Chromone studies. Part 15. Formation and condensation of Baylis–Hillman adducts in DABCO-catalysed reactions of chromone-3-carbaldehydes with acrylonitrile.

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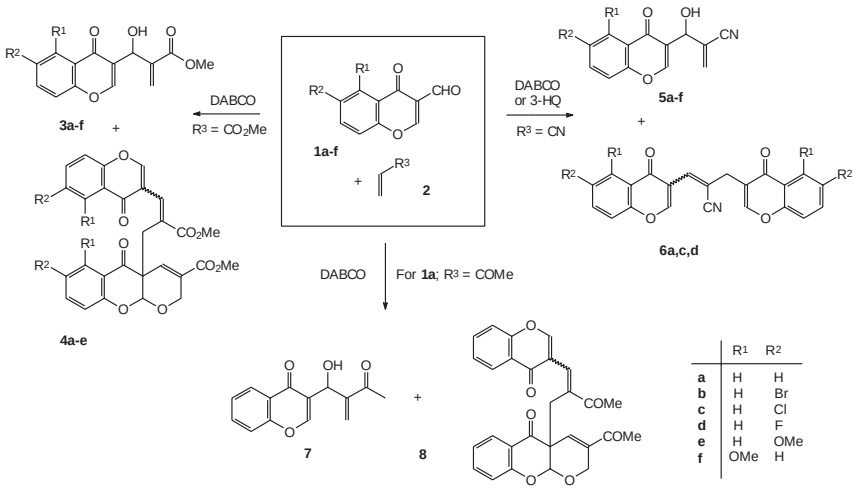
1,4-Diazabicyclo[2.2.2]octane(DABCO)-catalysed reactions of selected chromone-3-carbaldehydes with acrylonitrile (or methyl vinyl ketone) have led to the formation of Baylis–Hillman adducts and, in some cases, novel polycyclic condensation derivatives; electron-impact and electrospray MS fragmentation patterns have been examined for selected products.

Keywords: chromonecarbaldehydes, Bayliss-Hillman reaction.

Many chromone derivatives, natural and synthetic, are known to exhibit pharmacological activity. Classic examples include khellin, a furochromone present in the seeds of *Amni visnaga*, and the synthetic drug, disodium cromoglycate, both of which have found use in the treatment of bronchial asthma.[2,3] As part of our ongoing research on chromone derivatives, we have been investigating the use of chromone-3-carbaldehydes as Baylis–Hillman substrates, and recently reported[1] the dimerisation of Baylis–Hillman products obtained from 1,4-diazabicyclo[2.2.2]octane(DABCO)-catalysed reactions of chromone-3-carbaldehydes **1** with methyl acrylate **2** ($R^3 = CO_2Me$; Scheme 1). We now report an extension of this work in which acrylonitrile and methyl vinyl ketone were used as activated alkenes in place of methyl acrylate.

The chromone-3-carbaldehydes **1a–f** (prepared, as described previously,[1] using Vilsmeier-Haak methodology[4]) were initially reacted with acrylonitrile **2** (R^3 = CN) and DABCO in chloroform over periods of several weeks.[5] Three of the Baylis–Hillman products (**5a**,**c**,**d**) precipitated out of the reaction mixtures and were purified by elution through a silica plug using ethyl acetate as eluant; the remaining Baylis–Hillman products (**5b**,**e**,**f**) were purified by flash chromatography, followed by HPLC. In all cases, the yields were low (12–31%),[6] and substantial improvement was clearly needed.

In the reactions of the chromone-3-carbaldehydes **1a,c,d**, novel adducts (**6a,c,d**) were obtained in low yield (5–24%)[6] together with the Baylis–Hillman products **5a,c,d** (Scheme 1). Elemental (HRMS), IR and 1- and 2-D NMR analysis permitted identification of these adducts as the corresponding bis(chromone)-acrylonitrile adducts **6a,c,d**. The ^{1}H NMR and DEPT-135 spectra for compound **6a**, for example, indicate the presence of a single methylene group and 11 sp^2 CH nuclei, the latter resonating in the region, δ 7.6–8.7ppm; the ^{13}C NMR spectrum contains 22 signals corresponding to the CH_2 and C≡N groups, a pair of C=O groups and 11 methine and seven quaternary carbons, the signal assignments being supported by the HMQC and HMBC data. These structures are completely different from the dimers **4** obtained when methyl acrylate **2** ($R^3 = CO_2Me$) is used as the activated alkene, and their formation is presumably initiated by nucleophilic attack by DABCO at the electrophilic centre, C-2, of the chromone-3-carbaldehydes **1** (illustrated for the parent system **1a** in Scheme 2). Although DABCO normally attacks unhindered vinyl systems, some examples of attack at substituted vinylic centres have been reported.[7] In any event, the presence of *two* carbonyl groups in conjugation with the carbon–carbon double bond may well enhance electrophilicity at C-2 in the Baylis–Hillman products **5**. The resulting zwitterion **9a** could then attack the Baylis–Hillman product **5a** *via* an addition-elimination or (as shown in Scheme 2) S_N' pathway to afford the intermediate species **10a**, which, on elimination of formic acid and DABCO, would give the bis(chromone)-acrylonitrile adduct **6a**. Evidence for the intermediacy of the Baylis-Hillman product **5a** is provided by the formation of the adduct **6a** when chromone-3-carbaldehyde **1a** and the Baylis-Hillman product **5a** are treated with DABCO *in the absence of acrylonitrile*.[5]



Scheme 1

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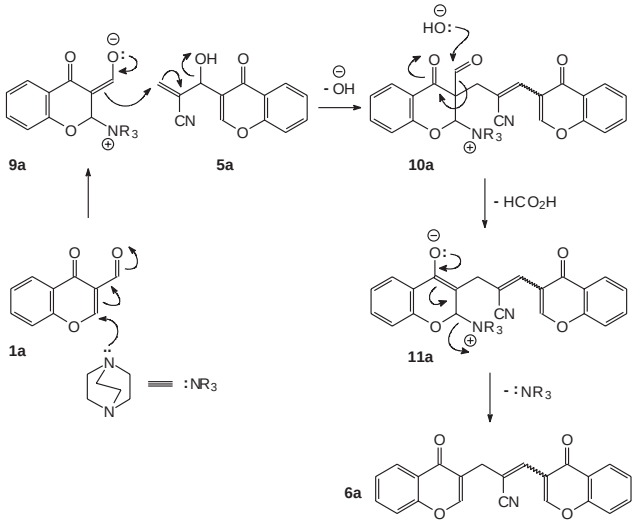
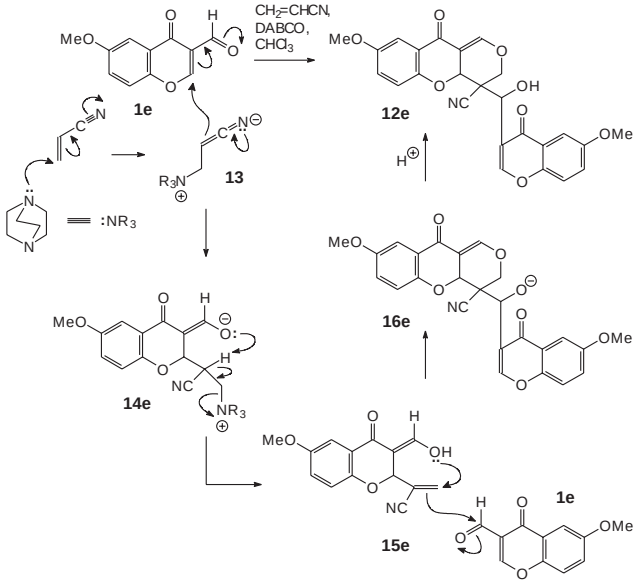


Scheme 2



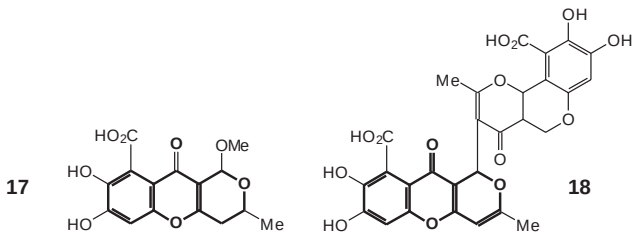
Scheme 3

Treatment of 6-nitrochromone-3-carbaldehyde with acrylonitrile and DABCO, however, failed to give either the expected Baylis–Hillman product or the bis(chromone)-acrylonitrile adduct. The 6-methoxy analogue **1e**, on the other hand, afforded, in addition to the Baylis–Hillman product **5e**, a trace quantity of a totally different bis(chromone)-acrylonitrile adduct, which was formulated, on the basis of the HRMS and NMR data, as the polycyclic compound **12e** (Scheme 3). The tricyclic moiety in dimer **12e** is, in fact, isomeric with that found in the dimers **4**.[1] However, several NMR features differentiate the adduct **12e** from the dimeric systems **4**, *viz.*, a *single* methylene carbon signal at δ 31.0 ppm (the attached, diastereotopic protons resonate as multiplets at 2.68 and 3.26 ppm) and an aliphatic methine carbon signal at 48.7ppm, with the attached proton resonating as a singlet at 3.29ppm. Formation of this novel system **12e** is proposed to involve:- initial attack of the Baylis–Hillman zwitterion **13** at C-2 of the aldehyde **1e**; proton transfer and elimination of DABCO (**14e** → **15e**); and intramolecular cyclisation and carbonyl addition steps (**15e** + **1e** → **16e**), possibly *via* the concerted mechanism detailed in Scheme 3.

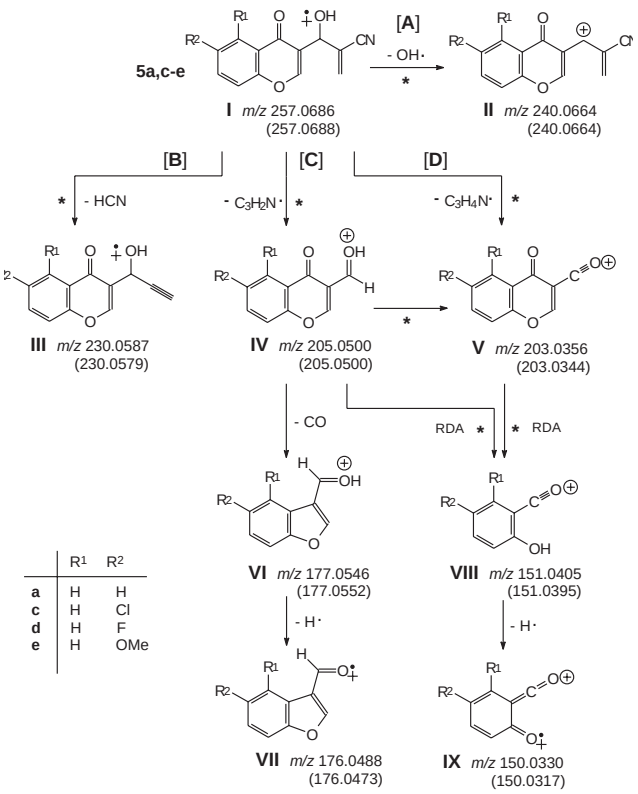
Interestingly, reaction of chromone-3-carbaldehyde **1a** with methyl vinyl ketone (MVK) **2** (R^3 = COMe) under similar conditions afforded the dimer **8** as the major product (33%) together with a very small quantity of the Baylis–Hillman product **7** (3%). The skeletal structure of the dimer **8** is identical to that of the dimeric products **4** obtained using methyl acrylate **2** (R = CO_2Me) as the activated alkene.[1]

In view of the generally low yields obtained for the Baylis–Hillman products **5**, attention was given to optimising the reaction conditions. In preliminary "NMR-scale" studies[5] of the reaction of chromone-3-carbaldehyde **1a** with acrylonitrile **2** (R = CN), it was observed that: (i) use of 2 equivalents of DABCO (instead of the usual 0.1 eq.) appeared to give 64% conversion in to the Baylis–Hillman product **5a** after 35 days; (ii) use of 2 equivalents of 3-hydroxyquinuclidine as the catalyst in place of DABCO led to 79% conversion after 24 h; and (iii) use of 5 equivalents of 3-hydroxyquinuclidine resulted in a conversion of *ca* 92% after 22 h! Based on these preliminary results, preparative-scale reactions were conducted,[8] using one equivalent of each of the aldehydes **1a**–**f**, 1.5 equivalents of acrylonitrile **2** (R^3 = CN) and 5 equivalents of 3-hydroxyquinuclidine as catalyst, dissolved in a minimal volume of chloroform (6–8 ml). After stirring for *ca* 25 h, the Baylis–Hillman products **5a–f** were isolated in yields of 53–67%, representing a significant improvement over the initial yields.

The tricyclic system in compound **12e** is present in a series of natural products, including **17**, which have been found to be potent, broad-spectrum metallo-β-lactamase inhibitors,[9] and in more complex semaphorin inhibitors, such as **18**.[10] However, the isomeric tricyclic system, present in compounds **4a–e** and **8**, and the 1,3-bis(chromone)propane skeleton, present in the bis(chromone)-acrylonitrile adducts **6**, appear to be unprecedented. Our ongoing research on applications of Baylis–Hillman methodology may well provide access to complex analogues with useful medicinal properties.



Electron impact (EI) mass spectrometric data were collected for the Baylis–Hillman products **5a,c,e**. The molecular ion **I**, in each case, appears to fragment *via* four general pathways (A–D; Scheme 4). In path A, loss of a hydroxyl radical affords resonance-stabilised cations of type **II** – a fragmentation which is paralleled by elimination of H_2O in the electrospray (ES) mass spectral data. In path B, loss of HCN leads to the radical cations of type **III**, while in paths C and D, elimination of C_3H_2N• and C_3H_4N• affords the even-electron species **IV** and **V** respectively. Paths C and D converge *via retro*-Diels-Alder processes, with the formation of acylium cations of type **VIII**, which deprotonate to afford the conjugated ketenes of type **IX**. Sequential decarbonylation and deprotonation account for the fragmentations **IV**→**VI**→**VII**. Decarbonylation of chromones to afford benzofuranoid fragments is, of course, well known.[11] The atomic composition of each of the ions detailed in Scheme 4 was established by high-resolution (HRMS) analysis. The proposed fragmentations are common (with very few exceptions) to all three of the compounds examined, and many of the pathways are supported by *B/E* linked scan data.



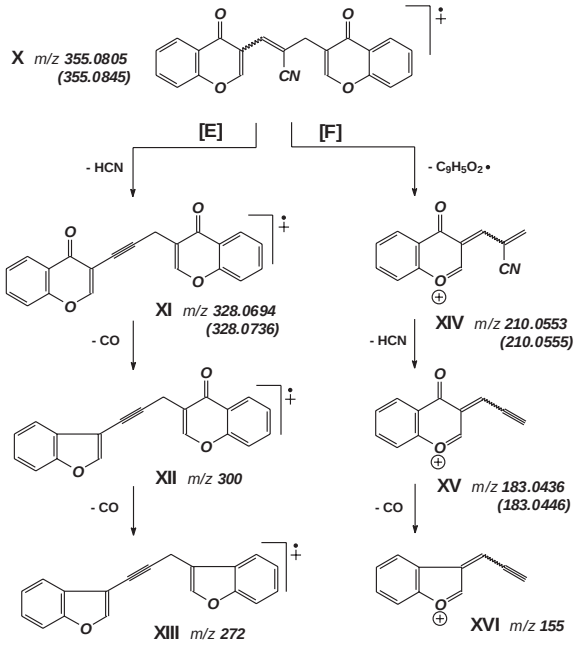
Scheme 4 EI fragmentation pathways exhibited by the Baylis–Hillman products **5a,c,e**. Accurate masses (*m/z*) are cited for the 6-methoxy derivative **5e** (R^1=H; R^2=OMe) and are followed, in parentheses, by the calculated formula masses; an asterisk indicates a pathway supported by *B/E* linked scan data.

The bis(chromone)-acrylonitrile adduct **6a** was subjected to both low-resolution ES MS^n and EI MS analysis, and two distinct fragmentation pathways were identified (E and F; Scheme 5). Where *m/z* correspondence between ES and EI mass spectral peaks was apparent, the atomic composition was determined by HRMS analysis. In path E, elimination of HCN from the molecular ion **X** (H• and HCN from MH^+ in the electrospray case) results in the formation of the odd-electron species **XI**, which undergoes sequential loss of CO (**XI**→**XII**→**XIII**). All three fragments (**XI, XII, XIII**) contain two heterocyclic moieties, *viz.*, chromonoid, benzofuranoid or a combination of both. In path F, elimination of a chromone moiety affords the oxonium ion **XIV**, which undergoes tandem loss of HCN and CO to give the even-electron ions **XV** and **XVI**, respectively.

Experimental

NMR spectra were recorded on Bruker AMX400 or AVANCE 400 MHz spectrometers at 303 K in $CDCl_3$ and calibrated using solvent signals. Infrared spectra were recorded on a Perkin Elmer FT–IR Spectrum 2000 spectrometer. Low-resolution mass spectra were obtained on Finnigan-Mat GCQ (EI) and LCQ (ES) mass spectrometers, and high-resolution (EI) mass spectra on a VG70-SEQ Micromass double-focusing magnetic sector spectrometer (Cape Technikon Mass Spectrometry Unit). The preparation and characterisation of compounds **1a–f**, **3a–f** and **4a–e** have been reported previously.[1] Synthetic procedures used in this study are illustrated by the following examples.

*3-(2-Cyano-1-hydroxy-2-propenyl)-4*H*-1-benzopyran-4-one* **5a:** Acrylonitrile (0.56 ml, 8.6 mmol) and 3-hydroxyquinuclidine (3.63 g, 28.8 mmol) were added to a stirred solution of chromone-3-carbaldehyde **1a** (1.0 g, 5.7 mmol) dissolved in a minimal volume of $CHCl_3$ (8.0 ml). The resulting intense red mixture was stirred at room temperature for 25 h. Flash chromatography on silica gel [elution with hexane-EtOAc (2:3)] afforded *3-(2-cyano-1-hydroxy-2-propenyl)-4H-1-benzopyran-4-one* **5a** as a yellow crystalline solid (0.83 g, 64%), m.p. 69–71°C (Found: $\mathbf{M}^+$, 227.0570. $C_{13}H_9NO_3$ requires *M*, 227.0582); ν_{max} (thin film)/cm^{-1} 3430 (br, OH), 2225 (CN) and 1630 (CO); δ_H (400 MHz; $CDCl_3$) 4.41 (1H, br s, 3'-OH), 5.30 (1H, s, 3'-H), 6.13 and 6.32 (2H, 2 × s, 1'-CH_2), 7.45 (1H, m, 6-H), 7.50 (1H, d, *J*=8.3 Hz, 8-H), 7.71 (1H, t, *J*=7.0 Hz, 7-H), 8.08 (1H, s, 2-H) and 8.18 (1H, dd, *J*=1.4 and 8.0 Hz, 5-H); δ_C (100 MHz; $CDCl_3$) 69.2 (C-3'), 116.8 (CN), 124.1 (C-2'), 118.4 (C-8), 121.2 (C-3), 123.7 (C-4a), 125.6 (C-6), 125.8 (C-5), 131.3 (C-1'), 134.5 (C-7), 153.9 (C-2), 156.3 (C-8a) and 177.7 (C=O); *m/z* 227 (M^+, 46%) and 210 (100).



Scheme 5 ES MS^n and HREIMS data for the bis(chromone)-acrylonitrile adduct **6a**.

*3-(2-Cyano-1-hydroxy-2-propenyl)-6-fluoro-4*H*-1-benzopyran-4-one* **5d** *and the corresponding bis(chromone)-acrylonitrile adduct* **6d**: 6–Fluoro-4*H*-1-benzopyran-4-one-3-carbaldehyde **1d** (1.00 g, 5.21 mmol) was dissolved in a minimal volume of $CHCl_3$. Acrylonitrile (0.38ml, 5.7 mmol) and DABCO (0.20 g, 1.8 mmol) were added, and the resulting solution was stirred at room temperature for 8 weeks. The resulting precipitate was filtered off and then eluted through silica with EtOAc; evaporation of the solvent from the eluate gave 3-(2-cyano-1-hydroxy-2-propenyl)-6-fluoro-4*H*-1-benzopyran-4-one **5d** (31%). Following filtration, the solvent was evaporated from the filtrate and the residue chromatographed [flash chromatography on silica gel; elution with hexane-EtOAc (1:1)] to give *1,3-bis(6-fluoro-*4H*-1-benzopran-4-on-3-yl)-2-cyano-1-propene* **6d** (24%), m.p. 242–244°C (Found: $\mathbf{M}^+$ 391.0651. $C_{22}H_{11}NO_4F_2$ requires *M*, 391.0656); ν_{max} (thin film)/cm^{-1} 2216 (C≡N), and 1650 and 1646 (C=O); δ_H (400 MHz; $CDCl_3$) 3.60 (2H, s, CH_2), 7.39–7.45 (3H, m, Ar–H), 7.48–7.53 (2H, m, Ar–H), 7.85 (2H, m, Ar–H), 7.98 and 8.67 (2H, 2 × s, 2- and 2'-H); δ_C (100 MHz; $CDCl_3$) 31.6 (CH_2), 110.2 (C≡N), 110.8, 111.2, 117.8, 118.6, 119.1, 120.4, 120.6, 122.3, 122.6, 124.8, 124.9, 135.6, 152.3, 152.8, 153.8, 155.1, 158.5 and 161.0 (C=CH and Ar-C), 174.7 and 176.1 (C=O); *m/z* 391 (M^+, 100%).

*3-(2-Cyano-1-hydroxy-2-propenyl)-6-methoxy-4*H*-1-benzopyran-4-one* **5e** *and the bis(chromone)-acrylonitrile adduct* **12e:** 6-Methoxy-4*H*-1-benzopyran-4-one-3-carbaldehyde **1e** (1.00g, 4.90mmol) was dissolved in a minimal volume of $CHCl_3$. Acrylonitrile (0.36ml, 5.4mmol) and DABCO (0.20g, 1.8mmol) were added, and the resulting solution was stirred at room temperature for 4 weeks. The solvent was then removed and the residue chromatographed [flash chromatography on silica gel; elution with $CHCl_3$-EtOAc (1:1)] to give two fractions: (i) 3-(2-cyano-1-hydroxy-2-propenyl)-6-methoxy-4*H*-1-benzopyran-4-one **5e** (20%); and (ii) the *bis(chromone)-acrylonitrile adduct* **12e** (4.0mg, 0.2%), m.p. 179–181 °C (Found: $\mathbf{M}^+$ 461.1110. $C_{25}H_{19}NO_8$ requires *M*, 461.1111); ν_{max} (thin film)/cm^{-1} 2930 (OH), 2213 (C≡N), 1694 and 1646 (C=O); δ_H (400 MHz; $CDCl_3$) 2.68 and 3.26 (2H, 2 × m, CH_2), 3.29 (1H, s, C*H*OH), 3.80 and 3.90 (6H, 2 × s, OCH_3), 5.43 (1H, d, COCH), 6.99 (1H, d, Ar–H), 7.14 (1H, Ar–H), 7.29 (1H, d, Ar–H), 7.31 (1H, t, Ar–H), 7.33 (1H, s, C=C*H*OCH_2), 7.44 (1H, d,

Ar–H), 7.58 (1H, d, Ar–H) and 8.71 (1H, s, C=CHOC); δ_C (100 MHz; $CDCl_3$) 31.0 (CH_2), 48.7 (CHOH), 55.8 and 56.0 (OCH_3), 100.8, 105.3 and 107.6 (Ar–C), 109.7 (*C*CN), 118.0, 118.4, 119.4, 119.9, 121.0, 124.3, 124.4, 124.9, 136.6, 151.0, 151.6, 154.4, 154.6 and 157.5 (C=CH, C≡N and Ar-C), 175.3 and 190.8 (C=O); *m/z* 461 (M^+, 8%) and 415 (100).

*3-(2-Acetyl-1-hydroxy-2-propenyl)-4*H*-1-benzopyran-4-one* **7** *and the corresponding dimer* **8:** 4*H*-1-benzopyran-4-one-3-carbaldehyde **1a** (1.00 g, 5.75 mmol) was dissolved in a minimal volume of $CHCl_3$. Methyl vinyl ketone **2** (R^3=Me; 0.53 ml, 6.3 mmol) and DABCO (0.20 g, 1.8 mmol) were added, and the resulting solution was stirred at room temperature for 3 weeks. The resulting precipitate was filtered off and then eluted through silica with EtOAc; evaporation of the solvent gave *the dimer* **8** (0.89 g, 33%), m.p. 266–268 °C (Found: $\mathbf{M}^+$ 470.1364. $C_{28}H_{22}O_7$ requires M, 470.1366); ν_{max} (thin film)/cm^{-1} 1698, 1669, 1642 and 1606 (C=O); δ_H (400 MHz; $CDCl_3$) 2.30 and 2.42 (6H, 2 × s, CH_3), 3.25 (2H, s, CH_2), 4.47 and 4.58 (2H, 2 × dd, OCH_2), 5.00 (1H, s, OCHO), 6.87–6.95 (2H, m, Ar–H), 7.17 (1H, s, C=CH), 7.26 (1H, m, Ar–H), 7.40–7.47 (3H, m, C=CH and Ar–H), 7.69–7.75 (2H, m, Ar–H), 7.89 (1H, s, Ar–H) and 8.13 (1H, dd, Ar–H); δ_C (100MHz; $CDCl_3$) 25.3 and 25.8 (CH_3), 25.9 (CH_2), 50.1 (CH_2*C*CO), 65.9 (OCH_2), 99.8 (OCHO), 117.5, 118.1, 120.0, 120.3, 122.9, 123.5, 125.8, 126.1, 128.0, 133.6, 134.2, 136.1, 136.6, 136.7, 139.1, 154.1, 155.9 and 157.0 (C=CH and Ar–C), 175.6, 191.5, 196.9 and 199.0 (C=O); *m/z* 470 (M^+, 23%) and 185 (100).

Following filtration, the solvent was evaporated from the filtrate to give an oil, which was then chromatographed [flash chromatography on silica gel; elution with hexane-EtOAc (7:3)]. Further chromatography [HPLC on Partisil 10; elution with hexane-EtOAc (2:3), followed by re-elution with the same mobile phase] gave *3-(2-acetyl-1-hydroxy-2-propenyl)-4H-1-benzopyran-4-one* **7** (3%), m.p. 86–88 °C (Found: $\mathbf{M}^+$ 244.0741. $C_{14}H_{12}O_4$ requires *M*, 244.0736); ν_{max} (thin film)/cm^{-1} 3420 (OH), and 1674 and 1638 (C=O); δ_H (400 MHz; $CDCl_3$) 2.34 (3H, s, CH_3), 4.71 (1H, d, *J*= 8.3 Hz, OH), 5.61 (1H, d, *J*= 8.3 Hz, C*H*OH), 6.29 and 6.35 (2H, 2 × s, $C=CH_2$), 7.41 (1H,m, 7-H), 7.47 (1H, d, *J*= 8.0 Hz, 5-H), 7.68 (1H, m, 6-H), 8.07 (1H, s, 2-H) and 8.17 (1H, dd, *J*= 1.6 and 8.0 Hz, 8-H); δ_C (100MHz; $CDCl_3$) 26.3 (CH_3), 67.6 (CHOH), 118.3, 122.8, 123.9, 125.3, 125.5, 127.3, 134.0, 147.6, 154.7 and 156.2 ($C=CH_2$ and Ar-C), 178.1 and 199.8 (C=O); *m/z* 244 (M^+, 19%) and 201 (100).

Data for other new compounds isolated in this study are as follows.

*6-Bromo-3-(2-cyano-1-hydroxy-2-propenyl)-4*H*-1-benzopyran-4-one* **5b**,[12] as an orange–yellow solid (0.40 g, 67%), m.p. 123–125 °C (Found: $\mathbf{M}^+$, 304.9724. $C_{13}H_8{}^{79}BrNO_3$ requires *M*, 304.9688); ν_{max} (thin film)/cm^{-1} 3420 (br, OH), 2225 (CN) and 1648 (CO); δ_H (400 MHz; $CDCl_3$) 4.10 (1H, br s, 3'-OH), 5.33 (1H, s, 3'-H), 6.14 and 6.32 (2H, 2 × s, 1'-H), 7.40 (1H, d, *J*=8.8 Hz, 8-H), 7.80 (1H, dd, *J*=2.3 and 8.8 Hz, 7-H), 8.09 (1H, s, 2-H) and 8.28 (1H, d, *J*=2.3 Hz, 5-H); δ_C (100 MHz; $CDCl_3$) 68.8 (C-3'), 116.6 (CN), 119.3 (C-6), 120.3 (C-8), 121.6 (C-2'), 123.9 (C-3), 124.9 (C-4a), 128.2 (C-5), 131.6 (C-1'), 137.5 (C-7), 154.1 (C-2), 155.1 (C-8a) and 176.1 (C=O); *m/z* 305 (M^+, 44%) and 253 (100).

*6-Chloro-3-(2-cyano-1-hydroxy-2-propenyl)-4*H*-1-benzopyran-4-one* **5c**,[12] as a yellow crystalline solid (0.37 g, 59%), m.p. 133–134 °C (Found: $\mathbf{M}^+$, 261.0196. $C_{13}H_8{}^{35}ClNO_3$ requires *M*, 261.0193); ν_{max} (thin film)/cm^{-1} 3440 (br, OH), 2300 (CN) and 1653 (CO); δ_H (400 MHz; $CDCl_3$) 4.16 (1H, d, *J*=6.8 Hz, 3'-OH), 5.34 (1H, d, *J*=6.5 Hz, 3'-H), 6.13 and 6.32 (2H, 2 × s, 1'-H), 7.47 (1H, d, *J*=8.9 Hz, 8-H), 7.66 (1H, dd, *J*=2.5 and 8.9 Hz, 7-H), 8.09 (1H, s, 2-H) and 8.11 (1H, d, *J*=2.4 Hz, 5-H); δ_C (100 MHz; $CDCl_3$) 68.7 (C-3'), 116.6 and 123.9 (C-2' and CN), 120.1 (C-8), 121.7 (C-3), 124.5 (C-4a), 125.0 (C-5), 131.6 (C-1'), 131.8 (C-6), 134.7 (C-7), 154.1 (C-2), 154.6 (C-8a) and 176.3 (C=O); *m/z* 261 (M^+, 52%) and 209 (100).

*3-(2-Cyano-1-hydroxy-2-propenyl)-6-fluoro-4*H*-1-benzopyran-4-one* **5d**:[12] as a yellow solid (0.34 g, 53%), m.p. 60–62 °C (Found: $\mathbf{M}^+$, 245.0490. $C_{13}H_8FNO_3$ requires *M*, 245.0488); ν_{max} (thin film)/cm^{-1} 3200 (br, OH), 2235 (CN) and 1640 (CO); δ_H (400 MHz; $CDCl_3$) 4.16 (1H, d, *J*=6.0 Hz, 3'-OH), 5.34 (1H, d, *J*=4.0 Hz, 3'-H), 6.13 and 6.32 (2H, 2 × s, 1'-H), 7.46 (1H, m, 7-H), 7.52 (1H, m, 8-H), 7.80 (1H, dd, *J*=2.9 and 8.0 Hz, 5-H) and 8.10 (1H, s, 2-H); δ_C (100 MHz; $CDCl_3$) 68.8 (C-3'), 110.5 (J_{CF} =23 Hz, C-5), 116.6 and 124.0 (C-2' and CN), 120.6 (J_{CF} =8.1 Hz, C-8), 120.9 (C-3), 122.8 (J_{CF} = 25.4 Hz, C-7), 124.8 (J_{CF} =7.5 Hz, C-4a), 131.4 (C-1'), 152.6 (C-8a), 154.1 (C-2), 159.7 (J_{CF} =246.8 Hz, C-6) and 176.7 (C=O); *m/z* 245 (M^+, 57%) and 193 (100).

*3-(2-Cyano-1-hydroxy-2-propenyl)-6-methoxy-4*H*-1-benzopyran-4-one* **5e**,[12] as a yellow solid (0.34 g, 54%), m.p. 114–117 °C (Found: $\mathbf{M}^+$, 257.0686. $C_{14}H_{11}NO_4$ requires *M*, 257.0688); ν_{max} (thin film)/cm^{-1} 3400 (br, OH), 2225 (CN) and 1650 (CO); δ_H (400 MHz; $CDCl_3$) 3.89 (3H, s, OCH_3), 4.50 (1H, s, *J*=4.0 Hz, 3'-OH), 5.33 (1H, d, *J*=3.8 Hz, 3'-H), 6.10 and 6.30 (2H, 2 × s, 1'-H), 7.27 (1H, dd, *J*=2.9 and 9.0 Hz, 7-H), 7.41 (1H, d, *J*=9.0 Hz, 8-H), 7.49 (1H, d, *J*=3.0 Hz, 5-H) and 8.08 (1H, s, 2-H); δ_C (100 MHz; $CDCl_3$) 55.9 (OCH_3), 68.8 (C-3'), 104.4 (C-5), 116.8 (C-3), 119.8 (C-8), 120.7 (C-4a), 124.2 and 124.3 (C-2' and CN), 124.6 (C-7), 131.2 (C-1'), 151.2 (C-8a), 153.7 (C-2), 157.3 (C-6) and 177.3 (C=O); *m/z* 257 (M^+, 75%) and 205 (100).

*3-(2-Cyano-1-hydroxy-2-propenyl)-5-methoxy-4*H*-1-benzopyran-4-one* **5f**,[12] as a yellow solid (0.38 g, 60%), m.p. 99–102 °C (Found: $\mathbf{M}H^+$, 258.0766. $C_{14}H_{11}NO_4$ requires *M*+1, 258.0766); ν_{max} (thin film)/cm^{-1} 3400 (br, OH), 2355 (CN) and 1650 (CO); δ_H (400 MHz; $CDCl_3$) 3.99 (3H, s, OCH_3), 4.60 (1H, s, *J*=7.2 Hz, 3'-OH), 5.18 (1H, d, *J*=5.6 Hz, 3'-H), 6.10 and 6.31 (2H, 2 × s, 1'-H), 6.84 (1H, d, *J*=8.3 Hz, 6-H), 7.15 (1H, d, *J*=8.4 Hz, 8-H), 7.60 (1H, t, *J*=8.4 Hz, 7-H) and 7.92 (1H, s, 2-H); δ_C (100 MHz; $CDCl_3$) 55.6 (OCH_3), 69.6 (C-3'), 106.8 (C-6), 110.3 (C-8), 114.4 (C-4a), 117.0 (CN), 121.9 (C-3), 124.1 (C-2'), 131.2 (C-1'), 134.7 (C-7), 152.1 (C-2), 158.3 (C-8a), 160.0 (C-5) and 177.7 (C=O); *m/z* 257 (M^+, 19%) and 239 (100).

*1,3-Bis(4*H*-1-benzopran-4-on-3-yl)-2-cyano-1-propene* **6a** (5%), m.p. 179–182°C (Found: $\mathbf{M}^+$ 355.0849. $C_{22}H_{13}NO_4$ requires *M*, 355.0845); ν_{max} (thin film)/cm^{-1} 2225 (C≡N) and 1630 (C=O); δ_H (400 MHz; $CDCl_3$) 3.59 (2H, s, CH_2), 7.39–7.49 (5H, m, C=CH and Ar–H), 7.68 (2H, m, Ar–H), 7.85 (2H, m, Ar–H), 7.97 and 8.66 (2H, 2 × s, Ar–H) and 8.21 (2H, m, Ar–H); δ_C (100 MHz; $CDCl_3$) 31.6 (CH_2), 110.0 (C≡N), 118.0, 118.2, 118.3, 119.3, 119.8, 123.7, 123.8, 125.4, 125.8, 125.9, 126.2, 133.9, 134.3, 135.9, 153.7, 155.0, 156.1 and 156.6 (C=CH and Ar–C), 175.4 and 176.8 (C=O); *m/z* 355 (M^+, 61%) and 121 (100).

*1,3-Bis(6-chloro-4*H*-1-benzopran-4-on-3-yl)-2-cyano-1-propene* **6c** (9%), m.p. 218–220°C (Found: MH^+ 424.0143. $C_{22}H_{11}{}^{35}Cl_2NO_4$ requires *M*+1, 424.0144); ν_{max} (thin film)/cm^{-1} 2361 (C≡N) and 1700 and 1654 (C=O); δ_H (400 MHz; $CDCl_3$) 3.59 (2H, s, CH_2), 7.40 (1H, s, Ar-H), 7.4–7.7 (4H, 2 × m, C=CH and Ar–H), 7.98 (1H, s, Ar–H), 8.16–8.21 (2H, m, Ar–H) and 8.65 (1H, s, Ar–H); δ_C (100 MHz; $CDCl_3$) 31.6 (CH_2), 110.0 (C≡N), 117.7, 119.3, 119.8, 120.0, 120.1, 124.6, 124.7, 125.4, 125.6, 131.5, 132.0, 134.2, 134.6, 135.6, 153.8, 155.4, 154.9 and 155.0 (C=CH and Ar-C), 174.3 and 175.7 (C=O); *m/z* 424 (MH^+, 17%) and 155 (100).

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