# Reactions of Formylchromone Derivatives. Part 5.[1] Transformations of 3-Formylchromones into Pyrroles and Pyridines

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4-Oxo-4*H*-1-benzopyran-3-carbaldehyde (3-formylchromone) (**1**) was treated with various bifunctional nucleophiles. With ethyl aminoethanoate it gave a mixture of ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine-2-carboxylate (**2**) and ethyl 4-(2-hydroxybenzoyl)pyrrole-2-carboxylate (**3**) whereas with 2-aminoethanonitrile, only the pyridine, 2-cyano-4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine (**7**) was obtained. Ethyl 2-aminopropanoate or ethyl 2-amino-2-phenylethanoate both gave the same pyrrole, 4-(2-hydroxybenzoyl)-2-(4-oxo-4*H*-1-benzopyran-3-yl)pyrrole (**8**), and *N*-methylethanoic acid yielded 3-(2-hydroxybenzoyl)-*N*-methylpyrrole (**9**). Corresponding products were usually obtained when various substituted 3-formylchromones were used in the reactions. Mechanistic pathways are proposed to account for all the products and the pyridine structure was confirmed by degradation.

Chromones possessing a formyl group in the 2- or 3-positions are useful intermediates in the synthesis of a wide variety of heterocycles and the applications of 3-formylchromones in this respect have recently been reviewed.[2] We now substantiate an earlier communication[3] on the transformations of 3-formylchromones into pyridines and pyrroles by interaction of the former with ethyl aminoethanoate and related compounds.

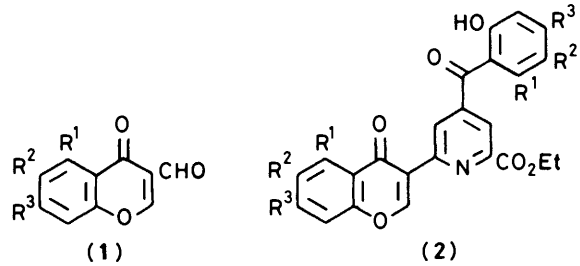
## Results and Discussion

Interaction of 3-formylchromone (**1a**) with ethyl aminoethanoate (**4a**) gave a mixture (50:50) of ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine-2-carboxylate (**2a**) and ethyl 4-(2-hydroxybenzoyl)-pyrrole-2-carboxylate (**3a**) which was separated chromatographically. The reaction, which was carried out in the presence of a trace of toluene-*p*-sulphonic acid in refluxing toluene under a Dean and Stark water-trap was repeated using various substituted 3-formylchromones and the results (Tables 1 and 2) show that pyridines and pyrroles are usually both formed and in fair overall yield although the proportions of the two products vary widely (Table 2).

In contrast, reaction of 3-acetylchromone (**5**) with ethyl aminoethanoate (**4a**) gave only ethyl 3-(2-hydroxybenzoyl)-2-methylpyrrole-5-carboxylate (**6a**).

Use of aminoethanonitrile (**4b**) in place of ethyl aminoethanoate in the reaction with 3-formylchromone (**1a**) gave 2-cyano-4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)-pyridine (**7a**). None of the anticipated pyrrole was obtained, and similarly, when the reaction was repeated using 3-formylchromones (**1c, d, f, g, h**), only the pyridines (**7b**—**f**) respectively, were obtained (Table 3).

Several reactions were also carried out using the *C*-methyl and *C*-phenyl derivatives (**4c, d**). Thus, 3-formylchromone (**1a**) and ethyl 2-aminopropanoate (**4c**) gave 4-(2-hydroxybenzoyl)-2-(4-oxo-4*H*-1-benzopyran-3-yl)pyrrole (**8a**), no pyridine being formed. Surprisingly, the same compound was formed when ethyl 2-amino-2-phenylethanoate (**4d**) was used in place of ethyl-2-aminopropanoate. This reaction also appears to be a general one, since the corresponding pyrrole (**8d**) was



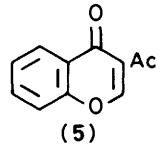
(1) (2) (3)

**a**; $R^1 = R^2 = R^3 = H$
**b**; $R^1 = R^2 = H, R^3 = OMe$
**c**; $R^1 = R^2 = H, R^3 = NO_2$
**d**; $R^1 = R^3 = H, R^2 = Cl$
**e**; $R^1 = R^3 = H, R^2 = Me$
**f**; $R^1 = R^3 = H, R^2 = NO_2$
**g**; $R^1 = R^3 = H, R^2 = OMe$
**h**; $R^1 = R^3 = Me, R^2 = H$
**i**; $R^1 = OMe, R^2 = R^3 = H$

$R^1NHCH(R^2)R^3$

(4)

**a**; $R^1 = R^2 = H, R^3 = CO_2Et$
**b**; $R^1 = R^2 = H, R^3 = CN$
**c**; $R^1 = H, R^2 = Me, R^3 = CO_2Et$
**d**; $R^1 = H, R^2 = Ph, R^3 = CO_2Et$
**e**; $R^1 = Me, R^2 = H, R^3 = CO_2H$



(5)

**Table 1.** Analytical data for ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine-2-carboxylates (**2**)

| Compound (Formula) | Yield (%) | M.p. (°C) | Found (%) (Required) C | H | N |
|---|---|---|---|---|---|
| (**2a**) ($C_{24}H_{13}NO_4$) | 23.5 | 202—204 | 69.6 (69.4) | 4.3 (4.1) | 3.7 (3.4) |
| (**2b**) ($C_{26}H_{21}NO_8$) | 9.7 | 203—204 | 65.7 (65.7) | 4.4 (4.45) | 3.1 (2.95) |
| (**2c**) ($C_{24}H_{15}N_3O_{10}$) | 13.6 | 231—232 | 57.3 (57.0) | 3.2 (3.0) | 7.85 (8.3) |
| (**2d**) ($C_{24}H_{15}Cl_2NO_6$) | 4.3 | 216—218 | 59.7 (59.5) | 3.1 (3.1) | 3.0 (2.9) |
| (**2e**) ($C_{26}H_{21}NO_6$) | 33.5 | 202—204 | 70.35 (70.4) | 4.8 (4.8) | 3.1 (3.2) |
| (**2g**) ($C_{26}H_{21}NO_8$) | 14.2 | 190.5—191 | 65.6 (65.7) | 4.5 (4.45) | 2.9 (2.95) |
| (**2h**) ($C_{28}H_{24}NO_6$) | 24.0 | 216—218 | 71.4 (71.5) | 5.3 (5.1) | 3.1 (3.0) |
| (**2i**) $C_{(26}H_{21}NO_8$) | 34.0 | 201—202 | 65.7 (65.7) | 4.5 (4.45) | 3.1 (2.95) |

**Table 2.** Analytical data for ethyl 4-(2-hydroxybenzoyl)pyrrole-2-carboxylates (**3**).

| Compound (Formula) | Yield (%) | M.p. (°C) | Found (%) (Requires) C | H | N | Ratio (**2**):(**3**) |
|---|---|---|---|---|---|---|
| (**3a**) ($C_{14}H_{13}NO_4$) | 22.4 | 112—113* | | | | 1:1 |
| (**3b**) ($C_{15}H_{15}NO_5$) | 33.1 | 128—130 | 62.2 (62.3) | 5.0 (5.2) | 4.6 (4.8) | 1:3.5 |
| (**3c**) ($C_{14}H_{12}N_2O_6$) | 41.4 | 151—152 | 55.6 (55.3) | 3.8 (4.0) | 8.9 (9.2) | 1:3 |
| (**3d**) ($C_{14}H_{12}ClNO_4$) | 51.5 | 173—174 | 57.1 (57.25) | 4.3 (4.1) | 4.6 (4.8) | 1:12 |
| (**3e**) ($C_{15}H_{15}NO_4$) | 29.4 | 198—200 | 65.8 (65.9) | 5.6 (5.5) | 5.0 (5.1) | 1:0.9 |
| (**3f**) ($C_{14}H_{12}N_2O_6$) | 36.4 | 207—209 | 55.2 (55.3) | 4.1 (4.0) | 9.2 (9.2) | No (**2f**) formed |
| (**3g**) ($C_{15}H_{15}NO_5$) | 22.2 | 131—132 | 62.6 (62.3) | 5.1 (5.2) | 4.8 (4.8) | 1:1.6 |
| (**3h**) ($C_{16}H_{17}NO_4$) | 11.0 | 176—177 | 66.5 (66.9) | 6.1 (6.0) | 4.8 (4.9) | 1:0.45 |
| (**3i**) ($C_{15}H_{15}NO_5$) | 24.0 | 130 | 62.7 (62.3) | 5.3 (5.2) | 4.9 (4.8) | 1:0.71 |

* Lit.,[6] 112—113 °C.

**Table 3.** Analytical data for 2-cyano-4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridines (**7**)

| Compound (Formula) | Yield (%) | M.p. (°C) | Found (%) (Required) C | H | N |
|---|---|---|---|---|---|
| (**7a**) ($C_{22}H_{12}N_2O_4$) | 20.0 | 259—261 | 71.65 (71.7) | 3.3 (3.3) | 7.6 (7.7) |
| (**7b**) ($C_{22}H_{10}N_4O_8$) | 7.8 | 235—236 | 54.1 (53.9) | 2.2 (2.1) | 11.7 (11.4) |
| (**7c**)($C_{22}H_{10}Cl_2N_2O_4$) | 15.0 | 232 | 60.3 (60.4) | 2.5 (2.3) | 6.5 (6.4) |
| (**7d**) ($C_{22}H_{10}N_4O_8$) | 9.0 | 267—268 | 58.0 (57.65) | 2.3 (2.2) | 12.2 (12.2) |
| (**7e**) ($C_{24}H_{16}N_2O_6$) | 14.0 | 237—238 | Satisfactory analysis not obtained (67.3) | (3.8) | (6.5) |
| (**7f**) ($C_{26}H_{20}N_2O_4$) | 21.4 | 215.5—216.5 | 73.7 (73.6) | 4.8 (4.8) | 6.4 (6.6) |

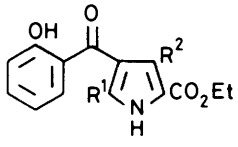
**Table 4.** Analytical data for 3-(2-hydroxybenzoyl)-5-(4-oxo-4*H*-1-benzopyran-3-yl)pyrroles (**8**)

| Compound (Formula) | Yield (%) | M.p. (°C) | Found (%) (Required) C | H | N |
|---|---|---|---|---|---|
| (**8a**) ($C_{20}H_{13}NO_4$) | 44 | 242—243 | 72.5 (72.5) | 4.2 (4.0) | 4.2 (4.2) |
| (**8b**) ($C_{22}H_{17}NO_4$) | 28 | 250—251 | 73.1 (73.5) | 4.8 (4.8) | 4.3 (4.9) |
| (**8c**) ($C_{22}H_{17}NO_6$) | 51 | 192—193 | 67.3 (67.5) | 4.4 (4.4) | 3.7 (3.6) |
| (**8d**) ($C_{24}H_{21}NO_4$) | 27 | 242—244 | 74.5 (74.4) | 5.4 (5.5) | 3.6 (3.6) |

obtained when the 3-formylchromone (**1h**) was treated with either the 2-methyl or 2-phenyl amino esters (**4c**) or (**4d**). The pyrroles (**8b**) and (**8c**) were prepared by interaction of the 3-formylchromones (**1e**) and (**1g**) with ethyl 2-aminopropanoate (Table 4).

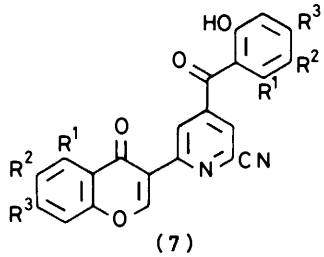
Interaction of *N*-methylaminoethanoic acid (**4e**) with 3-formylchromone gave 3-(2-hydroxybenzoyl)-*N*-methylpyrrole (**9a**) in high yield, and the reaction was repeated with 3-formylchromones (**1b**, **c**, **e**, **f**, **h**) when the corresponding *N*-methylpyrroles (**9b**—**f**) (Table 5) were obtained.

The various products were initially identified largely from their $^1$H n.m.r. spectra. For example, the pyridine (**2a**) displayed two doublets (*J* 2 Hz) centred at δ 8.24 and 8.90 which were



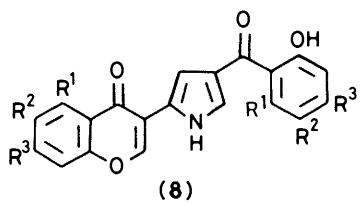
(**6**)

a; $R^1$ = Me, $R^2$ = H
b; $R^1$ = H, $R^2$ = Me



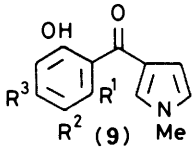
(**7**)

a; $R^1$ = $R^2$ = $R^3$ = H
b; $R^1$ = $R^2$ = H, $R^3$ = $NO_2$
c; $R^1$ = $R^3$ = H, $R^2$ = Cl
d; $R^1$ = $R^3$ = H, $R^2$ = $NO_2$
e; $R^1$ = $R^3$ = H, $R^2$ = OMe
f; $R^1$ = $R^3$ = Me, $R^2$ = H



(**8**)

a; $R^1$ = $R^2$ = $R^3$ = H
b; $R^1$ = $R^3$ = H, $R^2$ = Me
c; $R^1$ = $R^3$ = H, $R^2$ = OMe
d; $R^1$ = $R^3$ = Me, $R^2$ = H



(**9**)

a; $R^1$ = $R^2$ = $R^3$ = H
b; $R^1$ = $R^2$ = H, $R^3$ = OMe
c; $R^1$ = $R^2$ = H, $R^3$ = $NO_2$
d; $R^1$ = $R^3$ = H, $R^2$ = Me
e; $R^1$ = $R^3$ = H, $R^2$ = $NO_2$
f; $R^1$ = $R^3$ = Me, $R^2$ = H

**Table 5.** Analytical data for 3-(2-hydroxybenzoyl)-*N*-methylpyrroles (**9**)

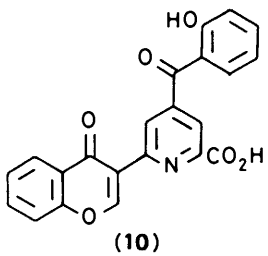
| Compound (Formula) | Yield (%) | M.p. (°C) | Found (%) (Required) C | H | N |
|---|---|---|---|---|---|
| (**9a**) ($C_{12}H_{11}NO_2$) | 72.0 | 83—84 | 71.5 (71.6) | 5.4 (5.5) | 6.95 (7.0) |
| (**9b**) ($C_{13}H_{13}NO_3$) | 51.0 | 122 | 58.2 (58.5) | 4.0 (4.1) | 11.6 (11.4) |
| (**9c**) ($C_{12}H_{10}N_2O_4$) | 61.3 | 125—126 | 58.5 (58.2) | 4.10 (4.00) | 11.4 (11.6) |
| (**9d**) ($C_{13}H_{13}NO_2$) | 73.5 | 95—96 | 72.6 (72.5) | 6.15 (6.1) | 6.65 (6.5) |
| (**9e**) ($C_{12}H_{10}N_2O_4$) | 53.4 | 116—117 | 58.4 (58.5) | 4.3 (4.1) | 11.4 (11.4) |
| (**9f**) ($C_{14}H_{15}NO_2$) | 77.6 | 151 | 73.2 (73.3) | 6.55 (6.6) | 6.2 (6.1) |

assigned respectively to the *meta*-coupled protons 5-H and 3-H of the pyridine ring. The spectrum also showed the presence of the chromone ring by the typical[4] signals of the 5-H proton as a doublet of doublets centred at δ 8.32 and the 2-H proton as a singlet at δ 9.10. Similarly, the lowfield (exchangeable) proton at δ 11.78 indicated the presence of a hydrogen-bonded hydroxy group suggesting that one chromone ring had been opened to an *o*-hydroxy ketone, and the proposed structure was supported by three i.r. carbonyl absorptions at $\nu_{max.}$ 1 710 (ester), 1 650 (benzoyl), and 1 635 (chromone). The spectral properties of the corresponding pyridines from other 3-formylchromones are shown in Table 6.

The presence of the pyridine ring was confirmed (see below) by degradation of (**2a**) to the known[5] 2-methylpyridine-4-carboxylic acid.

The corresponding pyrrole (**3a**) from the reaction of 3-formylchromone with ethyl aminoethanoate was identified by comparison with an authentic sample[6] and the $^1$H n.m.r. values for this and other examples are shown in Table 7.

The $^1$H n.m.r. spectrum of the single product (**7a**) from reaction of 3-formylchromone with aminoethanonitrile was similar to that of pyridine (**2a**). Although its i.r. spectrum showed no cyano absorption, its formulation as 2-cyano-4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine (**7a**)




(**10**)

followed from the fact that acid hydrolysis gave 4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine-2-carboxylic acid (**10**) identical with the product obtained from similar hydrolysis of the ethyl pyridine-2-carboxylate (**2a**). The $^1$H n.m.r. values for the cyanopyridines (**7**) are given in Table 8.

The structure of the product (**8a**) from reaction of 3-formylchromone (**1a**) with either ethyl 2-aminopropanoate (**4c**) or ethyl 2-amino-2-phenylethanoate (**4d**) was established spectroscopically. Two multiplets, replaced on deuteriation by doublets centred at δ 7.58 and 7.20 (*J* 2 Hz) were identified respectively, as the pyrrole 2-H and 5-H protons, the broad exchangeable signal at δ 12.04 being due to the NH. The doublet of doublets centred at δ 8.24 and the singlet at δ 8.93 again indicated the presence of the chromone ring, and the second exchangeable proton at δ 11.47 was assigned to the hydrogen-bonded hydroxy proton of a ring-opened chromone moiety. Spectroscopic details for the corresponding pyrroles (**8b—d**) are shown in Table 9.

The *N*-methylpyrrole structure (**9a**) also followed largely from its $^1$H n.m.r. spectrum. The three-proton multiplets between δ 6.55 and δ 7.53 were assigned to the pyrrole protons and the singlet at δ 3.69 to the *N*-methyl group. The lowfield singlet at δ 11.82 (removed on deuteriation) is again evidence for the exchangeable hydroxy proton of a ring-opened chromone moiety, the presence of which is confirmed by the strong i.r. benzoyl carbonyl absorption at 1 615 cm$^{-1}$. Spectroscopic details for the corresponding pyrroles (**9a—f**) appear in Table 10.

Finally, the structure of the product of interaction of 3-acetylchromone (**5**) with ethyl aminoethanoate (**4a**) was established as the 2-methylpyrrole (**6a**) by comparison of its spin-decoupled $^{13}$C n.m.r. spectrum with those of several related pyrroles (Table 11).[7] From the values for the chemical shifts of the pyrrole ring carbons, it is clear that the presence of a methyl group on a particular carbon generally causes a downfield shift of that carbon signal by *ca.* δ 12 [*cf.* (**11**), (**12**), and (**13**)]. It then follows from a comparison of the values for carbon 'a' of the methyl pyrrole in question (**6a**) with those of the closely related 3-acetylpyrrole (**14**), that the former possesses a methyl group in the 2-position and is unsubstituted in the 4-position.

The pathways to the various products are presumed to involve initial attack on the chromone by one of the two nucleophilic centres of the aminoethanoate derivatives, either at the formyl group or the conjugate chromone 2-position. Such reactions, involving nitrogen and active methylene nucleophiles are well-known,[2] but whereas the *order* of attack does not necessarily affect the identity of the product, the *point* of attack by one of the nucleophiles may well do so. Thus, although the reaction of ethyl aminoethanoate with 3-formylchromone was assumed to proceed (Scheme 1, route 'd') entirely *via* the initially formed azomethine (**15a**), the same products could have arisen *via* initial conjugate attack by the methylene at the chromone 2-position (route 'a') to give the imine (**19**). While not ruling out the former pathway ('d'), particularly for pyridine formation (**15**)→(**16**)→(**17**)→(**2a**), the latter is probably the more likely to explain pyrrole formation (**18**)→(**3a**), since it involves a favoured 5-*exo trig* process rather than the disfavoured 5-*endo trig* process of the former (**15**)→(**3a**).[8] It would also not preclude pyridine formation through interaction of the allylamine (**18**) with a second molecule of 3-formylchromone, (**18**)→(**19**)→(**2a**).

The regiochemistry of the initial attack of the amino esters onto the chromones to produce pyrroles is suggested by the position of the methyl substituent when 3-acetylchromone is used as substrate. The formulation of the product of this reaction as (**6a**) (see earlier) suggests that pathways 'b' and 'c' are not operating in this case, since these would lead to the isomeric 3-methylpyrrole derivative (**6b**). In the 3-acetylchromone reaction, no pyridine was formed, but the reduced reactivity of the acetyl, compared with the formyl group would suppress azomethine formation (pathway 'd') favouring pathway 'a' and therefore pyrrole formation.

Thus, assuming that the presence of the acetyl group plays no other role in influencing the initial reaction, it seems likely that the formylchromone reactions also follow pathways 'a' or 'd'.

Pyridine formation *via* initial pathway 'd' would involve interaction of two molecules of the azomethine (**15**) with ring-opening of one of the chromone rings. Cyclisation of the resulting tautomer (**16**) *via* an electrocyclic process[9—12] would then give the pyridine (**2a**) by elimination of amine from the dihydro derivative (**17**).

**Table 6.** Spectral data for ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine-2-carboxylates (**2**)

| | $\nu_{max.}$ (cm$^{-1}$) | | | δ (p.p.m.) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Pyridine H (d, *J* 2 Hz) | | Chromone H | | Substituents (R) on Chromone | | | Substituents (R) on Aryl | | | | | | | |
| Compound | $CO_2Et$ | CO | Pyrone CO | 3-H | 5-H | 2-H (s) | 5-H | $R^1$ | $R^2$ | $R^3$ | $R^1$ | $R^2$ | $R^3$ | ArH (m) | OH* | $CH_2Me$ $CH_2$ (q) | (*J* 7 Hz) Me (t) | $M^+$ |
| **(2a)** | 1 710 | 1 650 | 1 635 | 8.9 | 8.24 | 9.1 | 8.32 (dd) | | | | | | | 7.84—6.86 | 11.78 | 4.52 | 1.46 | 415 |
| **(2b)** | 1 740 | 1 645 | 1 630 | 7.67 | 7.19 | 7.9 | 7.79 (d) | | | 3.94 (OMe) | | | 3.86 (OMe) | 6.71—6.67 | 12.42 | 4.29 | 1.35 | 475 |
| **(2c)** | 1 700 | 1 655 | 1 635 | 8.75 | 8.60 | 9.16 | (in Ar-*H*) | | | | | | | 8.52—8.06 | | 4.41 | 1.35 | 505 |
| **(2d)** | 1 750 | 1 660 | 1 645 | 8.76 | 8.16 | 9.07 | 8.08 (d) | | | | | | | 7.85—7.0 | 10.65 | 4.40 | 1.39 | 484 |
| **(2e)** | 1 740 | 1 650 | 1 630 | 8.76 | 8.16 | 9.06 | 8.0 (d) | | 3.28 (Me) | | | 2.29 (Me) | | 7.67—6.9 | 10.4 | 4.44 | 1.38 | 443 |
| **(2g)** | 1 745 | 1 640 | 1 635 | 8.76 | 8.14 | 9.03 | 7.78 (d) | | 3.86 (OMe) | | | 3.73 (OMe) | | 7.73—6.81 | 9.95 | 4.40 | 1.33 | 475 |
| **(2h)** | 1 705 | 1 645 | 1 635 | 8.77 | 8.10 | 8.8 | | 2.78(Me) | | 2.41 (Me) | 2.30 (Me) | | 2.16 (Me) | 7.23—6.66 | 9.81 | 4.44 | 1.39 | 471 |
| **(2i)** | 1 750 | 1 660 | 1 645 | 8.63 | 8.08 | 8.77 | | 3.88 (OMe) | | | 3.65 (OMe) | | | 8.79—6.57 | 9.95 | 4.38 | 1.33 | 475 |

**Table 7.** Spectral data for ethyl 4-(2-hydroxybenzoyl)pyrrole-2-carboxylates (**3**)

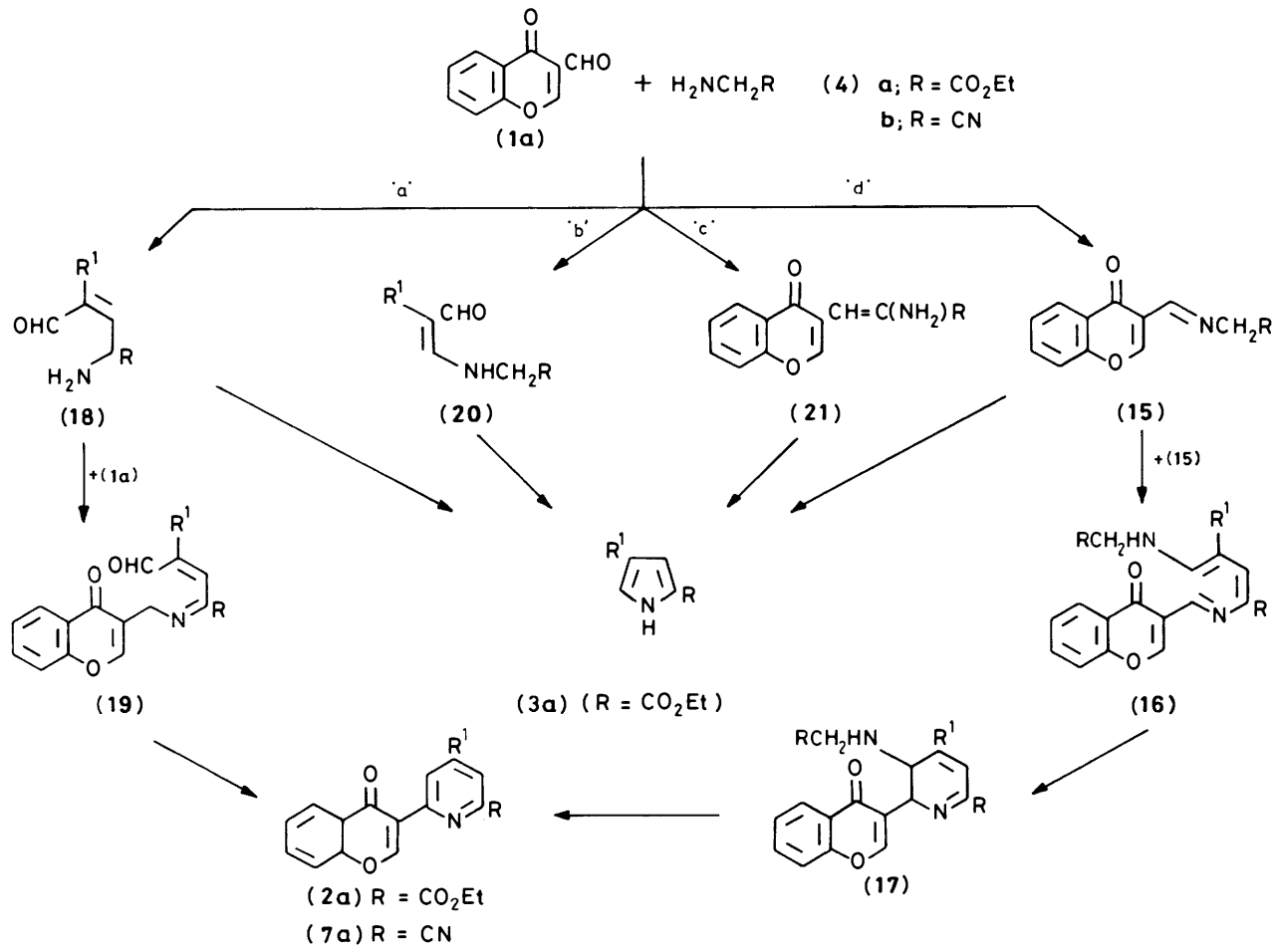
| | $\nu_{max.}$ (cm$^{-1}$) | | | δ (p.p.m.) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Pyrrole H | | | Substituents | | | | | | | | |
| Com-pound | NH | $CO_2Et$ | CO | 3-H (m) | 5-H (m) | NH (s)* | $R^1$ | $R^2$ | $R^3$ | ArH | OH* | $CH_2Me$ $CH_2$ (q) | (*J* 7 Hz) Me (t) | $M^+$ |
| **(3b)** | 3 200 | 1 710 | 1 625 | 7.3—7.03 | 7.71—7.56 | 12.48 | | | 3.83 (OMe) | 6.70—6.44 | | 4.3 | 1.29 | 289 |
| **(3c)** | 3 275 | 1 700 | 1 630 | 7.06—6.92 | 7.62—7.54 | 12.65 | | | | 7.84—7.38 | 10.84 | 4.25 | 1.27 | 304 |
| **(3d)** | 3 725 | 1 700 | 1 635 | 7.23—7.07 | 7.64—7.48 | 12.63 | | | | 7.39—6.98 | 10.81 | 4.30 | 1.30 | 293.5 |
| **(3e)** | 3 300 | 1 695 | 1 635 | 7.29—7.12 | 7.68—7.53 | 12.58 | | 2.28 (Me) | | 7.36—6.82 | 11.30 | 4.28 | 1.32 | 273 |
| **(3f)** | 3 275 | 1 700 | 1 640 | 7.25—7.09 | 7.69—7.50 | 12.68 | | | | 7.26—7.15 | 11.70 | 4.30 | 1.32 | 304 |
| **(3g)** | 3 275 | 1 690 | 1 640 | 7.17—7.08 | 7.67—7.44 | 12.59 | | 3.73 (OMe) | | 7.08—6.79 | 10.18 | 4.28 | 1.3 | 289 |
| **(3h)** | 3 250 | 1 720 | 1 620 | 7.24—7.06 | 7.37—7.21 | 11.38 | 2.2 (Me) | | 2.08 (Me) | 6.56—6.51 | 8.50 | 4.27 | 1.29 | 287 |
| **(3i)** | 3 325 | 1 700 | 1 635 | 7.08—6.92 | 7.37—7.21 | 12.31 | 3.67 (OMe) | | | 7.18—6.46 | 9.4 | 4.26 | 1.30 | 289 |

**Table 8.** Spectral data for 2-cyano-4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-benzopyran-3-yl)pyridines (**7**)

| | $\nu_{max.}$(cm$^{-1}$) | | δ (p.p.m.) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Pyridine H (d, *J* 1.4 Hz) | | Chromone H | | Substituents (R) on Chromone | | | Benzoyl | | | | | |
| Compound | CO | CO (Pyrone) | 3-H | 5-H | 2-H (s) | 5-H | R$^1$ | R$^2$ | R$^3$ | R$^1$ | R$^2$ | R$^3$ | ArH | OH* | *M*$^+$ |
| (**7a**) | 1 660 | 1 640 | 9.12 | 7.92 | 9.18 | 8.39 (dd) | | | | | | | 7.85—6.95 | 11.77 | 368 |
| (**7b**) | 1 660 | 1 640 | 8.62 | 7.68 | 9.24 | 8.78 (d) | | | | | | | 8.75—7.73 | 11.37 | 458 |
| (**7c**) | 1 660 | 1 640 | 9.03 | 7.85 | 9.12 | 8.31 (d) | | | | | | | 7.89—7.07 | 11.56 | 437 |
| (**7d**) | 1 660 | 1 640 | 8.75 | 8.26 | 9.18 | 8.83 (d) | | | | | | | 8.65—7.20 | | 458 |
| (**7e**) | 1 640 | 1 615 | 8.78 | 7.66 | 9.11 | 8.17 (d) | | 3.87 (OMe) | | | 3.71( OMe) | | 7.83—6.78 | 9.98 | 428 |
| (**7f**) | 1 630 | 1 620 | 8.71 | 8.03 | 8.89 | | 2.73 (Me) | | 2.40 (Me) | 2.27 (Me) | | 2.16 (Me) | 7.41—6.52 | 9.98 | 424 |

**Table 9.** Spectral data for 3-(2-Hydroxybenzoyl)-5-(4-oxo-4*H*-1-benzopyran-3-yl)pyrroles (**8**)

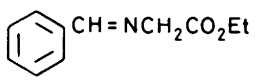
| | $\nu_{max.}$(cm$^{-1}$) | | | δ (p.p.m.) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Pyrrole H | | | Chromone H | | Chromone | | | Benzoyl | | | | | |
| Compound | NH | CO | Pyrone CO | 2-H (m) | 4-H (m) | NH* | 2-H (s) | 5-H | R$^1$ | R$^2$ | R$^3$ | R$^1$ | R$^2$ | R$^3$ | OH* | ArH | *M*$^+$ |
| (**8a**) | 3 425 | | 1 630 | 7.65—7.49 | 7.2—7.10 | 12.04 | 8.93 | 8.24 (dd) | | | | | | | 11.47 | 7.87—6.91 | 331 |
| (**8b**) | 3 325 | | 1 620 | 7.65—7.49 | 7.28—7.12 | 11.97 | 8.85 | 7.98 (d) | | 3.43 (Me) | | | 2.29 (Me) | | 11.32 | 7.75—6.83 | 359 |
| (**8c**) | 3 400—3 225 | | 1 620 | 7.70—7.60 | 7.43—7.33 | 11.57 | 8.89 | 7.75 (d) | | 3.89 (OMe) | | | 3.75 (OMe) | | 10.59 | 7.11—6.75 | 391 |
| (**8d**) | 3 475—2 700 | | 1 620 | 7.20—7.00 | 7.04—6.90 | 11.70 | 8.72 | | 2.78 (Me) | | 2.39 (Me) | 2.24 (Me) | | 2.17 (Me) | 9.22 | 7.30—6.56 | 387 |




**Scheme 1.** $R^1$ = *o*-$HOC_6H_4CO$

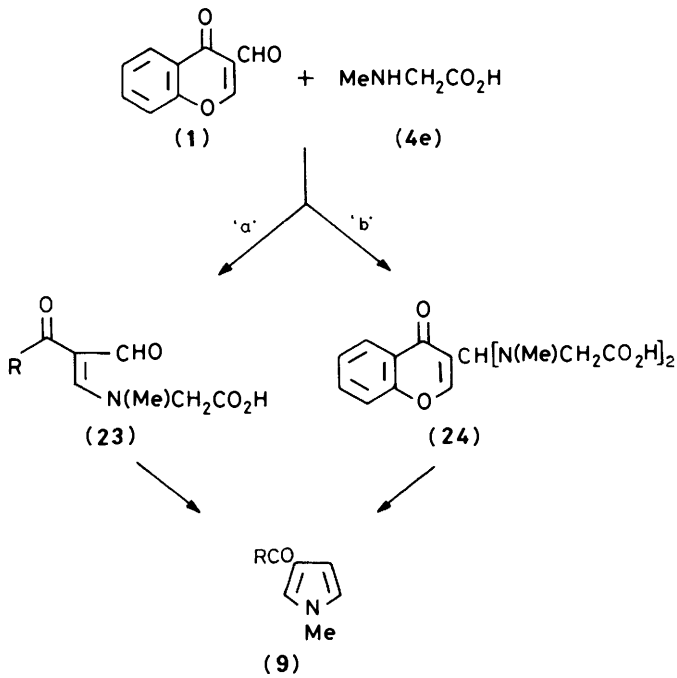
With the exception of (**1f**), all the 3-formylchromones gave both pyrroles and pyridines in fair overall yields although in widely differing ratios. The yield and ratio of the products from the 3-formylchromone (**1a**) reaction were unaltered when the volume of solvent was increased 25-fold and the absence of any dilution effect points clearly to the involveme it of separate pathways to the two products without a common intermediate.

We propose therefore, that initial pathway 'a' accounts for pyrrole formation, whereas pathway 'd' leads to the pyridine. [Isolation of the azomethine in order to confirm this point has not so far, proved possible, and all attempts to synthesise it, even using the method of Stork,[13] which was used to prepare the benzaldehyde analogue (**22**) were unsuccessful.]




(22)

The initial point of attack by the aminoethanoate on the chromone is likely also to be affected by the substituents in the benzene ring of the chromone and the various reactions using the range of 3-formylchromones were carried out primarily in an attempt to establish a correlation between the position and electronic nature of the substituents on the one hand and the

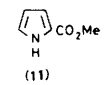
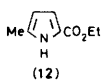
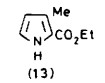
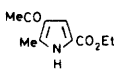
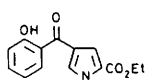
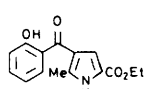



**Scheme 2.** R = *o*-$HOC_6H_4$

**Table 10.** Spectral data for 3-(2-hydroxybenzoyl)-*N*-methylpyrroles (**9**)

| | $\nu_{max.}$ ($cm^{-1}$) | | δ (p.p.m.) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Compound | OH | CO | Pyrrole H (m) (in range) | N-Me (s) | $R^1$ | $R^2$ | $R^3$ | OH* (s) | $M^+$ |
| (**9a**) | 3 200 | 1 615 | 7.53—6.55 | 3.69 | | | | 11.82 | 201 |
| (**9b**) | 3 080 | 1 620 | 7.30—7.03 | 3.92 | | | 3.25 (OMe) | 10.1 | 231 |
| (**9c**) | 3 100 | 1 620 | 7.30—6.37 | 3.63 | | | | 10.78 | 246 |
| (**9d**) | 3 300 | 1 620 | 7.29—6.62 | 3.69 | | 2.29 (Me) | | 12.02 | 215 |
| (**9e**) | 3 125 | 1 620 | 7.39—6.68 | 3.79 | | | | 13.07 | 246 |
| (**9f**) | 3 300 | 1 620 | 6.96—6.31 | 3.60 | 2.20 (Me) | | 2.0 (Me) | 8.99 | 229 |

**Table 11.** $^{13}C$ Chemical shifts for substituted pyrroles (δ)

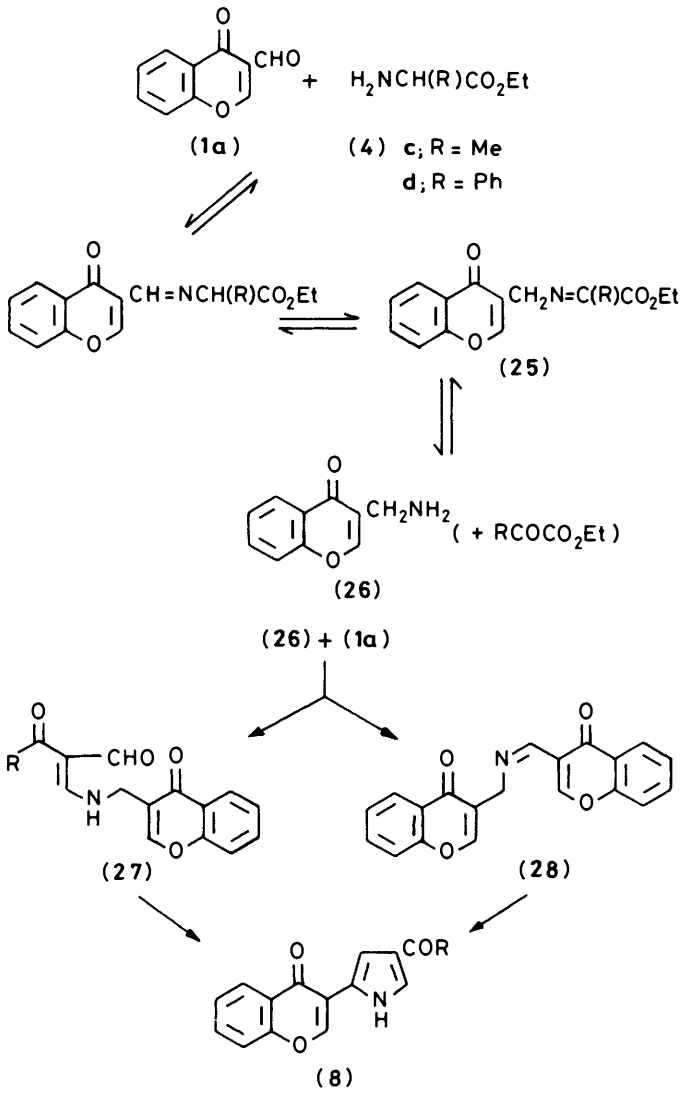
| | a | b | c | d |
|---|---|---|---|---|
|  | 117.3 | 107.6 | 107.6 | 117.3 |
|  (11) | 122.9 | 109.8 | 115.1 | 122.0 |
|  (12) | 135.4 | 108.4 | 115.8 | 120.8 |
|  (13) | 121.2 | 112.1 | 127.4 | 119.0 |
|  (14) | 139.6 | 122.0 | 117.2 | 119.9 |
|  (3a) | 129.42 | 124.07 | 116.02 | 122.72 |
|  (6a) | 140.67 | 120.89 | 116.98 | 120.52 |

proportions of the products on the other. No clear trend is apparent however, but the presence of both electron donating or withdrawing groups in the 6- or 7-positions apparently favours pyrrole formation whereas the presence of a substituent in the 5-position of the 3-formylchromone appears to favour pyridine formation.

In contrast to the ethyl aminoethanoate reactions which gave pyridines *and* pyrroles, use of 2-aminoethanonitrile (**4b**) led only to pyridines. In line with the above, this suggests that pathway 'd' predominates, the azomethine (**15b**) being formed preferentially owing to the lower reactivity of the nitrile methylene. Since intramolecular cyclisation of this azomethine would again be disfavoured, the intermolecular pathways (**15b**)→(**16b**) *etc* then leads to the pyridine (**7a**). Pyridine formation *via* pathway 'a' cannot be ruled out, but seems less likely since the participation of allylamine (**18b**) would be expected to lead to some pyrrole.

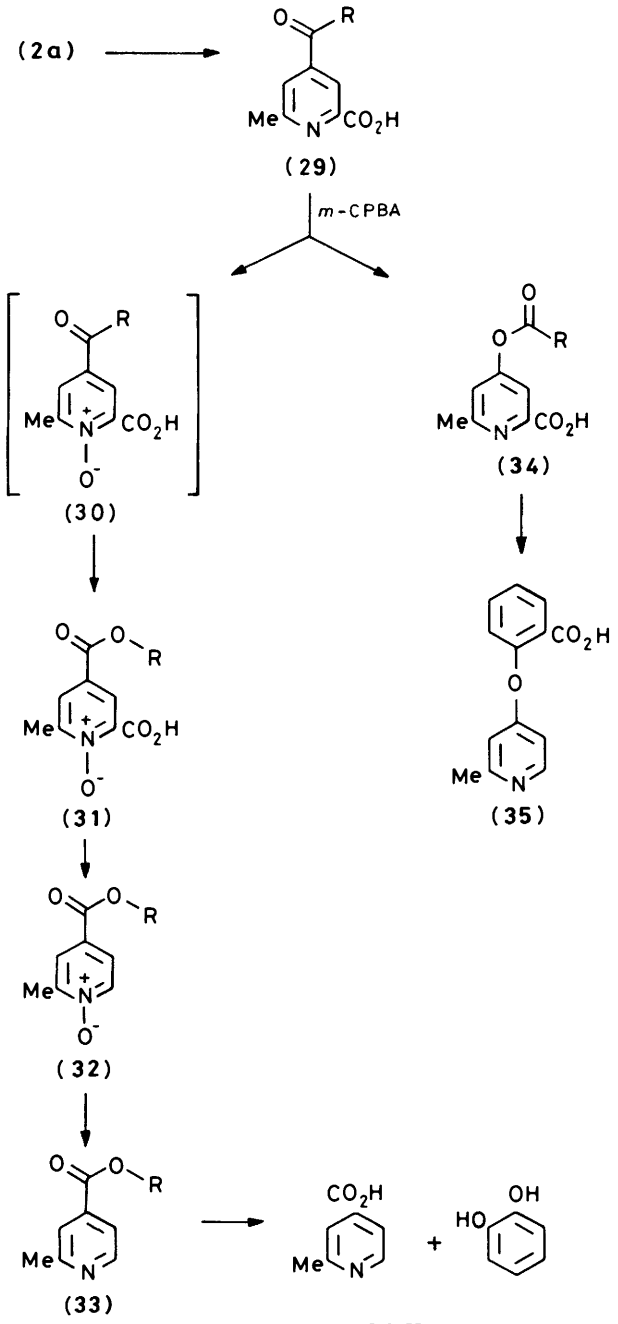
Interaction of *N*-methylaminoethanoic acid (**4e**) with the 3-formylchromones (Scheme 2) gave only the pyrroles (**9**). Although the four initial pathways considered in Scheme 1 would all lead to this product, initial attack by the methylene on the chromone now seems less likely and the pyrrole here is considered to arise *via* attack of the secondary amine (with ring-opening) at the chromone 2-position (Scheme 2, route 'a'). Subsequent cyclisation of the enamine (**23**) then leads to the pyrrole-2-carboxylic acid which is readily decarboxylated to the observed product. The alternative (route 'b') would involve an intermediate of type (**24**), cyclisation of which is again disfavoured.

Pyrroles only, were also obtained from the reactions of 3-formylchromones with ethyl 2-aminopropanoate (**4c**) or ethyl




**Scheme 3.** R = *o*-$HOC_6H_4$

2-amino-2-phenylethanoate (**4d**). With 3-formylchromone (**1a**) both reagents gave the same product (**8a**) thus pointing to a common intermediate, considered in this example to be 3-aminomethylchromone (**26**). It is presumed to arise (Scheme 3) *via* initial condensation of the amine and aldehyde followed by hydrolysis of the resulting tautomeric azomethine (**25**). Interaction of the 3-aminomethylchromone with a second molecule of 3-formylchromone with ring-opening of the latter gives the enamine (**27**), cyclisation of which yields the pyrrole. The alternative cyclisation of the azomethine (**28**) would again represent a disfavoured process. Support for the proposed intermediacy of 3-aminomethylchromone was obtained by treating it with 3-formylchromone when the pyrrole (**8a**) was again obtained and in comparable yield. The original reaction is thus independent of the α-substituent in the aminoethanoate.




**Scheme 4.** R = *o*-$HOC_6H_4$

The pyridine structure (**2a**), initially identified spectroscopically, was confirmed by degradation to the known[5] 2-methylpyridine-4-carboxylic acid (Scheme 4). Alkaline hydrolysis of (**2a**) gave 4-(2-hydroxybenzoyl)-6-methylpyridine-2-carboxylic acid (**29**) which was subjected to Baeyer-Villiger oxidation using *m*-chloroperbenzoic acid. This gave two products, 4-(2-hydroxyphenoxycarbonyl)-6-methylpyridine-2-carboxylic acid *N*-oxide (**31**) and 4-(2-hydroxybenzoyloxy)-6-methylpyridine-2-carboxylic acid (**34**). Treatment of the *N*-oxide (**31**) with triethylphosphite in refluxing bromobenzene gave firstly decarboxylation to 4-(2-hydroxyphenoxycarbonyl)-2-methylpyridine *N*-oxide (**32**) and then on further heating, deoxygenation to 4-(2-hydroxyphenoxycarbonyl)-2-methylpyridine (**33**). Finally, acid hydrolysis of the latter gave pyrocatechol and 2-methylpyridine-4-carboxylic acid. Attempted decarboxylation of the second ester (**34**) brought about a Smiles rearrangement to the ether (**35**).

The Baeyer-Villiger oxidation products (**31**) and (**34**) are considered to arise *via* two parallel reactions and, caused by initial partial conversion of the pyridine (**29**) into its *N*-oxide (**30**). The formation of the ester (**34**) is interesting since it must involve migration of the apparently less nucleophilic heterocyclic ring. This is probably explained by the reduced migratory aptitude of the phenyl ring due to the presence of its *o*-hydroxy group.[14] However, the migratory aptitude of the heterocyclic ring in (**30**) is presumably reduced to a level below that of the *o*-hydroxyphenyl ring by *N*-oxidation, and subsequent rearrangement then leads to the *N*-oxide ester (**31**).

## Experimental

M.p.s are uncorrected. I.r. spectra were determined for Nujol mulls on a Perkin-Elmer 297 spectrometer. Mass spectra were recorded on a Kratos MS 30 spectrometer at 70 eV. N.m.r. spectra were determined on a Varian Associates CFT 20 spectrometer operating at 80 MHz ($^1H$) and 20 MHz ($^{13}C$). Unless otherwise indicated, the spectra were recorded for $(CD_3)_2SO$ solutions using tetramethylsilane as internal standard. Signals for exchangeable protons are indicated by an asterisk.

Gradient elution column chromatography was carried out using BDH silica gel (60—120 mesh). Medium-pressure column chromatography was carried out using Merck Kieselgel (60 H). Exsiccated magnesium sulphate was used as drying agent for solutions in organic solvents.

*3-Formyl-7-nitrochromone* (**1c**).—To a solution of 4-nitro-2-hydroxyacetophenone (7.5 g) in dimethylformamide (20 ml) was added phosphorus oxychloride (12.61 g, 7.7 ml) dropwise with stirring over 20 min, the temperature being maintained at 40—50 °C. The mixture was stirred at this temperature for a further 40 min and then added to ice–water (31 ml). The resulting suspension was stirred at 0—20 °C for 2 h and then filtered and the residue washed with water (2 ml) and cold ethanol (2 ml). The crude product gave 3-formyl-7-nitrochromone (6.31 g, 75%) as light brown crystals, m.p. 209—210 °C (from acetone) (Found: C, 54.6; H, 2.35; N, 6.35. $C_{10}H_5NO_5$ requires C, 54.8; H, 2.3; N, 6.4%); $\nu_{max.}$ 1 705 (CHO), 1 645 $cm^{-1}$ (CO); ($M^+$ + 1) 220; δ 8.50—7.92 (m, 3 H, ArH), 8.58 (d, 1 H, 5-H), 9.03 (s, 1 H, 2-H), and 10.12 (s, 1 H, CHO).

*Reaction of Ethyl Aminoethanoate with 3-Formylchromone* (**1a**).—A solution of equimolar quantities (19 mmol) of ethyl aminoethanoate and 3-formylchromone containing toluene-*p*-sulphonic acid (2 crystals) in dry toluene (75 ml) was heated under reflux for 2 h using a Dean and Stark water trap. The solvent was evaporated and the residue was column chromatographed using medium pressure. Elution with chloroform–ethyl

acetate (9:1) gave first *ethyl* 4-(2-*hydroxybenzoyl*)-6-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*pyridine*-2-*carboxylate* (**2a**) as a yellow solid (1.16 g, 23.5%) and then 4-(2-hydroxybenzoyl)pyrrole-2-carboxylate (**3a**) as a pale yellow solid (1.04 g, 22.4%). Full details of these and the corresponding *pyridines* (**2b**—**i**) and *pyrroles* (**3b**—**i**) are given respectively in Tables 1 and 2. Ratios of pyridines to pyrroles appear in Table 2. Spectroscopic details are given in Tables 6 and 7, respectively.

*Ethyl* 4-(2-*Hydroxybenzoyl*)-5-*methylpyrrole*-2-*carboxylate* (**6a**).—A solution of ethyl aminoethanoate (2.75 g) and 3-acetylchromone[15] (5 g), containing toluene-*p*-sulphonic acid (2 crystals) in toluene (50 ml) was heated under reflux for 2 h using a Dean and Stark water trap. The solvent was evaporated and the residue was column chromatographed. Gradient elution with chloroform and ethyl acetate gave ethyl 4-(2-*hydroxybenzoyl*)-5-*methylpyrrole*-2-*carboxylate* (**6a**) (1.12 g, 16%) as yellow plates (from ethanol), m.p. 182—184 °C (Found: C, 66.0; H, 5.5; N, 5.0. $C_{15}H_{15}NO_4$ requires C, 65.9; H, 5.5; N, 5.1%); $\nu_{max.}$ 3 300 (NH) and 1 700 $cm^{-1}$ (ester); $M^+$, 273; δ 1.28 (t, *J* 7 Hz, 3 H, $CO_2CH_2Me$), 2.49 (s, 3 H, Me), 4.6 (q, *J* 7 Hz, 2 H, $CO_2CH_2Me$), 6.86 (d, *J* 1.8 Hz, 1 H, pyrrole 3-H), 7.5—6.93 (m, 4 H, ArH), 10.7 (s, 1 H, OH)*, and 12.4 (br s, 1 H, NH)*.

*Reaction of Aminoethanonitrile* (**4b**) *with* 3-*Formylchromone* (**1a**).—A solution of equimolar quantities (5 mmol) of aminoethanonitrile and 3-formylchromone containing toluene-*p*-sulphonic acid (2 crystals) in toluene (75 ml) was heated under reflux for 24 h, using a Dean and Stark water trap. The solvent was evaporated and the residue was column chromatographed using medium pressure. Elution with chloroform–ethyl acetate (9:1) gave 2-*cyano*-4-(2-*hydroxybenzoyl*)-6-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*pyridine* (**7a**) as a yellow solid (0.184 g, 20%). Full details of this and the corresponding *pyridines* (**7b**—**f**) are given in Table 3. Spectroscopic details are given in Table 8.

*Reaction of Ethyl* 2-*Aminopropanoate* (**4c**) *with* 3-*Formylchromone* (**1a**).—A solution of equimolar quantities (2.9 mmol) of ethyl 2-aminopropanoate and 3-formylchromone, containing toluene-*p*-sulphonic acid (2 crystals) in toluene (75 ml) was heated under reflux for 2 h using a Dean and Stark water trap. The solvent was evaporated and the residue was column chromatographed using medium pressure. Elution with chloroform–ethyl acetate (9:1) gave 4-(2-*hydroxybenzoyl*)-2-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*pyrrole* (**8a**) as a pale yellow solid (0.21 g, 44%). Full details of this and the corresponding pyrroles (**8b**—**d**) are given in Table 4.

*Note:* Pyrroles (**8a**, **d**) were also obtained (39 and 35% respectively) when, in this reaction, ethyl 2-aminopropanoate was replaced by ethyl 2-amino-2-phenylethanoate (**4d**). Spectroscopic details are given in Table 9.

*Reaction of* N-*Methylethanoic Acid* (**4e**) *with* 3-*Formylchromone* (**1a**).—A solution of equimolar quantities (5.7 mmol) of *N*-methylaminoethanoic acid and 3-formylchromone containing toluene-*p*-sulphonic acid (2 crystals) in toluene (100 ml) was heated under reflux using a Dean and Stark water trap for 6 h. The solvent was evaporated and the residue was column chromatographed using medium pressure. Elution with chloroform–ethyl acetate (9:1) gave 3-(2-*hydroxybenzoyl*)-N-*methylpyrrole* (**9a**) as a yellow solid (0.83 g, 72%). Full details of this and the corresponding N-*methylpyrroles* (**9b**—**f**) are given in Table 5. Spectroscopic details are given in Table 10.

4-(2-*Hydroxybenzoyl*)-6-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*pyridine*-2-*carboxylic Acid* (**10**).—(a) A solution of ethyl 4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine-2-carboxylate (1 g, 2.4 mmol) in a mixture of 5M-hydrochloric acid (10 ml) and dioxane (100 ml) was heated under reflux for 15 h and then cooled and poured into water (100 ml). The precipitated product was filtered off and gave 4-(2-*hydroxybenzoyl*)-6-(4-*oxo*-4H-1-*benzopyran*-3-*yl*)*pyridine*-2-*carboxylic acid* (0.55 g, 51%) as plates (from acetone), m.p. 220—221 °C (Found: C, 68.45; H, 3.2; N, 3.8. $C_{22}H_{13}NO_6$ requires C, 68.2; H, 3.4; N, 3.6%); $\nu_{max.}$ 3 350—2 500 ($CO_2H$), 1 730 ($CO_2H$), 1 660 (CO), and 1 640 $cm^{-1}$ (pyrone CO); $M^+$, 387; δ 7.95—7.0 (m, 8 H, ArH), 8.18 (d, *J* 2 Hz, 1 H, pyridine, 5-H), 8.22 (dd, *J* 6 Hz, 2 Hz, 1 H, chromone 5-H), 8.7 (d, *J* 2 Hz, 1 H, pyridine 3-H), and 9.31 (s, 1 H, chromone, 2-H).

(b) A solution of 2-cyano-4-(2-hydroxybenzoyl)-6-(4-oxo-4*H*-1-benzopyran-3-yl)pyridine (0.08 g, 0.22 mmol) in a mixture of concentrated sulphuric acid (2 ml), glacial acetic acid (2 ml), and water (2 ml) was heated under reflux for 2 h and then cooled and poured into water (25 ml). Isolation of the product as above gave the acid (**10**) (0.06 g), identical with the sample prepared in (a).

*Reaction of* 3-*Aminomethylchromone* (**26**) *with* 3-*Formylchromone* (**1a**).—To an equimolar mixture (3.2 mmol) of 3-formylchromone (0.55 g), and 3-aminomethylchromone hydrochloride (hemihydrate)[16] (0.7 g) in toluene (75 ml) was added sodium hydride (50% in oil, 0.152 g). The mixture was heated under reflux for 6 h in a nitrogen atmosphere using a Dean and Stark water trap and then filtered whilst hot. The filtrate was cooled and filtered and the residue was crystallised from ethanol, to yield 4-(2-hydroxybenzoyl)-2-(4-oxo-4*H*-1-benzopyran-3-yl)pyrrole (**8a**) (0.31 g, 30%) as yellow needles, m.p. 240—242 °C, identical with the sample prepared previously.

*Alkaline Hydrolysis of Ethyl* 4-(2-*Hydroxybenzoyl*)-6-(4-*oxo*-4H-*benzopyran*-3-*yl*)*pyridine*-2-*carboxylate* (**2a**).—A mixture of the title compound (15.1 g, 36 mmol) and potassium hydroxide (38.55 g) in water (40 ml) was heated under reflux for 1.5 h and then diluted with water (20 ml). The solution was neutralised with 4M-hydrochloric acid and the mixture was extracted with chloroform (3 × 50 ml). The combined extracts were dried and evaporated and the residue was column chromatographed on silica gel. Gradient elution with chloroform–ethyl acetate gave firstly salicylic acid (7.56 g, 65%) and then 4-(2-*hydroxybenzoyl*)-6-*methylpyridine*-2-*carboxylic acid* (**29**) (6.2 g, 69%) as yellow plates (from ethanol), m.p. 161—163 °C (Found: C, 65.4; H, 4.2; N, 5.4. $C_{14}H_{11}NO_4$ requires C, 65.4; H, 4.3; N, 5.4%); $\nu_{max.}$ 3 175—2 550 ($CO_2H$), 1 730 ($CO_2H$), and 1 650 $cm^{-1}$ (CO); $M^+$, 257; δ 2.75 (s, 3 H, Me), 7.52—6.86 (m, 4 H, ArH), 7.59 (d, *J* 2 Hz, 1 H, pyridine 5-H), and 8.14 (d, *J* 2 Hz, 1 H, pyridine 3-H).

*Baeyer-Villiger Oxidation of* 4-(2-*Hydroxybenzoyl*)-6-*methylpyridine*-2-*carboxylic Acid* (**29**).—A mixture of the title compound (2 g, 7.8 mmol) and *m*-chloroperbenzoic acid (3.27 g, 19 mmol) in chloroform (100 ml) was stirred at room temperature for 3 days. The mixture was filtered and the residue gave 2-*carboxy*-4-(2-*hydroxyphenoxycarbonyl*)-6-*methylpyridine* N-*oxide* (**31**) (0.7 g, 31%) as needles (from ethanol), m.p. 189—190 °C (Found: C, 58.25; H, 3.95; N, 4.7. $C_{14}H_{11}NO_6$ requires C, 58.1; H, 3.8; N, 4.8%); $\nu_{max.}$ 3 200—2 300 ($CO_2H$), 1 705 (ester), 1 695 ($CO_2H$), and 1 217 $cm^{-1}$ (N–O); $M^+$, 289; δ 2.69 (s, 3 H, Me), 7.18—6.88 (m, 4 H, ArH), 8.48 (d, *J* 2 Hz, 1 H, pyridine 5-H), 8.79 (d, *J* 2 Hz, pyridine 3-H), and 9.65 (br s, 1 H, $CO_2H$)*.

The filtrate was evaporated and the solid residue was column chromatographed on silica gel. Gradient elution with chloroform–ethyl acetate gave firstly *m*-chlorobenzoic acid (2.8 g, 96%) and then 4-[2-*hydroxybenzoyloxy*]-5-*methylpyridine*-2-*carboxylic acid* (**34**) (1 g, 47%) as yellow prisms (from ethanol), m.p. 179 °C (Found: C, 61.5; H, 4.1; N, 5.2. $C_{14}H_{11}NO_5$ requires

C, 61.5; H, 4.1; N, 5.1%); $\nu_{max.}$ 3 200—2 775 ($CO_2H$), 1 770 (ester), and 1 710 $cm^{-1}$ ($CO_2H$); $M^+$, 273; δ 2.68 (s, 3 H, Me), 7.55—6.89 (m, 4 H, ArH), 8.1 (d, *J* 2 Hz, 1 H, pyridine 5-H), 8.42 (d, *J* 2 Hz, 1 H, pyridine 3-H), and 10.6 (s, 1 H, OH)*.

*Deoxygenation of* 4-(2-*Hydroxyphenoxycarbonyl*)-6-*methylpyridine*-2-*carboxylic Acid* N-*Oxide* (**31**).—A mixture of the title compound (1 g, 3.5 mmol) and triethyl phosphite (0.59 g) was heated under reflux in bromobenzene (40 ml) for 6 h. The solvent was evaporated and the residue was column chromatographed. Gradient elution with chloroform and ethyl acetate gave 4-(2-*hydroxyphenoxycarbonyl*)-2-*methylpyridine* (**33**) (0.65 g, 79.2%) as grey plates (from ethanol), m.p. 176—178 °C (Found: C, 68.15; H, 4.9; N, 6.15. $C_{13}H_{11}NO_3$ requires C, 68.1; H, 4.8; N, 6.1%); $\nu_{max.}$ 3 600—2 400 (OH) and 1 750 $cm^{-1}$ (ester); $M^+$, 229; δ($CDCl_3$) 2.7 (s, 3 H, Me), 7.28—6.95 (m, 4 H, ArH), 7.78 (dd, *J* 5, 1.25 Hz, 1 H, pyridine 3-H), 7.82 (d, *J* 1.25 Hz, 1 H, pyridine 5-H), and 8.68 (dd, *J* 5, 1.25 Hz, 1 H, pyridine 2-H).

Further elution gave 4-(2-*hydroxyphenoxycarbonyl*)-6-*methylpyridine* N-*oxide* (**32**) (0.15 g, 17.5%) as brown plates (from ethanol), m.p. 197—199 °C (Found: C, 63.8;, H, 4.6; N, 5.8. $C_{13}H_{11}NO_4$ requires C, 63.7; H, 4.5; N, 5.7%); $\nu_{max.}$ 3 400—2 500 (OH), 1 725 (ester), and 1 230 $cm^{-1}$ ($\overset{+}{N}$–$\overset{-}{O}$); $M^+$, 245; δ 2.44 (s, 3 H, Me), 7.21—6.77 (m, 4 H, ArH), 7.81 (dd, *J* 6.2, 2.2 Hz, 1 H, pyridine 3-H), 8.18 (d, *J* 2.2 Hz, 1 H, pyridine 5-H), 8.43 (d, *J* 6.2 Hz, 1 H, pyridine 2-H), and 9.75 (s, 1 H, OH)*.

*Deoxygenation of* 4-(2-*Hydroxyphenoxycarbonyl*)-6-*methylpyridine* N-*Oxide* (**32**).—A solution of the title compound (0.2 g, 0.8 mmol) and triethyl phosphite (0.12 g) in bromobenzene (5 ml) was heated under reflux for 4 h. The solvent was evaporated and the mixture was column chromatographed on silica gel. Gradient elution with chloroform–ethyl acetate gave 4-(2-hydroxyphenoxycarbonyl)-2-methylpyridine (**33**) (60 mg, 32%) as grey plates (from ethanol), m.p. 176—178 °C, identical with the sample obtained from the previous experiment.

*Acid Hydrolysis of* 4-(2-*Hydroxyphenoxycarbonyl*)-6-*methylpyridine* (**33**).—A mixture of the title compound (0.12 g, 9 mmol) in glacial acetic acid (3 ml), concentrated sulphuric acid (3 ml), and water (3 ml) was heated under reflux for 2 h. The product was cooled and then neutralised with 10% aqueous sodium hydrogen carbonate and the whole then evaporated. The solid residue was column chromatographed on silica gel. Gradient elution with chloroform and ethyl acetate gave pyrocatechol (0.014 g), and further elution with ethanol gave 2-methylpyridine-4-carboxylic acid (31 mg, 25%) identical with an authentic sample.

*Attempted Decarboxylation of* 4-(2-*Hydroxybenzoyloxy*)-2-*methylpyridine*-2-*carboxylic Acid* (**34**).—A solution of the title compound (1 g, 3.7 mmol) in bromobenzene (35 ml) was heated under reflux for 2 h. The solvent was evaporated and the residual oil which solidified on scratching gave O-(2-*methyl*-4-*pyridyloxy*)*benzoic acid* (**35**) (0.56 g, 66.7%) as brown plates (from ethanol), m.p. 140—142 °C (Found: C, 68.1: H, 4.9; N, 6.1. $C_{13}H_{11}NO_3$ requires C. 68.1; H, 4.9; N, 6.1%); $\nu_{max.}$ 3 200—2 400 ($CO_2H$) and 1 660 $cm^{-1}$ ($CO_2H$); $M^+$, 229; δ 2.33 (s, 3 H, Me), 7.50—6.96 (m, 4 H, ArH), 7.56 (dd, *J* 7, 2 Hz, 1 H, pyridine 5-H), 7.76 (d, *J* 2 Hz, 1 H, pyridine 3-H), 8.34 (d, *J* 7 Hz, pyridine 6-H), and 10.52 (s, 1 H, $CO_2H$)*

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