Tetrahedron Vol. 30, pp. 2485 to 2492. Pergamon Press 1974. Printed in Great Britain

SYNTHESIS OF ROBUSTIN AND RELATED 4-HYDROXY-3-PHENYL COUMARINS AND ISOFLAVONES

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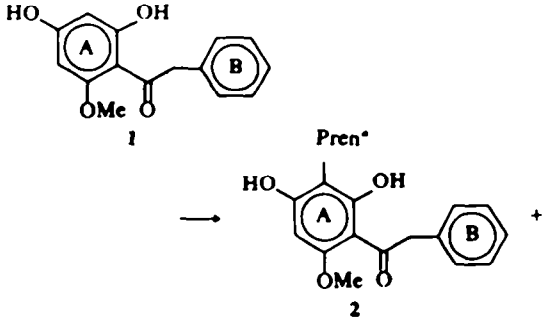
(*Received in the UK 4 November 1973; Accepted for publication 25 February 1974*)

Abstract—Robustin (**31a**) occurring in the roots of *Derris robusta* has been synthesised from mono-O-methylphloroglucinol (**20**) as follows. Hoesch condensation with homopiperonitrile (**21**) gave 2,4-dihydroxy-6-methoxyphenyl 3,4-methylenedioxybenzyl ketone (**22**) which on reaction with 2-hydroxy-2-methyl-3-butene in the presence of borontrifluoride-etherate afforded 5-C-(**24**) and 3-C-(**23**) prenyl derivatives. These on cyclodehydrogenation with DDQ followed by coumarin condensation with ethyl chloroformate yielded robustin (**31a**) and isorobustin (**32**) respectively. Model experiments with nuclear prenylation of 2,4-dihydroxy-6-methoxy-phenyl benzyl ketone (**1**), followed by oxidative cyclisation and either courmarin or isoflavone condensation have yielded new isopentenylated 4-hydroxy-3-phenylcourarins or isoflavones.

Five 4-hydroxy-3-phenyl coumarins were isolated by East, *et al.*[1] from the roots of the Indian tree *Derris robusta*; they are robustic acid, its methyl ether, robustin, its methyl ether, and derrusin. Of these, derrusnin[2] being only an oxygenated derivative, and robustic acid, and its methyl ether[3] have been synthesised.[3] Since robustin and its methyl ether were isolated only in milligram quantities, evidence regarding their structures was limited to their UV and IR spectra which suggested that robustin was possibly the piperonylic analogue of robustic acid. This suggestion was supported by partial synthesis;[1] hydrolysis of natural isoflavone robustone methyl ether (**30**) gave desoxybenzoin (**29**) which by reaction with methyl chloroformate afforded robustin (**31a**) identical with a natural sample. As robustone was synthesised[4] involving oxidative cyclisation of another natural isoflavone *viz* derrubone, it was considered a synthetic proof of the constitution of robustin and its methyl ether. In the present work, the desoxybenzoin (**29**) itself has been unambiguously synthesised which completes the total synthesis of robustin and its methyl ether. As the projected synthesis of **29** requires difficultly accessible 2,4-dihydroxy - 6-methoxyphenyl - 3,4 - methylenedioxybenzyl ketone (**22**) as a starting material, consideration was given to the various steps involved in the projected synthesis first on a simpler model *viz* 2,4 - dihydroxy - 6 - methoxy - phenyl benzyl ketone (**1**).

2,4-Dihydroxy-6-methoxy phenyl benzyl ketone[5] (**1**) was subjected to prenylation in two different ways: (i) with prenyl bromide in the presence of methanolic alkali and (ii) with 2 - hydroxy - 2 - methyl - 3 - butene in the presence of BF_3-etherate. Both the reactions gave the same two crystalline products **A** (m.p. 133–34°) and **B** (m.p. 93–94°) albeit in different yields; the latter method yielded more easily purifiable products and in better yields than the former. Both these products were suggested as isomeric monoprenyl derivatives by their elemental compositions and NMR data which further indicated the presence of a C-prenyl unit in the ring A. Thus there were signals of intact phenyl group, a singlet of only one aromatic proton of ring A, a singlet of methylene flanked by keto and phenyl groups, a doublet of benzylic methylene, a triplet of methine proton and doublet of gem dimethyl group at an unsaturated



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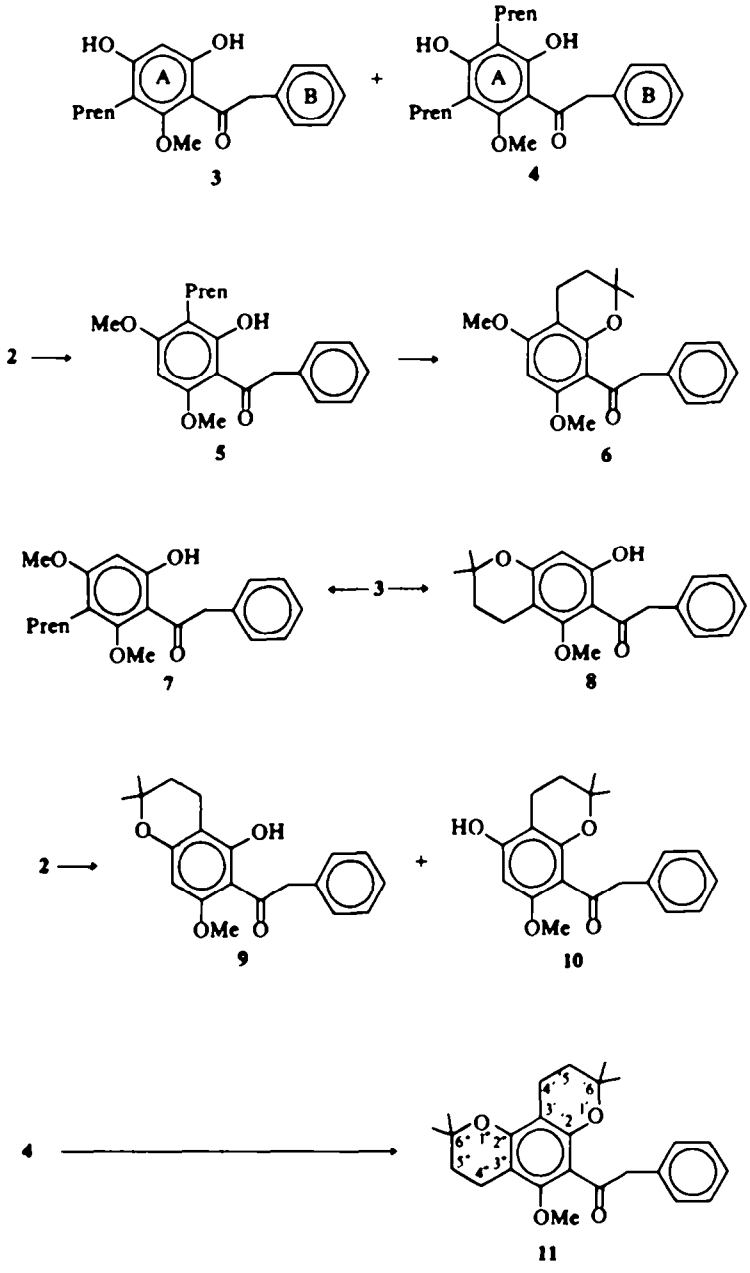
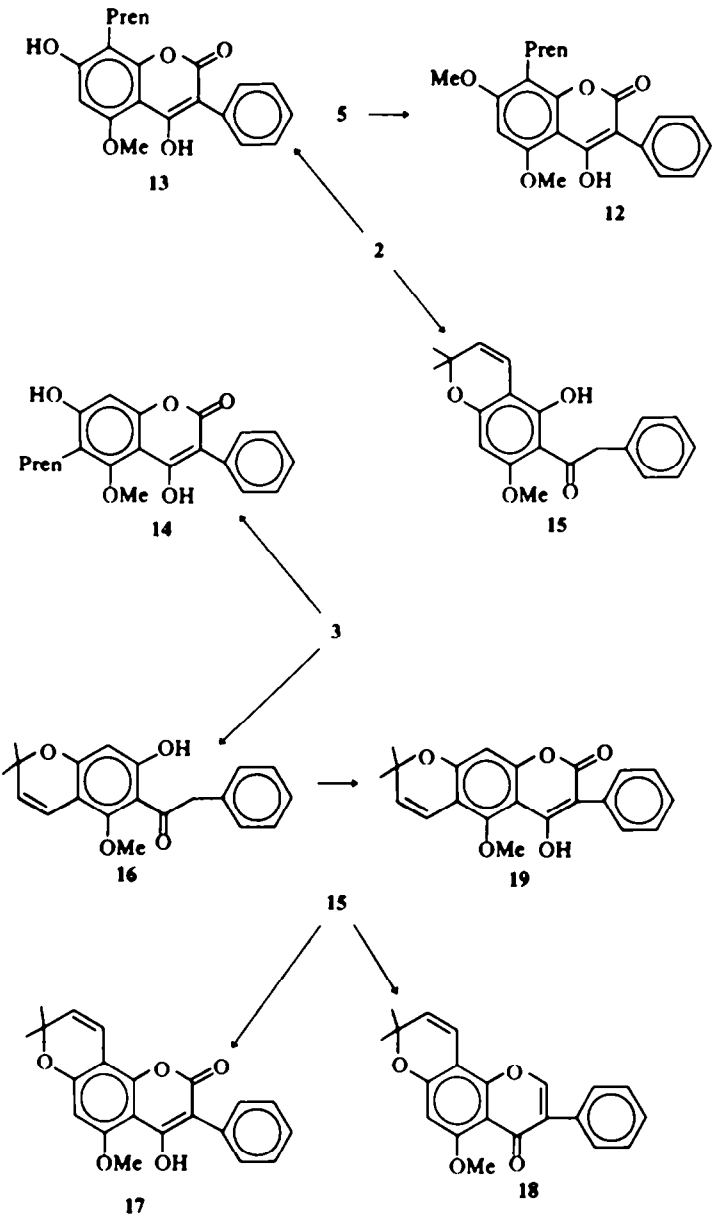
*Pren stands for γ,γ-dimethyl allyl group.



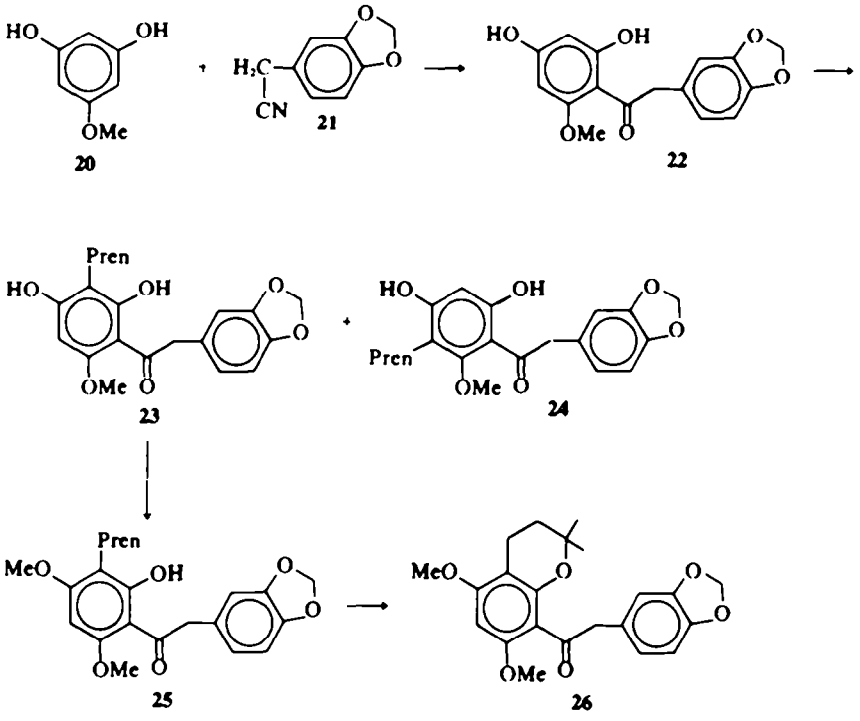
centre (Experimental). One of them is, therefore, a 3-C-prenyl derivative and the other a 5-C-prenyl derivative. To prove which is which, **A** and **B** were partially methylated in the 4 position to **A'** and **B'** respectively and then subjected to treatment with formic acid. Since **A'** yielded chroman **6** but **B'** underwent no reaction, **A** and **A'** were identified as 3-C-prenyl derivatives (**2** and **5** respectively) and **B** and **B'** as 5-C-prenyl derivatives (**3** and **7** respectively). This conclusion was further supported by acid cyclisation of **2** and **3**, the latter yielded only one monochroman (**8**); whereas the former gave two monochromans **9** (showing positive ferric reaction) and **10** (having no ferric reaction). Chroman structures at all the three compounds (**8** to **10**) were established by their NMR spectra which showed characteristic pairs of triplets (Experimental). It may be noted that in both the prenylation reactions, 3,5-di-C,C-prenyl derivative **4** was also formed but isolated only as an oil which on acid treatment afforded crystalline bischroman (**11**) as established by its NMR spectrum.



The above C-prenylated desoxybenzoins **5**, **2** and **3** could be converted with ethyl chloroformate into corresponding 4-hydroxy-3-phenylcoumarins **12**, **13**, and **14** respectively as established by their UV and IR spectra. Cyclodehydrogenation of **2** and **3** with DDQ yielded corresponding chromenes **15** and **16**, the structures of which were established by the presence of characteristic pairs of doublets for the olefinic protons of the pyran ring in their NMR spectra (Experimental). These chromenes **15** and **16**, could finally be converted into corresponding 4-hydroxy-3-phenyl coumarins **17** and **19** respectively and **15** into the isoflavone **18** in the usual manner.

Next the synthesis of robustin itself was attempted. The Hoesch condensation of mono-O-methyl phloroglucinol (**20**) with 3,4-methylenedioxybenzyl cyanide (**21**) yielded 2,4-dihydroxy-6-methoxyphenyl-3,4-methylenedioxybenzyl ketone (**22**) as established by its NMR spectrum which showed the expected signals. Prenylation of **22** with 2-hydroxy-2-methyl-3-butene in the presence of BF_3-etherate gave two crystalline products identified as 3-C-prenyl (**23**) and 5-C-prenyl (**24**) derivatives. The monomethyl ether (**25**) of the former gave on acid treatment the chroman (**26**); whereas the monomethyl ether (**27**) of the latter was recovered unchanged.

Oxidative cyclisation of **23** with DDQ yielded the



angular pyrano desoxybenzoin (**28**); whereas that of **24** afforded linear pyrano desoxybenzoin (**29**) which proved identical in m.p. and NMR spectrum with the desoxybenzoin isolated earlier by hydrolysis of robustone methyl ether (**30**). Since **29** could be converted into robustin (**31a**) as done earlier,[1] the synthesis of robustin (**31a**) and its methyl ether (**31b**) may be considered complete. The angular pyrano desoxybenzoin (**28**) and 3-C-prenyl desoxybenzoin (**23**) have also been converted into corresponding 4-hydroxy-3-phenyl coumarins **32** and **33** respectively. The former coumarin (**32**) may be named as isorobustin.

EXPERIMENTAL

Unless otherwise stated, m.p.s are uncorrected; NMR spectra were recorded in CDCl, with a Varian A-60 spectrometer using TMS as an internal reference standard; light petroleum had boiling range 60–80°; silica gel was used for column chromatography and TLC; solvent systems for TLC were : (A) benzene: EtOAc (9:1) (B) benzene : light petroleum (3:1) (C) benzene : EtOAc (19:1) (D) benzene : MeOH (4:1) (E) benzene : EtOAc (3:2) (F) benzene : MeOH (9:1) (G) benzene : EtOAc (1:1) (H) benzene : EtOAc (4:1); R_f values are those taken on TLC.

Prenylation of 2,4-dihydroxy-6-methoxy phenylbenzyl ketone (**1**)

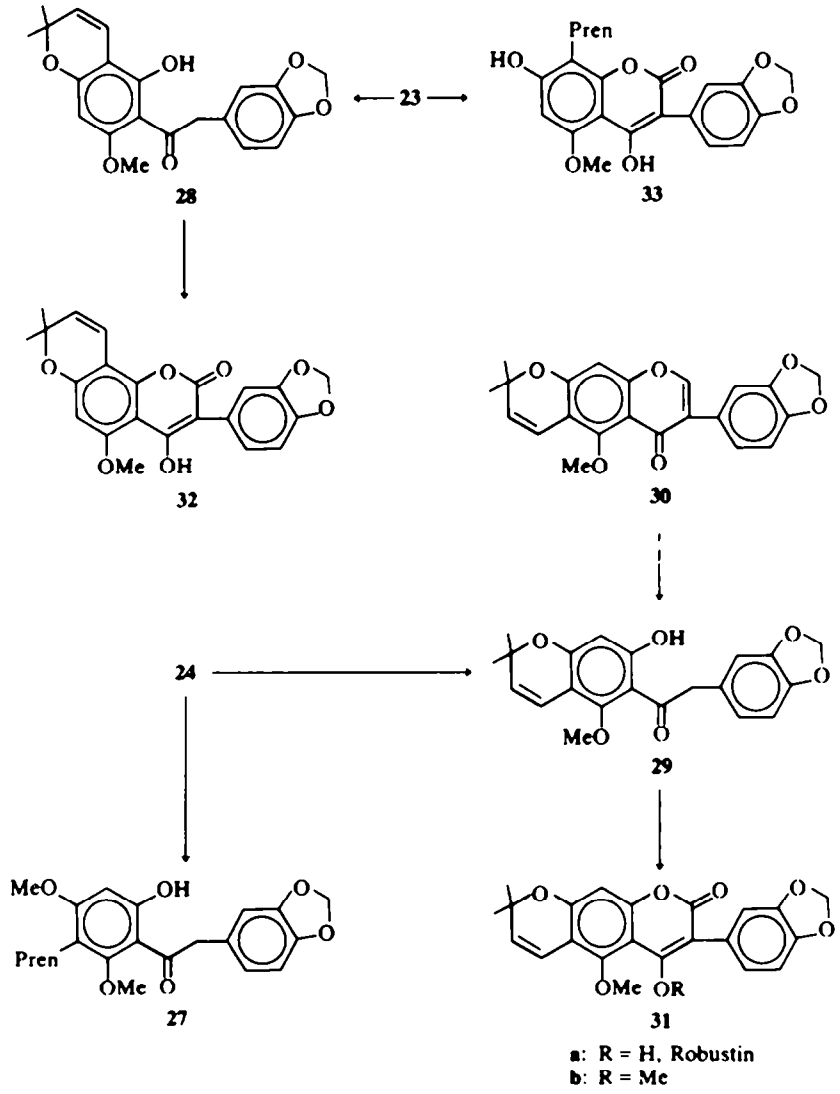
(*i*) *Using 2-hydroxy-2-methyl - 3-butene.* To an ice-cold soln of **1** (3g) in dioxan (25 ml) BF_3 etherate (1·8 ml) was added slowly with shaking followed by 2-hydroxy - 2-methyl-3-butene (1·6 ml) in dioxan (10 ml). The whole mixture was shaken (1 h) at room temp, diluted with moist ether (300 ml) and the ethereal extract washed with ice-cold water, dried over Na_2SO_4, concentrated and the residue subjected to column chromatography. The column was eluted successively with (i) benzene: light petroleum (1:19) (ii) benzene : light petroleum (1:9) (iii) benzene : light petroleum (2:3) and (iv) benzene alone, when four fractions A to D were obtained.

Fraction-A was obtained as an oil (100 mg), green ferric reaction; R_f 0·6 (solvent A). Treatment with formic acid (20 ml) yielded **11** which crystallised from MeOH as white needles, m.p. 125–26°; negative ferric reaction; R_f 0·5 (solvent A); NMR: δ 1·31 (1 s, 12 H, 2-$(CH_3)_2C$<), 1·69 and 2·62 (2t, J = 6Hz, 8H, 2-CH_2–CH_2–), 3·64 (1s, 3H, 1-OCH_3–), 4·12 (1s, 2H, 1-CO–CH_2–) and 7·27 ppm (1s, 5 aromatic H, C_6H_5–) (Found: C, 76·3; H, 7·6. $C_{23}H_{30}O_4$ requires: C, 76·1; H, 7·7%). Therefore the oil should be 3,5-di-C,C-prenyl derivative (**4**).

Fraction B crystallised from benzene : light petroleum mixture yielding **2** (300 mg), as pale yellow needles, m.p. 133–34°; R_f 0·50 (solvent A); green ferric reaction; NMR: δ 1·83 (1 broad s, 6H, 1-$(CH_3)_2C$=), 3·40 (1d, J = 7·5 Hz, 2H, 1-CH_2–), 3·83 (1s, 3H, 1-OCH_3), 4·34 (1s, 2H, 1-CO–CH_2–), 5·31 (1t, J = 7·5 Hz, 1H, 1-CH=), 5·91 (1s, 1 aromatic H at position 5) and 7·26 ppm (1s, 5 aromatic H, C_6H_5–) (Found: C, 74·1; H, 7·0. $C_{20}H_{22}O_4$ requires: C, 73·6; H, 6·8%).

Fraction C gave **3** (400 mg) which crystallised from benzene : light petroleum mixture as white plates, m.p. 93–94°; R_f 0·45 (solvent A); green ferric reaction; NMR: δ 1·78 (1 broad s, 6H, 1-$(CH_3)_2C$=), 3·36 (1d, J = 8·5 Hz, 2H, 1-CH_2–), 3·70 (1s, 3H 1-OCH_3–), 4·40 (1s, 2H, 1-CO–CH_2–), 5·30 (1t, J = 8·5 Hz, 1H, 1 CH=), 6·22 (1s, 1 aromatic H in position 3) and 7·24 ppm. (1s, 5 aromatic H, C_6H_5–) (Found: C, 73·3; H, 6·9. $C_{20}H_{22}O_4$ requires: C, 73·6; H, 6·8%).

Fraction D on crystallisation from benzene afforded the starting material (1·3g).



a: R = H, Robustin
b: R = Me

(*ii*) *Using prenyl bromide.* The ketone **1** (3g) was dissolved in abs. methanolic KOH (3·0g in 35 ml) and the resulting soln cooled and treated with prenyl bromide (4·5 ml) slowly while shaking. After keeping the mixture for 20 h at room temp, it was diluted with ice-cold water, acidified and the whole mixture extracted with ether. The ether residue on column chromatography and elution with solvents in the same order as in the first method gave four fractions A to D identical with those obtained above, albeit in different amounts: Fraction A (100 mg), B (300 mg), C (200 mg) and D (1·8g).

2-Hydroxy-4,6-dimethoxy-3-C-prenyl phenyl benzyl ketone (**5**)

3-C-Prenyl ketone (**2**, 200 mg) was refluxed (3·5 h) with Me_2SO_4 (0·06 ml) in the presence of anhyd K_2CO_3 (1g) and acetone (25 ml). Acetone was removed, water added and solid filtered. The product (**5**, 200 mg) crystallised from MeOH as white needles, m.p. 113–14°; R_f 0·60 (solvent B); dark green ferric reaction; NMR: δ 1·72 and 1·82 (2s, 6H, 1-$(CH_3)_2C$=), 3·35 (1d, J = 7 Hz, 2H, 1-CH_2- of prenyl unit), 3·94 (1s, 6H, 2-OCH_3-), 4·40 (1s, 2H, 1-CO-CH_2), 5·28 (1t, J = 7 Hz, 1-CH_2=), 6·02 (1s, 1 aromatic H at position 5) and 7·32 (1s, 5 aromatic H, C_6H_5-) (Found: C, 73·8; H, 7·2. $C_{21}H_{24}O_4$ requires: C, 74·1; H, 7·1%).

5,7-Dimethoxy-2,2-dimethyl-8-phenacylchroman (**6**)

The above ketone (**5**, 50 mg) was dissolved in warm formic acid (10 ml) and left at room temp (1 h). The yellow soln was then poured over ice-cold water and the whole mixture extracted with chloroform. The organic layer was dried over Na_2SO_4, evaporated and the solid (**6**) crystallised from MeOH as white needles (40 mg), m.p. 147–48°; R_f 0·81 (solvent A); negative ferric reaction; NMR: δ 1·27 (1s, 6H, 1-$(CH_3)_2C$<), 1·72, 2·50 (2t, J = 6 Hz, 4H, 1-CH_2-CH_2-), 3·73–3·82 (1 broad s, 6H, 2-OCH_3-), 4·03 (1s, 2H, 1-CO-CH_2-), 5·80 (1s, 1 aromatic H at position 6) and 7·25 ppm (1s, 5 aromatic H, C_6H_5-) (Found: C, 74·0; H, 7·1. $C_{21}H_{24}O_4$ requires: C, 74·1; H, 7·1%).

2-Hydroxy-4,6,dimethoxy-5-C-prenyl phenyl benzyl ketone (7)

The 5-C-prenyl ketone (3, 200 mg) was refluxed (4 h) with Me_2SO_4 (0·06 ml) in the presence of ignited K_2CO_3 (1g) and acetone (30 ml). The product (7) crystallised from MeOH as white plates, m.p. 80–81°; R_f 0·54 (solvent B); light green ferric reaction; NMR: δ 1·72 and 1·82 (2s, 6H, 1-$(CH_3)_2$C=), 3·34 (1d, J = 6·5 Hz, 2H, -CH_2- of prenyl unit), 3·95 (1s, 6H, 2-OCH_3-), 4·40 (1s, 2H, 1-CO-CH_2-), 5·28 (1t, 1H, 1-CH=), 6·05 (1s, 1 aromatic H at position 3) and 7·32 ppm (1s, 5 aromatic H, C_6H_5-) (Found: C, 74·1; H, 7·1; $C_{21}H_{24}O_4$ requires: C, 74·1; H, 7·1%). On heating with formic acid (2 h), it was recovered unchanged.

7-Hydroxy-5-methoxy-2,2-dimethyl-6-phenacylchroman (8)

5-C-Prenyl ketone (3, 80 mg) was warmed with formic acid (15 ml; 0·5 hr) on a water bath and then left at room temp (3 hr). The product was passed through silica gel and eluted with light petroleum when the chroman 8 was obtained. It crystallised from MeOH as white needles (50 mg), m.p. 53–54°; green ferric reaction; R_f 0·50 (solvent C); NMR: δ 1·31 (s, 6H, 1-$(CH_3)_2$C<), 1·76 and 2·60 (2t, J = 6 Hz, 4H, 1-CH_2-CH_2-), 3·8 (1s, 3H, 1-OCH_3), 4·32 (1s, 2H, 1-CO-CH_2), 5·82 (1s, 1 aromatic H at position 8) and 7·21 ppm (1s, 5 aromatic H, C_6H_5-) (Found: C, 73·1; H, 6·4. $C_{20}H_{22}O_4$ requires: C, 73·6; H, 6·8%).

Acid cyclisation of 2,4-dihydroxy-6-methoxy-3-C-prenyl phenyl-benzylketone (2)

Formation of 5-hydroxy-7-methoxy-2,2-dimethyl-6-phenacylchroman (9) *and its 8-phenacyl isomer* (10). The desoxybenzoin (2, 200 mg) was warmed with formic acid (20 ml; 0·5 h) and then left at room temp for 4 h. The product on TLC showed two spots. Hence the mixture was separated by column chromatography and eluting successively by (i) light petroleum and (ii) benzene, when two fractions A and B were obtained.

Fraction A crystallised from MeOH yielding 9 as white crystals (80 mg), m.p. 95–96°, green ferric reaction ; R_f 0·79 (solvent A); NMR: δ 1·32 (1s, 6H, 1-$(CH_3)_2$C<), 1·89 and 2·61 (2t J = 6 Hz, 4H, 1-CH_2-CH_2-), 3·80 (1s, 3H, 1-OCH_3), 4·34 (1s, 2H, 1-CO-CH_2), 5·85 (1s, 1 aromatic H at position 8) and 7·25 ppm (1s, 5 aromatic H, C_6H_5-) (Found: C, 74·1; H, 7·3. $C_{20}H_{22}O_4$ requires: C, 73·6; H, 6·8%).

Fraction B crystallised from MeOH affording 10 as white needles (60 mg), m.p. 192–93°; negative ferric reaction; R_f 0·5 (solvent E); NMR: δ 1·36 (1s, 6H, 1-$(CH_3)_2$C<), 1·81 and 2·64 (2t, J = 6 Hz, 4H, 1-CH_2-CH_2-), 3·84 (1s, 3H, 1-OCH_3), 4·36 (1s, 2H, 1-CO-CH_2), 5·87 (1s, 1 aromatic H at position 6) and 7·27 ppm (1s, 5 aromatic H, C_6H_5-) (Found: C, 73·8; H, 7·0 $C_{20}H_{22}O_4$ requires; C, 73·6; H, 6·8%).

4-Hydroxy-5,7-dimethoxy-8C-prenyl-3-phenylcoumarin (12)

A mixture of 3-C-prenyl ketone (5, 100 mg), ethyl chloroformate (0·06 ml), anhyd K_2CO_3 (1g) and acetone (20 ml) was refluxed (3 h), poured over water and acidified. The product was crystallised from MeOH when the coumarin (12) was obtained as white shining needles (50 mg), m.p. 206–7°; R_f 0·58 (solvent D); ν_{max}^{KBr} 1710 cm^{-1} (C=O) (Found: C, 71·9; H, 6·2 $C_{22}H_{22}O_5$ requires: C, 72·1; H, 6·0%).

4,7-Dihydroxy-5-methoxy-8-C-prenyl-3-phenylcoumarin (13)

A mixture of 3-C-prenyl ketone (2, 100 mg), ethyl chloroformate (0·10 ml), anhyd K_2CO_3 (1g) and acetone (10 ml) was refluxed (3 h). The resulting solid was hydrolysed with 4% Na_2CO_3 aq on a water bath (1 h). The mixture was cooled and acidified when 13 was obtained. It crystallised from MeOH as white crystals (40 mg), m.p. 241–42°; R_f 0·65 (solvent D); λ_{max}^{MeOH} 322 and 242 nm; ν_{max}^{Nujol} 1670 cm^{-1} (C=O) (Found: C, 71·3; H, 5·7. $C_{21}H_{20}O_5$ requires: C, 71·6; H, 5·7%).

4,7-Dihydroxy-5-methoxy-6-C-prenyl-3-phenylcoumarin (14)

5-C-Prenylketone (3, 100 mg), ethyl chloroformate (0·1 ml), anhyd K_2CO_3 (1g) and acetone (20 ml) was refluxed (3·5 h). The product 14 crystallised from MeOH as white silky needles (40 mg), m.p. 231–32°; R_f 0·60 (solvent D); λ_{max}^{MeOH} 322 and 243 nm; ν_{max}^{Nujol} 1670 cm^{-1} (C=O) (Found: C, 71·1; H, 5·9. $C_{21}H_{20}O_5$ requires: C, 71·6; H, 5·7%).

5-Hydroxy-7-methoxy-2,2-dimethyl-6-phenacylchromene (15)

To a soln of 3-C-prenyl ketone (2, 200 mg) in dry benzene (25 ml) was added DDQ (180 mg) and the resulting soln heated on a water bath (1 h) when colourless hydro-quinone separated out. It was filtered while hot and the residue washed with dry benzene. The filtrate was distilled to remove the solvent and the residue chromatographed. Elution with light petroleum gave 15 (150 mg) as yellow needles, m.p. 116–17°; green ferric reaction; R_f 0·8 (solvent C); NMR: δ 1·30 (1s, 6H, 1-$(CH_3)_2$C<), 3·82 (1s, 3H, 1-OCH_3), 4·30 (1s, 2H, 1-CO-CH_2-), 5·44 and 6·68 (2d, J = 10 Hz each, 2H at positions 3 and 4), 5·88 (1s, 1 aromatic H at position 8) and 7·25 ppm. (1s, 5 aromatic H, C_6H_5-) (Found: C, 73·7; H, 5·9. $C_{20}H_{20}O_4$ requires: C, 74·0; H, 6·2%).

4-Hydroxy-5-methoxy-6",6"-dimethyl-3-phenyl pyrano (2",3":7,8) coumarin (17)

The chromene (15, 100 mg), ethyl chloroformate (0·07 ml) and acetone (10 ml) were refluxed together with anhyd K_2CO_3 on a water bath (4·5 h). 17 crystallised from MeOH as white shining needles (40 mg), m.p. 202–3°; R_f 0·52 (solvent F); λ_{max}^{EtOH} 313 and 266 nm; ν_{max}^{Nujol} 1675 cm^{-1} (C=O) (Found: C, 72·3; H, 5·2. $C_{21}H_{18}O_5$ requires: C, 72·0; H, 5·2%).

4-Hydroxy-5-methoxy-6",6"-dimethyl-3-phenyl pyrano (2",3":7,6) coumarin (19)

To a soln of the 5-C-prenyl ketone (3, 150 mg) in dry benzene (125 ml) was added DDQ (100 mg) and the whole soln heated on water bath (1 h). The product was chromatographed and elution with light-petroleum gave 16 as yellow oil (100 mg); light green ferric reaction; R_f 0·75 (solvent A); NMR: δ 1·48 (1s, 6H, 1-$(CH_3)_2$C<), 3·82 (1s, 3H, 1-OCH_3), 4·30 (1s, 2H, 1-CO-CH_2-), 5·44 and 6·68 (2d, J = 10 Hz each, 2H at 3 and 4 positions), 5·92 (1s, 1 aromatic H at position 8) and 7·29 ppm (1s, 5 aromatic H of phenyl ring). It was directly converted into coumarin (19) by heating with ethyl chloroformate (0·09 ml), anhyd

K_2CO_3 (1g) and acetone (10 ml) on a water bath (3·5 h). The product crystallised from acetone as white silky needles (100 mg), m.p. 231–32°; R_f 0·5 (solvent F); λ_{max}^{EtOH} 302 and 242 nm: ν_{max}^{KBr} 1675 cm^{-1} (C=O) (Found: C, 72·3; H, 5·0. $C_{21}H_{18}O_5$ requires: C, 72·0; H, 5·2%).

5-Methoxy-6'':6'' dimethyl pyrano (2'',3'':7,8) isoflavone (**18**)

A soln of **15** (120 mg) in ethyl formate (20 ml) was added slowly while shaking to a flask containing powdered Na (120 mg) and ethyl formate (20 ml) at 0° during 1h. After keeping in fridge (12 h), water was added and the whole mixture extracted with ether. The dried ether residue was refluxed with Ac_2O (10 ml), 0·5 h), poured into water and the solid crystallised from MeOH when **18** was obtained as shining needles (50 mg), m.p. 165–66°; R_f 0·77 (solvent G); λ_{max}^{EtOH} 308 and 265 nm; ν_{max}^{KBr} 164 cm^{-1} (C=O) (Found: C, 74·9; H, 5·4. $C_{21}H_{18}O_4$ requires: C, 75·4; H, 5·4%).

2,4 - Dihydroxy - 6 - methoxy phenyl 3,4 - methylene - dioxybenzyl ketone (**22**)

Phloroglucinol mono-methyl ether[7] (**20**, 5g) and **21** (5·0g) were dissolved in dry ether (75 ml) and the soln treated with fused $ZnCl_2$ (1g). The mixture was cooled to 0° and a stream of dry HCl gas passed (4 h). After leaving it over night at 0°, the ketimine hydrochloride separated as an oil. The upper layer of the ether was decanted off and the oily liquid washed twice with dry ether. The residue was then treated with ice-cold water (75 ml) and heated on water bath (2 h). The product was cooled, extracted with ether and the residue subjected to column chromatography. The fraction eluted with benzene:light petroleum (3:1) crystallised from benzene when **22** separated as white silky needles (2g), m.p. 138–39°; reddish brown ferric reaction; R_f 0·6 (solvent H); NMR: δ 3·90 (1s, 3H, 1–OCH_3); 4·29 (1s, 2H, 1–CO–CH_2), 5·98 (1s, 2H, 1–O–CH_2–O–), 6·02 (1s, 2 aromatic H at positions 3 and 5), 6·78 ppm (1s, 3 aromatic H at 2', 5', 6' positions of benzyl unit) (Found: C, 63·6; H, 4·6. $C_{16}H_{14}O_6$ requires: C, 63·6; H, 4·7%).

Prenylation of 2,4-dihydroxy - 6-methoxy phenyl-3,4-methylene - dioxybenzyl ketone (**22**)

To an ice-cold soln of **22** (4g) in dry dioxan (200 ml) was added BF_3-etherate (2 ml) slowly while shaking, followed by 2 - hydroxy - 2 - methyl - 3 - butene (0·19 ml) in dioxan (10 ml) in one lot. The whole mixture was shaken for 1 h at room temp and the product subjected to column chromatography. Successive elution with (i) benzene:light petroleum (1:1), (ii) benzene:light petroleum (2:3), and (iii) 100% benzene gave three fractions A to C.

Fraction A crystallised from benzene:light petroleum yielding **23** (300 mg) as yellow needles, m.p. 155–56°; R_f 0·61 (solvent H); brownish green ferric reaction; NMR δ 1·74 and 1·77 (2s, 6H, 1–(CH_3)$_2$C=), 3·36 (1d, J = 7·5 Hz, 2H, 1–CH_2– of prenyl unit), 3·82 (1s, 3H, 1–OCH_3), 4·24 (1s, 2H, 1–CO–CH_2–), 5·30 (1t, J = 7·5 Hz, 1H, 1–CH=), 5·92 (1s, 3H, 1–O–CH_2–O and one aromatic H of phenyl ring) and 6·72 ppm (1s, 3 aromatic H of benzyl unit) (Found C, 68·2; H, 6·4. $C_{21}H_{22}O_6$ requires: C, 68·1; H, 6·0%).

Fraction B crystallised from benzene:light petroleum giving **24** (0·2g) as white plates, m.p. 105–6°; R_f 0·58 (solvent H); light green ferric reaction; NMR: δ 1·82 (1s, 6H, 1–(CH_3)$_2$C=), 3·42 (1d, J = 7·5 Hz, 2H, 1–CH_2–), 3·82 (1s, 3H, 1–O–CH_3–), 4·40 (1, 2H, 1–CO–CH_2–), 5·36 (1t, J = 7·5 Hz, 1H, 1–CH=), 6·05 (1s, 2H, 1–O–CH_2–O–), 6·34 (1s, 1 aromatic H of phenyl ring) and 6·98 ppm (1s, 3 aromatic H in benzyl ring) (Found: C, 68·1; H, 5·9. $C_{21}H_{22}O_6$ requires: C, 68·1; H, 6·0%).

Fraction C crystallised from benzene yielding starting material **22**, (2g)

2-Hydroxy-4,6-dimethoxy-3-C-prenylphenyl 3,4-methylenedioxy-benzyl ketone (**25**)

The above 3-C-prenyl ketone (**23**, 200 mg) was refluxed with Me_2SO_4 (0·067 ml) in the presence of anhyd K_2CO_3 (1g) and acetone (20 ml) for 3·5 h. The product **25** crystallised from MeOH as yellow needles (200 mg), m.p. 118–19°; green ferric reaction; R_f 0·60 (solvent A); NMR: δ 1·64 and 1·73 (2s, 6H, 1–(CH_3)$_2$C=), 3·28 (1d, J = 8·5 Hz, 2H, 1–CH_2– of prenyl unit), 3·86 (1s, 6H, 2–OCH_3), 4·22 (1s, 2H, 1–CO–CH_2–), 5·20 (1t, J = 8·5 Hz, 1H, 1–CH=), 5·90 (1s, 2H, 1–O–CH_2–O–), 5·95 (1s, 1 aromatic H of phenyl unit) and 6·70 ppm (1s, 3 aromatic H of benzyl unit) (Found: C, 68·4: H, 5·9. $C_{22}H_{24}O_6$ requires: C, 68·8; H, 6·2%).

5 - 7 - Dimethoxy - 2,2 - dimethyl - 8 - (3,4 - methylenedioxy phenacyl chroman (**26**)

The above ketone (**25**, 150 mg) was dissolved in warm formic acid (20 ml) and then left at room temp (1 h). **26** crystallised from MeOH as white shining needles (130 mg), m.p. 160–61°; negative ferric reaction; R_f 0·65 (solvent H); NMR: δ 1·28 (1s, 6H, 1–(CH_3)$_2$C<), 1·75 and 2·58 (2t, J = 6 Hz, 4H, 1–CH_2–CH_2–) 3·74 & 3·82 (2s, 6H, 2–OCH_3), 3·98 (1s, 2H, 1–CO–CH_2), 5·88 (1s, 2H, 1–O–CH_2–O–), 6·1 (1s, 1 aromatic H at position 6) and 6·69 ppm. (1s, 3 aromatic H of phenacyl unit) (Found: C, 68·4; H, 6·0. $C_{22}H_{24}O_6$ requires: C, 68·8; H, 6·2%).

2 - Hydroxy - 4,6 - dimethoxy - 5 - C - prenylphenyl 3,4-methylenedioxy - benzyl ketone (**27**)

The ketone **24** (200 mg) was refluxed with Me_2SO_4 (0·06 ml) in the presence of ignited K_2CO_3 (1g) and acetone (25 ml) (4 h). The product (**27**) crystallised from MeOH as white needles (200 mg), m.p. 83–84°; violet ferric reaction; R_f 0·58 (solvent A); NMR: δ 1·64 and 1·74 (2s, 6H, 1–(CH_3)$_2$C=), 3·26 (1d, J = 7·5 Hz, 2H, 1–CH_2– of prenyl unit), 3·86 (1s, 6H, 2–CH_3), 4·22 (1s, 2H, 1–CO–CH_2–), 5·18 (1t, J = 7 Hz, 1H, 1–CH=), 5·89 (1s, 2H, 1–O–CH_2–O–), 5·95 (1s, 1 aromatic H of phenyl part) and 6·70 ppm (1s, 3 aromatic H of benzyl part) (Found: C, 69·2; H, 6·2. $C_{22}H_{24}O_6$ requires: C, 68·8; H, 6·2%). Heating with formic acid brought no change.

5 - Hydroxy - 7 - methoxy - 2,2 - dimethyl - 6 - (3,4 methylenedioxyphenacyl) chromene (**28**)

The ketone **23** (150 mg) was refluxed with DDQ (100 mg) in dry benzene (20 ml). The product on column chromatography and elution with benzene:light petroleum (1:1) gave a solid which on crystallisation from light-petroleum yielded **28** as yellow crystals (100 mg), m.p. 128–29°; green ferric reaction; R_f 0·64 (solvent C); NMR: δ 1·46 (1s, 6H, 1–(CH_3)$_2$C<), 3·92 (1s, 3H, 1–OCH_3), 4·32 (1s, 2H, 1–CO–CH_2), 5·55 and 6·80 (2d, J = 10 Hz, 2 olefinic H at 3,4 positions), 6·08 (1s, 2H, 1–O–CH_2–O–), 6·22 (1s, 1 aromatic H at position 8) and 6·88 ppm (1s, 3 aromatic H of phenacyl part) (Found: C, 68·5; H, 5·8. $C_{21}H_{20}O_6$ requires: C, 68·5: H, 5·4%).

7 - *Hydroxy* - 5 - *methoxy* - 2,2 - *dimethyl* - 6 - (3,4 - *methylenedioxyphenacyl*) *chromene* (**29**)

The ketone **24**, 70 mg) was refluxed with DDQ (100 mg) in dry benzene (20 ml). The product on column chromatography and elution with light petroleum gave a solid which on crystallisation from light petroleum yielded **29** as yellow plates (50 mg), m.p.83–84°; green ferric reaction; R_f 0·6 (solvent C); NMR: δ 1·46 (1s, 6H, 1–$(CH_3)_2C$<, 3·82 (1s, 3H, 1–OCH_3), 4·32 (1s, 2H, 1–CO–CH_2–), 5·64 and 6·54 (2d, J = 10 Hz each, 2 olefinic H at 3,4 positions), 5·95 (1s, 2H, 1–O–CH_2–O–); 6·22 (1s, 1 aromatic H at position 8) and 6·75 ppm (1s, 3 aromatic H of phenacyl part) (Found: C, 68·0; H, 5·8. $C_{21}H_{20}O_6$ requires: C, 68·5; H, 5·4%). This agrees in m.p. with the desoxybenzoin obtained earlier[1] from robustone methyl ether (**30**). Further it could be converted into robustin as described earlier.[1]

4,7 - *Dihydroxy* - 5 - *methoxy* - 8 - *C* - *prenyl* - 3 - (3,4-*methylenedioxyphenyl*) *coumarin* (**33**)

The ketone **23** (100 mg), ethylchloroformate (0·08 ml), ignited K_2CO_3 (1g) and acetone (20 ml) were refluxed together (3·5 h). **33** crystallised from MeOH as white silky needles (50 mg), m.p. 192–93°; R_f 0·68 (solvent I); λ_{max}^{EtOH} 314 and 262 nm; ν_{max}^{Nujol} 1670 cm^{-1} (C=O) (Found: C, 66·4: H, 5·5. $C_{22}H_{20}O_7$ requires: C, 66·7: H, 5·1%).

4 - *Hydroxy* - 5 - *methoxy* - 6",6" - *dimethyl* - *pyrano* (2",3":7,8) - 3 - (3,4 - *methylenedioxyphenyl*) *coumarin or isorobustin* (**32**)

The chromene **28** (130 mg), ethylchloroformate (0·075 ml), ignited K_2CO_3 (1g), acetone (20 ml) was refluxed (3·5 h) on a water bath. Compound **32** crystallised from acetone as white solid (60 mg), m.p. 197–98°; R_f 0·54 (solvent G); λ_{max}^{EtOH} 316 and 268 nm; ν_{max}^{KBr} 1650 cm^{-1} (C=O) (Found: C, 66·9; H, 4·3. $C_{22}H_{18}O_7$ requires: C, 67·0; H, 4·6%).

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