Aryllead-mediated synthesis of linear 3-arylpyranocoumarins: synthesis of robustin and robustic acid

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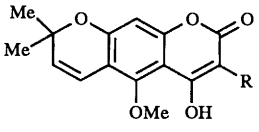
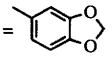
The two naturally occurring linear 3-arylpyranocoumarins, robustin **1** and robustic acid **2**, have been synthesised in nine steps from methyl 2,4,6-trihydroxyphenyl ketone, in 19% overall yield for robustin and 18% for robustic acid. Their syntheses involved, as a key step, the regioselective arylation of a functionalised 4-hydroxybenzo[1,2-*b*:5,4-*b*']dipyran-2-one with the appropriate aryllead triacetate.

Introduction

3-Aryl-4-hydroxy-2*H*-1-benzopyran-2-ones constitute a group of isoflavonoid natural products which have been isolated from the genus *Derris* (Dalbergieae) and from the genus *Millettia* (Millettieae), of the Leguminosae, subfamily Papilionoideae.[1] With the exception of derrusnin, all the members of this group are both methoxylated at C-5 and prenylated in the A-ring. Cyclisation of the prenyl side chain onto a neighbouring phenol function leads to two structural types: (i) the furanobenzopyran type found in thonningin-A, thonningin-B and glabrescin, and (ii) the pyranobenzopyran type, itself subdivided into the linear system and the angular system. The angular arrangement is found in isorobustin, isorobustin methyl ether and scandenin. In contrast, robustin **1**, robustic acid **2**, lonchocarpic and their methyl ethers possess the linear arrangement. Robustic acid **2** was first isolated in 1942 from the indian tree *Derris robusta*, independently by Krishna and Ghose[2] and by Harper.[3] It was later isolated from the seeds of *Millettia thonningii*, a deciduous tree found in moist situations in the savanna areas of West Africa.[4] Its structure was elucidated by Pelter and co-workers,[5] and by Ollis and co-workers[6] who also reported the isolation of robustin **1** from *Derris robusta*. Because of their relatively narrow distribution in Nature, the biological activities of 3-arylpyranocoumarins have not been much studied. Nevertheless, robustic acid and other structurally related pyranobenzopyrans, isolated from *Millettia thonningii*, possess a significant antimalarial activity.[7]



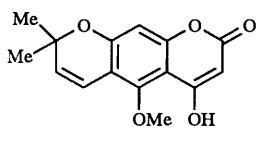
1 R = 

2 R = C_6H_4OMe-*p*

A limited number of syntheses of the 3-arylpyranocoumarins has been described and they fall into two categories. In the linear type, a final ring closure for the elaboration of either pyran rings occurs on the complete skeleton.[8-10] The major drawback of these approaches is the very low-yielding preparation of the ring cyclisation reactants. In the second type, a C-3 arylation of a pre-formed 4-hydroxy-2*H*-1-benzopyran-2-one substrate links together the two heterocyclic systems. A number of efficient methods for the α-C-arylation of ketones, β-keto esters, enols and phenols has been described in the past 15 years.[11] Among them, the ligand coupling method using aryllead triacetates has been developed by Pinhey and his group.[12] As part of our studies on the application of aryllead reagents to the chemistry of natural products, we have recently described the synthesis of 3-aryl-4-hydroxycoumarins and, in particular, of isorobustin.[13-15] We now would like to report the total synthesis of the two linear pyranocoumarins, robustin **1** and robustic acid **2**.

Results and discussion

Our retrosynthetic analysis of robustin **1** and robustic acid **2** involved the C-3 arylation of the 4-hydroxy-5-methoxy-2*H*-1-benzopyran-2-one derivative **3** by the appropriate aryllead reagents, respectively **4** and **5**. If the synthesis of most



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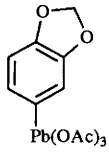

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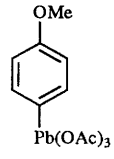

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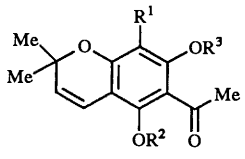
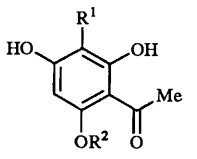
4-hydroxycoumarins can be easily performed from the corresponding 2'-hydroxyacetophenones, the synthesis of the linear pyranocoumarin system **3** requires the regioselective construction of the 2,2-dimethylchromene **6**. However, reaction of 2,4-dihydroxy-6-methoxyphenyl methyl ketone **7** with dimethylchromenylating reagents leads preferentially to the angular isomer **8**, unless the more reactive C-3 position is protected by substitution, for example, with an iodine atom, as shown by Ahluwalia and co-workers in their synthesis of robustin and isorobustin.[10] To obtain selectively the chromene **6**, the iodo compound **9** could react with a classical chromenylating agent to give **10**, which, upon treatment with *N*,*N*-dimethylaniline, should lead to the desired isomer **6**.

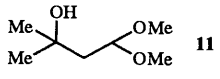
Compound **9** was synthesised in 86% yield from 2,4-dihydroxy-6-methoxyphenyl methyl ketone **7**,[16] using iodine and periodic acid. The introduction of the 2,2-dimethylchromene ring system onto 2,4-dihydroxy-3-iodo-6-methoxyphenyl methyl ketone **9** was initially attempted by base-catalysed condensation of compound **9** with the dimethylchromenylating reagent **11**.[17] However, the condensation of acetal **11** with a phenol possessing a halogen atom on the



$R^1 = R^3 = H$, $R^2 = Me$ **6**
$R^1 = R^2 = H$, $R^3 = Me$ **8**
$R^1 = I$, $R^2 = Me$, $R^3 = H$ **10**



$R^1 = H$, $R^2 = Me$ **7**
$R^1 = I$, $R^2 = Me$ **9**
$R^1 = R^2 = H$ **13**



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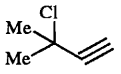

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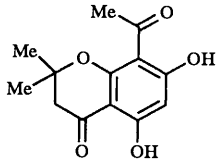

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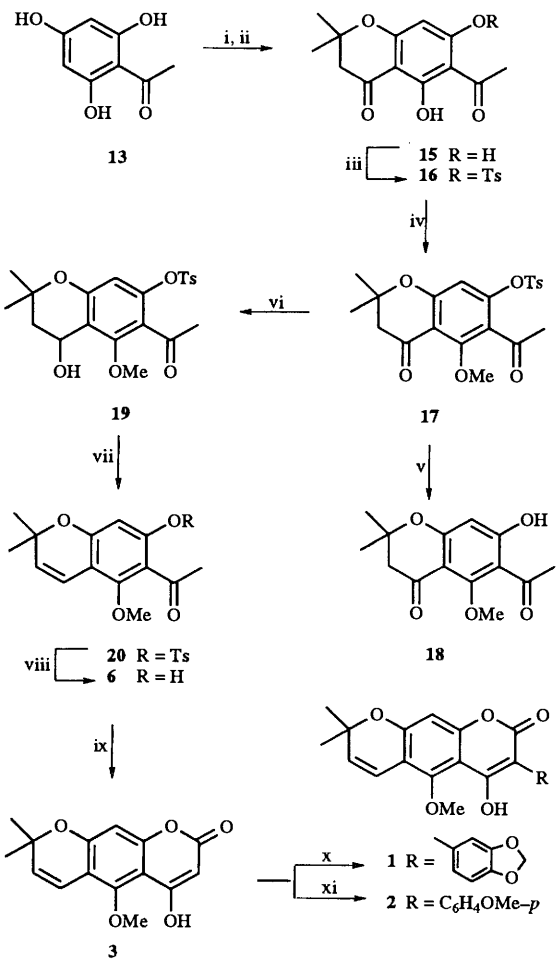
ring was unsuccessful, only starting materials being recovered. When the condensation was attempted over a longer reaction time at 175 °C, a crystalline precipitate of 5-hydroxy-7-methoxy-2,2-dimethyl-2*H*-1-benzopyran-6-yl methyl ketone **8** was obtained. Prolonged heating of the iodo compound **9** in refluxing pyridine had resulted in deiodination to give 2,4-dihydroxy-6-methoxyphenyl methyl ketone **7**, which underwent condensation with the dimethyl acetal derivative **11** to give the angular isomer **8**, previously described in the total synthesis of isorobustin.[15] When **9** was treated with **12** under a variety of basic conditions,[18] only complex intractable mixtures were obtained. Similarly, treatment of the iodo compound **9** with isoprene in xylene under reflux, in the presence of ortho-phosphoric acid,[19] again afforded only complex mixtures.

In view of the failure of the various methods used to introduce directly the 2,2-dimethylchromene ring system onto phenols possessing a halogen atom on the ring, it was thus decided to introduce the 2,2-dimethylchromene ring system *via* a corresponding 2,2-dimethylchroman-4-one derivative. 6-Acetyl-7-hydroxy-5-methoxy-2,2-dimethylchroman-4-one **18**[20] is a possible precursor for the required substrate **3** for the synthesis of robustin and robustic acid. In acetylchromanone derivatives, the carbonyl group of a chromanone ring can be specifically reduced to the corresponding acetylchromanol in preference to the carbonyl of the acetyl group, by using a sodium boranuide–palladium chloride system.[21] Consequently, it was expected that specific reduction of the chromanone carbonyl group of compound **18** would afford a chromanol derivative, which, on dehydration, would give the 2,2-dimethylchromene derivative **20**. Condensation of compound **20** with diethyl carbonate in the presence of sodium hydride could then afford the 2*H*-1-benzopyran-2-one derivative **3**, which, on C-3 arylation, will furnish either robustin **1** or robustic acid **2**.

6-Acetyl-7-hydroxy-5-methoxy-2,2-dimethylchroman-4-one **18** was synthesised in five steps from 2,4,6-trihydroxyphenyl methyl ketone in 44% overall yield following the sequence described by Tsukayama and co-workers.[20] Unfortunately, various attempts to reduce selectively the chromanone carbonyl group in the acetylchromanone derivative **18** by the sodium boranuide–palladium chloride system in aqueous tetrahydrofuran yielded only a complex mixture of products. Attempted separation and purification of this mixture were unsuccessful. ^{1}H NMR analysis of the crude reaction mixture suggested that partial reduction of both the acetyl and chromanone carbonyl



Scheme 1 *Reagents and conditions:* i, 3-methylbut-2-enoic acid (1.4 mol equiv.), polyphosphoric acid (0.4 g per mmol of **13**), dioxane, 60 °C, 3 h, (**14** + **15**) 89%; ii, K_2CO_3, anhydrous acetone, reflux, 50 h, **15** 87%; iii, TsCl, K_2CO_3, acetone, reflux, 2 h, 64%; iv, Me_2SO_4, K_2CO_3, acetone, reflux, 4 h, 93%; v, K_2CO_3, MeOH, reflux, 2 h, 95%; vi, $NaBH_4$, $PdCl_2$, THF, H_2O, 0–5 °C, 1.5 h, 70%; vii, TsOH, toluene, reflux, 20 min, 92%; viii, K_2CO_3, MeOH, reflux, 1.5 h, 95%; ix, NaH, Et_2CO_3, 45 °C, 30 min, 80%; x, **4**, pyridine, $CHCl_3$, 60 °C, 14 h, 84%; xi, **5**, pyridine, $CHCl_3$, 60 °C, 14 h, 79%

groups had occurred and the reaction was not investigated further. Though the mechanism of action of the sodium boranuide–palladium chloride system is not known, it is likely that the palladium salt is complexed to the acetyl carbonyl group allowing only reduction of the chromanone carbonyl group. The failure to achieve specific reduction of the chromanone carbonyl in compound **18** may be due to the presence of the 7-hydroxy group which is hydrogen bonded to the acetyl carbonyl group. This hydrogen bonding may prevent complexation of the palladium metal to the group which is thus ultimately reduced by sodium boranuide along with the chromanone carbonyl group. In contrast, reduction of the protected 7-tosyloxy derivative **17** by the sodium boranuide–palladium chloride system proved selective and afforded the corresponding chromanol derivative **19** in 68% yield. Subsequently, acid-catalysed dehydration of this alcohol **19** (*p*-TsOH, toluene, reflux) led to the 2,2-dimethylchromene derivative **20** in 95% yield. Detosylation of compound **20** with potassium carbonate in methanol followed by condensation of the sodium enolate of **6** with diethyl carbonate furnished the required precursor **3** for the synthesis of robustin **1** or robustic acid **2**. Reaction of the 4-hydroxycoumarin **3** with the aryllead reagent **4** under the classical arylation conditions ($CHCl_3$,

pyridine, 60 °C, 14 h) afforded robustin **1** in 84% yield, and the aryllead reagent **5** led to robustic acid **2** in 79% yield.

In summary, the sequence we have now reported allows the synthesis of robustin **1** in nine steps in 19% overall yield and of robustic acid **2** in 18% from commercially available methyl 2,4,6-trihydroxyphenyl ketone. This sequence affords a facile access to a range of linear pyranocoumarins, as the 3-aryl group is introduced only at the last step by arylation with easily accessible aryllead reagents. Moreover, the mild conditions used throughout the sequence are compatible with acid-sensitive substrates.

Experimental

For the general procedures, see previous papers.[22] 3,4-Methylenedioxyphenyllead triacetate **4** and 4-methoxyphenyllead triacetate **5** were prepared as previously described.[15]

2,4-Dihydroxy-3-iodo-6-methoxyphenyl methyl ketone 9

2,4-Dihydroxy-6-methoxyphenyl methyl ketone **7** (4.5 g, 24.6 mmol) was dissolved in the minimum of ethanol and iodine (2.66 g, 12.6 mmol) and periodic acid (0.79 g, 3.47 mmol) were added to the solution. The mixture was stirred at 60–70 °C for 2 h after which it was cooled and diluted with water to afford a precipitate. This was filtered and recrystallised from methanol to give the title ketone **9** (6.2 g, 86%) as plates, mp 198–200 °C; ν_{max}(KBr)/cm^{-1} 3248, 1629, 1429 and 1280; δ_H(DMSO; 270 MHz) 2.54 (3 H, s, COMe), 3.84 (3 H, s, OMe), 6.20 (1 H, s, Ar H), 11.57 (1 H, s, 4-OH) and 14.97 (1 H, br s, 2-OH); δ_C(DMSO; 67.80 MHz) 202.10 (C=O), 165.15 (C-6), 164.16 (C-2), 163.24 (C-4), 104.63 (C-1), 90.59 (C-5), 65.47 (C-3), 55.84 (MeO) and 32.19 (CO*Me*); *m*/*z* 308 (M$^+$, 75%), 292.9 (100), 277.9 (10), 167 (9.7), 95 (7.3), 69 (14.6), 53 (8.4) and 43 (30) (Found: C, 35.1; H, 3.0; I, 41.2. $C_9H_9IO_4$ requires C, 35.09; H, 2.92; I, 41.6%).

Reaction of compound 9 with 1,1-dimethoxy-3-methylbutan-3-ol

The ketone **9** (1 g, 5.5 mmol), dry pyridine (0.43 g, 5.5 mmol) and 1,1-dimethoxy-3-methylbutan-3-ol[18] (0.98 g, 6.6 mmol) were heated together under reflux at 170–175 °C for 8 h after which 1,1-dimethoxy-3-methylbutan-3-ol (0.98 g, 6.6 mmol) was added to the mixture and heating continued for a further 8 h. The mixture was allowed to reach room temperature when the precipitate was filtered off and recrystallised from ethanol to give 5-hydroxy-7-methoxy-2,2-dimethyl-2*H*-1-benzopyran-6-yl methyl ketone **8** (0.8 g, 65%) as plates, mp 127–128 °C (lit.,[23] 128.5–129 °C); ν_{max}(KBr)/cm^{-1} 3115, 1641, 1620, 1598 and 730; δ_H($CDCl_3$; 270 MHz) 1.41 (6 H, s, 2 × Me), 2.55 (3 H, s, COMe), 3.86 (3 H, s, OMe), 5.56 (1 H, d, *J* 9.90, 3-H), 6.03 (1 H, s, ArH), 6.52 (1 H, d, *J* 9.9, 4-H) and 14.28 (1 H, s, OH); δ_C($CDCl_3$; 67.80 MHz) 202.85 (C=O), 162.64 (C-5), 160.60 (C-9), 159.82 (C-7), 125.72 (C-3), 115.15 (C-4), 104.98 (C-6), 101.67 (C-10), 91.40 (C-8), 77.90 (C-2), 55.98 (MeO), 32.71 (CO*Me*) and 27.95 (2 × Me); *m*/*z* 248 (M$^+$, 23%), 233 (100), 215 (27), 200 (9), 109 (11) and 43 (22) (Found: C, 67.8; H, 6.3. Calc. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.49%).

6-Acetyl-5-methoxy-2,2-dimethyl-7-tosyloxychroman-4-ol 19

Sodium boranuide (0.95 g) was added in small portions over a period of 1.5 h to a mixture of compound **17** (1.7 g) and palladium(II) chloride (0.675 g) in THF (50 cm^3) and water (10 cm^3) kept at 0–5 °C. Acetone (5 cm^3) was added to the mixture after which the solid catalyst was filtered off and the filtrate diluted with water (5 cm^3). After concentration of the filtrate under reduced pressure (temperature kept below 35 °C), the residue was extracted with ethyl acetate (3 × 50 cm^3). The combined extracts were washed with 5% aqueous HCl (20 cm^3) and saturated brine (20 cm^3), dried (Na_2SO_4) and distilled under reduced pressure. The residue was purified by column chromatography on silica [eluent: dichloromethane–ethyl acetate–light petroleum (50:2:1)] to give the *title compound* **19** (1.2 g, 70%) as colourless needles, mp 100–102 °C; ν_{max}(KBr)/cm^{-1} 3570, 1700, 1605, 1370 and 1190; δ_H($CDCl_3$; 270 MHz) 1.34 and 1.41 (2 × 3 H, 2 s, *Me*$_2$C-2), 2.0 (1 H, dd, *J* 5.68 and 14.29, 3-H$_A$), 2.08 (1 H, dd, *J* 6.23 and 14.47, 3-H$_B$), 2.45 and 2.46 (2 × 3 H, 2 s, MeC-4′ and COMe), 3.09 (1 H, br s, 4-OH), 3.79 (3 H, s, 5-OMe), 4.96 (1 H, dd, *J* 5.68 and 6.05, 4-H), 6.47 (1 H, s, 8-H), 7.34 (2 H, d, *J* 8.24, 3′-H and 5′-H) and 7.75 (2 H, d, *J* 8.24, 2′-H and 6′-H); δ_C($CDCl_3$; 67.80 MHz) 198.53 (CO), 157.72 (C-1′), 155.6 (C-9), 146.27 (C-7), 145.71 (C-5), 132.06 (C-4′), 129.82 (C-3′ and -5′), 128.34 (C-2′ and -6′), 121.5 (C-10), 116.97 (C-6), 108.11 (C-8), 75.97 (C-2), 62.95 (5-OMe), 60.07 (C-4), 40.0 (C-3), 31.92 (COMe), 27.17 and 26.83 (Me$_2$C-2) and 21.67 (MeC-4′); *m*/*z* 420 (M$^+$, 21%), 405 (24), 387 (23), 349 (25), 155 (39), 91 (100), 65 (21) and 43 (33) (Found: C, 59.65; H, 5.7; S, 7.75. $C_{21}H_{24}O_7S$ requires: C, 59.99; H, 5.75; S, 7.62%).

6-Acetyl-5-methoxy-2,2-dimethyl-7-tosyloxy-2*H*-chromene 20

A mixture of compound **19** (0.96 g) and toluene-*p*-sulfonic acid monohydrate (0.12 g) in toluene (50 cm^3) was stirred under reflux for 20 min. The organic phase was washed with water, dried (Na_2SO_4) and concentrated under reduced pressure. The solid was recrystallised from methanol–acetone (1:1) to give the *title compound* **20** (0.84 g, 92%) as colourless needles, mp 69–72 °C; ν_{max}(KBr)/cm^{-1} 3104, 1701, 1636 and 1599; δ_H($CDCl_3$; 270 MHz) 1.42 (6 H, s, Me$_2$C-2), 2.40 and 2.45 (2 × 3 H, 2 s, COMe and MeC-4′), 3.70 (3 H, s, 5-OMe), 5.66 (1 H, d, *J* 10.1, 3-H), 6.45 (1 H, s, 8-H), 6.48 (1 H, d, *J* 10.1, 4-H), 7.34 (2 H, d, *J* 8.6, 3′- and 5′-H) and 7.75 (2 H, d, *J* 8.6, 2′- and 6′-H); δ_C($CDCl_3$; 67.80 MHz) 198.67 (CO), 155.35 (C-1′), 154.15 (C-9), 145.71 (C-7), 145.67 (C-5), 132.41 (C-4′), 130.99 (C-3), 129.85 (C-3′ and -5′), 128.54 (C-2′ and -6′), 122.90 (C-10), 115.85 (C-6), 113.91 (C-4), 107.47 (C-8), 76.56 (C-2), 63.60 (5-OMe), 32.03 (COMe), 27.95 (Me$_2$C-2) and 21.20 (MeC-4′); *m*/*z* 402 (M$^+$, 17%), 387 (100), 215 (34), 91 (35), 65 (15) and 43 (32) (Found: C, 62.7; H, 5.85; S, 7.7. $C_{21}H_{22}O_6S$ requires: C, 62.67; H, 5.51; S, 7.97%).

6-Acetyl-7-hydroxy-5-methoxy-2,2-dimethyl-2*H*-chromene 6

A mixture of compound **20** (0.79 g) and potassium carbonate (1.78 g) in methanol (30 cm^3) was stirred under reflux for 1.5 h. The reaction mixture was then poured onto ice–cold water, acidified with 10% aqueous HCl and extracted with ethyl acetate. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was recrystallised from methanol to give the *title compound* **6** (0.47 g, 95%) as colourless needles, mp 81–83 °C; ν_{max}(KBr)/cm^{-1} 3600–3100br, 2930 and 1641; λ_{max}(MeCN)/nm 261.9 (21 850) and 342.4 (2600); δ_H($CDCl_3$; 270 MHz) 1.44 (6 H, s, Me$_2$C-2), 2.68 (3 H, s, COMe), 3.80 (3 H, s, 5-OMe), 5.60 (1 H, d, *J* 10.1, 3-H), 6.18 (1 H, s, 8-H), 6.49 (1 H, d, *J* 10.1, 4-H) and 13.42 (1 H, s, 7-OH); δ_C($CDCl_3$; 67.80 MHz) 203.05 (CO), 165.85 (C-9), 160.68 (C-5), 158.95 (C-7), 128.17 (C-3), 116.35 (C-4), 107.23 (C-6), 101.11 (C-8), 76.52 (C-2), 63.02 (5-OMe), 31.18 (COMe) and 28.17 (Me$_2$C-2); *m*/*z* 248 (M$^+$, 25%), 233 (100), 203 (22) and 43 (18) (Found: C, 67.4; H, 6.5. $C_{14}H_{16}O_4$ requires: C, 67.73; H, 6.49%).

4-Hydroxy-5-methoxy-8,8-dimethyl-2*H*,8*H*-benzo[1,2-*b*:5,4-*b*′]-dipyran-2-one 3

Sodium hydride (80% dispersion in oil; 0.336 g) was added slowly to a solution of compound **6** (0.15 g) in dry diethyl carbonate (34 cm^3) and was slowly heated to 45 °C at which temperature it was stirred for 30 min. After cooling the mixture was diluted with methanol (40 cm^3) and extracted with water

(2 × 50 cm^3). The aqueous extracts were acidified with 10% aqueous HCl and exhaustively extracted with $CHCl_3$ (2 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and concentrated to give a yellow solid which was purified by column chromatography [eluent: ethyl acetate–light petroleum (2:1)] to afford the *title compound* **3** as needles after crystallisation from ethanol (0.134 g, 80%), mp 76–78 °C; ν_{max}(KBr)/cm^{-1} 3600–2800br, 2974, 1612 and 1373; λ_{max} (MeCN)/nm 228.5 (12 025), 264.9 (16 375) and 328.9 (5875); δ_H($CDCl_3$; 270 MHz) 1.48 (6 H, s, Me_2C-8), 3.99 (3 H, s, 4-OMe), 5.57 (1 H, s, 3-H), 5.78 (1 H, d, *J* 10.1, 7-H), 6.50 (1 H, d, *J* 10.1, 6-H), 6.59 (1 H, s, 10-H) and 9.70 (1 H, br s, 4-OH); δ_C($CDCl_3$; 67.80 MHz) 165.64 (C-4), 163.0 (C-2), 157.63 (C-11), 155.05 (C-5), 152.29 (C-13), 131.41 (C-7), 114.97 (C-6), 101.87 (C-10), 101.46 (C-12), 100.84 (C-14), 91.05 (C-3), 77.6 (C-8), 64.40 (5-OMe) and 28.01 (Me_2C-8); *m/z* 274 (M^+, 24%), 259 (86), 217 (100), 202 (12), 115 (8), 91 (8), 71 (12), 69 (23) and 43 (7).

4-Hydroxy-5-methoxy-8,8-dimethyl-3-(3′,4′-methylenedioxyphenyl)-2*H*,8*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-2-one (robustin)

A mixture of compound **3** (0.1 g), 3,4-methylenedioxyphenyllead triacetate **4** (0.2 g) and dry pyridine (0.1 cm^3) in dry $CHCl_3$ (0.6 cm^3) was stirred at 60 °C for 14 h. The mixture was diluted with $CHCl_3$ (60 cm^3) and washed with 3 mol dm^{-3} sulfuric acid (2 × 50 cm^3). The aqueous phase was washed with $CHCl_3$ (4 × 50 cm^3) and the combined extracts were dried ($MgSO_4$), filtered through Celite and concentrated to yield a residue which was purified by PTLC [eluent: $CHCl_3$–MeOH (36:1)] to give compound **1** as a solid which crystallised as needles from ethanol (0.119 g, 84%), mp 202–204 °C (lit.,[6] 207 °C); ν_{max}(KBr)/cm^{-1} 1707 and 1629; λ_{max}(MeCN)/nm 229.5 (9100), 266.1 (10 725) and 344.1 (5500); δ_H($CDCl_3$; 270 MHz) 1.48 (6 H, s, Me_2C-8), 3.99 (3 H, s, 5-OMe), 5.79 (1 H, d, *J* 10.1, 7-H), 5.97 (2 H, s, OCH_2O), 6.51 (1 H, d, *J* 10.1, 6-H), 6.64 (1 H, s, 10-H), 6.87 (1 H, d, *J* 8.44, 5′-H), 6.69–7.03 (2 H, m, 2′- and 6′-H) and 9.98 (1 H, s, 4-OH); δ_C($CDCl_3$; 67.80 MHz) 162.0 (C-4), 160.46 (C-2), 157.0 (C-11), 153.77 (C-5), 152.15 (C-13), 147.28 (C-4′), 146.96 (C-3′), 131.48 (C-7), 124.49 (C-1′), 124.3 (C-6′), 115.01 (C-6), 111.12 (C-5′), 108.13 (C-2′), 103.94 (C-14), 101.74 (C-3), 101.65 (C-10), 101.01 (OCH_2O), 96.09 (C-12), 77.60 (C-8), 64.43 (5-OMe) and 27.98 (Me_2C-8); *m/z* 394 (M^+, 91%), 379 (81), 351 (15), 233 (38), 232 (12), 217 (100), 189 (21), 162 (30), 91 (10), 69 (13), 32 (22) and 28 (73).

4-Hydroxy-5-methoxy-3-(4′-methoxyphenyl)-8,8-dimethyl-2*H*,8*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-2-one (robustic acid)

A mixture of compound **3** (0.08 g), 4-methoxyphenyllead triacetate **5** (0.158 g) and dry pyridine (0.095 cm^3) in dry $CHCl_3$ (0.5 cm^3) was stirred at 60 °C for 14 h. After treatment as above, robustic acid **2** crystallised from ethanol as needles (0.083 g, 79%), mp 206–209 °C (lit.,[5] 208–210 °C); ν_{max}(KBr)/cm^{-1} 3436br, 1708, 1610, 1460 and 1386; λ_{max}(MeCN)/nm 229.4 (7510), 268.2 (7620) and 245 (2000); δ_H($CDCl_3$; 270 MHz) 1.49 (6 H, s, Me_2C-8), 3.83 (3 H, s, 4′-OMe), 3.99 (3 H, s, 5-OMe), 5.79 (1 H, d, *J* 10.1, 7-H), 6.52 (1 H, d, *J* 10.1, 6-H), 6.64 (1 H, s, 10-H), 6.97 (2 H, d, *J* 8.97, 3′- and 5′-H), 7.48 (2 H, d, *J* 8.97, 2′- and 6′-H) and 9.94 (1 H, s, 4-OH); *m/z* 380 (M^+, 35%), 365 (32), 233 (60), 135 (100), 77 (40), 57 (49) and 43 (50).

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