

Synthesis of (\pm)-Eriobrucinol and Regioisomeric Monoterpenoid Coumarins, using Intramolecular Cycloadditions

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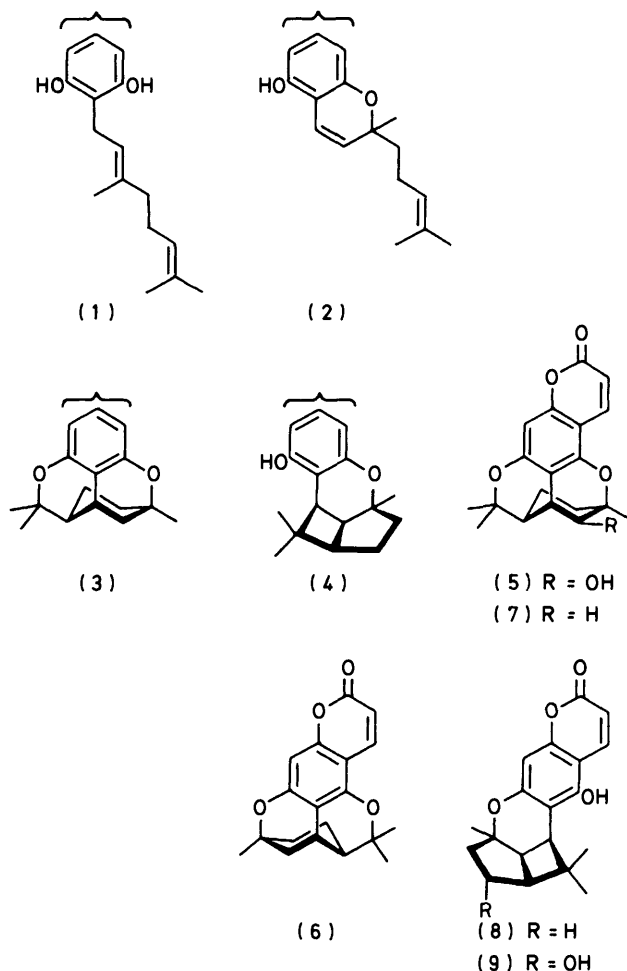
Unambiguous syntheses of the three regioisomers (8), (13), and (16), of the eriobrucinol structure, are reported. The (\pm)-cyclol (8) is spectrally identical with natural ($-$)-eriobrucinol from *Eriostemon brucei*, thus confirming Jefferies and Worth's structural proposal by synthesis.

Biogenetic condensation of terpenes with natural acetate-derived phenols leads to 'meroterpene' metabolites. Prenyl-phenols formed in the first instance, e.g. compound (1), are likely starting points for elaboration, *in vivo*, giving rise to chromens (2) and tetracyclic systems such as (3) and (4), known generically as 'citrans' and 'cyclols', respectively. Although direct evidence on the biosynthetic pathways is sparse, various synthetic transformations, e.g. (2) \rightarrow (3) and (2) \rightarrow (4), have been effected in our laboratory.¹⁻⁶

A group of prenylated coumarins of types (3) and (4) have been extracted from the Australian shrub *Eriostemon brucei*.⁷ Individually these have set difficult problems in both structure determination and regioisomer differentiation and, moreover, biogenetic relationships among the known set are not readily rationalised. Thus, *E. brucei* contains the citrans bruceol (5) and deoxybruceol, now known to have the orientation (6) (the latter name is thus misleading). The original structure (7) has been revised to (6) on synthetic grounds, and opposite orientations for the two compounds were confirmed by X-ray analysis.^{5,8b} Both bruceol and deoxybruceol occur in optically active form (absolute configurations unknown), and racemic (6) has also been found in nature. Circular dichroism data for optically active (5) and (6) are very similar, and it has been predicted⁹ that bruceol and deoxybruceol can be represented stereochemically either as (5) and (6), or as *ent*-(5) and *ent*-(6), thus raising interesting biosynthetic questions.

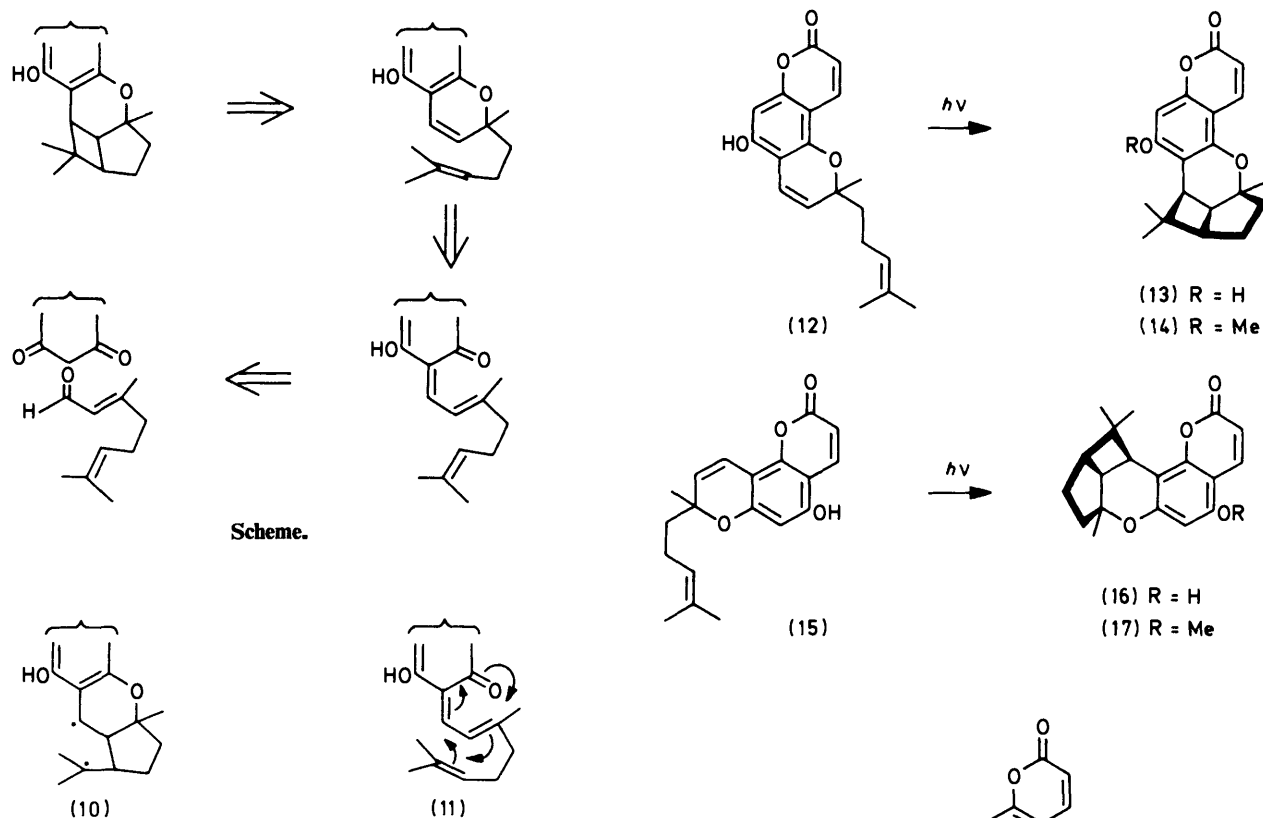
Two related cyclols, eriobrucinol and hydroxyeriobrucinol have also been discovered,¹⁰ and have been assigned structures (8) and (9), respectively; they have the same orientation (that of deoxybruceol), but their absolute chirality is undetermined. At the start of the present work, constitutions (8) and (9) were based on chemical and n.m.r. evidence, and in view of previous orientation difficulties in the area we embarked on synthesis of (\pm)-eriobrucinol and its two regioisomers. In this paper we report our results which confirm structure (8) for eriobrucinol by unambiguous synthesis. Since preliminary communication¹¹ of this work, a confirmatory X-ray analysis has appeared.^{8a}

Our earlier work has shown that the disconnections of the retrosynthetic Scheme provide the basis for a successful approach to cyclol synthesis in suitable phenols. Direct chromenylation of substituted resorcinols using α -enals or certain derivatives, under base catalysis, is possible,^{3,4,12} and the intramolecular cycloaddition required for cyclol formation has been induced thermally,^{1,2} photochemically,^{2,6,13} or with acid catalysis.^{1,2} Mechanistically, the (2 + 2) process may be concerted in a light-induced process, in accord with well known theory. It is possible that the thermal reaction proceeds by way of the diradical (10),² but an attractive alternative mechanism involves initial electrothermal opening to afford the dienone (11) (this is a known reaction of chromens), followed by concerted bicyclisation as shown.



A ($\pi 6s + \pi 2a$) process is thermally allowed in frontier orbital theory, and models show it to be geometrically feasible in the case shown. Acid catalysis of such a pathway would be understandable, as in the Diels-Alder or ene processes.

For synthesis of eriobrucinol (8) and its regioisomers (13) and (16), we required the chromens (12), (15), and (18). Chromenylation of 5,7-dihydroxycoumarin, using citral and pyridine, has been described by us in another context;⁵ the formation of only two major isomers, (12) and (15), can be rationalised.³ The chromen (12) was dissolved in [²H₅]pyridine and irradiated, using a 100-W medium-pressure mercury lamp, monitoring the reaction by ¹H n.m.r. at intervals. After 24 h no olefinic proton signals could be

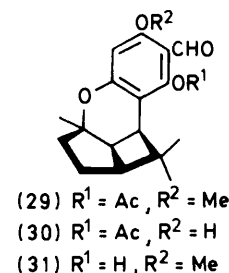
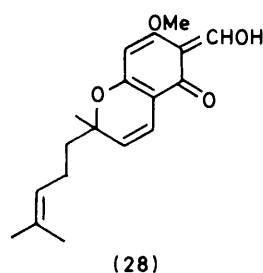
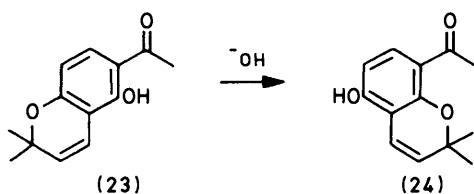
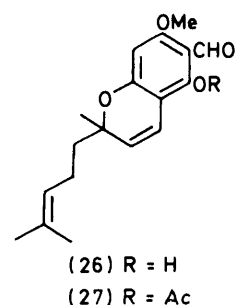
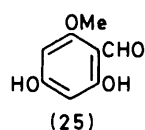
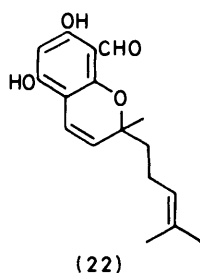


observed, and methyl resonances attributable to a single cyclol product had appeared. Isolation through preparative layer chromatography (p.l.c.) and crystallisation gave the cyclol (13) (32%), showing the shielded methyl at τ 9.04 (CDCl_3), a position characteristic for this system.² Other n.m.r. data (Experimental section) fully support the cyclol formulation, and are unexceptional. Treatment with diazomethane gave the ether (14), τ 9.36 (C-Me) and 6.20 (OMe); irradiation of the second n.m.r. band induced an increase (32%) in intensity of the signal from the aryl proton (τ 3.63), while the lactone β -H resonance (τ 1.96) was unchanged. The observed n.o.e. (nuclear Overhauser effect) supports the orientation shown for compounds (13) and (14).

The isomeric chromen (15) was similarly irradiated, but in an acetone-*t*-butyl alcohol (1 : 1) solvent mixture. A single cyclol product (16) was isolated (18% after p.l.c. and crystallisation), with τ 9.16 (shielded C-Me). The same product (34%) was obtained by heating compound (15) in pyridine at 110 °C for seven days. The corresponding methyl ether (17), from diazomethane treatment, had τ 6.18 (OMe); on irradiation at this chemical shift, reproducible n.o.e. enhancements of the aryl proton (τ 3.78, 28%) and the lactone β -H (τ 2.09, 4%) were seen. These data are consistent only with the cyclol orientation (17). Interestingly, the yield of compound (16) from (15) fell to 10% on repetition in pure acetone, and reduced to zero in pyridine. In contrast, the yield of the cyclol (13) from the chromen (12) was, as stated above, 32% in pyridine, but declined to 8% in acetone-*t*-butyl alcohol.

In none of the above experiments was a second cyclol product observed, and the orientation of the cyclols obtained indicates that no regioisomerisation occurred in the reactions. Such rearrangement has been noticed in thermal chromen \rightarrow citran conversion⁴ *via* dienone intermediates which could equally arise by photochemical means. Further, Montero

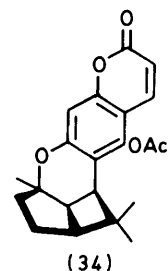
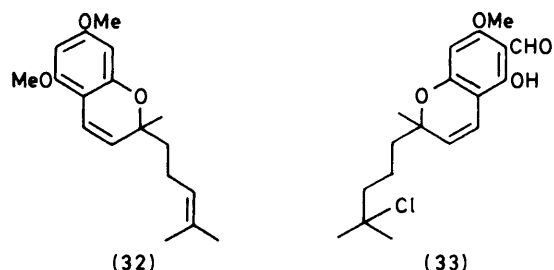
and Winternitz¹⁴ claimed to have formed both the cyclols (20) and (21) from the chromen (19) on irradiation; they invoked C-O cleavage to radicals, followed by reclosure at a second oxygen site. Dienone-mediated reorientation of chromens before intramolecular cycloaddition appears to be a more plausible explanation for their results. Hydrolysis of the lactone (16) would be expected to lead to an *o,o'*-dihydroxycinnamate, and reclosure in acid could lead to a mixture of compound (16) and eriobrucinol (8). However, a solution of compound (16) in aqueous alkali afforded only regenerated (16) on acidification after 15 min at ambient temperature, and gave back no cyclols after 3 h. The behaviour of the chromens (22) and (12) in aqueous alkali was also investigated, in view of the observation by Manners and Jurd¹⁵ that the transformation (23) \rightarrow (24) was effected by hydroxide ion. After



initial difficulties* we could repeat this experiment satisfactorily; however, similar treatment of the chromens (22) and (12) led only to unpromising mixtures. An alternative route to eriobrucinol (8), under regiocontrol, had therefore to be devised.

Formylation of 1,3-dihydroxy-5-methoxybenzene affords a methyl ether of phloroglucinaldehyde (2,4,6-trihydroxybenzaldehyde) which has been assigned both the 4-methyl ether¹⁶ and 2-methyl ether (25)¹⁷ structures. Karrer,¹⁸ on the basis of his work on this ether, favoured structure (25), and we found that the ¹H n.m.r. spectrum of this product accords with this structure, displaying resonances for both chelated and free hydroxy groups¹⁹ (τ -2.30 and 0.36; [²H₆]acetone). Reaction of the phenol (25) with citral-pyridine at 90 °C for 72 h gave a single chromen (26) (50%). The orientation of compound (26) can be predicted with confidence³ and was confirmed when irradiation at the ¹H n.m.r. OMe signal (τ 6.10) induced an n.o.e. (12%) in the aryl proton band (τ 4.08). Further, in the derived acetate (27), the olefinic protons are shifted from their position in the parent phenol by +0.3 p.p.m. (chromen-H_a) and -0.1 p.p.m. (chromen-H_b), an effect originally observed by Merlini and his co-workers²⁰ in such structures. Since compound (26) is a chelated phenol [τ -2.72 (OH); ν_{\max} 1 630 cm⁻¹ (CH=O)], the chromen orientation is demonstrated.

Irradiation, using a medium-pressure mercury lamp, of the chromen (26) in pyridine, acetone, or benzene (Pyrex) or in acetonitrile (quartz) failed to induce cycloaddition, and gave only quantitative recovery of starting material. The compound was also unaffected by heating in pyridine at 120 °C for 144 h, while boron trifluoride-diethyl ether caused rapid decomposition. However, irradiation of the acetate (27) in acetone gave, in 12 h, the desired (29) (78%). The failure of the phenol (26) to react photochemically may plausibly be explained by invoking energy dissipation through the enol (28). However, the situation is probably more complex, since the chromen (32) (prepared from 3,5-dimethoxyphenoxymagnesium bromide and citral dimethyl acetal^{12,21}) was also stable under irradiation, in either acetone or acetonitrile solution.



Attempted demethylation of the chromen (26) using boron trichloride, to try to reach a precursor to compound (18), led only to the hydrogen chloride adduct (33). However, the cyclol (29) could be demethylated with magnesium iodide-diethyl ether in benzene, with retention of the acetyl group (τ 7.60; ν_{\max} 1 755 cm⁻¹) in the major product (30) (62%). The deacetylated cyclol (31) (15%) was also obtained and the same compound could be prepared from its acetate (29) by boron trichloride treatment. Next, elaboration of the *o*-hydroxyaldehyde function of compound (30) to give a coumarin was required, at the same time avoiding deacetylation. The reagents 1,1-dimethoxy-1-(dimethylamino)ethane and 1,1-bismorpholinoethene,²² although successfully employed in deoxybruceol synthesis,⁴ both reacted with compound (30) to give complex mixtures containing none of the desired product. Neither reagent converted 2,4-diacetoxy-6-hydroxybenzaldehyde into a coumarin product, and it appears that they are unsuitable for benzaldehydes with two free or latent *o*-hydroxy groups.

* Dr. Manners has informed us that the reagent for isomerisation of compound (23) is 5% aqueous potassium hydroxide, not 50% aqueous sodium hydroxide as published. The latter reagent leads only to formation of 2,4-dihydroxyacetophenone.

Finally we resorted to the classical Perkin reaction. Treatment of the aldehyde (30) with potassium acetate-acetic anhydride provided two compounds, separated by p.l.c. The less polar (29%) was, from spectroscopic data, a coumarin acetate retaining the cyclol moiety. Deacetylation with methanol-hydrochloric acid yielded the cyclol (16), identical (^1H n.m.r., i.r., t.l.c., mixed m.p.) with the sample prepared by irradiation of compound (15). The more polar product (30%) proved to be (\pm)-eriobrucinol acetate (34); deacetylation gave (\pm)-eriobrucinol (8), m.p. 176–178 °C. Its ^1H n.m.r. and i.r. spectra were indistinguishable from those of an authentic specimen of (–)-eriobrucinol, kindly supplied by Professor Jefferies. Clear differences between the ^1H n.m.r. spectra of eriobrucinol (8) and its two regioisomers (13) and (16) could be seen. The orientation and structure of natural eriobrucinol are thus rigorously confirmed by unambiguous synthesis.

Experimental

Unless otherwise stated, the following generalisations apply. M.p.s were determined with a hot-stage microscope. I.r., ^1H n.m.r., and u.v. spectra were recorded in chloroform, deuteriochloroform, and ethanol solution, respectively. Hydroxylic protons were located in n.m.r. spectra by deuterium exchange. Log ϵ follows λ_{max} in u.v. data. Silica gel HF₂₅₄ was used for analytical t.l.c. (0.3-mm layers) and for preparative work (p.l.c.; 0.5–1-mm layers) and products were observed using u.v. irradiation. Organic solutions were dried over anhydrous (MgSO_4), and were evaporated under reduced pressure.

2,4-Dihydroxy-6-methoxybenzaldehyde (25).—Dry hydrogen chloride was passed through a stirred mixture of 1,3-dihydroxy-5-methoxybenzene (2 g) and zinc cyanide (2.2 g) in dry diethyl ether (50 cm³) for 4 h. The residue, obtained after decantation of the ethereal layer, was boiled with water (20 cm³) and the solution was allowed to cool and provided the title aldehyde (1.2 g, 50%), m.p. 202–203 °C (from benzene) (lit.,¹⁸ 203 °C), $\tau(\text{CD}_3\text{COCD}_3)$ –2.30 (1 H, s, OH), 0.00 (1 H, s), 0.36 (1 H, s, OH), 3.98 (1 H, d, J 3 Hz), 4.10 (1 H, d, J 3 Hz), and 6.08 (3 H, s).

Chromenylation of 2,4-Dihydroxy-6-methoxybenzaldehyde.—Citral (0.53 g, 3.5 mmol), 2,4-dihydroxy-6-methoxybenzaldehyde (25) (0.59 g, 3.5 mmol), and dry pyridine (0.28 g, 3.5 mmol) were stirred and heated together at 90 °C for 72 h. The product was diluted with chloroform and chromatographed [p.l.c.; n-hexane-diethyl ether (3 : 1)]. The major band afforded the *chromen* (26) (507 mg, 50%), m.p. 68–68.5 °C (from acetonitrile) (Found: C, 71.6; H, 7.55%; M^+ , 302.151. $\text{C}_{18}\text{H}_{22}\text{O}_4$ requires C, 71.5; H, 7.3%; M , 302.152); λ_{max} 225 (3.95), 232infl (3.90), 269infl (4.42), 276 (4.50), 298 (4.09), 310 (4.09), and 361 nm (3.44); ν_{max} 3 000, 1 630, and 1 575 cm⁻¹; τ –2.72 (1 H, s, OH), –0.12 (1 H, s, CHO), 3.38 (1 H, d, J 10 Hz, 4-H), 4.08 (1 H, s, 8-H), 4.64 (1 H, d, J 10 Hz, 3-H), 4.86 (1 H, br t, $\text{CH}=\text{CMe}_2$), 6.10 (3 H, s, OMe), 7.75–8.25 (4 H, m), and 8.32, 8.40, and 8.56 (each 3 H, s, Me).

Treatment of this *chromen* with acetic anhydride-pyridine at ambient temperature for 16 h gave, after the usual isolation procedure, the corresponding acetate (27) as an oil (93%) after p.l.c. [n-hexane-diethyl ether (3 : 1)] (Found: M^+ , 344.163. $\text{C}_{20}\text{H}_{24}\text{O}_5$ requires M , 344.162); λ_{max} 223 (4.03), 256infl (4.39), 262 (4.41), 291infl (3.80), 304infl (3.62), and 343 nm (3.77); ν_{max} 2 950, 1 760, 1 665, 1 640, 1 610, and 1 570 cm⁻¹; τ –0.28 (1 H, s, CHO), 3.68 (1 H, d, J 10 Hz, 4-H), 3.66 (1 H, s, 8-H), 4.52 (1 H, d, J 10 Hz, 3-H), 4.88 (1 H,

br t, $\text{CH}=\text{CMe}_2$), 6.08 (3 H, s, OMe), 7.56 (3 H, s, COMe), 7.7–8.3 (4 H, m), and 8.32, 8.42, and 8.56 (each 3 H, s, Me).

Reaction of the Chromen (26) with Boron Trichloride.—A solution of the *chromen* (26) (90 mg) in dry dichloromethane (10 cm³) was cooled to –78 °C and boron trichloride vapour was bubbled through the solution for 5 min. The solution was then allowed to warm to room temperature during 30 min, when it was washed with water, dried, and evaporated to dryness. Purification of the residue by p.l.c. [n-hexane-diethyl ether (4 : 1)] gave the *chromen* (33) (66 mg, 65%), m.p. 74–75 °C (from acetonitrile) (Found: C, 63.55; H, 6.65; Cl, 12.15%; M^+ , 338.127. $\text{C}_{18}\text{H}_{23}\text{ClO}_4$ requires C, 63.8; H, 6.8; Cl, 10.5%; M , 338.128); ν_{max} 225 (3.96), 232infl (3.90), 269infl (4.42), 275 (4.48), 298 (4.10), 310 (4.10), and 359 nm (3.47); ν_{max} (KBr) 2 998, 2 100, 1 640, 1 630, 1 590, and 1 550 cm⁻¹; τ –2.78 (1 H, s, OH), –0.14 (1 H, s, CHO), 3.30 (1 H, d, J 10 Hz, 4-H), 4.08 (1 H, s, 8-H), 4.54 (1 H, d, J 10 Hz, 3-H), 6.12 (3 H, s, OMe), 8.28 (6 H, br, $3 \times \text{CH}_2$), 8.42 (6 H, s, $2 \times \text{Me}$), and 8.56 (3 H, s, Me).

Chromenylation of 3,5-Dimethoxyphenol.—A solution of 3,5-dimethoxyphenol (3.08 g, 0.02 mol) in dry diethyl ether (25 cm³) was added, under nitrogen, to methylmagnesium bromide prepared from magnesium (0.49 g, 0.02 g-atom) in diethyl ether (25 cm³), and the mixture was stirred for 3 h. Dry benzene (100 cm³) was then added, and the diethyl ether was distilled off. A solution of citral dimethyl acetal (4.25 g, 0.02 mol) in benzene (25 cm³) was added dropwise during 30 min to the stirred slurry of aryloxymagnesium bromide in refluxing benzene. The resulting mixture was refluxed for 18 h when it was cooled, treated with dilute hydrochloric acid, and extracted with diethyl ether. The extracts were washed (aqueous hydrogen carbonate, then water), dried, and evaporated to dryness. The residue was distilled to yield the *chromen* (32) (4.73 g, 82%), b.p. 140–142 °C at 0.1 mmHg (Found: M^+ , 288.174. $\text{C}_{18}\text{H}_{24}\text{O}_3$ requires M , 288.173); λ_{max} 228infl (4.24), 234 (4.26), 240infl (4.15), 289 (3.85), and 304infl nm (3.65); τ 3.40 (1 H, d, J 12 Hz, 3-H), 3.94 (1 H, d, J 2 Hz, ArH), 3.98 (1 H, d, J 2 Hz, ArH), 4.60 (1 H, d, J 12 Hz, 4-H), 4.90 (1 H, br t, $\text{CH}=\text{CMe}_2$), 6.20 and 6.24 (each 3 H, s, OMe), 7.75–8.15 (4 H, m, $2 \times \text{CH}_3$), and 8.36, 8.44, and 8.66 (each 3 H, s, Me).

Preparation of the Cyclol (29).—The *chromen* (27) (344 mg) was dissolved in [$^2\text{H}_6$]acetone (0.75 cm³) in an n.m.r. sample tube and the solution was irradiated with a medium-pressure mercury vapour lamp (100 W). Reaction progress was monitored by ^1H n.m.r. spectroscopy which indicated completion after 12 h when the solution was evaporated to dryness. The residue was subjected to p.l.c. [n-hexane-diethyl ether (3 : 1)] to provide the *cyclol* (29) (268 mg, 78%), m.p. 141–141.5 °C (from acetonitrile) (Found: C, 69.15; H, 6.8%; M^+ , 344.162. $\text{C}_{20}\text{H}_{24}\text{O}_5$ requires C, 69.75; H, 7.0%; M , 344.162); λ_{max} 216 (4.23), 220 (4.23), 237 (4.22), 281 (4.13), and 322 nm (3.89); ν_{max} (KBr) 2 950, 2 850, 1 762, 1 670, 1 630, 1 600, and 1 585 cm⁻¹; τ –0.36 (1 H, s, CHO), 3.52 (1 H, s, ArH), 6.06 (3 H, s, OMe), 6.98 (1 H, d, J 10 Hz, ArCH), 7.4–7.55 (2 H, m), 7.56 (3 H, s, COMe), 7.95–8.5 (4 H, m), and 8.56, 8.62, and 9.20 (each 3 H, s, Me).

Deacetylation of the Cyclol (29).—A solution of the *cyclol* (29) (55 mg) in dichloromethane (10 cm³) at –78 °C was treated with boron trichloride (0.2 cm³) and the mixture was kept at –78 °C for 15 min before being poured onto ice. The organic layer was separated, dried, and evaporated to dryness. The residue after p.l.c. [n-hexane-diethyl ether (4 : 1)] gave the *cyclol* (31) (36 mg, 75%), m.p. 152–153 °C (from aceto-

nitrile) (Found: C, 71.6; H, 7.35%; M^+ , 302.153. $C_{18}H_{22}O_4$ requires C, 71.5; H, 7.3%; M , 302.152); λ_{\max} , 219 (4.20), 223infl (4.18), 233infl (4.04), 3.01 (4.31), and 339infl nm (3.48); ν_{\max} (KBr) 3 450, 2 940, 2 900, 1 610, and 1 585 cm^{-1} ; τ -2.60 (1 H, s, OH), -0.12 (1 H, s, CHO), 3.12 (1 H, s, ArH), 6.16 (3 H, s, OMe), 6.96 (1 H, d, J 8 Hz, ArCH), 7.3—7.8 (2 H, m), 8.0—8.5 (4 H, m), and 8.60, 8.64, and 9.20 (each 3 H, s, Me).

Demethylation of the Cyclol (29).—Magnesium iodide-diethyl ether was prepared from magnesium (0.4 g), iodine (2 g), dry diethyl ether (2.5 cm^3), and dry benzene (5 cm^3), and a portion (2.2 cm^3) of this solution was added to a solution of the cyclol (29) (380 mg) in benzene (40 cm^3). The mixture was refluxed for 3 h under nitrogen, when it was cooled, diluted with diethyl ether, and washed in turn with dilute hydrochloric acid and water. Evaporation of the solvents and p.l.c. (n-hexane-diethyl ether) of the residue gave two products. The less polar (52 mg, 15%), m.p. 152—153 °C (from acetonitrile), was shown to be the deacetylated cyclol (31) by spectroscopic comparisons. The more polar product was the cyclol (30) (205 mg, 62%), m.p. 127—127.5 °C (from acetonitrile) (Found: C, 68.55; H, 7.0%; M^+ , 330.146. $C_{19}H_{22}O_5$ requires C, 69.0; H, 6.7%; M , 330.147); λ_{\max} , 220 (4.23), 224 (4.23), 236 (4.07), 289 (4.16), and 329infl nm (3.71); ν_{\max} (KBr) 3 400, 2 950, 2 850, 1 755, 1 640, and 1 580 cm^{-1} ; τ -1.68 (1 H, s, OH), 0.20 (1 H, s, CHO), 3.60 (1 H, s, ArH), 7.06 (1 H, d, J 8 Hz, ArCH), 7.3—7.55 (2 H, m), 7.60 (3 H, s, COMe), 8.00—8.4 (4 H, m), and 8.49, 8.60, and 9.22 (each 3 H, s, Me).

(±)-Eriobrucinol (8).—The cyclol (30) (280 mg, 0.85 mmol), acetic anhydride (180 mg, 1.70 mmol), and fused potassium acetate (90 mg, 0.85 mmol) were heated together at 160 °C for 1.5 h and the mixture was then poured into water. The mixture was extracted with ethyl acetate and the extracts were washed (aqueous hydrogen carbonate, then water), dried, and evaporated to dryness. The residue was chromatographed [p.l.c.; n-hexane-diethyl ether (3 : 1), four elutions]. The less polar product (88 mg, 29%) was the acetate of compound (16), m.p. 141—142 °C (from diethyl ether) (Found: C, 70.85; H, 6.25%; M^+ , 354.149. $C_{21}H_{22}O_5$ requires C, 71.2; H, 6.2%; M , 354.147); λ_{\max} , 226infl (4.11), 255 (3.73), 264 (3.77), and 328 nm (4.11); ν_{\max} (KBr) 2 930, 1 760, 1 715, and 1 605 cm^{-1} ; τ 2.44 (1 H, d, J 10 Hz, CH=CHCO), 3.42 (1 H, s, ArH), 3.88 (1 H, d, J 10 Hz, CH=CHCO), 6.70 (1 H, d, J 8 Hz), 7.3—7.6 (2 H, m), 7.64 (3 H, s), 8.2—8.4 (4 H, m), and 8.48, 8.60, and 9.12 (each 3 H, s, Me). Deacetylation of this acetate (methanol-hydrochloric acid; reflux; 1 h) afforded the cyclol (16), m.p. 266—268 °C (from acetone), with 1H n.m.r., u.v., and i.r. spectra indistinguishable from those of the sample prepared as described below.

The more polar reaction product (90 mg, 30%) was (±)-*eriobrucinol acetate* (34), m.p. 151.5—152 °C (from diethyl ether) (Found: C, 71.4; H, 6.25%; M^+ , 354.148. $C_{21}H_{22}O_5$ requires C, 71.2; H, 6.2%; M , 354.147); λ_{\max} , 228 (4.19), 249 (3.65), 259 (3.51), 299infl (3.94), 310infl (4.03), and 333 nm (4.16); ν_{\max} (KBr) 2 590, 1 765, 1 720, 1 630, and 1 610 cm^{-1} ; τ 2.54 (1 H, d, J 10 Hz, CH=CHCO), 3.24 (1 H, s, ArH), 3.80 (1 H, d, J 10 Hz, CH=CHCO), 6.98 (1 H, d, J 9 Hz, ArCH), 7.3—7.6 (2 H, m), 7.58 (3 H, s, COMe), 8.2—8.4 (4 H, m), and 8.60, 8.62, and 9.14 (each 3 H, s, Me). Deacetylation of this acetate with methanol-1% concentrated hydrochloric acid (12 h at reflux; 18 h at room temperature) gave, after p.l.c. [n-hexane-ethyl acetate (4 : 1)], (±)-*eriobrucinol* (8) (32 mg, 58%), m.p. 176—178 °C (from benzene) (Found: C, 73.5; H, 6.25%; M^+ , 312.136. $C_{19}H_{20}O_4$ requires C, 73.05; H, 6.4%; M , 312.136). The 1H n.m.r. and i.r. spectra of the

synthetic specimen were indistinguishable from those of a sample of natural (—)-*eriobrucinol*.

Preparation of the Cyclol (16).—(a) The chromen (15) (150 mg) was heated at 110 °C in pyridine (750 mg) for 7 d. The reaction mixture was chromatographed [p.l.c.; benzene-ethyl acetate (9 : 1)]. The single band observable under u.v. light was eluted with chloroform, and the product was extracted with hot cyclohexane to yield unchanged chromen (15) (24 mg, 16% recovery). The residue from this extraction was crystallised from acetone to yield the cyclol (16) (51 mg, 34%), m.p. 268—269 °C (from acetone) (Found: C, 72.65; H, 6.5%; M^+ , 312.136. $C_{19}H_{20}O_4$ requires C, 73.05; H, 6.45; M , 312.136); λ_{\max} , 227infl (4.05), 260infl (3.90), 266 (3.95), and 332 nm (4.08); ν_{\max} , 3 400 and 1 700 cm^{-1} ; τ ($[^2H_5]$ pyridine) 1.70 (1 H, d, J 10 Hz, CH=CHCO), 3.40 (1 H, s, ArH), 3.75 (1 H, d, J 10 Hz, CH=CHCO), 5.20 (1 H, s, OH), 6.71 (1 H, d, J 10 Hz, ArCH), 7.7—8.3 (6 H, m), and 8.47, 8.66, and 9.16 (each 3 H, s, Me). Methylation of this compound with diazomethane in diethyl ether-ethanol gave the methyl ether (17), m.p. 199—200 °C (from benzene-light petroleum) (Found: M^+ , 326.151. $C_{20}H_{22}O_4$ requires M , 326.152); λ_{\max} , 226infl (4.12), 258infl (3.87), 265 (3.91), and 333 nm (4.08); ν_{\max} (KBr) 1 730, 1 719, 1 625, and 1 601 cm^{-1} ; τ 2.09 (1 H, d, J 10 Hz), 3.78 (1 H, s, ArH), 3.92 (1 H, d, J 10 Hz), 6.18 (3 H, s, OMe), 6.72 (1 H, d, J 10 Hz), and 8.50, 8.59, and 9.24 (each 3 H, s, Me).

(b) A solution of the chromen (15) (100 mg) in acetone (180 cm^3) was irradiated for 2.5 h by a mercury vapour lamp (100 W, medium pressure) with a Pyrex filter. Evaporation of the solvent gave a residue which afforded, after p.l.c. [benzene-ethyl acetate (9 : 1)] the cyclol (16) (10 mg, 10%), m.p. 263—265 °C; the u.v., i.r., and 1H n.m.r. spectra of this product were indistinguishable from those of the above sample. Repetition of this experiment but with acetone-*t*-butyl alcohol (1 : 1) as solvent raised the yield to 18 mg (18%).

Preparation of the Cyclol (13).—(a) The chromen (12) (90 mg) was dissolved in a mixture of acetone (90 cm^3) and *t*-butyl alcohol (90 cm^3) and the solution was irradiated as in the previous experiment. Product isolation as above gave the cyclol (13) (8.0 mg, 8%), m.p. 278—280 °C (from ethanol) (Found: C, 72.45; H, 7.05%; M^+ , 312.137. $C_{19}H_{20}O_4$ requires C, 73.05; H, 6.45%; M , 312.136); λ_{\max} , 234infl (4.16), 252 (3.82), 261 (3.77), and 339 nm (4.23); ν_{\max} (KBr) 3 200, 1 685, 1 610, and 1 595 cm^{-1} ; τ ($[^2H_5]$ pyridine) 1.92 (1 H, d, J 10 Hz, CH=CHCO), 3.41 (1 H, s, ArH), 3.76 (1 H, d, J 10 Hz, CH=CHCO), 5.15 (1 H, s, OH), 6.66 (1 H, d, J 10 Hz, ArCH), and 8.52, 8.55, and 9.04 (each 3 H, s, Me).

(b) In a similar experiment the chromen (12) (250 mg) was irradiated in pyridine (0.5 cm^3) for 25 h (reaction monitored by n.m.r.). Product isolation as before gave the cyclol (13) (82 mg, 32%), m.p. 278—280 °C, with the same spectroscopic and chromatographic characteristics as the above sample. Methylation of this product in ethanol-diethyl ether with diazomethane gave the corresponding methyl ether (14), m.p. 173—174 °C (from benzene-light petroleum) (Found: M^+ , 326.149. $C_{20}H_{22}O_4$ requires M , 326.152); λ_{\max} , 238 (4.16), 257 (3.79), and 329 nm (4.21); ν_{\max} (KBr) 1 729, 1 615, and 1 569 cm^{-1} ; τ 1.96 (1 H, d, J 10 Hz), 3.63 (1 H, s), 3.87 (1 H, d, J 10 Hz), 6.20 (3 H, s, OMe), 6.93 (1 H, d, J 10 Hz), and 8.60, 8.69, and 9.36 (each 3 H, s).

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