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CONJUGATE ADDITION OF CUPRATE REAGENTS TO CHROMONES: A ROUTE TO 2-SUBSTITUTED CHROMAN-4-ONES

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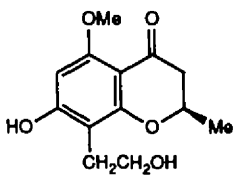
Abstract Chromones (4-oxo-4*H*-1-benzopyrans) activated by electron-withdrawing groups attached to C-3 undergo efficient 1,4-addition of cuprate reagents, producing 2,3-disubstituted chroman-4-ones. The addition products from methyl chromone-3-carboxylates can be converted into 2-substituted chroman-4-ones by treatment with sodium chloride in wet dimethylsulphoxide.

The chroman-4-one (2,3-dihydro-4-oxo-4*H*-1-benzopyran) ring system occupies a prominent position among the oxygen heterocycles. It occurs naturally with a variety of substituents at C-2, exemplified in the antibiotic LL-D253α **1**,[1] the flavanone hesperetin **2**,[2] and the plant product myrochromanone **3**.[3] In addition, some of the many biologically active natural products which contain a chroman ring system[4,5] have been synthesised *via* 2-substituted chroman-4-one intermediates. These include structures as diverse as α-tocopherol (vitamin E) **4**,[6] the antimalarial robustadial A **5**,[7] and the psychotropic tricycle Δ^9-tetrahydrocannabinol **6**.[8]



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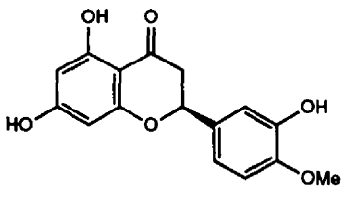

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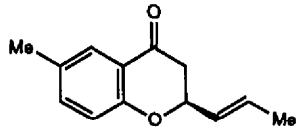

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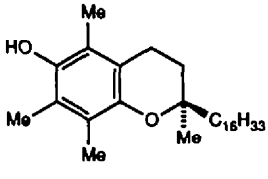

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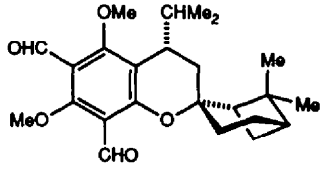

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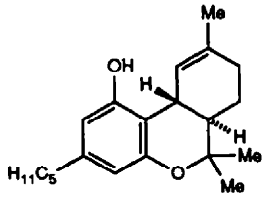

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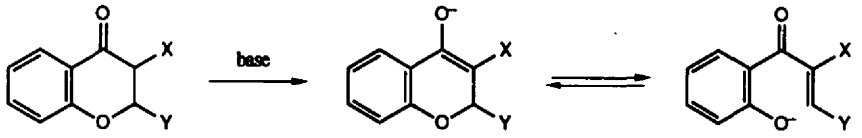
Notwithstanding these examples, the preparation[5,9,10] and manipulation of substituted chroman-4-ones can be problematic, due in part to the ease with which they undergo ring opening *via* the equilibrium shown in

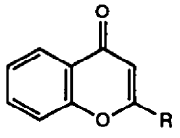
Scheme 1.[11] With this in mind we chose to evaluate the potential of conjugate addition of organocuprate reagents to substituted chromones, anticipating that a procedure based upon this type of reaction would be sufficiently mild for ring opening to be suppressed, and our experiments are herein described in detail.[12]



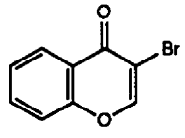
SCHEME 1

Conjugate Addition of Homocuprates to 3-Substituted Chromones

It was rapidly established that chromones with no activating substituent in the 3-position were poor cuprate acceptors, the parent system **7**, 2-methylchromone **8**, 3-bromochromone **9**, and the isoflavone **10** all giving complex reaction mixtures.[13] However, the process proved efficient when an extra electron-withdrawing substituent was incorporated at C-3 of the substrate, and the results of a series of reactions of 3-substituted chromones with homocuprate reagents (1.5 equivalents) proceeded as shown in Table 1. The products were easily identified *via* their ^{1}H n.m.r. spectra, and displayed varying degrees of keto-enol tautomerism. In the enolic forms **12**, **15**, **18** and **21**, the respective signals due to H-2 are quartets ($J \approx 6$ Hz), whereas in the keto forms **14**, **17**, and **20** they appear as overlapping double quartets ($J \approx 6$, 12 Hz). The larger of these coupling constants indicates a *trans*-diaxial relationship between H-2 and H-3 in each case, thus confirming the expected preference for a *trans*-diequatorial arrangement of the bulky 2,3-substituents. This preference has also been assumed in assigning the structure **27** to the major of the two keto products obtained from the ester **26** (entry 7), although the n.m.r. evidence in this case is equivocal. Chromone-3-carbonitrile **30** also reacted with the methyl cuprate reagent to give predominantly the 2,3-*trans*-disubstituted addition product **31**.



7 R = H
8 R = Me



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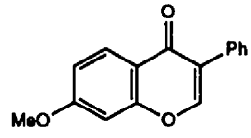

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From a synthetic point of view it is notable that the conjugate addition process is not adversely affected by the potentially inhibiting presence of a 2-alkyl substituent (*cf.* entries 6 and 7). Moreover, the lack of reactivity of unactivated chromones such as **7** and **8** is of little consequence, since the ester group of the substrates **19** and **24** can be exploited very effectively as a removable activating substituent. This strategy provides an alternative route to the chromanones which were not directly accessible. For example, heating the mixture of **20** and **21** with sodium chloride in wet dimethylsulphoxide[14] effected a smooth decarbomethoxylation, producing 2-methylchroman-4-one **35**, isolated as the derived 2,4-dinitrophenylhydrazone (2,4-DNP) in 77% overall yield. In a similar fashion the ketoester **25** was readily transformed into 2,2-dimethylchroman-4-one **36** (2,4-DNP, 86% overall), while the mixture of **33** and **34** derived from the reaction of methyl chromone-3-carboxylate **19** with lithium diphenylcuprate was converted into 2-phenylchroman-4-one (flavanone) **37** in 89% yield.

TABLE 1 REACTIONS OF 3-SUBSTITUTED CHROMONES WITH CUPRATE REAGENTS

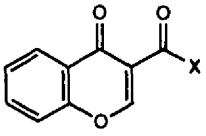
ENTRY	SUBSTRATE	CUPRATE	PRODUCT(S)*	RATIO†	YIELD (%)
1	**11**	Me_2CuLi	**12**	-	50‡
2	**13**	Me_2CuLi	**14, 15**	1:4.5	70
3	**16**	Me_2CuLi	**17, 18**	7:1	77
4	**19**	Me_2CuLi	**20, 21**	5:1	78
5	**22**	Me_2CuLi	**23**	-	42¶
6	**24**	Me_2CuLi	**25**	-	74
7	**26**	Me_2CuLi	**27, 28, 29**	3:1:1	91
8	**30**	Me_2CuLi	**31, 32**	5:1	62
9	**19**	Ph_2CuLi	**33, 34**	4:3	89

* All compounds are racemic

† After isolation by distillation or chromatography; estimated by ^1H n.m.r. spectroscopy

‡ Decomposes during distillation or chromatography

¶ Starting material remained even after prolonged reaction



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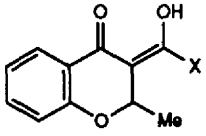
13 X = Me
16 X = Ph
19 X = OMe



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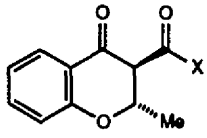
18 X = Ph



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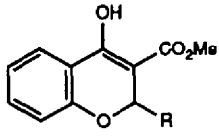
17 X = Ph
20 X = OMe



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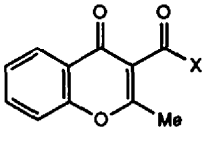
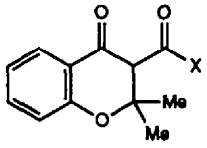
34 R = Ph



22 X = Me
24 X = OMe



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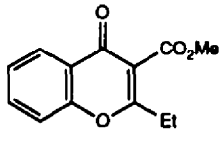

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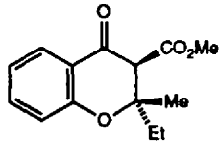

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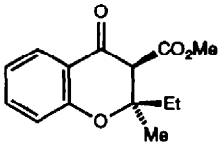

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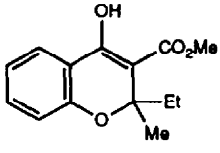

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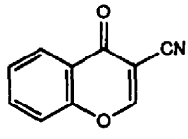

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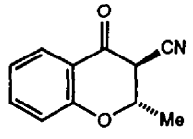

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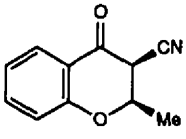

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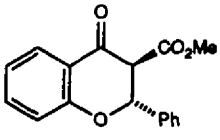

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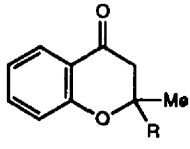

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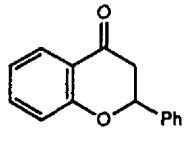
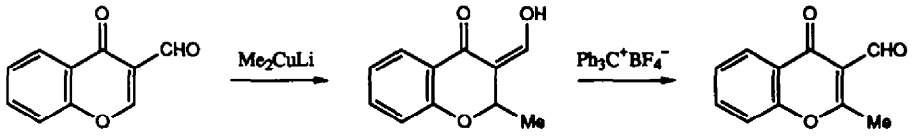
36 R = Me



37

In a later study[13] it was established that the cuprate addition products were susceptible to oxidation, which regenerates the chromone nucleus and allows a second cuprate addition using a different reagent. With the hydroxymethylene compound **12** proving difficult to isolate in a pure state, it was eventually characterised *via* such an oxidation, which gave 2-methylchromone-3-carboxaldehyde **38** in 56% yield. The overall sequence leading to **38** (Scheme 2) represents a considerable improvement over existing routes to this compound.[15,16]



11 **12** **38**

SCHEME 2

With the conjugate addition route to chromanones clearly viable, we next sought to establish a route to homochiral 2-substituted chroman-4-ones. Our experiments, based on the use of an arylsulphinyl substituent as an activating group and chiral auxiliary, will be described in detail elsewhere.[17]

EXPERIMENTAL

Melting points were determined using an Electrothermal apparatus and are uncorrected. Unless otherwise stated, i.r. spectra were of liquid paraffin mulls on sodium chloride plates, recorded on Pye-Unicam SP3-100, or Perkin-Elmer 297 spectrometers. N.m.r. spectra were measured for solutions in deuteriochloroform unless otherwise indicated, with tetramethylsilane as the internal standard, on Varian EM 360 (60 MHz), Perkin-Elmer R32 (90 MHz), or Bruker AC300 (300 MHz) instruments. Mass spectra were measured on a Kratos MS30 instrument with a 70 eV electron impact source.

Starting materials and solvents were routinely purified by conventional techniques.[18] Distillation of liquid products was performed using a Kugelröhr bulb-to-bulb apparatus, and the temperatures quoted are those of the oven. Organic solutions were dried using anhydrous magnesium sulphate and concentrated by rotary evaporation. Analytical thin layer chromatography (t.l.c.) was carried out on Camlab Polygram SIL G/UV_{254} plates. Preparative (column) chromatography was carried out using 60H silica gel (Merck 7736 and hand-bellows pressure, or Merck 9385 and the flash technique[19]). Compositions of solvent mixtures are quoted as ratios of volume. 'Petroleum' refers to a light petroleum fraction, b.p. 40–60 °C, unless otherwise stated. 'Ether' refers to diethyl ether.

Chromones **8**,[20] **9**,[21] **10**,[22] **11**,[23] **13**,[24] **16**,[24] **19**,[25] **22**,[20] **24**,[26] and **30**[27] were prepared *via* published routes.

*Methyl 2-ethyl-4-oxo-4*H*-1-benzopyran-3-carboxylate* **26**. – A stirred mixture of methyl 3-(2-hydroxyphenyl)-3-oxopropanoate[28] (0.99 g, 5.1 mmol), anhydrous potassium carbonate (2.7 g, 19.6 mmol), and propanoic anhydride (3.7 ml, 3.76 g, 29 mmol) in toluene (50 ml) was heated at 80 °C until the generation of carbon dioxide had ceased. The temperature of the mixture was then raised to 125–130 °C for 3 h. The cooled mixture was treated with water (20 ml), extracted with ether (3 x 25 ml), and the extract washed with water (25 ml) and brine (25 ml), dried, and evaporated. The residue was chromatographed (elution with ethyl

acetate - petroleum 1:9), giving 4-hydroxy-3-propanoyl-2*H*-1-benzopyran-2-one (0.62 g, 56%), m.p. 122 - 123 °C (ether) (lit.[29] 123 °C), followed by the *title compound* **26** (0.284 g, 24%), m.p. 54–55 °C (ether - petroleum) (Found: C, 67.0; H, 5.2. $C_{13}H_{12}O_4$ requires C, 67.2; H, 5.2%); ν_{max} 1720, 1635, and 1610 cm^{-1}; δ (60 MHz) 1.37 (3 H, t, *J* 7 Hz, Me), 2.80 (2 H, q, *J* 7 Hz, CH_2), 3.95 (3 H, s, OMe), 7.2–7.8 (3 H, m, 6-H, 7-H, and 8-H), and 8.05–8.3 (1 H, m, 5-H); M^+, 232.

General Procedure for Cuprate Additions (Table 1, entries 1 - 8). – A solution of the chromone (2 mmol) in tetrahydrofuran (10 ml) was added dropwise at 0 °C under nitrogen to a stirred solution of lithium dimethylcuprate (3 mmol), prepared by treating copper(I) iodide (3.05 mmol) in ether (10 ml) with methyllithium in ether (6 mmol) at -10 to -5 °C and stirring until the orange solid had dissolved. After 0.5 h the reaction was quenched by stirring vigorously with saturated aqueous ammonium chloride (15 ml), and the products extracted into ethyl acetate (3 x 20 ml). The extract was washed successively with 2 M hydrochloric acid (20 ml), water (2 x 20 ml), and brine (20 ml), dried, and evaporated. The residue was dissolved in a small quantity of dichloromethane and the solution filtered through a short plug of silica gel (Merck 7736) using dichloromethane. The filtrate was evaporated and the residue examined by 60 MHz ^1H n.m.r. spectroscopy. The products were isolated by column chromatography, eluting with dichloromethane - petroleum mixtures.

Entry 1: The aldehyde **11** was treated as described above. Bulb-to-bulb distillation (105–110 °C, 0.2 mmHg) gave 2,3-dihydro-3-(hydroxymethylene)-2-methyl-4*H*-1-benzopyran-4-one **12** as an impure oil (50%); ν_{max} (neat) 1670 and 1585 cm^{-1}; δ (60 MHz) 1.55 (3 H, d, *J* 6 Hz, Me), 5.1 (1 H, q, *J* 6 Hz, 2-H), 6.85–7.95 (5 H, m, =CHOH and ArH), and 12.0 (1 H, br s, OH). The benzopyran **12** was characterised by conversion into 2-methylchromone-3-carboxaldehyde **38** (*vide infra*).

Entry 2: 3-Acetylchromone **13** was treated as described above. Chromatography gave the product mixture **14** + **15** (total 70%; ratio *ca.* 1:4.5 by n.m.r.) as a pale yellow oil. Crystallisation gave *2,3-dihydro-3-(1-hydroxyethylidene)-2-methyl-4*H*-1-benzopyran-4-one* **15**, m.p. 72–74 °C (petroleum - ether) (Found: C, 70.45; H, 6.2. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9%); ν_{max} 1700–1300 (br), 1160, 915, 770, 720, and 700 cm^{-1}; δ (90 MHz) 1.40 (3 H, d, *J* 7 Hz, 2-Me), 2.13 (3 H, s, C(OH)Me), 5.37 (q, *J* 7 Hz, 2-H), 6.8–7.5 (3 H, m, ArH), 7.84 (1 H, dd, *J* 2, 8 Hz, 5-H), and 16.1 (1 H, s, exchanges with D_2O, OH). The keto form **14** had characteristic signals at δ (60 MHz) 3.69 (d, *J* 11 Hz, 3-H) and 4.75 (dq, *J* 6, 11 Hz, 2-H).

Entry 3: 3-Benzoylchromone **16** was treated as described above. Crystallisation of the product mixture **17** + **18** (or the alternative tautomer) (total 77%; ratio *ca.* 7:1 by n.m.r.) gave the pure *3-benzoyl-2,3-dihydro-2-methyl-4*H*-1-benzopyran-4-one* **17**, m.p. 91–93 °C (ethanol) (Found: C, 76.7; H, 5.2. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%); ν_{max} 1690, 1680, and 1615 cm^{-1}; δ (90 MHz) 1.45 (3 H, d, *J* 6 Hz, 2-Me), 4.61 (1 H, d, *J* 12 Hz, 3-H), 5.06 (1 H, dq, *J* 6, 12 Hz, 2-H), and 6.9–8.1 (9 H, m, ArH). The enol form **18** had characteristic signals at δ (60 MHz) 5.4 (q, *J* 6 Hz, 2-H) and 16.4 (br s, exchanges with D_2O, OH).

Entry 4: The ester **19** was treated as described above. Bulb-to-bulb distillation (115–120 °C, 0.2 mmHg) gave a mixture of *methyl* trans-*3,4-dihydro-2-methyl-4-oxo-2*H*-1-benzopyran-3-carboxylate* **20** and *methyl 4-hydroxy-2-methyl-2*H*-1-benzopyran-3-carboxylate* **21** (total 78%; ratio *ca.* 5:1 by n.m.r.) as a colourless oil (Found: C, 65.65; H, 5.4. $C_{12}H_{12}O_4$ requires C, 65.45; H, 5.5%); ν_{max} (neat) 1740, 1690, 1655, and 1615 cm^{-1}; δ (90 MHz) [keto form **20**] 1.50 (3 H, d, *J* 6 Hz, 2-Me), 3.60 (1 H, d, *J* 11.5 Hz, 3-H), 3.8 (3 H, s, OMe), 4.83 (1 H, dq, *J* 6, 11.5 Hz, 2-H), and 6.8–8.0 (4 H, m, ArH); the enol form **21** had characteristic signals at δ 1.34 (3 H, d, *J* 6 Hz, 2-Me), 5.35 (1 H, q, *J* 6 Hz, 2-H), and 12.03 (1 H, s, exchanges with D_2O, OH).

Entry 5: 2-Methyl-3-acetylchromone **22** was treated as described above. Bulb-to-bulb distillation (105–110 °C, 0.2 mmHg) gave *3-acetyl-2,3-dihydro-2,2-dimethyl-4*H*-1-benzopyran-4-one* **23** (42%) as a pale yellow oil (Found: C, 71.4; H, 6.3. $C_{13}H_{14}O_3$ requires C, 71.5; H, 6.5%); ν_{max} (neat) 1720, 1680, and 1610 cm^{-1}; δ (90 MHz) 1.48 (3 H, s, 2-Me), 1.53 (3 H, s, 2-Me), 2.28 (3 H, s, COMe), 3.87 (1 H, s, 3-H), and 6.9–7.9 (4 H, m, ArH).

Entry 6: The ester **24** was treated as described above. Bulb-to-bulb distillation (110–115 °C, 0.2 mmHg) gave *methyl 3,4-dihydro-2,2-dimethyl-4-oxo-*2H*-1-benzopyran-3-carboxylate* **25** (74%) as a colourless oil (Found: C, 66.6; H, 5.9. $C_{13}H_{14}O_4$ requires C, 66.7; H, 6.0%); ν_{max} (neat) 1740, 1690, and 1615 cm^{-1}; δ (90 MHz) 1.53 (3 H, s, 2-Me), 1.57 (3 H, s, 2-Me), 3.74 (1 H, s, 3-H), 3.77 (3 H, s, OMe), and 6.9–8.0 (4 H, m, ArH).

Entry 7: The ester **26** was treated as described above. Chromatography (elution with ether - petroleum 1:9) yielded a mixture of keto forms **27** + **28**, and enol **29** (0.450 g, 91%; ratio *ca.* 3:1:1 by n.m.r.). Bulb-to-bulb distillation (95–100 °C, 0.1 mmHg) gave a colourless oil containing *rel-(2S,3S)-methyl 2-ethyl-2,3-dihydro-2-methyl-4-oxo-*2H*-1-benzopyran-3-carboxylate* **27** and *rel-(2R,3S)-methyl 2-ethyl-2,3-dihydro-2-methyl-4-oxo-*2H*-1-benzopyran-3-carboxylate* **28** (ratio *ca.* 3:2 by n.m.r.) (Found: C, 67.75; H, 6.4. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.5%); ν_{max} (neat) 1740, 1685, and 1605 cm^{-1}; δ (300 MHz) 0.95 and 1.0 (total 3 H, 2 x t, *J* 7 Hz, 2 x MeCH$_2$), 1.42 (s, 2-Me of **28**), 1.48 (s, 2-Me of **27**), 1.6–2.2 (total 2 H, m, 2 x CH$_2$), 3.72 (s, OMe of **28**), 3.74 (s, OMe of **27**), 3.79 (s, 3-H of **27**), 3.80 (s, 3-H of **28**), 6.9–7.05 (total 2 H, m, 6-H, 8-H), 7.4–7.5 (total 1 H, m, 7-H), and 7.8–7.85 (total 1 H, m, 5-H); m/z 248 (M^+, 13%), 219 (10), 187 (24), 122 (10), 121 (100), 120 (53), 97 (12), and 92 (15). The enol form **29** had distinguishable signals at δ (300 MHz) 1.54 (s, 2-Me) and 13.0 (s, OH).

Entry 8: The nitrile **30** was treated as described above. Chromatography (elution with dichloromethane - petroleum 1:4) yielded a mixture of **31** and **32** (0.232 g, 62%; ratio *ca.* 5:1 by n.m.r.). trans-*2,3-dihydro-2-methyl-4-oxo-*2H*-1-benzopyran-3-carbonitrile* **31** had m.p. 96–97 °C (petroleum - dichloromethane) (Found: C, 70.7; H, 4.9; N, 7.4. $C_{11}H_9NO_2$ requires C, 70.6; H, 4.85; N, 7.5%); ν_{max} 2250, 1685, and 1600 cm^{-1}; δ (300 MHz) 1.75 (3 H, d, *J* 6 Hz, 2-Me), 3.77 (1 H, d, *J* 12 Hz, 3-H), 4.65 (1 H, dq, *J* 6, 12 Hz, 2-H), 6.95–7.15 (2 H, m, 6-H, 8-H), 7.5–7.6 (1 H, m, 7-H), and 7.91 (1 H, dd, *J* 2, 8 Hz, 5-H); m/z 187 (M^+, 20%), 172 (10), 121 (20), 120 (100), and 92 (52). The *cis*-isomer **32** had characteristic signals at δ (300 MHz) 1.66 (d, *J* 6 Hz, 2-Me), 3.68 (d, *J* 3 Hz, 3-H), and 4.70 (1 H, dq, *J* 3, 6 Hz, 2-H).

Entry 9: To a stirred solution of lithium diphenylcuprate (3 mmol), prepared from copper(I) iodide (0.58 g, 3.0 mmol) and phenyllithium (2.4 M; 2.5 ml, 6.0 mmol) in ether (10 ml) at 0 °C under nitrogen, was added dropwise at -78 °C a solution of the ester **19** (0.41 g, 2.0 mmol) in tetrahydrofuran (10 ml). After 0.5 h the mixture was allowed to warm slowly to 0 °C (approx. 1 h) and then quenched with saturated aqueous ammonium chloride solution (15 ml). The organic layer was separated and the aqueous layer washed with ethyl acetate (3 x 20 ml). The combined extracts were washed successively with 2 M hydrochloric acid (20 ml), water (20 ml), and brine (20 ml), and the solution dried and evaporated. The ^{1}H n.m.r. spectrum of the residue indicated the presence of the keto and enol forms **33** and **34** (ratio *ca.* 4:3). Chromatography (elution with ether - petroleum 3:17) yielded a mixture of **33** and **34** (0.50 g, 89%; ratio *ca.* 3:7). Crystallisation from petroleum then gave two crops of colourless crystals; the first was a mixture of **33** and **34** (0.22 g, ratio *ca.* 1:1), while the second was pure *methyl 4-hydroxy-2-phenyl-*2H*-1-benzopyran-3-carboxylate* **34** (0.2 g), m.p. 93–94 °C (Found: C, 72.2; H, 5.0. $C_{17}H_{14}O_4$ requires C, 72.3; H, 5.0%); ν_{max} 1660 and 1630 cm^{-1}; δ (300 MHz) 3.74 (3 H, s, CO_2Me), 6.23 (1 H, s, 2-H), 6.78 (1 H, dd, *J* 1, 8 Hz, 8-H), 6.93 (1 H, ddd, *J* 1,

8, 8 Hz, 6-H), 7.2–7.5 (6 H, m, 7-H and phenyl H), 7.67 (1 H, dd, *J* 2, 8 Hz, 5-H), and 12.3 (1 H, s, exchanges with D_2O, OH); M^+, 282. The keto form **33** had ν_{max} 1735 cm^{-1}; δ (300 MHz) 3.62 (3 H, s, CO_2Me), 4.09 (1 H, d, *J* 12 Hz, 3-H), 5.69 (1 H, d, *J* 12 Hz, 2-H), 7.0–7.55 (8 H, m, 6-H, 7-H, 8-H, and phenyl H), and 7.94 (1 H, dd, *J* 2, 8 Hz, 5-H).

*2,3-Dihydro-2-methyl-4*H*-1-benzopyran-4-one* **35**. – A mixture of **20** and **21** (*ca.* 5:1 by n.m.r.; 70 mg, 0.32 mmol), sodium chloride (50 mg, 0.85 mmol), water (0.1 ml), and dimethylsulphoxide (3 ml) was heated at 155–165 °C for 5 h, allowed to cool, poured into water (30 ml), and extracted with ether - petroleum (2:1; 3 x 15 ml). The extract washed with water (20 ml) and brine (20 ml), dried, and evaporated under slightly reduced pressure to obtain the title compound **35**. The oily product was dissolved in methanol (1 ml) and added to a solution prepared[30] from 2,4-dinitrophenylhydrazine (0.25 g), methanol (5 ml), and conc. sulphuric acid (0.5 ml), which produced a red precipitate of the 2,4-dinitrophenylhydrazone (84 mg, 77%), m.p. 234–236 °C (ethyl acetate) (lit.[31] 236 °C).

*2,3-Dihydro-2,2-dimethyl-4*H*-1-benzopyran-4-one 2,4-dinitrophenylhydrazone* **36**. – A mixture of **25** (92 mg, 0.39 mmol), sodium chloride (50 mg, 0.85 mmol), water (0.1 ml), and dimethylsulphoxide (3 ml) was heated at 155–165 °C for 5 h, allowed to cool, poured into water (30 ml), and extracted with ether - petroleum (2:1; 3 x 15 ml). The extract washed with water (20 ml) and brine (20 ml), dried, and evaporated under slightly reduced pressure to obtain the title compound **36**. The oily product was dissolved in methanol (1 ml) and added to a solution prepared[30] from 2,4-dinitrophenylhydrazine (0.25 g), methanol (5 ml), and conc. sulphuric acid (0.5 ml), which produced a red precipitate of the 2,4-dinitrophenylhydrazone (121 mg, 86%), m.p. 223–224 °C (ethanol) (lit.[32] 220–221 °C).

*2,3-Dihydro-2-phenyl-4*H*-1-benzopyran-4-one* **37**. – A mixture of **33** and **34** (*ca.* 1:1 by n.m.r.; 170 mg, 0.60 mmol), sodium chloride (44 mg, 0.75 mmol), and water (22 mg, 1.2 mmol) in dimethylsulphoxide (2 ml) was heated at 155–160 °C for 5 h, cooled, poured into water (20 ml), and extracted with petroleum - ether (1:1; 3 x 20 ml). The extract was washed with water (2 x 20 ml) and brine (20 ml), dried, and evaporated. Chromatography of the residue (eluting with ether) gave flavanone **37** (120 mg, 89%), m.p. 75–76 °C (petroleum) (lit.[33] 76 °C); ν_{max} 1695 and 1615 cm^{-1}; δ (60 MHz) 2.92 (1 H, d, *J* 5.5 Hz, 3-H *trans* to Ph), 2.95 (1 H, d, *J* 11 Hz, 3-H *cis* to Ph), 5.40 (1 H, dd, *J* 5.5, 11 Hz, 2-H), and 6.7–8.1 (9 H, m, ArH).

*2-Methyl-4-oxo-4*H*-1-benzopyran-3-carboxaldehyde* **38**. – A crude (undistilled) sample of 2,3-dihydro-2-methyl-3-hydroxymethylene-4*H*-1-benzopyran-4-one **12**, prepared from lithium dimethylcuprate (3.2 mmol) and the aldehyde **11** (0.35 g, 2 mmol) as described above, was diluted with dichloromethane (10 ml) and treated with a solution of triphenylcarbenium tetrafluorborate (1.0 g, 3 mmol) in dichloromethane (10 ml) at room temperature for 20 h. The reaction was quenched with saturated aqueous sodium hydrogen carbonate (20 ml), and the layers separated. The organic phase was washed with water (2 x 5 ml) and brine (5 ml), dried, and evaporated. Flash chromatography of the residue, eluting with dichloromethane - ethyl acetate (19:1), gave the title compound **38** (0.21 g, 56%) as pale yellow prisms, m.p. 139–140 °C (ether - dichloromethane) [lit.[16] m.p. 142 °C (benzene)]; ν_{max} 1695, 1645, and 1615 cm^{-1}; δ (60 MHz) 2.8 (3 H, s, Me), 7.1–7.9 (3 H, m, 6-H, 7-H, 8-H), 8.2 (1 H, dd, *J* 2, 8 Hz, 5-H), and 10.5 (1 H, s, CHO).

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