Benzopyrones. Part 23.[1] Cyclization of *o*-Amino Carboxamides and Related Compounds

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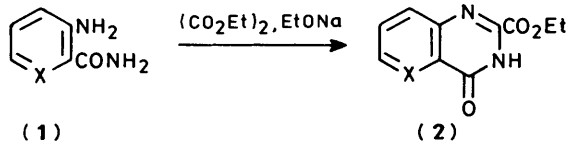
Cyclization of 2-amino-6-bromo-4-oxochromene-3-carboxamide (**5**) with diethyl oxalate–sodium ethoxide gave the benzopyrano[2,3-*d*]pyrimidine-4,6-dione (**6**). Ethyl 3-amino-2-carbamoyl-4-oxochromene-6-carboxylate (**10a**) in a similar reaction gave derivatives of a novel ring system benzopyrano[3,2-*d*]pyrimidine (**8**) but when 3-amino-4-oxochromene-2-carboxamide (**10b**) was subjected to the same reaction, the novel ring system benzopyrano[3,2-*e*]-1,4-diazepine (**14a**) was obtained in high yield. This structure, which contains the hitherto unknown 1,4-diazepine-2,3,5-trione ring, is supported by spectroscopic and chemical evidence. The presence of a 3-amino and a 2-carbonyl group in a chromone has an unexpected shielding effect on the chemical shift of C-8. The course of the cyclization was studied. Attempts to cyclize 3-aminomethyl-4-oxochromene-2-carboxamide (**28**; X = Y = H), a homologue of (**10b**), failed but a new ring system (**31**) was obtained when ethyl 3-bromo-4-oxochromene-2-carboxylate (**29**; R^1 = OEt) reacted with *o*-phenylenediamine.

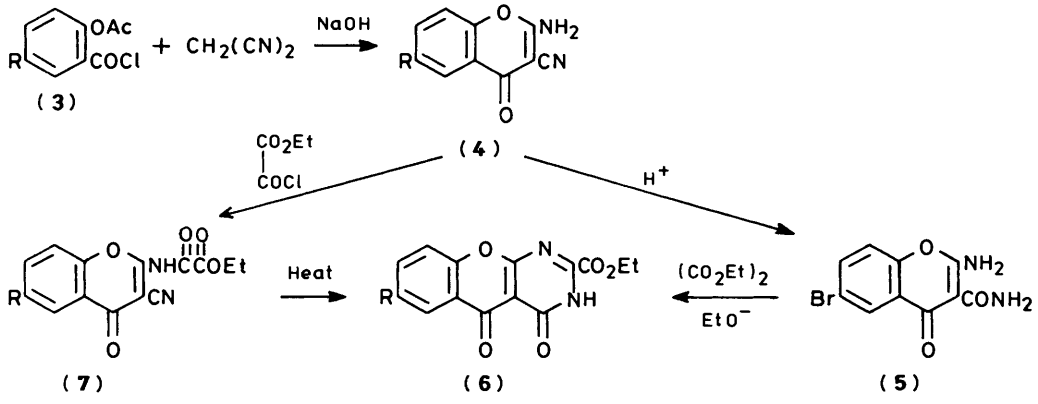
A number of chromones in which a third heterocyclic ring is fused at the 2,3-bond have recently been described.[2] Pyridine, pyrrole, 1,2,3-triazole, 1,2-, 1,4-, and 1,5-diazepine rings have been fused to chromone in this way; several of these were formed from functional groups at C-2 and C-3 of the chromone and some of the products possessed pharmacological properties. We now describe the synthesis of several other new ring systems and related compounds.

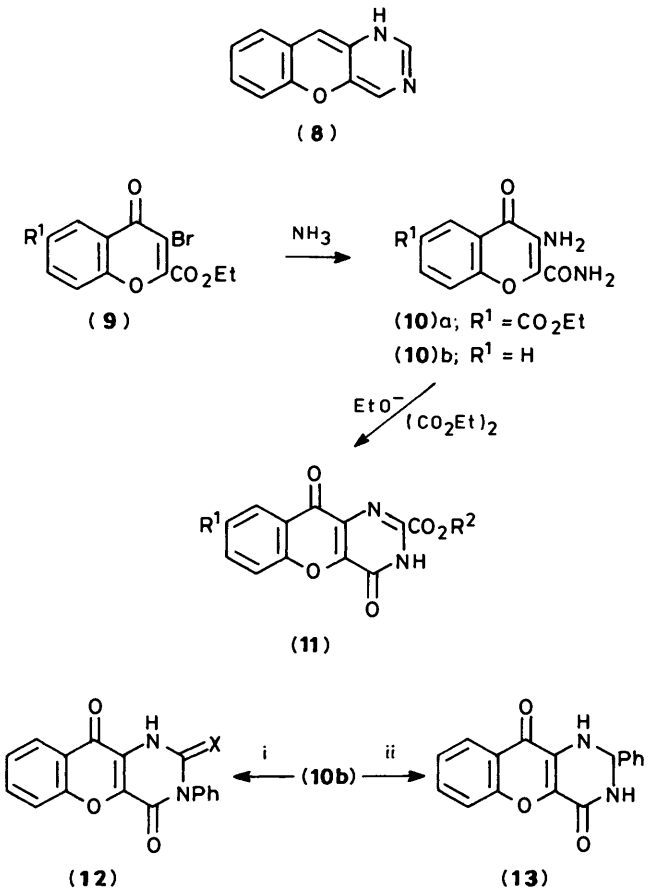


(1) (2)

Anthranilamides are readily cyclized by reaction with various reagents to give quinazolines.[3] For example, Nakanishi and Massett[4] obtained high yields of 4-oxoquinazoline-2-carboxylic acid derivatives (**2**; X = CH) by heating anthranilamide (**1**; X = CH) with diethyl oxalate and sodium ethoxide. Heterocyclic analogues of anthranilamide gave similar products (**2**; X = N). Cyclizations of this type do not appear to have been attempted in the chromone series although suitable precursors, 3-amino-4-oxochromene-2-carboxamide[5,6] and 2-amino-4-oxochromene-3-carboxamide[7] have been available for some time. In order to prepare 2-amino-6-bromo-4-oxochromene-3-carboxamide (**5**), we cyclized 2-acetoxy-5-bromobenzoyl chloride (**3**; R = Br) by reaction with malononitrile and sodium hydroxide.[7] The product, 2-amino-6-bromo-4-oxochromene-3-carbonitrile (**4**; R = Br) was converted into the 3-carboxamide (**5**). When Nakanishi and Massett's method was applied to this amino carboxamide, ethyl 7-bromo-4,5-dioxo-3*H*-[1]benzopyrano[2,3-*d*]pyrimidine-2-carboxylate (**6**; R = Br) was formed in moderate yield. The amino nitrile (**4**; R = H)[7] was converted into the tricyclic ester (**6**; R = H) by successive acylation with ethoxalyl chloride [which first yielded the carboxamide (**7**; R = H)] and thermal cyclization to the pyrimidine (**6**; R = H). The latter procedure gave a better yield than that using hydrogen chloride–ethanol.

Derivatives of the novel isomeric ring system, [1]benzopyrano[3,2-*d*]pyrimidine (**8**) have been synthesized by applying the method described above for the synthesis of the benzopyrano[2,3-*d*]pyrimidine (**6**) to a 3-amino-4-oxochromene-2-carboxamide, namely, ethyl 3-amino-2-carbamoyl-4-oxochromene-6-carboxylate (**10a**). The latter was synthesized by successive bromination and amination of diethyl 4-oxochromene-2,6-dicarboxylate. Cyclization of the amino carboxamide (**10a**) with diethyl oxalate gave a high yield of the diester (**11**; R^1 = CO_2Et, R^2 = Et) which was hydrolysed to the dicarb-





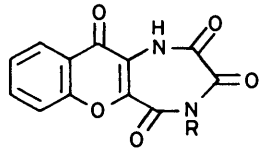
oxylic acid (**11**; $R^1 = CO_2H$, $R^2 = H$) by a boiling acetic–hydrochloric acid mixture.

Other derivatives of the novel ring system of compound (**11**) were synthesized by reaction of the amino carboxamide (**10b**)[6] with aryl isocyanates or isothiocyanates. For example, reaction with phenyl isocyanate gave 3-phenyl[1]benzopyrano[3,2-*d*]-pyrimidine-2,4,10-trione (**12**; X = O) while phenyl isothiocyanate gave the corresponding 2-thione (**12**; X = S). Alkyl isothiocyanates failed to react. A low yield of 1,2-dihydro-2-phenyl[1]benzopyrano[3,2-*d*]pyrimidine-4,10-dione (**13**) was obtained by reaction of the amino carboxamide (**10b**) with benzaldehyde.

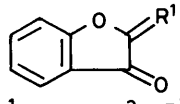
Treatment of the amino carboxamide (**10b**) with diethyl oxalate–sodium ethoxide was similarly expected to yield the benzopyranopyrimidine ($C_{14}H_{10}N_2O_5$) (**11**; $R^1 = H$, $R^2 =$ Et) but the sole product (A), a bright yellow crystalline compound isolated in good yield, had a molecular formula of $C_{12}H_6N_2O_5$ (as determined by microanalysis and mass spectrometry). N.m.r. spectroscopy showed that (A) did not have an ethoxycarbonyl group and its infrared spectrum contained absorptions at 3 200, 3 150, 3 100 (NH stretching), 1 735 and 1 680 (CONHCO or large ring lactam[8]), and 1 640 cm^{-1} (pyran CO). From these and other considerations (see below), it was concluded that product (A) had a [1]benzopyrano[3,2-*e*]-1,4-diazepine-2,3,5,11-tetraone ring structure (**14**). Alkylation of this compound by iodoethane, benzyl chloride, or 4-bromophenacyl bromide in the presence of sodium hydride gave the expected products, the N(4)-alkyl derivatives (**14b—d**), which had lower melting points and higher solubility than the substrate in organic solvents. N.m.r. and i.r. spectra of each of the three derivatives supported the structure.

The diazepine (**14a**) was characterized by ^{13}C n.m.r. spectroscopy. No published data were found on the chemical shifts of carbon atoms of 1,4-diazepine-2,3,5-triones; earlier attempts to synthesize 1,4-benzodiazepine-2,3,5-trione were unsuccessful.[9] The spectrum of quinoxaline-2,3-dione (C-2 and C-3 absorb at δ 155.3)* provided a useful parallel for the 1,2-dicarbonyl (δ 152.4 and 154.9) part of the molecule. However, when the shifts of the benzenoid carbon atoms of (**14a**) were compared with published data[10] for chromones, some significant differences were found. For example, C-8, -7, -6, and -2 were shielded by about 4—5 p.p.m. while C-8a and -4 were deshielded by 3—5 p.p.m. compared with chromone derivatives possessing a range of substituents on the pyrone ring.

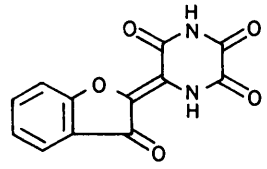
Gammill, Nash, and Mizsak[11] recently reported that when some 3-bromochromen-4-ones are treated for 18 h with primary (but not secondary) aliphatic amines in acetonitrile containing potassium carbonate, they underwent contraction of the pyran ring and the formation of benzofuran-3-ones (**15**; $R^1 = CHNHR^2$, R^2 = Bu, $PhCH_2$, cyclohexyl). We considered whether or not compound (A) might have structure (**19**) (or its geometric isomer) as its precursor (**10b**) had been prepared by amination of a 3-bromochromen-4-one (**9**; $R^1 = H$), although under different reaction conditions (gaseous ammonia was passed into an ethanolic solution at −3 °C for 15 min) from those employed by Gammill, *et al.* By analogy, ring contraction of the bromo ester (**9**; $R^1 = H$) would have produced (**16**) instead of (**10b**).



(**14**) **a**; R = H
b; R = Et
c; R = CH_2Ph
d; R = $CH_2COC_6H_4Br$-*p*



(**15**) $R^1 = CHNHR^2$; R^2 = Bu, $PhCH_2$, or cyclo-C_6H_{11}
(**16**) $R^1 = C(NH_2)CONH_2$
(**17**) $R^1 = CHPh$
(**18**) $R^1 = O$



(**19**)

The chemical shifts of the methine carbon atom *ortho* to the furan oxygen atom of compound (**15**; $R^1 = CHNHCH_2Ph$)† and of the model compounds (**17**)[12] and (**18**)[13] are in the range 112.2 to 113.7 whereas many chromones show a signal for C-8 at about 118 p.p.m. On the other hand, C-8 of compounds such

* We thank Dr. G. W. H. Cheeseman for providing this spectrum.
† We are grateful to Dr. R. B. Gammill for providing this spectrum and other valuable information.

Table. ^{13}C Data of some chromen-4-ones[a]

	C-8	C-7	C-6[b]	C-5[b]	C-4a	C-8a	C-4	C-3	C-2	C(2)=O	Other
(**10b**)	112.3	134.5	123.5	122.6	124.5	159.9	175.7	131.7	139.3	160.7	
(**14a**)[c]	113.5	138.3	124.4	124.4	119.8	158.1	186.4	120.1	135.1	165.6	154.6, 152.4 (COCO)
(**14b**)[c]	113.4	138.5	124.6	124.6	119.1	156.9	186.3	120.1	135.5	165.6	154.5, 151.5, 35.5, 12.0
(**20**)[d]	118.2	132.7	125.6	124.1	122.0	156.0	173.4	131.6	137.8[e]		
(**21**)[d]	117.7	138.7	126.0	123.8	123.4	155.5	174.5	135.3	132.5		
(**22**)	112.5	134.0	122.7	122.5	123.2	161.0	177.4	134.5	126.8	162.4	50.3, 41.2, 40.4 ($NCH_2CH_2CH_2$), 62.3, 13.5 (CH_2Me)
(**23**)[d]	112.8	133.5	123.0	122.2	123.7	160.9	180.6	140.1	130.6	162.2	31.5 (NMe), 62.8, 14.1 (CH_2Me)
(**26a**)	113.3	137.7	124.1	123.9	121.2	158.7	184.2	125.4	136.0	160.5	154.0, 164.7 ($COCO_2$) 63.1, 13.7 (CH_2Me)

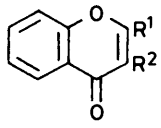
[a] Numbering refers to chromen-4-one ring. [b] Assignments may be reversed. [c] Solvent: $(CD_3)_2SO$ unless otherwise stated. [d] Solvent: $CDCl_3$. [e] Assignment confirmed by specific irradiation of ^1H signal.

as (**10b**), (**14a**), and (**14b**) resonated at 112.7 ± 0.6 (see Table) and so these compounds may possibly have a ring-contracted structure. However, comparison of the chemical shift of C-8 in 3-piperidinochromen-4-one (**21**) (δ 117.7), or 3-aminochromen-4-one (**20**) (δ 118.2) with that of the corresponding carbon atom of ethyl 4-oxo-3-piperidinochromene-2-carboxylate (**22**) (δ 112.2) shows that the combination of an amine at C-3 and a carbonyl group at C-2 produces a shielding effect on the C-8 atom. Neither amine (**20**) [prepared by the reduction of 3-nitrochromen-4-one] nor (**22**) [obtained from the 3-bromo ester (**9**) and a secondary amine by the method of Gammill, Nash, and Mizsak [11]] can have a benzofuran structure. Moreover, the 3-methylamino (**23**) and the 3-ethoxalylamino (**26a**) 2-carboxylate esters have similar chemical shifts (112.8 and 113.3 respectively) for their C-8 atoms. We therefore conclude that compound (A) [its C-7 (*ortho* to the pyran ring oxygen atom) resonates at 113.5] and its derivatives have the structure shown in (**14**).

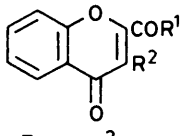
The amino carboxamide (**10b**) was initially cyclized in 77.5% yield by stirring the reactants at ambient temperature for 1.5 h but when the unusual nature of the product was realised, attempts were made to isolate an intermediate by shortening the reaction time to 10 min. The yield of product (74%) was little affected by this reduction and even when the temperature was reduced to −30 °C, a yield of 16% was obtained after stirring the reaction for 1.5 h. T.l.c. of the reaction mixture showed the presence of only reactant and product. The amino carboxamide and diethyl oxalate did not react on being heated at 160 °C for 10 h—conditions which Baker and Almaula [14] used successfully to cyclize anthranilamide to the quinazolinedione.

We surmised that the cyclization could proceed through the initial formation of the anion (**24**) and that this would attack the oxalate ester to give the imide (**25**) which cyclized to give (**14a**). A rather less likely possibility under the reaction conditions is that the amino group may first be deprotonated and then acylated to give the diamide (**26a**). Finally, it is possible that a dianion (**27**) may be an intermediate in a concerted reaction which leads to the diazepine.

The diamide (**26a**) appeared to be easier to synthesize than the imide (**25**) but treatment of the amino carboxamide with ethoxalyl chloride in pyridine gave a low yield of the diamide (**26a**). A satisfactory yield was obtained when pyridine was replaced by dry dimethylformamide. The diamide (as a suspension in ethanol containing sodium) cyclized to the diazepine (**14a**) on stirring. This supports the suggestion that in a strongly basic medium, initial N^3-acylation would be followed by cyclization. This supports the suggestion that (**26a**) is an intermediate in the formation of the diazepinetrione (**14a**). We were unable to demonstrate the formation and cyclization of the imide (**25**).



(**20**) $R^1 = H$; $R^2 = NH_2$
(**21**) $R^1 = H$; $R^2 = N(CH_2)_5$
(**22**) $R^1 = CO_2Et$; $R^2 = N(CH_2)_5$
(**23**) $R^1 = CO_2Et$; $R^2 = NHMe$

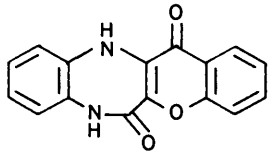


(**24**) $R^1 = {}^-NH$; $R^2 = NH_2$
(**25**) $R^1 = NHCOCO_2Et$; $R^2 = NH_2$
(**26**) **a**; $R^1 = NH_2$; $R^2 = NHCOCO_2Et$
b; $R^1 = NH_2$; $R^2 = NHCOCO_2Bu^t$
(**27**) $R^1 = {}^-NH$; $R^2 = {}^-NH$
(**28**) $R^1 = NHX$; $R^2 = CH_2NHY$
(**29**) $R^1 = OEt, OMe, OBu^t, OH,$ or Cl; $R^2 = Br$
(**30**) $R^1 = OBu^t$; $R^2 = NH_2$

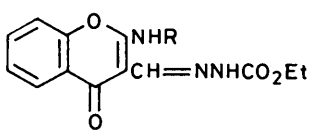
Attempts were also made to arrest the formation of the diazepine (**14a**) by replacing diethyl oxalate by t-butyl ethyl oxalate. The bulky t-butyl group of (**26b**) was expected to react more slowly with the 2-carboxamide but in the presence of sodium ethoxide, this reaction gave a 71% yield of the diazepine (**14a**), probably because of ester exchange of the t-butyloxy by ethoxy group supplied by the base. On replacing diethyl oxalate by ethyl *N*,*N*-diethyloxamate, t.l.c. showed the presence of a considerable amount of the amino carboxamide even after a period of warming at about 60 °C and only the amino carboxamide and a dark unidentifiable product were isolated.

Although we were unable to isolate or detect the presence of an intermediate product in the cyclization of the amino carboxamide (**10b**) to the diazepine (**14a**), the facile cyclization of diamide (**26a**) under basic conditions supports the possibility of this being an intermediate. On the other hand, the failure of ethyl *N*,*N*-diethyloxamate to react with the amino carboxamide implies that the diazepine is formed by a concerted mechanism, possibly through the dianion (**27**). The ease of formation of the latter is enhanced by the apparently low basicity of the amino group, as demonstrated by its reluctance to react with an acylating agent under mild conditions.

In view of the different products obtained by the reaction of amino carboxamides (**5**) and (**10a**) on the one hand, and (**10b**) on the other, with diethyl oxalate, the behaviour of 3-aminomethyl-4-oxochromene-2-carboxamide (**28**; X = Y = H) was examined. This compound was reported to be unreactive towards acetylating agents[5] but we now find that acetylation with acetic anhydride at ambient temperature in the presence of a catalytic amount of *N,N*-dimethylpyridin-4-amine yields either the 3-acetamidomethyl (**28**; X = H, Y = Ac) or the *N,N'*-diacetyl (**28**; X = Y = Ac) derivative, according to the molar proportion of reagent. Two molar equivalents of ethoxalyl chloride similarly gave the diacyl derivative (**28**; X = Y = $COCO_2Et$) in low yield. When the amino carboxamide (**28**; X = Y = H) was treated with diethyl oxalate and sodium ethoxide, the monoacyl derivative (**28**; X = H; Y = $COCO_2Et$) was isolated in low yield and none of the expected cyclized product was detected. Similarly, reaction of (**28**; X = Y = H) with phenyl isocyanate gave the urea (**28**; X = H; Y = CONHPh) rather than the seven-membered ring homologue of (**12**; X = O).



(**31**)



(**32**)

2-Amino-4-oxochromene-3-carbaldehyde reacted with ethyl carbazate to form the hydrazone (**32**; R = H) but attempts to cyclize this by heating with ethyl chloroformate–pyridine[15] gave the carbamate (**32**; R = CO_2Et).

The amino carboxamide (**10b**) was synthesized by amination of ethyl 3-bromo-4-oxochromene-2-carboxylate (**29**; R^1 = OEt).[6] The parent carboxylic acid (**29**; R^1 = OH) of the latter and a few of its derivatives have now been prepared as potentially useful intermediates. They are the methyl (**29**; R^1 = OMe) and t-butyl (**29**; R^1 = OBu^t) esters, the acid chloride (**29**; R^1 = Cl), t-butyl 3-amino-4-oxochromene-2-carboxylate (**30**) and the 3-methylamino (**23**) and 3-piperidino derivatives (**22**) of the ethyl ester. A compound belonging to a novel ring system, [1]benzopyrano[3,2-*e*][1,5]benzodiazepine, was obtained when the bromo ester (**29**; R^1 = OEt) was stirred with *o*-phenylenediamine and anhydrous potassium carbonate. Spectral and analytical evidence identified the product as [1]benzopyrano[3,2-*b*][1,5]benzodiazepine-6,13-dione (**31**).

Experimental

M.p.s were determined on a Reichert hot-stage apparatus. I.r. spectra were recorded as potassium bromide discs on a Perkin-Elmer model 577 spectrophotometer. ^1H N.m.r. spectra were recorded on a Perkin-Elmer S32 (90 MHz) instrument using Me_4Si as an internal standard and deuteriochloroform as the solvent unless otherwise stated. ^{13}C N.m.r. spectra were determined as described in an earlier paper.[11] Mass spectra were obtained on VG Analytical Instrument ZAB-IF at 70 eV.

2-Acetoxy-5-bromobenzoyl Chloride (**3**; R = Br).—Phosphorus pentachloride (20.8 g, 0.1 mol) was added in portions over 1 h to a suspension of 2-acetoxy-5-bromobenzoic acid (25.9 g, 0.1 mol) in boiling benzene (100 ml). Refluxing was continued for another hour and the solvent was removed under reduced pressure to give an oil which was purified by distillation under reduced pressure to give the *chloride* (**3**; R = Br) (11.4 g, 41%), m.p. 92—93 °C (Found: C, 39.4; H, 2.4. $C_9H_6BrClO_3$ requires C, 39.0; H, 2.2%).

2-Amino-6-bromo-4-oxochromene-3-carbonitrile (**4**; R = Br).—A mixture of malononitrile (12.2 g, 0.18 mol), 20% aqueous sodium hydroxide (19.4 ml), 2-acetoxy-5-bromobenzoyl chloride (25.6 g, 0.92 mol), and ice (197 g) was stirred vigorously for 10 min. A second portion of malononitrile and alkali was added with vigorous stirring for 10 min. The mixture was warmed to 40 °C and stirred while 50% aqueous potassium hydroxide solution (60 ml) was added until the pH of the solution reached 9. Cooling and acidification with hydrochloric acid gave the *amino nitrile* (**4**; R = Br) (11.0 g, 45%), m.p. >340 °C (Found: C, 44.9; H, 1.9; N, 10.2. $C_{10}H_5BrN_2O_2$ requires C, 45.3; H, 1.9; N, 10.6%); $\nu_{max.}$ 3 335, 3 278, 3 100, 2 236, 1 650, and 1 600 cm^{-1}; δ[$(CD_3)_2CO$–$(CD_3)_2SO$] 8.94 (2 H, s, NH_2), 8.02 (1 H, d, *J* 2 Hz, 5-H), 7.88 (1 H, dd, *J* 9 and 2 Hz, 7-H), and 7.41 (1 H, d, *J* 9 Hz, 8-H).

2-Amino-6-bromo-4-oxochromene-3-carboxamide (**5**; R = Br).—A mixture of the above nitrile (**4**; R = Br) (5.1 g, 0.02 mol) and sulphuric acid–water (80:20 v/v; 25 ml) was heated on a steam bath for 1 h. Cooling and pouring into ice–water (150 g) gave a precipitate of the *carboxamide* (**5**; R = Br) (3.5 g, 66%), m.p. >325 °C (from dimethylformamide–ethanol) (Found: C, 42.4; H, 2.5; N, 9.6. $C_{10}H_7BrN_2O_3$ requires C, 42.4; H, 2.4; N, 9.9%); $\nu_{max.}$ 3 350, 3 260, 3 060, 1 640, 1 607, and 1 595 cm^{-1}; δ[$(CD_3)_2CO$–$(CD_3)_2SO$] 9.50 (1 H, br s, NH), 9.15 (1 H, br s, NH), 8.09 (1 H, d, *J* 2 Hz, 5-H), 8.33 (1 H, dd, *J* 9 and 2 Hz, 7-H), and 7.39 (1 H, d, *J* 9 Hz, 8-H).

Ethyl 7-Bromo-4,5-dioxo-3H-[1]benzopyrano[2,3-d]pyrimidine-2-carboxylate (**6**; R = Br).—The above carboxamide (3.5 g, 0.01 mol) and freshly distilled diethyl oxalate (5.6 g, 0.03 mol) were stirred with sodium (0.9 g, 0.038 mol) in anhydrous ethanol (85 ml) for 3 h at 70—75 °C under nitrogen. The mixture was allowed to cool and acidified with acetic acid to yield the *ester* (**6**; R = Br) (1.37 g, 30%), m.p. 289 °C (decomp.) (from dimethylformamide–ethanol) (Found: C, 45.9; H, 2.6; N, 8.1. $C_{14}H_9BrN_2O_5$ requires C, 46.0; H, 2.5; N, 7.7%); $\nu_{max.}$ 1 749 and 1 536 cm^{-1}; δ[$(CD_3)_2CO$–$(CD_3)_2SO$] 8.17 (1 H, d, *J* 2 Hz, 6-H), 8.04 (1 H, dd, *J* 9 and 2 Hz, 8-H), 7.72 (1 H, d, *J* 9 Hz, 9-H), 4.45 (2 H, q, *J* 7 Hz, OCH_2), and 1.41 (3 H, t, *J* 7 Hz, Me).

Ethyl N-(3-Cyano-4-oxochromen-2-yl)oxamate (**7**; R = H).—Ethoxalyl chloride (2.3 g, 17.0 mmol) was added dropwise to a suspension of 2-amino-4-oxochromene-3-carbonitrile[7] (3.0 g, 16.0 mmol) in dry pyridine (14 ml) at 0 °C. After the reaction had been stirred for 30 min at ambient temperature, the reaction mixture was poured into water (70 ml) and acidified with 5M-hydrochloric acid. Extraction with dichloromethane, decolourization with charcoal and removal of the solvent gave the *oxamate* (**7**; R = H) (3.2 g, 69%), m.p. 157 °C (Found: C, 58.4; H, 3.5; N, 9.7. $C_{14}H_{10}N_2O_5$ requires C, 58.7; H, 3.5; N, 9.8%); $\nu_{max.}$ 2 230, 1 740, 1 664, and 1 645 cm^{-1}; δ 8.16 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.90—7.20 (3 H, m, ArH), 6.73 (1 H, s, NH, exchangeable with D_2O), 4.45 (2 H, q, *J* 7 Hz, CH_2), and 1.44 (3 H, t, *J* 7 Hz, Me).

Ethyl 4,5-Dioxo-3H-[1]benzopyrano[2,3-d]pyrimidine-2-carboxylate (**6**; R = H).—(*a*) *Acid cyclization.* Dry hydrogen chloride was passed into a suspension of the above oxamate (**7**; R = H) (2.0 g, 7.0 mmol) in dry ethanol (70 ml). Within 15 min an exothermic reaction raised the temperature to the reflux point and this was maintained for *ca.* 10 min. The gas was bubbled through for a total time of 1.5 h. Removal of the solvent under reduced pressure gave the *pyrimidine ester* (**6**; R = H) (0.13 g, 6.5%), m.p. 255 °C (from ethanol) (Found: C, 58.6; H, 3.6; N, 9.7%; M^+, 286.0592. $C_{14}H_{10}N_2O_5$ requires C, 58.7; H, 3.5; N, 9.8%; *M* 286.0589); $\nu_{max.}$ 1 760, 1 755, and 1 710 cm^{-1};

δ(CF_3CO_2D) 8.33 (1 H, d, *J* 8 Hz, 6-H), 8.21—7.50 (3 H, m, ArH), 4.66 (2 H, q, *J* 7 Hz, CH_2), and 1.56 (3 H, t, *J* 7 Hz, Me); *m/z* 286 (34%, M^+), 214 (100, $M^+ - 72$), and 213 (31, $M^+ - 73$).

(*b*) *Thermal cyclization.* The oxamate (100 mg, 0.35 mmol) was refluxed in ethanol (6 ml) for 10 min and the solid which separated was washed with ethanol to give the pyrimidine ester (25 mg, 25%), m.p. and mixed m.p. with the above sample 255 °C.

Ethyl 3-Amino-2-carbamoyl-4-oxochromene-6-carboxylate (**10a**).—Anhydrous ammonia was passed for 15 min into diethyl 3-bromo-4-oxochromene-2,6-dicarboxylate[1] (5.7 g, 15.4 mmol) suspended in dry ethanol (120 ml) and stirred at −3 °C. Water (300 ml) was added and stirring was continued for 15 min. The precipitate was crystallized from dimethylformamide to give the *carboxamide* (2.2 g, 52%), m.p. 267 °C (Found: C, 56.2; H, 4.4; N, 10.0. $C_{13}H_{12}N_2O_5$ requires C, 56.5; H, 4.4; N, 10.1%); $\nu_{max.}$ 1 740, 1 696, 1 650, and 1 615 cm^{-1}; δ[$(CD_3)_2CO$–$(CD_3)_2SO$] 8.27—7.80 (6 H, m, 5- and 6-H, NH_2 and $CONH_2$), 7.47 (1 H, d, *J* 9 Hz, 8-H), 4.34 (2 H, q, *J* 6 Hz, CH_2), and 1.37 (3 H, t, *J* 6 Hz, Me).

Diethyl 4,10-Dioxo[1]*benzopyrano*[3,2-d]*pyrimidine-2,8-dicarboxylate* (**11**; R^1 = CO_2Et, R^2 = Et).—Sodium ethoxide [from sodium (0.3 g, 0.013 mol) and anhydrous ethanol (88 ml)], the above carboxamide (**10a**) (1.20 g, 4.3 mmol), diethyl oxalate (1.3 g, 8.7 mmol) and ethanol (47 ml) were stirred for 10 min and then acidified to pH 5 with dilute hydrochloric acid. This gave the *diester* (**11**; R^1 = CO_2Et, R^2 = Et) (1.32 g, 85%), m.p. 292 °C (from dimethylformamide–ethanol) (Found: C, 57.3; H, 3.5; N, 8.2. $C_{17}H_{14}N_2O_7$ requires C, 57.0; H, 3.9; N, 7.8%); $\nu_{max.}$ 1 755, 1 720, 1 675, 1 632, and 1 605 cm^{-1}; δ[$(CD_3)_2CO$–$(CD_3)_2SO$] 8.45—8.34 (2 H, m, 5- and 7-H), 7.73 (1 H, d, *J* 9 Hz, 9-H), 4.36 (4 H, q, *J* 7 Hz, 2 × CH_2), 1.38 (3 H, t, *J* 7 Hz, Me), and 1.07 (3 H, t, *J* 7 Hz, Me).

Heating the diester with acetic acid and hydrochloric acid for 6 h gave the *dicarboxylic acid* (**11**; R^1 = CO_2H; R_2 = H) (80%), m.p. >320 °C (from dimethylformamide–ethanol) (Found: C, 51.9; H, 2.1; N, 9.2. $C_{18}H_{16}N_2O_7$ requires C, 51.7; H, 2.0; N, 9.3%); $\nu_{max.}$ 3 400—2 600, 1 780, 1 700, 1 660, and 1 613 cm^{-1}; δ[C_5D_5N–$(CD_3)_2SO$] 8.76 (1 H, d, *J* 2 Hz, 9-H), 8.52 (1 H, dd, *J* 10 and 2 Hz, 7-H), and 7.33 (1 H, d, *J* 10 Hz, 6-H).

3-Phenyl[1]*benzopyrano*[3,2-d]*pyrimidine-2,4,10-trione* (**12**; X = O).—3-Amino-4-oxochromene-2-carboxamide[6] (204 mg, 1.0 mmol) was heated under reflux for 16 h with phenyl isocyanate (1.2 g, 10 mmol) in dry benzene. The cool mixture was filtered and the yellow solid obtained was stirred in boiling ethanol (300 ml) to give the yellow *trione* (**12**; X = O) (200 mg, 65.0%), m.p. >330 °C (Found: C, 66.5; H, 3.4; N, 9.3%; M^+, 306.0640. $C_{17}H_{10}N_2O_4$ requires C, 66.7; H, 3.3; N, 9.2%; *M*, 306.0641); $\nu_{max.}$ 1 780, 1 725, 1 685, 1 650, and 1 600 cm^{-1}; *m/z* 306 (100%, M^+), 264 (49, $M^+ - 42$), and 159 (90, $C_9H_5NO_2$).

3-Phenyl-2-thioxo[1]*benzopyrano*[3,2-d]*pyrimidine-4,10-dione* (**12**; X = S).—3-Amino-4-oxochromene-2-carboxamide (750 mg, 3.67 mmol), phenyl isothiocyanate (5.65 g, 41.8 mmol) were heated under reflux in pyridine (5.0 g, 61 mmol) for 5 h. Concentration of the solution under reduced pressure gave a viscous oil which solidified on trituration with ethanol. Heating the insoluble product in ethanol (300 ml) gave on cooling, orange coloured crystals of the *dione* (**12**; X = S) (500 mg, 42%), m.p. 314—315 °C (decomp.) (Found: C, 63.8; H, 3.2; N, 8.3. $C_{17}H_{10}N_2O_3S$ requires C, 63.4; H, 3.1; N, 8.7%); $\nu_{max.}$ 1 740, 1 685, 1 640, and 1 590 cm^{-1}; δ[$(CD_3)_2SO$] 7.98 (1 H, s, NH) and 7.89—7.11 (9 H, m, ArH).

1,2-Dihydro-2-phenyl[1]*benzopyrano*[3,2-d]*pyrimidine-4,10-dione* (**13**).—The amino carboxamide (**10b**) (750 mg, 3.67 mmol), freshly distilled benzaldehyde (3.9 g, 36.7 mmol) and zinc chloride (50 mg, 0.36 mmol) were heated at 150 °C for 15 min. Addition of diethyl ether to the cooled mixture precipitated a red solid which was washed successively with water and ethanol and recrystallized several times from dimethylformamide to give brick-red crystals of the *dione* (**13**) (110 mg, 10%), m.p. 293 °C (decomp.) (Found: C, 69.7; H, 4.0; N, 9.2. $C_{17}H_{12}N_2O_3$ requires C, 69.9; H, 4.1; N, 9.6%); $\nu_{max.}$ 1 690 and 1 640 cm^{-1}.

[1]*Benzopyrano*[3,2-e]-*1,4-diazepine-2,3,5,11-tetraone* (**14a**).—(*a*) *From 3-amino-4-oxochromene-2-carboxamide.* A suspension of 3-amino-4-oxochromene-2-carboxamide[6] (0.51 g, 2.5 mmol) in diethyl oxalate (0.73 g, 5.0 mmol) and dry ethanol (20 ml) was added to a solution of sodium ethoxide [prepared from sodium (0.17 g, 7.5 mmol) and dry ethanol (50 ml)]. The carboxamide dissolved rapidly and a new red solid was precipitated. After 1.5 h of stirring at ambient temperature, 5M-hydrochloric acid was added until the mixture reached pH 5. The yellow solid was washed successively with water and ethanol, then stirred in boiling ethanol (150 ml); cooling and filtration gave the yellow crystalline *diazepine* (**14a**) (0.50 g, 77.5%), m.p. 326—328 °C (decomp.) (Found: C, 55.8; H, 2.4; N, 10.9%; M^+, 258.0278. $C_{12}H_6N_2O_5$ requires C, 55.8; H, 2.3; N, 10.9%; *M*, 258.0277; $\nu_{max.}$ 3 200, 3 150, 3 100 (NH), 1 735 and 1 680 (diazepine CO), and 1 640 cm^{-1} (pyran CO); δ_C [$(CD_3)_2SO$] 186.4 (C-11), 165.6 (C-5), 158.1 (C-6a), 154.9 (C-3), 152.4 (C-2), 138.3 (C-8), 135.1 (C-5a), 124.4 (C-9 and C-10), 120.1 (C-11a), 119.8 (C-10a), and 113.5 (C-7); *m/z* 258 (7.9%, M^+), 215 (42, $M^+ - 43$), 159 (100, $M^+ - 99$), and 76 (28, C_6H_4).

(*b*) Reducing the reaction time to 10 min gave a 74% yield of the diazepine, identical with the above sample (mixed m.p. and i.r.). Reducing the temperature to −30 °C and monitoring the reaction with t.l.c. showed the presence of substrate and diazepine only after 1.5 h. This gave a yield of 16% of the diazepine but at temperatures below −30 °C no reaction was detected.

(*c*) *From ethyl N-(2-carbamoyl-4-oxochromen-3-yl)oxamate* (**26a**). Ethoxalyl chloride (0.29 g, 2.1 mmol) was added to a stirred mixture of the amino carboxamide (**10b**) (0.21 g, 1.0 mmol) in dry dimethylformamide (6 ml). After 1 h, water (50 ml) was added to precipitate the yellow *oxamate* (**26a**) (0.18 g, 57.5%), m.p. 189 °C (decomp.) (from ethanol) (Found: C, 55.2; H, 4.0; N, 9.0. $C_{14}H_{12}N_2O_6$ requires C, 55.3; H, 4.0; N, 9.2%); $\nu_{max.}$ 1 720, 1 695, 1 670, and 1 627 cm^{-1}; δ[$(CD_3)_2SO$] 11.5 (1 H, s, NHCO), 8.35—7.25 (6 H, m, ArH and $CONH_2$), 4.44 (2 H, q, *J* 7 Hz, CH_2), and 1.45 (3 H, t, *J* 7 Hz, Me).

The oxamate (**26a**) (0.1 g, 0.33 mmol) was stirred for 2 h with sodium ethoxide [prepared from sodium (22 mg, 0.94 mmol) and dry ethanol (5 ml)] in ethanol (2 ml). Addition of dilute hydrochloric acid gave a precipitate which was collected, washed with water and purified by stirring in boiling ethanol (4 ml) to give the diazepine (**14a**) (46 mg, 54%), m.p. and mixed m.p. with a sample prepared as described in (*a*) above, 326 °C (decomp.).

Alkylation of the Diazepine (**14a**).—A suspension of the diazepine (0.51 g, 2.0 mmol) in dry dimethylformamide (25 ml) was added to a stirred suspension of sodium hydride (50% in oil; 0.1 g, 2.1 mmol) in dimethylformamide (3 ml) under dry nitrogen. After the initial reaction had subsided, the mixture was warmed to 50—60 °C for 30 min to complete the reaction. To the cooled mixture was added dry benzyl chloride (0.27 g, 2.2 mmol) in dimethylformamide (2 ml). After heating this for 3 h at 100 °C, water (150 ml) was cautiously added to the cooled

mixture, which was then acidified with hydrochloric acid and left to stand for 1 h. The resulting yellow precipitate was identified as 4-*benzyl*[1]*benzopyrano*[3,2-e]-1,4-*diazepine*-2,3,5,11-*tetraone* (**14c**) (0.21 g, 31%), m.p. 253 °C (Found: C, 65.9; H, 3.6; N, 8.3. $C_{19}H_{12}N_2O_5$ requires C, 65.5; H, 3.5; N, 8.0%); $\nu_{max.}$ 1 725, 1 693, 1 667, and 1 637 cm^{-1}; δ[$(CD_3)_2SO$] 11.41 (1 H, s, NH), 8.05—7.22 (9 H, m, ArH), and 5.01 (2 H, s, CH_2); ^{13}C n.m.r. data are given in the Table.

The following compound was prepared similarly from the diazepine (**14a**) and iodoethane: 4-*ethyl*[1]*benzopyrano*[3,2-e]-1,4-*diazepine*-2,3,5,11-*tetraone* (**14b**) (35% yield), m.p. 279 °C (from ethanol) (Found: C, 59.1; H, 3.6; N, 9.8. $C_{14}H_{10}N_2O_5$ requires C, 58.9; H, 3.5; N, 9.8%); $\nu_{max.}$ 1 740, 1 712, 1 668, and 1 640 cm^{-1}; δ[$(CD_3)_2SO$] 7.97—7.22 (4 H, m, ArH), 3.79 (2 H, q, *J* 7 Hz, CH_2), and 1.14 (3 H, t, *J* 7 Hz, Me); ^{13}C n.m.r. data are given in the Table.

Heating the diazepine (**14a**) (0.5 g, 1.94 mmol), anhydrous potassium carbonate (0.11 g, 0.8 mmol), and 4-bromophenacyl bromide (0.53 g, 1.94 mmol) in dry dimethylformamide (6 ml) at 110 °C for 2 h followed by cooling and pouring into water (100 ml), gave 4-(4-*bromophenacyl*)[1]*benzopyrano*[3,2-e]-1,4-*diazepine*-2,3,5,11-*tetraone* (**14d**) (0.41 g, 46.5%), m.p. 296 °C (decomp.) (from ethanol) (Found: C, 52.6; H, 2.6; N, 6.4. $C_{20}H_{11}BrN_2O_6$ requires C, 52.8; H, 2.4; N, 6.2%); $\nu_{max.}$ 1 736, 1 724, 1 690, 1 661, and 1 634 cm^{-1}; δ[$(CD_3)_2SO$] 8.08—7.30 (8 H, m, ArH) and 5.36 (2 H, s, CH_2).

Ethyl 3-*Piperidino*-4-*oxochromene*-2-*carboxylate* (**22**).—A solution of ethyl 3-bromo-4-oxochromene-2-carboxylate[6] (0.75 g, 2.5 mmol) and piperidine (0.64 g, 7.5 mmol) in dry acetonitrile (7 ml) was stirred with anhydrous potassium carbonate for 18 h. Water was added and the solution was extracted with diethyl ether. Work-up gave yellow crystals of the *ethyl ester* (0.59 g, 77%), m.p. 121 °C [from ethyl acetate–light petroleum, (b.p. 60—80 °C)] (Found: C, 68.2; H, 6.4; N, 4.9. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.3; N, 4.7%); $\nu_{max.}$ 1 730 and 1 655 cm^{-1}; δ_H 7.74 (1 H, d, *J* 8 Hz, 5-H), 7.61—7.00 (3 H, m, ArH), 4.50 (2 H, q, *J* 7 Hz, OCH_2), 3.68 (4 H, s, CH_2NCH_2), 1.74 [6 H, s, $(CH_2)_3$], and 1.42 (3 H, t, *J* 7 Hz, Me).

Ethyl 3-*Methylamino*-4-*oxochromene*-2-*carboxylate* (**23**).—Ethyl 3-bromo-4-oxochromene-2-carboxylate (3.0 g, 10 mmol) was suspended in dry ethanol (30 ml) at −5 °C. Methylamine (33% w/w solution in ethanol; 3.6 ml, 30 mmol) was added to the stirred solution at a rate which maintained the temperature at less than 0 °C. After a further period of 20 min of stirring at 0 °C, the mixture was poured into saturated sodium chloride (120 ml). Extraction with diethyl ether and isolation of the product from the extract in the usual way gave yellow crystals of the *amine* (1.0 g, 40%), m.p. 112 °C [from ethyl acetate–light petroleum (b.p. 60—80 °C)] (Found: C, 63.4; H, 5.3; N, 5.6. $C_{13}H_{13}NO_4$ requires C, 63.2; H, 5.3; N, 5.7%); $\nu_{max.}$ 1 735 and 1 650 cm^{-1}; δ 7.82 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.69—7.05 (3 H, m, ArH), 5.30 (1 H, s, NH, exchangeable with D_2O), 4.53 (2 H, q, *J* 7 Hz, OCH_2), and 1.49 (3 H, t, *J* 7 Hz, CH_2Me); ^{13}C n.m.r. data are given in the Table.

Acetylation of 3-*Aminomethyl*-4-*oxochromene*-2-*carboxamide* (**28**; X = Y = H).—The amine[5] (1.0 g, 4.6 mmol) and *N,N*-dimethylpyridin-4-amine (0.02 g, 0.2 mmol) were stirred with acetic anhydride (1.08 g, 1.0 ml, 10.6 mmol) and triethylamine (0.73 g, 1.0 ml, 0.07 mmol). Acetic acid (7.0 ml) was added a few minutes later and after allowing the mixture to stand for 30 min, the solid was collected, washed successively with dilute aqueous sodium hydroxide, water, and a little ice-cold methanol to give yellow crystals of N,N′-*diacetyl*-3-*aminomethyl*-4-*oxochromene*-2-*carboxamide* (**28**; X = Y = Ac) (0.36 g, 26%), m.p. 165—167 °C (from ethanol) (Found: C, 59.3; H, 4.8; N, 9.0. $C_{15}H_{14}N_2O_5$ requires C, 59.6; H, 4.7; N, 9.3%); $\nu_{max.}$ 1 730, 1 685, 1 650, 1 580, and 1 530 cm^{-1}; δ 7.63 (4 H, m, ArH), 6.70—6.00 (2 H, br, CONH, CH_2NH), 4.37 (2 H, s, CH_2), 2.58 (3 H, s, CONHCO*Me*), and 2.20 (3 H, s, $CH_2NHCOMe$).

Repetition of the above reaction using half the quantities of acetic anhydride gave yellow crystals of 3-*acetylaminomethyl*-4-*oxochromene*-2-*carboxamide* (**28**; X = H, Y = Ac) (23%), m.p. 182 °C (Found: C, 60.4; H, 4.6; N, 10.7. $C_{13}H_{12}N_2O_4$ requires C, 60.0; H, 4.7; N, 10.8%); $\nu_{max.}$ 1 710, 1 700, 1 630, and 1 570 cm^{-1}.

N,N′-*Bisethoxalyl*-3-*aminomethyl*-4-*oxochromene*-2-*carboxamide* (**28**; X = Y = $COCO_2Et$).—A mixture of ethoxalyl chloride (1.32 g, 9.7 mmol) and 3-aminomethyl-4-oxochromene-2-carboxamide[5] (1.0 g, 4.6 mmol) was stirred in dimethylformamide (28 ml) for 1 h. Pouring this reddish mixture into water gave the *diamide* (**28**; X = Y = $COCO_2Et$) (0.22 g, 11.5%), m.p. 197 °C (from ethanol) (Found: C, 54.4; H, 4.4; N, 6.5. $C_{19}H_{18}N_2O_9$ requires C, 54.5; H, 4.3; N, 6.7%); $\nu_{max.}$ 1 735, 1 700, 1 625, 1 605, and 1 570 cm^{-1}; δ[$CDCl_3$–$(CD_3)_2SO$] 7.93—6.96 (4 H, m, ArH), 4.97 (2 H, s, CH_2NH), 4.90—4.30 (4 H, m, 2-CO_2CH_2, 3-CO_2CH_2), and 1.82—1.40 (6 H, m, 2 × Me).

3-*Ethoxalylaminomethyl*-4-*oxochromene*-2-*carboxamide* (**28**; X = H, Y = $COCO_2Et$).—Following the method described earlier for the preparation of the diazepine (**14a**) from the amino carboxamide (**10b**), but replacing the latter by 3-aminomethyl-4-oxochromene-2-carboxamide, the product was the orange 3-*acylaminomethyl derivative*, (**28**; X = H, Y = $COCO_2Et$), m.p. 227 °C (from dimethylformamide–ethanol) (7%) (Found: C, 57.0; H, 4.1; N, 8.9. $C_{15}H_{14}N_2O_6$ requires C, 56.6; H, 4.4; N, 8.8%; $\nu_{max.}$ 1 730, 1 720, 1 700, 1 640, 1 610, and 1 570 cm^{-1}.

4-*Oxo*-3-*phenylureylenemethylchromene*-2-*carboxamide* (**28**; X = H, Y = PhNHCO).—The amino carboxamide (**28**; R^1 = R^2 = H) (0.70 g, 2.8 mmol) and phenyl isocyanate (0.33 g, 0.3 ml, 2.8 mmol) were heated under reflux in dry toluene (10 ml) for 6 h and allowed to cool. The precipitated yellow solid was the *urea* (**28**; X = H, Y = PhNHCO) (0.69 g, 64%), m.p. 237 °C (Found: C, 63.7; H, 4.5; N, 12.3. $C_{18}H_{15}N_3O_4$ requires C, 64.1; H, 4.5; N, 12.5%); $\nu_{max.}$ 1 700, 1 630, 1 605, and 1 595 cm^{-1}.

3-*Bromo*-4-*oxochromene*-2-*carboxylic Acid* (**29**; R^1 = OH, R^2 = Br) *and its Methyl Ester* (**29**; R = OMe).—Ethyl 3-bromo-4-oxochromene-2-carboxylate[5] (8.0 g, 27 mmol) was hydrolysed by heating with hydrobromic acid (40 ml) and acetic acid (30 ml) for 3.5 h to give the *carboxylic acid* (**29**; R^1 = OH, R^2 = Br) (4.60 g, 63.5%), m.p. 215 °C (decomp.) (from ethyl acetate) (Found: C, 45.0; H, 2.0. $C_{10}H_5BrO_4$ requires C, 44.7; H, 1.9%); $\nu_{max.}$ 1 710 and 1 650 cm^{-1}; δ[$(CD_3)_2SO$–$(CD_3)_2CO$] 8.60 (1 H, s, OH, exchangeable with D_2O), 8.14 (1 H, dd, *J* 8 and 2 Hz, 5-H), and 8.00—7.45 (3 H, m, ArH).

Heating the carboxylic acid with methanol and sulphuric acid for 6 h gave the *methyl ester* (**29**; R^1 = OMe, R^2 = Br) (63% yield), m.p. 115 °C (from aqueous ethanol) (Found: C, 46.7; H, 2.5. $C_{11}H_7BrO_4$ requires C, 46.6; H, 2.5%); $\nu_{max.}$ 1 726 and 1 656 cm^{-1}; δ 8.25 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.94—7.26 (3 H, m, ArH), and 4.06 (3 H, s, Me).

t-*Butyl* 3-*Bromo*-4-*oxochromene*-2-*carboxylate* (**29**; R^1 = OBu^t, R^2 = Br).—The bromo carboxylic acid (**29**; R = OH) (8.65 g, 32 mmol) was heated under reflux with phosphorus pentachloride (7.08 g, 34 mmol) in dry cyclohexane (160 ml) for 2 h. Cooling gave a crystalline sample of the *acid chloride* (**29**; R^1 = Cl, R^2 = Br) (6.20 g, 67%), m.p. 150 °C (from cyclohexane) (Found: C, 41.7; H, 1.5. $C_{10}H_4BrClO_3$ requires C, 41.7;

H, 1.4%); $\nu_{max.}$ 1 760 and 1 650 cm^{-1}; δ[$(CD_3)_2CO$] 8.18 (1 H, dd, *J* 8 and 2 Hz, 5-H) and 8.04—7.54 (3 H, m, ArH).

The acid chloride (5.5 g, 19 mmol) in dichloroethane (150 ml) was added dropwise to a stirred solution of t-butyl alcohol (1.48 g, 20 mmol) and dry pyridine (1.5 ml, 19 mmol) in dichloroethane (100 ml) at 0 °C. The solution was stirred at 0 °C for 4 h, left overnight at room temperature and diluted with water (150 ml). The organic layer was separated, washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water. Drying and removal of the solvent gave the *t-butyl ester* (**29**; R^1 = OBu^t, R^2 = Br) (3.4 g, 55%), m.p. 103 °C (Found: C, 52.1; H, 4.2. $C_{14}H_{13}BrO_4$ requires C, 51.7; H, 4.0%); $\nu_{max.}$ 1 730 and 1 650 cm^{-1}; δ[$(CD_3)_2CO$] 8.02 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.90—7.30 (3 H, m, ArH), and 1.52 (9 H, s, Bu^t).

t-Butyl 3-Amino-4-oxochromene-2-carboxylate (**30**).—Anhydrous ammonia was passed for 20 min into a suspension of t-butyl 3-bromo-4-oxochromene-2-carboxylate (1.5 g, 4.6 mmol) in dry ethanol (40 ml) kept at −5 to −10 °C. The red solution was poured into water to give the yellow *amino ester* (0.67 g, 55%), m.p. 108 °C (Found: C, 64.2; H, 5.7; N, 5.4. $C_{14}H_{15}NO_4$ requires C, 64.4; H, 5.8; N, 5.4%); $\nu_{max.}$ 1 700 and 1 655 cm^{-1}; δ 7.79 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.69—6.40 (5 H, m, ArH, and NH_2 exchangeable with D_2O), and 1.64 (9 H, s, Bu^t).

[1]*Benzopyrano*[3,2-e][1,5]*benzodiazepine-6,13-dione* (**31**).—A mixture of ethyl 3-bromo-4-oxochromene-2-carboxylate (3.0 g, 10 mmol), *o*-phenylenediamine (1.09 g, 10 mmol) and anhydrous potassium carbonate (1.38 g, 10 mmol) was stirred in dry ethanol for 4 h. About two-thirds of the ethanol was removed by distillation and the residue was diluted with water (200 ml) to precipitate the orange *diazepine* (1.0 g, 35.6%), m.p. 323—325 °C (decomp.) (Found: C, 69.5; H, 3.8; N, 10.1%; M^+, 278.0691. $C_{16}H_{10}N_2O_3$ requires C, 69.1; H, 3.6; N, 10.1%; *M*, 278.0691); $\nu_{max.}$ 1 640 and 1 610 cm^{-1}; δ[$(CD_3)_2SO$] 13.36 (2 H, s, NH) and 8.05—7.20 (8 H, m, ArH); *m/z* 278.0691 (100%, M^+), 250.0735 (10, $C_{15}H_2O_2$), and 194.0834 (19, $C_{13}H_{10}N_2$).

2-Amino-4-oxochromene-3-carbaldehyde Ethoxycarbonylhydrazone (**32**; R = H).—2-Amino-4-oxochromene-3-carbaldehyde (4.0 g, 21.1 mmol) was dissolved in ethanol (400 ml). Sufficient water was added to cause slight turbidity which was then removed by addition of a few drops of ethanol. Acetic acid (3 ml) and ethyl carbazate (4.0 g, 38.4 mmol) were added and the mixture was heated under reflux for 3 h. Cooling produced needle-shaped crystals of the *hydrazone* (**32**; R = H) (5.08 g, 87%), m.p. 290 °C (decomp.) (from dimethylformamide–ethanol) (Found: C, 57.0; H, 4.9; N, 15.2. $C_{13}H_{13}N_3O_4$ requires C, 56.7; H, 4.8; N, 15.3%); $\nu_{max.}$ 1 710, 1 630, 1 600, and 1 565 cm^{-1}; δ[$(CD_3)_2SO$] 9.55—8.60 (2 H, br, NH_2), 8.48 (1 H, s, CH), 7.97 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.82—7.25 (3 H, m, ArH), 4.11 (2 H, q, *J* 7.0 Hz, CH_2), and 1.22 (3 H, t, *J* 7.0 Hz, Me).

Attempted Cyclization of the Hydrazone (**32**; R = H).—To the hydrazone (2.0 g, 7.3 mmol) dissolved in dry pyridine (184 ml) and cooled in an ice bath, was added dropwise ethyl chloroformate (15.2 g, 13.4 ml, 0.14 mmol) over 5 min. After stirring at 0 °C for 3 h and at 18 °C for 15 h, the temperature was raised to reflux for 3 h. Dilution of the cooled mixture with water gave the *ethoxycarbonylhydrazone* of *ethyl* N-(*3-formyl-4-oxochromen-2-yl*)*carbamate* (**32**; R = CO_2Et) (1.57 g, 62%), m.p. 236 °C (from dimethylformamide–ethanol) (Found: C, 55.2; H, 4.9; N, 11.9. $C_{16}H_{17}N_3O_6$ requires C, 55.3; H, 4.9; N, 12.1%); $\nu_{max.}$ 1 740, 1 625, and 1 565 cm^{-1}.

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