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HETEROANNULATION OF 4-OXO-4*H*-1-BENZOPYRANS (CHROMONES) *VIA* THE CONJUGATE ADDITION OF HALOALKANOLS IN THE PRESENCE OF BASE

Peter J. Cremins, Roy Hayes, and Timothy W. Wallace*

Department of Chemistry and Applied Chemistry
University of Salford, Salford M5 4WT, U.K.

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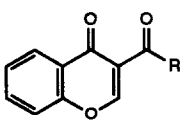
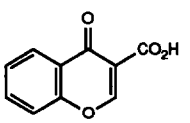
Abstract: Chromones (4-oxo-4*H*-1-benzopyrans) bearing electron-withdrawing substituents at C-3 react with 2-haloethanols and potassium carbonate in acetone to produce tetrahydrofuro[2,3-*b*][1]benzopyran-4-ones, the heteroannulation proceeding *via* the conjugate addition of the haloethanol to the chromone, followed by intramolecular alkylation. Under the conditions of the reaction, the products derived from chromone-3-carbaldehydes undergo *in situ* deformylation.

Chromones (4-oxo-4*H*-1-benzopyrans) bearing electron-withdrawing substituents at C-3 are highly versatile molecules. Acyl derivatives **1** and the carboxylic acid **2** are effective as 4π components (heterodienes) in inverse electron demand [4π + 2π] cycloadditions to electron-rich alkenes,[1,2] while systems of the types **1–4** can also function as 2π components (dienophiles) in conventional Diels-Alder reactions with electron-rich dienes.[3] Treating such compounds with nucleophiles often provokes rearrangement of the chromone nucleus,[4] but organocopper reagents undergo clean conjugate addition to C-2 of **1**, **3**, and **4**, providing a general route to 2-substituted chroman-4-ones[5,6] which in the case of the sulphoxides **4** is usefully diastereoselective.



1 R = H, Me, Ph



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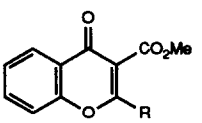
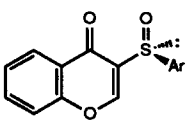


3 R = H, alkyl



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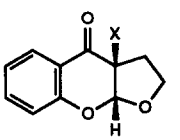

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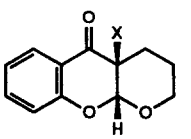

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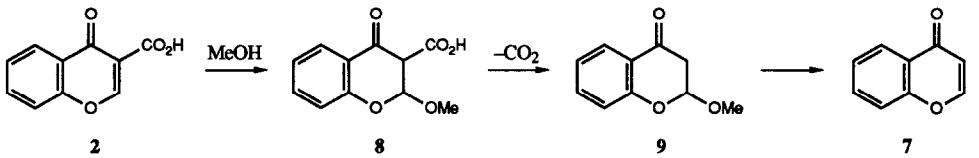
3-Acylchromones are also susceptible to the uncatalysed conjugate addition of alkanols, although the adducts readily undergo the reverse reaction and may go undetected,[7] and we herein describe in detail[8] an application of this process in which the addition engenders a second, irreversible, transformation leading to a fused cyclic acetal, a class of compound which features widely in nature.[9] The sequence offers a simple route to derivatives of tetrahydrofuro[2,3-*b*][1]benzopyran-4-one **5** and tetrahydropyrano[2,3-*b*][1]benzopyran-5-one **6**.

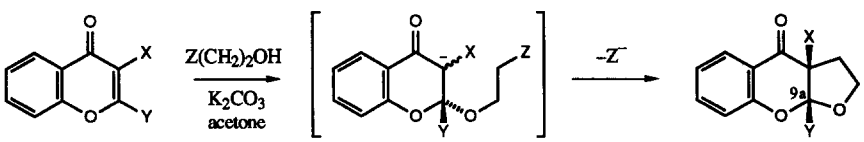
The underlying principle of this work is illustrated by the behaviour of the acid **2**, which might be expected to undergo decarboxylation in the event of reversible nucleophilic addition at C-2 due to the transient formation of an unstable β-ketoacid moiety. Indeed, while the acid **2** was unaffected when heated in toluene at 110 °C for 5 h, heating it in methanol under reflux for 2–3 h brought about its quantitative conversion into chromone **7**. When the reaction was carried out at a lower temperature in the presence of sodium acetate trihydrate, the intermediate **9** was isolated in 34% yield, suggesting that the decarboxylation proceeds as shown in Scheme 1. An earlier report, by Ghosh and Khan,[10] that the decarboxylation of **2** can be induced with triethylamine in refluxing ethanol is therefore rather misleading, since the ethanol alone elicits the observed transformation.



2 **8** **9** **7**

SCHEME 1

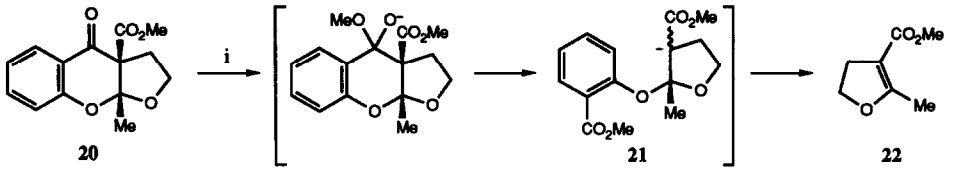
ω-Haloalkanols also undergo conjugate addition to activated chromones, and in the presence of base the initial adduct has the opportunity of cyclising *via* intramolecular alkylation. This heteroannulation process turns out to be a particularly effective route to tetrahydro[2,3-*b*][1]benzopyran-4-ones. For example, heating the ester **10** with 2-bromoethanol and potassium carbonate in acetone for 6 h gave the furochromanone **11** in 79% yield. Other activated chromones behaved similarly (Table 1), although the products obtained from 3-acetylchromone **12** included a substantial amount of the parent furochromanone **14**, which is formed as a result of the facile base-induced retro-Claisen deacetylation of the initial product **13**. Methyl 2-methylchromone-3-carboxylate **19** also gave a corresponding furochromanone **20**, but the presence of a methyl substituent at C-2 of the substrate resulted in a significant rate decrease, and the conversion was poor even after prolonged reaction with 2-iodoethanol. It is noteworthy that treatment of **20** with sodium methoxide induced ring-fission to **21**, which eliminated methyl salicylate anion to give the known dihydrofuran **22**[11] (Scheme 2).



Chromone	X	Y	Z	Time (h)	Product	Yield (%)	$\delta_{H\text{-}9a}$
10	CO_2Me	H	Br	6	**11**	79	6.10
12	COMe	H	Br	6	**13**	27†	6.10
15	COPh	H	Br	8	**16**	80	6.26
17	CN	H	Br	6	**18**	79	6.03
19	CO_2Me	Me	I	48	**20**	24‡	–

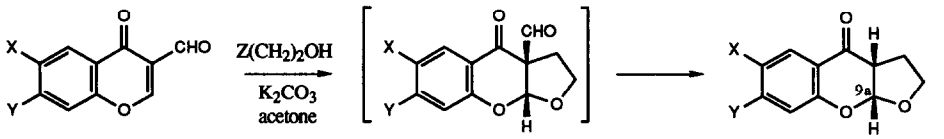
† A substantial amount of the deacetylated product **14** (X = Y = H) was also formed in this reaction.
‡ The material balance was unreacted starting material.

TABLE 1 Heteroannulation of 3-substituted chromones using haloethanols and base



SCHEME 2 *Reagents:* i, NaOMe, MeOH, reflux, 24 h (64%).

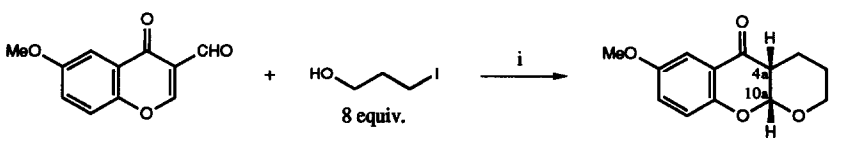
When chromone-3-carbaldehyde **23** was treated with 2-iodoethanol under the heteroannulation conditions, the product was found to be exclusively derived *via* the retro-Claisen process previously observed with the product from 3-acetylchromone **12**. The structure of **14** was apparent from its i.r. and ^{1}H n.m.r. spectra, both indicating that the formyl group had been lost, and the latter including a characteristic signal at 5.93 ppm (1 H, d, *J* 4 Hz) due to the acetal hydrogen (9a-H). Other chromone-3-carbaldehydes reacted in similar fashion, with yields which varied according to the electron demand of the aromatic substituent (Table 2). The results are consistent with a rate-limiting nucleophilic displacement (*i.e.* cyclisation) step, since the process is facilitated by a donor group (*e.g.* OMe) in the aromatic ring, and an acceptor group (*e.g.* NO_2) has the opposite effect.



Aldehyde	X	Y	Z	Time (h)	Product	Yield (%)	$\delta_{H\text{-}9a}$
23	H	H	I	8	**14**	53	5.93
24	OH	H	I	4	**25**	65	5.90
26	OMe	H	I	4	**27**	70	5.86
28	NO_2	H	I	4	**29**	40	6.02
30	H	OAc	Br	8	**31**	65	5.93

TABLE 2 Heteroannulation of chromone-3-carbaldehydes using haloethanols and base

The heteroannulation reaction was found to be less effective when used as a route to tetrahydropyrano[2,3-*b*][1]benzopyranones. Heating 6-methoxychromone-3-carbaldehyde **26** with an excess of 3-iodopropanol and potassium carbonate in acetone for an extended period produced the tricycle **32** in only 26% yield (Scheme 3). The stereochemistry of **32** was established from its ^{1}H n.m.r. spectrum, which incorporated a doublet at 5.5 ppm which can be attributed to the acetal hydrogen (10a-H). The coupling constant $J_{4a,10a}$ (3 Hz) is similar to that observed in comparable *cis*-fused pyranobenzopyrans.[12]



26 **32**

SCHEME 3 *Reagents:* i, excess K_2CO_3, acetone, reflux, 72 h (26%).

The procedure described above provides a simple and flexible method for the fusion of a furan ring on to an activated α,β-unsaturated carbonyl system. The scope and limitations of the process, particularly with regard to the construction of pyran rings and the use of chiral substrates, are the subject of further studies which will be described in due course.

EXPERIMENTAL

All compounds are racemic. 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, and Perkin-Elmer 177, 257, or 580B spectrometers. ^{1}H N.m.r. spectra were measured for solutions in deuteriochloroform unless otherwise indicated, with tetramethylsilane as the internal standard, on Varian EM360 (60 MHz), CFT-20 (80 MHz), or XL-200 (200 MHz), Perkin-Elmer R32 (90 MHz), Jeol FX100 (100 MHz), and Bruker AM250 (250 MHz) or AC300 (300 MHz) instruments. U.v. spectra were recorded for ethanolic solutions using a Pye-Unicam SP800 spectrometer. Mass spectra were measured on a Kratos MS30 instrument using 70 eV electron impact ionisation.

Starting materials and solvents were routinely purified by conventional techniques.[13] 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[14]). 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.

Starting Materials. – The chromones **2**,[3] **10**,[3] **12**,[15] **15**,[15] **17**,[16] **19**,[17] **23**,[18] **24**,[19] **26**,[20] **28**,[20] and **30**,[20] and 3-iodopropanol,[21] were prepared *via* the procedures cited. 2-Iodoethanol and 2-bromoethanol were purchased from the Aldrich Chemical Co.

Thermal Stability of Chromone-3-carboxylic acid **2**. – The acid **2** (190 mg, 1.0 mmol) in toluene (25 ml) was heated under reflux for 5 h and then allowed to cool to room temperature. A colourless solid crystallised out and was collected. Evaporation of the supernatant liquid gave a second quantity of white solid. Both of the solids thus obtained were identical (by ^{1}H n.m.r., i.r., and m.p.) with the starting material **2**.

Decarboxylation of Chromone-3-carboxylic acid **2**. – The acid **2** (190 mg, 1.0 mmol) in methanol (25 ml) was heated under reflux for 3 h. Removal of the methanol *in vacuo* gave an oil (145 mg, 99%) which slowly solidified. The product was identical (^{1}H n.m.r., i.r., t.l.c.) to a commercial sample of chromone **7** (Aldrich 19,922-2).

*2,3-Dihydro-2-methoxy-4*H*-1-benzopyran-4-one* **9**. – Method A: A stirred mixture of the acid **2** (190 mg, 1.0 mmol) and sodium acetate trihydrate (245 mg, 1.8 mmol) in methanol (25 ml) was heated under reflux for 3 h. T.l.c. analysis, eluting with ethyl acetate:petroleum (1:4), indicated the presence of two products, one of which had the same chromatographic mobility as chromone **7**. The mixture was filtered, the residue washed

with dichloromethane (2 x 10 ml), and the combined washings and filtrate were evaporated. Chromatography of the residue, eluting with ethyl acetate - petroleum (1:3), gave chromone **7** (133 mg, 91%), and the *title compound* **9** (16 mg, 9%) as an oil (Found: C, 67.4; H, 5.7. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.7%); ν_{max} (neat) 2900, 1680, and 1600 cm^{-1}; δ (80 MHz) 2.8–2.9 (2 H, m, 3-H_2), 3.5 (3 H, s, OMe), 5.4 (1 H, t, *J* 3.5 Hz, 2-H), 6.9–7.15 (2 H, m, 6,8-H), 7.35–7.6 (1 H, m, 7-H), and 7.75–7.95 (1 H, m, 5-H).

Method B: A mixture of the acid **2** (190 mg, 1.0 mmol) and sodium acetate trihydrate (245 mg, 1.8 mmol) in methanol (25 ml) was stirred at room temperature for 24 h. Isolation of the products as in Method A gave chromone **7** (96 mg, 66%), and the acetal **9** (61 mg, 34%).

General Procedure for the Heteroannulation of 3-Substituted Chromones (*cf.* Table 1)

A mixture of the chromone (1.0 mmol), the 2-haloalkanol (2.0 mmol), and anhydrous potassium carbonate (0.28 g, 2.0 mmol) in acetone (20 ml) was heated under reflux until t.l.c. analysis (elution with ethyl acetate - petroleum 1:1) indicated that the starting chromone had been consumed. The cooled reaction mixture was then evaporated and the residue extracted with ethyl acetate or dichloromethane (3 x 20 ml). The extract was washed with water (20 ml), dried, and evaporated. Chromatography or crystallisation of the residue gave the pure product.

*Methyl (*3aβ,9aβ*)-2,3,3a,9a-tetrahydro-4-oxo-*4H*-furo[2,3-*b*][1]benzopyran-3a-carboxylate* **11**. – Heating the ester **10** (204 mg) with 2-bromoethanol for 6 h as above, followed by chromatography (elution with ethyl acetate - petroleum 1:4), gave the *title compound* **11** (195 mg, 79%) as a white solid, m.p. 70–71 °C (Found: C, 63.1; H, 4.9. $C_{13}H_{12}O_5$ requires C, 62.9; H, 4.9%); ν_{max} 1740, 1680, 1605, and 1570 cm^{-1}; λ_{max} 253.5 nm (ε 10500) and 322 (3420); δ (250 MHz) 2.25–2.45 (1 H, m, 3-H), 2.85–3.05 (1 H, m, 3-H), 3.79 (3 H, s, OMe), 4.1–4.4 (2 H, m, 2-H_2), 6.10 (1 H, s, 9a-H), 7.0–7.15 (2 H, m, 6,8-H), 7.5–7.6 (1 H, m, 7-H), and 7.91 (1 H, dd, *J* 2, 8 Hz, 5-H).

*(*3aβ,9aβ*)-3a-Acetyl-2,3,3a,9a-tetrahydro-*4H*-furo[2,3-*b*][1]benzopyran-4-one* **13**. – Heating the chromone **12** (188 mg) with 2-bromoethanol for 6 h as above gave an oil with two main components. It was evident that one of these was the furobenzopyran **14** (identical by t.l.c. and 60 MHz ^1H n.m.r. spectroscopy with a sample prepared from the aldehyde **23** as described below). Chromatography (elution with ethyl acetate - petroleum 1:3) gave a mixed fraction and a fraction containing the pure *title compound* **13** (63 mg, 27%), m.p. 108–109 °C (ether) (Found: C, 67.1; H, 5.2. $C_{13}H_{12}O_4$ requires C, 67.2; H, 5.2%); ν_{max} 1720, 1655, and 1600 cm^{-1}; δ (60 MHz) 2.0–3.1 (2 H, m, 3-H_2), 2.3 (3 H, s, Me), 3.9–4.3 (2 H, m, 2-H_2), 6.10 (1 H, s, 9a-H), and 6.9–8.0 (4 H, m, 5,6,7,8-H).

*(*3aβ,9aβ*)-3a-Benzoyl-2,3,3a,9a-tetrahydro-*4H*-furo[2,3-*b*][1]benzopyran-4-one* **16**. – Heating the chromone **15** (250 mg) with 2-bromoethanol for 8 h as above, followed by chromatography (elution with ethyl acetate - petroleum 1:4), gave the *title compound* **16** (235 mg, 80%) as a white needles, m.p. 125–126 °C (ether) (Found: C, 73.3; H, 4.8. $C_{18}H_{14}O_4$ requires C, 73.5; H, 4.8%); ν_{max} 1680, 1665, 1600, 1590, and 1575 cm^{-1}; λ_{max} 252 nm (ε 21300) and 323 (3600); δ (250 MHz) 2.25–2.4 (1 H, m, 3-H), 3.2–3.35 (1 H, m, 3-H), 4.1–4.4 (2 H, m, 2-H_2), 6.26 (1 H, s, 9a-H), and 7.1–8.0 (9 H, m, ArH).

(3aβ,9aβ)-2,3,3a,9a-Tetrahydro-4-oxo-4H-furo[2,3-b][1]benzopyran-3a-carbonitrile **18**. – Heating the nitrile **17** (171 mg) with 2-bromoethanol for 6 h as above, followed by chromatography (elution with ethyl acetate - petroleum 1:3), gave the *title compound* **18** (170 mg, 79%) as a white needles, m.p. 131–132 °C (ether) (Found: C, 66.7; H, 4.2; N, 6.5. $C_{12}H_9NO_3$ requires C, 67.0; H, 4.2; N, 6.5%); ν_{max} 2240, 1680, 1605, and 1575 cm^{-1}; λ_{max} 255 nm (ε 10500) and 322 (3190); δ (200 MHz) 2.5–2.8 (2 H, m, 3-H_2), 4.25–4.45 (2 H, m, 2-H_2), 6.03 (1 H, s, 9a-H), 7.06 (1 H, d, 8-H), 7.0–7.2 (2 H, m, 6,8-H), 7.55–7.7 (1 H, m, 7-H), and 7.94 (1 H, dd, *J* 2, 8 Hz, 5-H).

Methyl (3aβ,9aβ)-2,3,3a,9a-tetrahydro-9a-methyl-4-oxo-4H-furo[2,3-b][1]benzopyran-3a-carboxylate **20**. – Heating the ester **19** (218 mg) with 2-iodoethanol for 48 h as above, followed by chromatography (elution with ethyl acetate - petroleum 1:4), gave the starting chromone **19** (166 mg, 76%) and the *title compound* **20** (62 mg, 24%) as a white solid, m.p. 127–128 °C (ether) (Found: C, 64.2; H, 5.5. $C_{14}H_{14}O_5$ requires C, 64.1; H, 5.4%); ν_{max} 1730, 1675, 1600, and 1575 cm^{-1}; λ_{max} 254 nm (ε 10600) and 321.5 (3450); δ (300 MHz) 1.60 (3 H, s, Me), 2.45–2.55 (1 H, m, 3-H), 2.83–2.93 (1 H, m, 3-H), 3.75 (3 H, s, OMe), 4.00–4.10 (1 H, m, 2-H), 4.12–4.20 (1 H, m, 2-H), 7.00 (1 H, d, *J* 8 Hz, 8-H), 7.07 (1 H, t, *J* 8 Hz, 6-H), 7.4–7.65 (1 H, dt, *J* 1.3, 8, 7-H), and 7.90 (1 H, dd, *J* 1.3, 8, 5-H).

Methyl 4,5-Dihydro-2-methylfuran-3-carboxylate **22**. – A solution of the ester **20** (87 mg, 0.33 mmol) in methanol (4 ml) in which had been dissolved sodium metal (8 mg) was heated under reflux for 24 h, cooled, and evaporated to dryness *in vacuo*. Flash chromatography of the residue, eluting with ethyl acetate - hexane (1:4), gave the title compound **22** (30 mg, 64%) as a colourless oil, δ (300 MHz) 2.13 (3 H, t, *J* 1.5 Hz, Me), 2.85 (2 H, tq, *J* 1.5, *J* 10 Hz, 4-H_2), 3.67 (3 H, s, OMe), and 4.37 (2 H, t, *J* 10 Hz, 5-H_2) [lit.[10] (60MHz, CCl_4) 2.13 (3 H, t, *J* 1.6 Hz, Me), 2.82 (2 H, tm, 4-H_2), and 4.38 (2 H, tm, 5-H_2)].

General Procedure for the Heteroannulation of Chromone-3-carbaldehydes (*cf.* Table 2)

A mixture of the chromone (1.0 mmol), the haloalkanol, and anhydrous potassium carbonate in acetone (25–30 ml) was heated under reflux for the time indicated in Table 2. The cooled reaction mixture was then evaporated and the residue extracted with ethyl acetate or dichloromethane (3 x 20 ml). The extract was washed with water (20 ml), dried, and evaporated. Chromatography and/or crystallisation of the residue gave the pure product.

cis-*2,3,3a,9a-Tetrahydro-4H-furo[2,3-b][1]benzopyran-4-one* **14**. – Treating the chromone **23** (174 mg), 2-iodoethanol (0.5 g, 3 mmol), and potassium carbonate (0.3 g, 2.2 mmol) as described above, followed by chromatography (elution with ethyl acetate - petroleum 1:3) and crystallisation, gave the *title compound* **14** (101 mg, 53%) as colourless needles, m.p. 112–113 °C (ethyl acetate - petroleum 1:3) (Found: C, 69.1; H, 5.3. $C_{11}H_{10}O_3$ requires C, 69.45; H, 5.3%); ν_{max} ($CHBr_3$) 1680 and 1610 cm^{-1}; λ_{max} 254 nm (ε 8950) and 322 (3150); δ (200 MHz) 2.1–2.55 (2 H, m, 3-H_2), 3.1 (1 H, ddd, *J* 4, 8.5, 10.5 Hz, 3a-H), 4.0–4.3 (2 H, m, 2-H_2), 5.93 (1 H, d, *J* 4 Hz, 9a-H), 6.95–7.10 (2 H, m, 6,8-H), 7.45–7.65 (1 H, m, 7-H), and 7.90 (1 H, dd, *J* 2, 8 Hz, 5-H).

cis-*2,3,3a,9a-Tetrahydro-6-hydroxy-4H-furo[2,3-b][1]benzopyran-4-one* **25**. – Treating the chromone **24** (190 mg), 2-iodoethanol (0.5 g, 3 mmol), and potassium carbonate (0.5 g, 3.6 mmol) as described above, and crystallisation, gave the *title compound* **25** (134 mg, 65%) as colourless crystals, m.p. 174–175 °C (ethyl

acetate - petroleum 1:1) (Found: C, 64.2; H, 4.8. $C_{11}H_{10}O_4$ requires C, 64.1; H, 4.9%); ν_{max} 3425 and 1670 cm^{-1}; δ (80 MHz) 2.0–2.5 (2 H, m, 3-H_2), 3.05 (1 H, ddd, *J* 4, 8.5, 10.5 Hz, 3a-H), 3.9–4.4 (2 H, m, 2-H_2), 5.2 (1 H, s, OH), 5.9 (1 H, d, *J* 4 Hz, 9a-H), and 6.8–7.3 (3 H, m, 5,7,8-H); M^+, 206.

cis-*2,3,3a,9a-Tetrahydro-6-methoxy-4*H-*furo[2,3*-b*][1]benzopyran-4-one* **27**. – Treating the chromone **26** (204 mg), 2-iodoethanol (0.5 g, 3 mmol), and potassium carbonate (0.3 g, 2.2 mmol) as described above, followed by crystallisation, gave the *title compound* **27** (154 mg, 70%) as cream coloured crystals, m.p. 108–109 °C (ethyl acetate - petroleum 1:3) (Found: C, 65.2; H, 5.5. $C_{12}H_{12}O_4$ requires C, 65.45; H, 5.5%); ν_{max} ($CHBr_3$) 1680, 1620 and 1235 cm^{-1}; λ_{max} 226 nm (ε 15400), 257 (6820), and 354.5 (3410); δ (100 MHz) 1.9–2.6 (2 H, m, 3-H_2), 3.08 (1 H, ddd, *J* 4, 8.5, 10.5 Hz, 3a-H), 3.80 (3 H, s, OMe), 3.9–4.4 (2 H, m, 2-H_2), 5.86 (1 H, d, *J* 4 Hz, 9a-H), and 6.8–7.3 (3 H, m, 5,7,8-H).

cis-*2,3,3a,9a-Tetrahydro-6-nitro-4*H-*furo[2,3*-b*][1]benzopyran-4-one* **29**. – Treating the chromone **28** (219 mg), 2-iodoethanol (0.5 g, 3 mmol), and potassium carbonate (0.5 g, 3.6 mmol) as described above, followed by chromatography (elution with ethyl acetate - petroleum 1:3), gave the *title compound* **29** (95 mg, 40%) as a pale yellow powder, m.p. 167–168 °C (Found: C, 56.3; H, 3.9; N, 6.0. $C_{11}H_9NO_5$ requires C, 56.2; H, 3.9; N, 6.0%); ν_{max} ($CHBr_3$) 1695, 1615, and 1230 cm^{-1}; λ_{max} 241 nm (ε 16600) and 294.5 (10200); δ (100 MHz) 1.95–2.7 (2 H, m, 3-H_2), 3.23 (1 H, ddd, *J* 4.5, 8, 11 Hz, 3a-H), 4.0–4.5 (2 H, m, 2-H_2), 6.02 (1 H, d, *J* 4.5 Hz, 9a-H), 7.10 (1 H, d, *J* 8.5 Hz, 8-H), 8.35 (1 H, dd, *J* 2, 8.5 Hz, 7-H), and 8.73 (1 H, d, *J* 2 Hz, 5-H).

cis-*7-Acetoxy-2,3,3a,9a-tetrahydro-4*H-*furo[2,3*-b*][1]benzopyran-4-one* **31**. – Treating the chromone **30** (248 mg), 2-bromoethanol (0.25 g, 2 mmol), and potassium carbonate (0.28 g, 2 mmol) as described above, followed by chromatography (elution with ethyl acetate - petroleum 1:3), gave the *title compound* **31** (161 mg, 65%) as colourless crystals, m.p. 115–116 °C (Found: C, 62.8; H, 4.8. $C_{13}H_{12}O_5$ requires C, 62.9; H, 4.9%); ν_{max} 1750, 1675, 1600, and 1575 cm^{-1}; δ (200 MHz) 2.1–2.5 (2 H, m, 3-H_2), 2.31 (3 H, s, Me), 3.10 (1 H, ddd, *J* 4.5, 8, 11 Hz, 3a-H), 4.0–4.4 (2 H, m, 2-H_2), 5.93 (1 H, d, *J* 4.5 Hz, 9a-H), 6.75–6.85 (2 H, m, 6,8-H), and 7.9 (1 H, dd, *J* 1, 8 Hz, 5-H).

cis-*3,4,4a,10a-Tetrahydro-7-methoxy-*2H,5H-*pyrano[2,3*-b*][1]benzopyran-5-one* **32**. – Treating the chromone **26** (204 mg), 3-iodopropanol (1.5 g, 8 mmol), and potassium carbonate (2 g, 14.5 mmol) as described above, followed by chromatography (elution with ethyl acetate - petroleum 1:8) and crystallisation, gave the *title compound* **32** (60 mg, 26%) as a white solid (Found: C, 66.6; H, 6.1. $C_{13}H_{14}O_4$ requires C, 66.7; H, 6.0%); δ (80 MHz) 1.5–2.3 (4 H, m, 3-H_2 and 4-H_2), 2.7–2.95 (1 H, m, 4a-H), 3.6–4.3 (2 H, m, 2-H_2), 3.8 (3 H, s, OMe), 5.5 (1 H, d, *J* 3 Hz, 10a-H), and 7.0–7.4 (3 H, m, 6,8,9-H).

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