Benzopyrones. Part 17.[1] The Synthesis of some Bischromones and the Reaction of Cyanomethyl Esters with Sodium Azide

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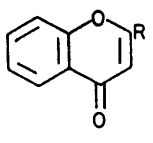
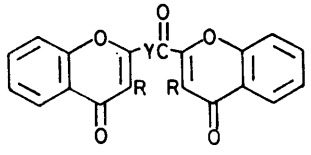
Treatment of 4-oxochromen-2-carbonyl chloride with dimethylcadmium gave 1-methyl-1-(4-oxochromen-2-yl)-ethyl 4-oxochromen-2-carboxylate (11) which was synthesized unequivocally and degraded to the carboxylic acid and 2-(1-methylvinyl)chromen-4-one. 2-Acetylchromen-4-one was synthesized by a new and more efficient method from 4-oxochromen-2-carbonyl chloride.

The synthesis and some reactions of 4-oxochromen-2-yl isocyanate, and the cyanomethyl esters of 4-oxochromen-2-carboxylic and -2,6-dicarboxylic acids are described.

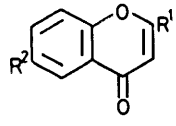
2-ACETYLCHROMEN-4-ONE (1) was required as an intermediate. Schmutz, Hirt, and Lauener [2] obtained a 17% yield of this ketone by oxidation of 2-ethylchromen-4-one with selenium dioxide. In an attempt to find a more efficient method of producing the ketone, we treated 4-oxochromen-2-carbonitrile [3] with a molar proportion of methylmagnesium iodide under various conditions but no trace of the 2-acetyl compound was found in the oily product. The reaction of a dialkylcadmium with an acyl halide usually yields a ketone; [4] when dimethylcadmium was heated with 4-oxochromen-2-carbonyl chloride in refluxing benzene and the product isolated in the usual way, a compound, m.p. 204—205 °C, was isolated in moderate yield. Elemental analysis and mass spectrometric determination of molecular weight showed the compound to have a molecular formula $C_{22}H_{16}O_6$, compared with $C_{11}H_8O_3$ expected for 2-acetylchromen-4-one. That the product (11) was not simply a dimeric form of the target molecule was evident from the n.m.r. spectrum



(1) R = Ac
(2) R = CO_2H
(3) R = $CMe{=}CH_2$
(4) R = $NHCO_2Et$
(5) R = NCO
(6) R = $NHCOCX_3$
X = Cl or F
(7) R = CONHPh
(8) R = CONMePh
(9) R = CO_2CH_2CN
(10) R = $CONH_2$

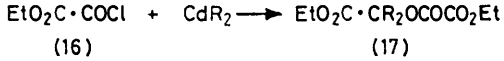


(11) R = H, Y = CMe_2O
(12) R = Me, Y = CMe_2O
(13) R = H, Y = NH



(14) $R^1 = R^2 = CO_2CH_2CN$
(15) $R^1 = CONH_2$, $R^2 = CO_2CH_2$ 

which showed two singlets at δ 6.54 and 7.20, and a pair of double doublets at 8.10 and 8.25. The molecule therefore contained two nonequivalent 3-H atoms and similarly a different pair of 5-H atoms. The presence of two dissimilar chromen-4-one moieties was confirmed by the ratio of areas under the singlet at δ 2.00 and that at 6.54 (or that at 7.20) which was not the expected 3 : 1 but 6 : 1. I.r. absorption in the carbonyl region consisted of three peaks: 1 705s, 1 670s, and 1 655s cm^{-1}. The last two are within the range commonly found for the pyran carbonyl stretching absorption but that at 1 705 cm^{-1} could be due to either an exocyclic keto or an ester group. The singlet δ 2.0 represents six hydrogen atoms and so a Me_2C grouping must be present; the chemical shift of the geminal dimethyl group shows that it is likely to be adjacent to an oxygen atom rather than a carbonyl, *i.e.* $Me_2C{-}O{-}$ rather than $Me_2C{-}CO{-}$, and hence



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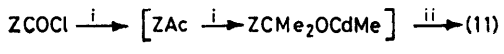


z = 4-oxochromen-2-yl;

SCHEME 1 *Reagents:* i, $CdMe_2$; ii, ZCOCl

the compound is likely to contain an ester group. When 3-methyl-4-oxochromen-2-carbonyl chloride was subjected to a similar reaction the product, $C_{24}H_{20}O_6$, gave spectra which showed only the expected differences from those of the 3-normethyl homologue and indicated the presence of two chromen-4-one ring systems in a molecule of formula (11) or (12). It is apparent that the 2-acetyl compound first formed reacts with another molecule of dimethylcadmium to give the tertiary alcoholate which is then acylated by the acyl chloride. The known low electron density of position 2 of chromones encourages attack on the exocyclic carbonyl group at that position (Scheme 1), a reaction which is similar to that described by Stacy and McCurdy [4] who isolated the triester (17) as the major product of the reaction of dialkylcadmium with ethyloxalyl chloride (16). The structure of the dimeric ester (11) was confirmed by (*a*) hydrolysis to the carboxylic acid (2) and the alkene (3) formed by dehydration of the alcohol and (*b*) synthesis from the acid chloride and the alcohol which was synthesized by a Grignard reaction on ethyl 4-oxochromen-2-carboxylate.

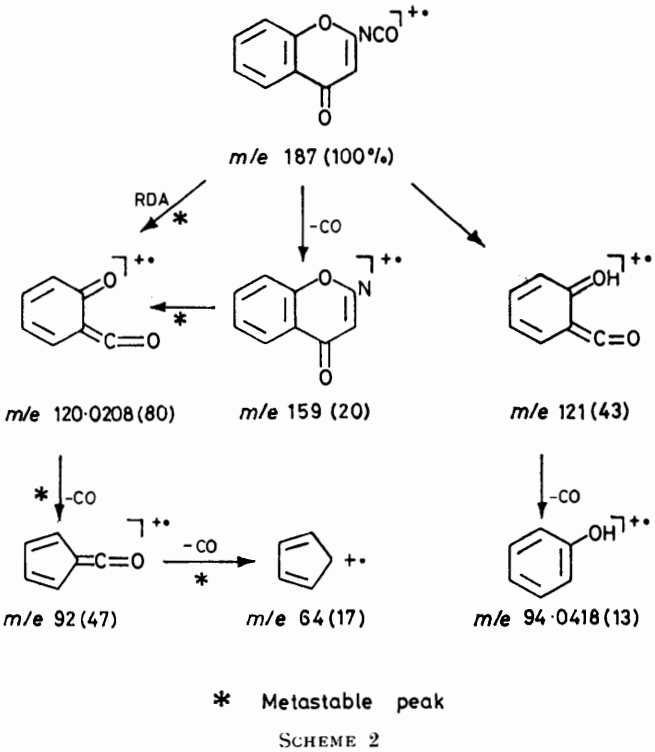
Grignard reactions on acyl halides give t-alcohols when a two- or three-fold excess of the reagent is present but

ketones are obtained when equimolar proportions are used. A low temperature (−70 °C) and iron(III) chloride as catalyst have been recommended [5,6] in the synthesis of dialkyl ketones by this method. When a Grignard reaction under these conditions was attempted on 4-oxochromen-2-carbonyl chloride, the unchanged halide was recovered, but when repeated at −5 to 0 °C, the reaction gave a high yield of 2-acetylchromen-4-one. This is a much more convenient and efficient route than that using selenium dioxide.[2]

4-Oxochromen-2-carboxylic acid (2) has been converted *via* the acid azide into ethyl *N*-(4-oxochromen-2-yl)carbamate (4).[7] Some chromones which contain an acidic function at C-2 possess antiallergic properties [8] and the modest activity displayed by the carbamate (4) encouraged us to synthesize (*a*) analogues in which the acidity of NH is increased, and (*b*) the isocyanate (5) which is an intermediate in the synthesis of several analogous compounds. The isocyanate was produced *in situ* and converted without isolation into other products.[7] It is a very reactive compound but by rigid exclusion of moisture and other compounds with which it reacts, it was possible to isolate the isocyanate. It did not absorb i.r. radiation at *ca.* 2 270 cm^{-1} (N=C=O) (*cf.* the absence of C≡N absorption in the corresponding nitrile [9]). The presence of the isocyanate was demonstrated by its conversion into the carbamate (4) by ethanol, and into *N*-trichloro- and *N*-trifluoro-acetylaminochromen-4-one (6) by the trihalogenoacetic acid. Its mass spectrum confirmed the structure and contained several fragmentations (supported by metastable peaks and accurate mass measurements) which are characteristic of chromen-4-ones, such as retro-Diels–Alder and successive loss of carbon monoxide (Scheme 2).

Attempts to react the isocyanate with ammonia, urea or oxalic acid, however, all led to a neutral compound, m.p. 262 °C, in varying amounts and none of the products expected.[10] Elemental analysis and mass spectrometry of the compound showed that its molecular formula was $C_{19}H_{11}NO_5$. Its low solubility in suitable solvents precluded examination of its n.m.r. spectrum but structure (13) was in accordance with available data and was confirmed by its synthesis in high yield by conversion of 4-oxochromen-2-carbonyl azide into the isocyanate and treatment of this with 4-oxochromen-2-carboxylic acid. The fragmentation pattern of this amide (Scheme 3) was interpreted by comparison with those of the *N*-phenyl- (7) and *N*-methyl-*N*-phenyl-2-carboxamide (8) and of published data.[11]

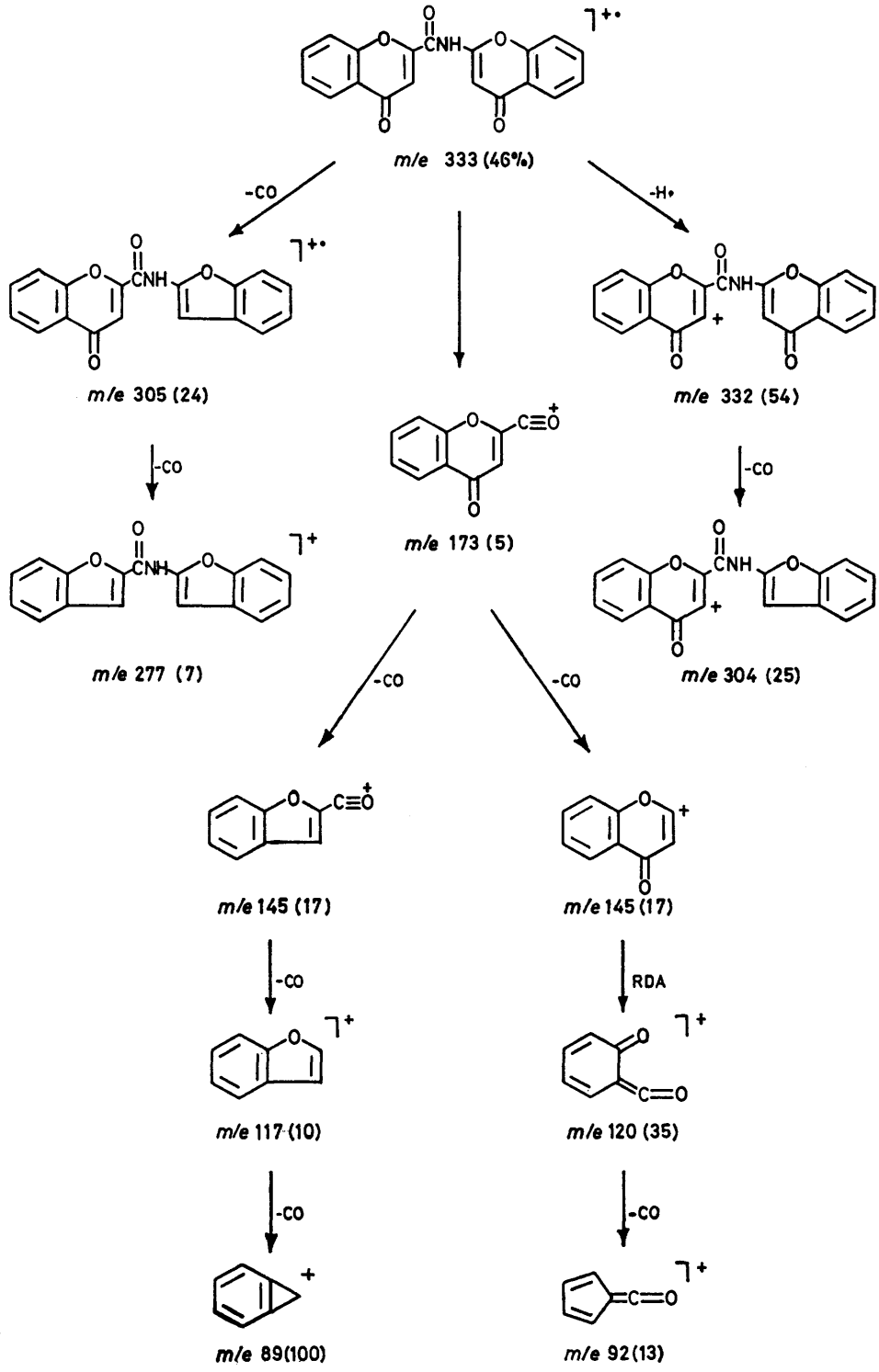
Earlier work in these Laboratories [3] showed that the acidity which is characteristic of some pharmacologically active chromones may be provided by the tetrazole ring. Such tetrazoles are often synthesized from a nitrile and sodium azide but when cyanomethyl 4-oxochromen-2-carboxylate (9) was thus treated, a high yield of 4-oxochromen-2-carboxamide (10) was obtained. In an attempt to determine the source of the amide nitrogen, the experiment was repeated several times but with each component (sodium azide, ammonium chloride, dimethylformamide) being omitted in turn. In other experiments, ammonium chloride was replaced by lithium chloride (which has been shown to be a good substitute [12]), or triethyleneglycol was used as solvent. The only product obtained in each of these experiments was the



SCHEME 2

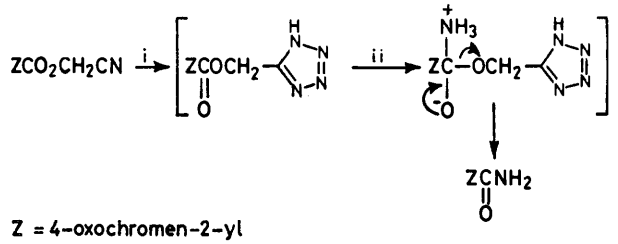
carboxylic acid (2). It therefore appears that an intermediate or complex which is formed only when all three reagents are present, is essential for the formation of the carboxamide. The possibility that the ester is hydrolysed to the carboxylic acid which then reacts with sodium azide, ammonium chloride and dimethylformamide was discounted by subjecting the carboxylic acid to the three reagents but it was recovered unchanged. A possibility which has not been discounted is that the tetrazolyl methyl ester is formed and that this labile ester is attacked by ammonia ($NH_4Cl \rightleftharpoons NH_3 + HCl$) to give the amide (Scheme 4).

Cyanomethyl 4-chlorobenzoate reacted normally to give the tetrazolylmethyl ester but cyanomethyl 2,4-dinitrobenzoate gave a low yield of ester and much tarry material. The low electron density at C-2 of chromone is comparable with that of C-1 in 2,4-dinitrobenzoate and different from the high electron density of C-6 of chromone.[13] It was, therefore, of interest to subject bis(cyanomethyl) 4-oxochromen-2,6-dicarboxylate (14) to one molar proportion of the same reagents. The product was a monotetrazole monoamide ($C_{13}H_9N_5O_5$) and from the behaviour of the 4-oxochromen-2-carboxylate (9), its structure would be expected to be (15). I.r. and ^1H n.m.r. spectroscopy were of no avail in distinguishing between structure (15) and that in which the substituents were interchanged but ^{13}C n.m.r. spectro-


m/e 333 (46%)
-CO
-H•
m/e 305 (24)
m/e 332 (54)
m/e 173 (5)
-CO
-CO
m/e 277 (7)
m/e 304 (25)
-CO
-CO
m/e 145 (17)
m/e 145 (17)
-CO
RDA
m/e 117 (10)
m/e 120 (35)
-CO
-CO
m/e 89(100)
m/e 92(13)

SCHEME 3

scopy of this and related compounds confirmed structure (15) (see following paper). The same compound was formed when diester (14) was treated with two molar proportions of reagents but the same reagents had no effect on ethyl 4-oxochromen-2-carboxylate.



SCHEME 4 *Reagents:* i, NaN_3, NH_4Cl, DMF; ii, NH_3

EXPERIMENTAL

M.p.s were determined on a Reichert hot-stage apparatus. I.r. spectra were recorded as potassium bromide discs on Perkin-Elmer model 157G spectrophotometer. N.m.r. spectra were recorded on a Perkin-Elmer R32 (90 MHz) instrument using Me_4Si as internal standard and deuteriochloroform as solvent unless otherwise stated. T.l.c.s were obtained on Polygram silica gel plates.

1-*Methyl*-1-(4-*oxochromen*-2-*yl*)*ethyl* 4-*Oxochromen*-2-*carboxylate* (11).—(*a*) To a solution of methylmagnesium iodide [prepared from methyl iodide (28.4 g, 0.2 mol) and magnesium (4.9 g, 0.2 g-atom)] in dry diethyl ether (50 cm^3) at 5 °C was added finely powdered anhydrous cadmium chloride (19.6 g, 0.011 mol). The mixture was stirred vigorously and heated under reflux for 15 min. The ether was rapidly removed under reduced pressure and replaced by dry benzene (65 cm^3). Roughly a third of this solvent was removed similarly. More benzene (120 cm^3) was added and the solution heated to boiling. 4-Oxochromen-2-carbonyl chloride (20.8 g, 0.1 mol) in warm benzene (100 cm^3) was added rapidly and the mixture heated under reflux for 30 min. After being allowed to cool, the mixture was added to stirred dilute sulphuric acid. The aqueous layer was separated and extracted with benzene (100 cm^3). This extract was combined with the organic layer and after being washed with water, dried (Na_2SO_4) and the solvent distilled off, it gave the *ester* (8.8 g, 47%), m.p. 204—205 °C (from ethanol) (Found: C, 70.0; H, 4.2%; M^+, 376.0944. $C_{22}H_{16}O_6$ requires C, 70.2; H, 4.3%; M^+, 376.0947); $\nu_{max.}$ 2 925, 2 860, 1 705, 1 670, and 1 655 cm^{-1}; δ 8.28—8.10 (2 H, dd, *J* 8 and 2 Hz, 5,5′-H_2), 8.00—7.21 (6 H, m, 6,6′,7,7′,8,8′-H_6), 7.20 (1 H, s, 3′-H), 6.54 (1 H, s, 3-H), and 2.00 (6 H, s, Me_2).

(*b*) A solution of 2-(4-oxochromen-2-yl)propan-2-ol (2.0 g, 0.01 mol) [prepared by heating ethyl 4-oxochromen-2-carboxylate (1 mol) with methylmagnesium iodide (2.2 mol) in diethyl ether for 1 min and pouring the mixture into cold dilute sulphuric acid] and 4-oxochromen-2-carbonyl chloride (2.1 g, 0.01 mol) in benzene (100 cm^3) was heated on a steam-bath for 5 min. The solvent was removed under reduced pressure and the residue crystallized from ethanol to give the ester (11) (3.2 g, 85%), m.p. 204—205 °C. The i.r. spectrum of this was identical with that obtained as described under (*a*) above.

Hydrolysis of 1-*Methyl*-1-(4-*oxochromen*-2-*yl*)*ethyl* 4-*Oxochromen*-2-*carboxylate* (11).—The ester (3.5 g) was hydrolysed with concentrated sulphuric acid (10 cm^3) at 20 °C for 5 min. The resulting syrup was poured into cold water to give a white solid and an oil. The solid was collected and crystallized from ethanol to give 4-oxochromen-2-carboxylic acid (1.0 g, 56%), m.p. alone and with an authentic sample, 260 °C (lit.,[15] 261 °C). The oil was 2-(1-*methylvinyl*)*chromen*-4-*one* (Found: C, 77.6; H, 5.5. $C_{12}H_{10}O_2$ requires C, 77.3; H, 5.4%) δ 8.04 (1 H, dd, *J* 8 and 2 Hz, 5-H), 5.96 (1 H, s, =CH), 5.36 (1 H, s, =CH), and 2.00 (3 H, s, Me).

1-*Methyl*-1-(3-*methyl*-4-*oxochromen*-2-*yl*)*ethyl* 3-*Methyl*-4-*oxochromen*-2-*carboxylate* (12).—Treatment of 3-methyl-4-oxochromen-2-carbonyl chloride with dimethylcadmium under the conditions described for the synthesis of ester (11) under (*a*) above gave a comparable yield of the *dimethyl homologue* (12), m.p. 178—179 °C (from ethanol) (Found: C, 71.4; H, 5.2. $C_{24}H_{20}O_6$ requires C, 71.3; H, 5.0%), $\nu_{max.}$ 2 930, 2 860, 1 738, 1 651, 1 626, 1 615, and 1 578 cm^{-1}; δ 8.40—8.14 (2 H, dd, *J* 8 and 2 Hz, 5,5′-H_2), 7.98—7.26 (6 H, m, 6,6′,7,7′,8,8′-H_6), 3.38 (3 H, s, 3-Me), 2.26 (3 H, s, 3′-Me), and 1.85 (6 H, s, Me_2).

2-*Acetylchromen*-4-*one* (1).—A solution of methylmagnesium iodide [from methyl iodide (0.035 mol) and magnesium in dry diethyl ether] was added during 1 h to a stirred ethereal solution of 4-oxochromen-2-carbonyl chloride (6.4 g, 0.03 mol) maintained at between −5 and 0 °C. Addition of the reaction mixture to dilute sulphuric acid and isolation of the product in the usual way gave 2-acetylchromen-4-one (4.1 g, 72%), m.p. 137 °C (from ethanol) (lit.,[2] 135—137 °C), $\nu_{max.}$ 1 702 (COMe), 1 655 (pyrone CO), and 1 605 cm^{-1}; δ 8.14 (1 H, dd, *J* 8 and 2.5 Hz, 5-H), 7.8—7.2 (3 H, m, 6-, 7-, 8-H), 7.07 (1 H, s, 3-H), and 2.14 (3 H, s, Me).

When the temperature was maintained at −70 °C in the presence of iron(III) chloride (0.1 g),[5,6] the halide was recovered.

4-*Oxochromen*-2-*yl Isocyanate* (5).—4-Oxochromen-2-carbonyl azide [7] (2.1 g) was heated in dry benzene (70 cm^3) for 3 h. On cooling, a small quantity of material was precipitated and on rapid crystallization from dry benzene gave the *isocyanate* (0.6 g, 33%), m.p. 255—258 °C (Found: C, 64.6; H, 3.1; N, 7.9. $C_{10}H_5NO_3$ requires C, 64.2; H, 2.7; N, 7.5%), $\nu_{max.}$ 3 600—2 700, 1 740, and 1 640 cm^{-1}; *m/e* 187 (M^+, 100%), 159 (M − CO, 20), 121 (M − 66, 43), 120 (M − 67, 80), and 92 (M − 95, 47).

N-(4-*Oxochromen*-2-*yl*)*trifluoroacetamide* (6; X = F).—4-Oxochromen-2-carbonyl azide (2.15 g, 0.01 mol) was heated under reflux in dry benzene (50 cm^3) for 3 h. The solution was cooled and trifluoroacetic acid (1.14 g, 0.01 mol) was added to it; the mixture was then shaken. The orange precipitate that formed gave the *acetamide* (2.0 g, 78%), m.p. 244—245 °C (from ethanol) (Found: C, 51.2; H, 2.3; N, 5.3. $C_{11}H_6F_3NO_3$ requires C, 51.4; H, 2.3; N, 5.5%), $\nu_{max.}$ 3 060—2 600, 1 730, 1 655, 1 610, and 1 560 cm^{-1}.

N-(4-*Oxochromen*-2-*yl*)*trichloroacetamide* (6; X = Cl).—Replacement of trifluoroacetic acid by trichloroacetic acid in the above reaction gave an 83% yield of the trichloroacetamide, m.p. 192—194 °C (ethanol) (lit.,[7] 187—190 °C) (Found: C, 43.1; H, 1.8; N, 4.5. Calc. for $C_{11}H_6Cl_3NO_3$: C, 43.1; H, 2.0; N, 4.6%), $\nu_{max.}$ 3 120, 3 080, 2 980, 1 740, 1 640, 1 620, and 1 535 cm^{-1}.

N-(4-*Oxochromen*-2-*yl*)-4-*oxochromen*-2-*carboxamide* (13).—(*a*) A solution of the isocyanate (5) (1 g) in warm benzene was prepared as above and gaseous ammonia was slowly bubbled through the stirred solution for 30 min. The mixture was left overnight in a refrigerator and the solid col-

lected. Extraction of this with ethanol gave the *carboxamide*, m.p. 262 °C (decomp.) (from ethanol) (Found: C, 68.5; H, 3.4; N, 4.2. $C_{19}H_{11}NO_5$ requires C, 68.5; H, 3.3; N, 4.2%), $\nu_{max.}$ 3 200—2 800, 1 705, 1 665, 1 610, and 1 550 cm^{-1} (Found: M^+ 333.0621. $C_{19}H_{11}NO_5$ requires 333.0637) 332 (M − 1, 54%), 305 (M − CO, 24), and 304 (M − HCO, 25).

(*b*) 4-Oxochromen-2-carbonyl azide (1 g) was heated under reflux in dry benzene (20 cm^3) for 3 h. 4-Oxochromen-2-carboxylic acid (2) (1 g) was added and the mixture was refluxed for 2 h. The solid which crystallized out on cooling was the carboxamide [1.45 g, 82% based on (2)], m.p. and mixed m.p. with sample from (*a*) above, 262—263 °C (decomp.).

N-Methyl-N-phenyl-4-oxochromen-2-carboxamide (8).—4-Oxochromen-2-carbonyl chloride (4.5 g, 0.02 mol) was added slowly to a stirred solution of *N*-methylaniline (2 g, 0.02 mol) in dry diethyl ether (50 cm^3). Filtration gave the amide (4.35 g, 72%), m.p. 115—116 °C (from ethanol) lit.,[7] 115—116 °C) (Found: C, 72.8; H, 4.6; N, 4.8. Calc. for $C_{17}H_{13}NO_3$: C, 73.1; H, 4.7; N, 5.0%); *m/e* 279 (M^+, 9%), 278 (M − 1, 22), 250 (M − 29, 23), 234 (M − 45, 15), and 186 (M − 93, 17).

N-Phenyl-4-oxochromen-2-carboxamide (7).—Replacement of *N*-methylaniline in the above preparation of (8) by aniline gave an 86% yield of the amide, m.p. 225—226 °C (lit.,[15] 223—224.5 °C) (Found: C, 72.1; H, 4.0; N, 5.2. Calc. for $C_{16}H_{11}NO_3$: C, 72.5; H, 4.2; N, 5.3%); *m/e* 265 (M^+, 9%), 264 (M − 1, 11), 235 (M − 30, 15), 220 (M − 45, 10), and 145 (M − 120, 20).

Cyanomethyl 4-Oxochromen-2-carboxylate (9).—4-Oxochromen-2-carboxylic acid (7.6 g, 4 mmol), chloroacetonitrile (4.5 g, 7 mmol), and triethylamine (6.1 g) were heated under reflux in ethyl acetate (60 cm^3) for 3 h. The hot solution was filtered and the solvent was removed under reduced pressure. The residue was washed with dilute sodium carbonate solution, dilute hydrochloric acid, and water to give the *ester* (5.7 g, 62%), m.p. 112 °C (from diethyl ether) (Found: C, 62.8; H, 2.8; N, 6.1. $C_{12}H_7NO_4$ requires C, 62.9; H, 3.1; N, 6.1%) $\nu_{max.}$ 3 060, 1 752, 1 648, 1 635, 1 615, 1 604, and 1 563 cm^{-1}.

4-Oxochromen-2-carboxamide (10).—When the ester (9) (1 g, 4.0 mmol) was treated [12] with sodium azide (0.45 g, 7 mmol), and ammonium chloride (0.35 g, 7 mmol) in dimethylformamide (10 cm^3), the product was the carboxamide (10) (0.7 g, 85%), m.p. 257—258 °C (decomp.) (from ethanol) [lit.,[3] 256—257 °C) (decomp.)] (Found: C, 63.1; H, 3.8; N, 7.2. Calc. for $C_{10}H_7NO_3$: C, 63.5; H, 3.9; N, 7.3%), δ(CF_3CO_2H) 8.37 (1 H, dd *J* 9 and 2 Hz, 5-H), 8.27—7.57 (5 H, m, 6,7,8-H, NH_2), and 7.64 (1 H, s, 3-H).

Cyanomethyl 4-Chlorobenzoate and Cyanomethyl 2,4-Dinitrobenzoate.—These compounds were prepared as described above for the ester (9): the *4-chlorobenzoate* (in 80% yield), m.p. 40—41 °C (from ethanol) (Found: C, 55.3; H, 3.2; N, 7.1. $C_9H_6ClNO_2$ requires C, 55.3; H, 3.1; N, 7.2%); the *2,4-dinitrobenzoate* (in 63% yield), m.p. 105 °C (from ethanol) (Found: C, 43.0; H, 2.1; N, 16.3. $C_9H_5N_3O_6$ requires C, 43.0; H, 2.0; N, 16.7%).

Tetrazol-5-ylmethyl 4-Chlorobenzoate.—Cyanomethyl 4-chlorobenzoate (2.0 g, 0.01 mol), sodium azide (0.7 g, 0.01 mol) and ammonium chloride (0.56 g, 0.01 mol) were heated on a steam-bath for 4 h in dimethylformamide (DMF) (40 cm^3) under the usual conditions.[12] This gave the *chlorobenzoate* (2.0 g, 82%), m.p. 150—151 °C (from aqueous ethanol) (Found: C, 45.3; H, 2.9; N, 23.3. $C_9H_7ClN_4O_2$ requires C, 45.3; H, 2.9; N, 23.5%).

Tetrazol-5-ylmethyl 2,4-Dinitrobenzoate.—Cyanomethyl 2,4-dinitrobenzoate was treated in the same way as the 4-chlorobenzoate and gave *tetrazol-5-ylmethyl 2,4-dinitrobenzoate* (8.6% yield), m.p. 198—199 °C (Found: C, 36.5; H, 1.9; N, 28.4. $C_9H_6N_6O_6$ requires C, 36.7; H, 2.0; N, 28.6%).

Bis(cyanomethyl) 4-Oxochromen-2,6-dicarboxylate (14).—The method described for the preparation of the ester (9) was applied to 4-oxochromen-2,6-dicarboxylic acid and gave the *bis(cyanomethyl)ester* (51% yield), m.p. 181—183 °C (from ethanol) (Found: C, 58.0; H, 2.9; N, 8.8. $C_{15}H_8N_2O_6$ requires C, 57.7; H, 2.6; N, 9.0%).

Reaction of Bis(cyanomethyl) 4-Oxochromen-2,6-dicarboxylate with Sodium Azide–Ammonium Chloride–DMF.—(a) *With 1 molar equivalent of reagents.* The diester (14) (5.0 g, 16 mmol), sodium azide (1.0 g, 16 mmol) and ammonium chloride (0.85 g, 16 mmol) and DMF (40 cm^3) reacted together as described above for similar reactions and produced *tetrazol-5-ylmethyl 2-carbamoyl-4-oxochromen-6-carboxylate* (15) (2.6 g, 52%), m.p. 281—282 °C (decomp.) (from ethanol) (Found: C, 49.9; H, 3.0; N, 21.8; $C_{13}H_9N_5O_5$ requires C, 49.5; H, 2.9; N, 22.2%), $\nu_{max.}$ 3 100 broad, 1 728 (ester C=O), 1 697 (amide C=O), 1 641 (pyrone C=O), and 1 612 cm^{-1}. The structure of this compound was confirmed by ^{13}C n.m.r. spectroscopy (see following paper).

(b) *With 2 molar equivalents of reagents.* The reaction described in (1) was repeated using twice as much sodium azide and ammonium chloride; the ester-amide (15) was the only product isolated.

We thank Glaxo Group Research (Ware) for financial support for one of us (H. R. W.), this Institute for a Tutorial Assistant (to P. S. B.), Mr. D. Jervis for analytical services and the S.R.C. and P.C.M.U., Harwell for mass spectrometry. We are grateful to Dr. G. J. P. Becket for preparing compounds (1), (3), and (11), and Dr. R. F. Newton for valuable discussions.

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