21 H, m, 6'-H, 4 × Ph), 7.85 and 8.20 (2 H, AB, *J* 16 Hz, $COCH_A{=}CH_B$), and 13.35 (1 H, s, OH) (Found: C, 76.5; H, 5.85. $C_{45}H_{40}O_8$ requires C, 76.25; H, 5.69%).

2',3',4',8-Tetrabenzyloxy-6',7-dimethoxyisoflavone (27).—The chalcone (24) (3.1 g) was treated similarly to the chalcone (25) used to prepare the isoflavone (28) (see later) and the crude product was chromatographed (eluant: benzene–ethyl acetate, 8 : 1) to give the isoflavone (27) as a resin (2.46 g); δ 3.68 and 3.95 (6 H, s, 3 × OMe), 5.08—5.20 (8 H, m, 4 × OCH_2), 6.47 (1 H, s, 5'-H), 7.0—7.6 (2 H, m, 6-H, 4 × Ph), 7.60 (1 H, s, 2-H), and 8.00 (1 H, d, *J* 8 Hz, 5-H).

Debenzylation and acetylation of the isoflavone (27) (0.14 g) gave *2',3',4',8-tetra-acetoxy-6,7-dimethoxyisoflavone* (0.10 g) (from ethyl acetate), m.p. 219—221 °C; δ 2.10, 2.25, 2.29, and 2.43 (12 H, s, 4 × OAc), 3.74 and 3.97 (6 H, s, OMe), 6.78 (1 H, s, 5'-H), 7.10 (1 H, d, *J* 9 Hz, 6-H), 7.76 (1 H, s, 2-H), and 8.13 (1 H, d, *J* 9 Hz, 5-H) (Found: C, 58.15; H 4.2. $C_{25}H_{22}O_{12}$ requires C, 58.36; H, 4.31%).

2',3',4',8-Tetrabenzyloxy-6',7-dimethoxyisoflavan-4-one (30).—The isoflavone (27) (1.61 g) was reduced similarly to the isoflavone (25) used to prepare compound (31) (see below) and the crude product was chromatographed on silica gel (eluant: benzene–acetone, 20 : 1) to give *compound* (30) (0.93 g), m.p. 123—124 °C; δ 3.66 and 3.88 (6 H, s, 2 × OMe), 3.8—4.7 (3 H, m, 3-H, 2-CH_2), 4.99, 5.04, 5.12 (8 H, s, 4 × OCH_2Ph), 6.34 (1 H, s, 5'-H), 6.57 (1 H, d, *J* 9 Hz, 6-H), 7.1—7.6 (20 H, m, 4 × Ph), and 7.66 (1 H, d, *J* 9 Hz, 5-H) (Found: C, 76.0; H, 5.75. $C_{45}H_{40}O_8$ requires C, 76.25; H, 5.69%).

4-Hydroxy-3,7-dimethoxy-6H-benzofuro[2,3-c][1]benzopyran-9,10-quinone (18).—The isoflavanone (30) (0.29 g) was debenzylated by catalytic hydrogenation in ethanol (25 ml) after which 2 drops of concentrated hydrochloric acid were added. The mixture was kept at 65 °C for 1 h, evaporated, dissolved in dichloromethane, and silver carbonate on Celite (2.0 g) was added. The mixture was stirred in the dark for 6 h, filtered, and passed through a short column of silica gel to yield compound (18) as dark violet *crystals* (0.033 g) not melting up to 360 °C, $\lambda_{max.}$ 231, 291, 392, and 532 nm; δ 3.84 and 3.89 (6 H, s, 2 × OMe), 5.47 (2 H, s, CH_2), 5.64 (1 H, s, 8-H), 6.53 (1 H, d, *J* 9 Hz, 2-H), and 7.51 (1 H, d, *J* 9 Hz, 1-H) (Found: C, 62.0; H, 3.6. $C_{17}H_{12}O_7$ requires C, 62.20; H, 3.69%).

4,9,10-Triacetoxy-3,7-dimethoxy-6H-benzofuro[3,2-c][1]-benzopyran (4).—The isoflavanone (30) (0.14 g) was hydrogenated and cyclized as described in the preparation of compound (18). The reaction mixture was evaporated under nitrogen and immediately acetylated with acetic anhydride–pyridine to give, after recrystallization from ethanol, *compound* (4) (0.040 g), m.p. 182—184 °C (lit., m.p.

of bryaquinone leucoacetate 205 °C); δ 2.32, 2.36, and 2.39 (9 H, s, 3 × OAc), 3.83 (6 H, s, 2 × OMe), 5.66 (2 H, s, OCH_2), 6.45 (1 H, s, 8-H), 6.54 (1 H, d, *J* 8.5 Hz, 2-H), and 7.29 (1 H, d, *J* 8.5 Hz, 1-H); δ_C 20.39, 20.48, and 20.65 (3 × CO*Me*), 55.96 and 56.16 (2 × OMe), 66.25 (C-6), 99.95 (C-8), 104.25 (C-11b), 106.68 (C-2), 110.37 (C-6b), 115.66 (C-10), 117.85 (C-1), 122.30 (C-6a), 124.99 (C-4), 138.65 (C-9), 146.55 (C-4a), 147.35 (C-7), 150.32 (C-10a), 153.01 (C-11a), 153.34 (C-3), 167.76, 168.49, and 168.63 (3 × CO) (Found: 60.35; H, 4.2. $C_{23}H_{20}O_{10}$ requires C, 60.52; H, 4.42%).

Bryaquinone leucoacetate gave δ_C 20.51, 20.51, 20.89, 56.16, 57.04, 65.73, 102.96, 104.43, 105.04, 110.19, 114.55,* 118.09, 123.00,* 128.21,* 139.73, 146.37,* 147.75,* 148.22,* 148.98, 150.79, 153.10, 168.14, 168.40, and 168.96.

2,3,4-*Tribenzyloxy*-2′-*hydroxy*-4′,6-*dimethoxychalcone* (25).—The aldehyde (8) (6.6 g) and 2-hydroxy-4-methoxyacetophenone (8.32 g) were stirred on a steam-bath in a mixture of methanol (32 ml) and 50% sodium hydroxide (64 g) for 2 h. Dilution with water and neutralization to pH 8 precipitated the product, which was recrystallized from acetic acid as yellow *needles* (6.3 g), m.p. 128—130 °C; δ 3.77 and 3.82 (6 H, s, 2 × OMe), 4.96, 5.07, and 5.09 (6 H, s, 3 × OCH_2), 6.2—6.4 (3 H, m, 3′, 5-, 5′-H), 7.1—7.6 (16 H, m, 6′-H, 3 × Ph), 7.88 and 8.23 (2 H, AB, *J* 16 Hz, $COCH_A$=CH_B), and 13.20 (1 H, s, OH) (Found: C, 75.5; H, 5.9. $C_{38}H_{34}O_7$ requires C, 75.73; H, 5.69%).

2′,3′,4′-*Tribenzyloxy*-6′,7-*dimethoxyisoflavone* (28).—To a vigorously stirred suspension of the chalcone (25) (2.8 g) in methanol (90 ml), $Tl(NO_3)_3 \cdot 3H_2O$ (2.78 g and, after 24 h, 1.0 g) was added. After 30 h the mixture was filtered and to the filtrate were added saturated brine (40 ml) and saturated sodium hydrogen carbonate (20 ml). The precipitate was extracted with chloroform, the extract was evaporated, and the residue refluxed with methanol–hydrochloric acid (10% 10 : 1, 48 ml) for 1 h. The neutralized solution was evaporated, the residue triturated with water, and recrystallized from ethanol to give compound (28) as *prisms* (1.7 g), m.p. 141—143 °C; δ 3.60 and 3.78 (6 H, s, 2 × OMe), 4.98, 5.00, and 5.08 (6 H, s, 3 × OCH_2), 6.36 (1 H, s, 6′-H), 6.6—6.9 (2 H, m, 6-, 8-H), 7.0—7.3 (15 H, m, 3 × Ph), 7.40 (1 H, s, 2-H), and 8.07 (1 H, d, *J* 8 Hz, 5-H) (Found: C, 76.0; H, 5.6. $C_{38}H_{32}O_7$ requires C, 75.98; H, 5.53%).

Hydrogenation of compound (28), immediate acetylation of the product, and recrystallization from ethyl acetate afforded the 2′,3′,4′-*triacetate* of compound (28) (1.1 g), m.p. 174—176 °C; δ 2.05, 2.08, and 2.25 (9 H, s, 3 × OAc), 3.78 and 3.83 (6 H, s, 2 × OMe), 6.70 (1 H, s, 5′-H), 6.7—7.0 (2 H, m, 6-, 8-H), 7.65 (1 H, s, 2-H), and 8.05 (1 H, d, *J* 8.5 Hz, 5-H) (Found: C, 60.4; H, 4.6. $C_{23}H_{20}O_{10}$ requires C, 60.53; H, 4.41%).

2′,3′,4′-*Tribenzyloxy*-6′,7-*dimethoxyisoflavan*-4-*one* (31).—The isoflavone (28) (3.71 g) was dissolved in a mixture of dry toluene (120 ml) and dry tetrahydrofuran (THF) (60 ml), cooled to −60 °C and treated with di-isobutylaluminium hydride (1.73 g, in toluene). After 5 h, hydrochloric acid (5%) and benzene were added. The organic phase was separated off, washed with water, evaporated, and the residue crystallized from diethyl ether to give *compound* (31) (2.11 g), m.p. 122—124 °C (from diethyl ether); δ 3.65 and 3.81 (6 H, s, 2 × OMe), *ca.* 3.7 (1 H, overlapped, 3-H), 4.6 (2 H, mc, 2-CH_2), 4.99 (2 H), and 5.12 (4 H, s, 3 × OCH_2), 6.3—6.6 (3 H, m, 5′-, 6-, 8-H), 7.1—7.5 (15 H, m, 3 × Ph), and 7.80 (1 H, d, *J* 8.5 Hz, 5-H) (Found: C, 75.55; H, 6.3. $C_{38}H_{34}O_7$ requires C, 75.73; H, 6.02%).

* Low intensity signals, difficult to distinguish from noise.

2′,3′,4′-*Triacetoxy*-6′,7-*dimethoxyisoflavan*-4-*one* (32).—The isoflavanone (31) (0.60 g) was debenzylated and acetylated to give, after recrystallization from ethanol, *compound* (32) (0.89 g), m.p. 198—200 °C; δ 2.12, 2.17, 2.21 (9 H, s, 3 × OAc), 3.17 and 3.26 (6 H, s, 2 × OMe), 4.1—4.5 (3 H, m, 2-CH_2, 3-H), 6.3—6.6 (2 H, m, 6-, 8-H), 6.63 (1 H, s, 5′-H), and 7.80 (1 H, d, *J* 9 Hz, 5-H) (Found: C, 60.3; H, 4.7. $C_{23}H_{22}O_{10}$ requires C, 60.26; H, 4.84%).

3,7-*Dimethoxy*-6H-*benzofuro*[2,3-c][1]*benzopyran*-9,10-*quinone* (19).—The isoflavanone triacetate (32) (0.30 g) was heated in a sealed tube under CO_2 with a mixture of ethyl acetate (6 ml), ethanol (6 ml), and concentrated hydrochloric acid (0.6 ml) for 6 h. After evaporation under nitrogen the residue was dissolved in dichloromethane (20 ml), silver carbonate on Celite (2.0 g) was added, and the mixture was stirred in the dark for 6 h. The oxidant was filtered off and washed several times with dichloromethane. Evaporation of the combined filtrate and chromatography (eluant: chloroform) gave compound (19) as dark violet *crystals* (0.14 g) which did not melt nor sublime up to 300 °C (deoxybryaquinone sublimes at 200 °C); δ 3.82 and 3.93 (6 H, s, 2 × OMe), 5.47 (2 H, s, CH_2), 5.64 (1 H, s, 8-H), 6.3—6.7 (2 H, m, 2-, 4-H), and 7.50 (1 H, d, *J* 9 Hz, 1-H); $\nu_{max.}$ 1 650 (shoulder), 1 625, and 1 580 cm^{-1}; *m/e* 312 (68%), 297 (21), 288 (100), 269 (12), 185 (16), 141 (9.6), 73 (11), and 44 (66); $\lambda_{max.}$ (EtOH) 209, 227 (shoulder), 301, 391, and 518 nm (Found: C, 65.05; H, 3.9. $C_{17}H_{12}O_6$ requires C, 65.38; H, 3.87%).

9,10-*Diacetoxy*-3,7-*dimethoxy*-6H-*benzofuro*[3,2-c][1]-*benzopyran*.—The isoflavanone (31) (0.30 g) was debenzylated, cyclized and acetylated similarly to the isoflavanone (30) used to prepare compounds (18) and (4). The crude product was recrystallized from methanol–acetone to give the product as *plates* (0.15 g), m.p. 161—163 °C; δ 2.32 and 2.38 (6 H, s, 2 × OAc), 3.78 and 3.84 (6 H, s, 2 × OMe), 5.63 (s, 2 H, CH_2), 6.4—6.55 (2 H, m, 2-, 4-H), 6.43 (1 H, s, 8-H), and 7.35 (1 H, d, *J* 9 Hz, 1-H); δ_C 20.18 and 20.33 (q, CO*Me*), 55.37 and 55.87 (q, OMe), 65.96 (t, C-6), 99.81 (d, C-8), 102.29 (d, C-4), 105.83 and 109.14 (s, C-6b, -11b), 107.15 (d, C-2), 155.81 (s, C-10), 121.45 (d, C-1), 122.30 (s, C-6a), 139.27 (s, C-9), 147.19 (s, C-11a), 148.07 and 150.18 (s, C-7, -11a), 155.32 (s, C-4a), 161.23 (s, C-3), and 167.76 and 168.63 (s, CO) (Found: C, 63.0; H, 4.85. $C_{21}H_{16}O_8$ requires C, 63.31; H, 4.55%).

3,4′,5′-*Tribenzyloxy*-2′-*hydroxy*-2,4-*dimethoxychalcone* (26).—3,4-Dibenzyloxy-2-hydroxyacetophenone [16] (6.1 g) and 3-benzyloxy-2,4-dimethoxybenzaldehyde [17] (7.15 g) were treated similarly to the reactants used to prepare compound (9). The crude chalcone was boiled out with methanol to give the pure *compound* (26) (7.6 g), m.p. 143—144 °C; δ 3.90 and 3.94 (6 H, s, 2 × OMe), 5.10 (2 H) and 5.32 (4 H) (s, 3 × OCH_2), 6.64 and 6.88 (2 H, s, 3′-, 6′-H), and 7.3—7.8 (19 H, m, 3 × Ph, 5-, 6-H, CH=CH) (Found: C, 74.75; H, 5.7. $C_{38}H_{34}O_7$ requires C, 75.73; H, 5.69%).

The *acetate* gave m.p. 98—101 °C (from methanol) (Found: C, 74.2; H, 5.6. $C_{40}H_{36}O_7$ requires C, 74.52; H, 5.63%).

3′,6,7-*Tribenzyloxy*-2′,4′-*dimethoxyisoflavone* (29).—A solution of the acetate of compound (26) (0.64 g) in methanol (125 ml) was treated similarly to the acetate of compound (9) used to prepare compound (12). The crude product was purified by boiling with ethanol to give the *isoflavone* (29) (0.19 g), m.p. 145—146 °C; δ 3.80 and 3.87 (6 H, s, 2 × OMe), 5.08, 5.26, and 5.28 (6 H, s, 3 × OCH_2), 6.76 (1 H, d, *J* 8.5 Hz, 5′-H), 6.95 (1 H, s, 8-H), 7.08 (1 H, d, *J* 8.5 Hz, 6′-H), 7.3—7.6 (15 H, m, 3 × Ph), 7.78 (1 H, s,

5-H), and 7.90 (1 H, s, 2-H) (Found: C, 76.35; H, 5.45. $C_{38}H_{32}O_7$ requires C, 75.98; H, 5.37%).

The isoflavone (29) (0.60 g) was debenzylated by catalytic hydrogenation to give *3',6,7-trihydroxy-2',4'-dimethoxyisoflavone*, m.p. 282—284 °C (from methanol), which was characterized as the *triacetate*, m.p. 173—175 °C; δ 2.30 and 2.32 (9 H, s, 3 × OAc), 3.66 and 3.82 (6 H, s, 2 × OMe), 6.75 (1 H, d, *J* 8.5 Hz, 5'-H), 7.30 (1 H, d, *J* 8.5 Hz, 6'-H), 7.40 (1 H, s, 8-H), 7.98 (1 H, s, 2-H), and 8.04 (1 H, s, 5-H) (Found: C, 60.25; H, 4.55. $C_{23}H_{20}O_{10}$ requires C, 60.52; H, 4.42%).

(±)-*3',6,7-Trihydroxy-2',4'-dimethoxyisoflavan*, (±)-*Bryaflavan* (33).—The triacetate isoflavone (29) (0.60 g) was hydrogenated over palladium-on-charcoal in acetic acid until uptake of the calculated amount of hydrogen was complete. The usual work-up yielded *3',6,7-triacetoxy-2',4'-dimethoxyisoflavan* (34) as a non-crystalline solid [δ 2.24, 2.26, and 2.34 (9 H, s, 3 × OAc), 2.95 (2 H, pseudo-doublet, 4-CH_2), 3.50 (1 H, mc, 3-H), 3.80 and 3.83 (6 H, s, 2 × OMe), 4.00 (1 H, q, ^2J 11, ^3J 10 Hz, 2-H_{ax}), 4.30 (1 H, q, ^2J 11, ^3J 4 Hz, 2-H_{eq}), 6.72 and 6.90 (2 H, s, 5-, 8-H), 6.74 (1 H, d, *J* 8.5 Hz, 5'-H), and 6.94 (1 H, d, *J* 8.5 Hz, 6'-H)].

The acetate was treated under nitrogen with ethanol (10 ml), which contained concentrated hydrochloric acid (0.5 ml), for 6 days. Evaporation and crystallization from diethyl ether afforded compound (33) (25 mg) m.p. 190—195 °C [lit.,[1] m.p. 188—189 °C, (3*S*)-bryaflavan]. (±)- and (3*S*)-Bryaflavan were compared by t.l.c. in several solvent systems.

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