Studies of Chromenes. Part 5.[1] Reaction of the Vilsmeier Reagent with 7-Methoxy-2,2-dimethylchroman-4-ones. 4-Chloro-7-methoxy-2,2-dimethyl-2*H*-chromenes and their Nitration Products.

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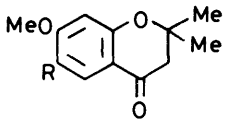
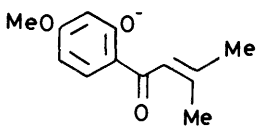
Action of the Vilsmeier reagent on 7-methoxy-2,2-dimethylchroman-4-one and its 6-bromo and 6-methoxy analogues gave low yields of 4-chlorochromene-3-carbaldehydes. 4-Chloro-2*H*-chromenes, which are not precursors of the carbaldehydes, were obtained in high yields. 4-Chloro-7-methoxy-2,2-dimethyl-6-nitrochroman was too labile to allow a dehydrogenation to the 6-nitrochlorochromene but the latter was obtained by regioselective nitration of 4-chloro-7-methoxy-2,2-dimethyl-2*H*-chromene. 6-Amino-7-methoxy-2,2-dimethylchroman-4-one, protected as the *N*-ethoxycarbonyl derivative, gave the 6-aminochlorochromene. The 6-amino-5-chloro analogue largely underwent *N*-formylation. The chlorochromenes have potential synthetic value since those without electron-withdrawing substituents are readily hydrolysed back to the chroman-4-one.

In Part 2[2] we commented on the difficulty in alkylating or acylating 7-methoxy-2,2-dimethylchroman-4-one (**1a**) at C-3 under basic conditions. The difficulty arises because of ring-opening of the carbanion to give the more stable phenolate ion (**2**). Substitution at C-3 by cationic reagents avoids this problem so that, for example, bromination of (**1a**) with an excess of reagent affords the 3,3,6-tribromo derivative (**3a**). Similarly, nitration under more forcing conditions than are required for 6-nitration[3] gave the 3,3,6-trinitro derivative (**3b**) in 89% yield. Consequently one of our attempts to functionalise C-3 had involved reaction of the Vilsmeier reagent with 7-methoxy-2,2-dimethylchroman-4-one (**1a**), our intention being to generate the 4-chloro-2*H*-chromene-3-carbaldehyde (**4a**).



(1)

a; R = H
b; R = NO_2
c; R = Br
d; R = OMe



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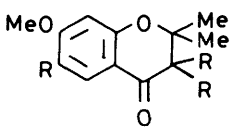
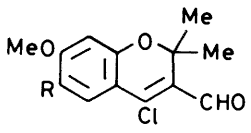


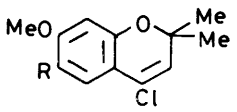
(3)

a; R = Br
b; R = NO_2



(4)

a; R = H
b; R = CHO
c; R = Br
d; R = OMe



(5)

a; R = H
b; R = CHO
c; R = Br
d; R = OMe
e; R = NO_2
f; R = NH_2

Under standard conditions[4] the action of the Vilsmeier reagent on the chromanone (**1a**) gave only minor quantities of the chlorocarbaldehyde (**4a**), the major product being the chlorochromene (**5a**). Prolonged reaction times did not increase the yield of the chlorocarbaldehyde but merely resulted in 6-formylation, giving (**4b**) and (**5b**), as shown by the presence of two singlets in the aromatic region of the ^1H n.m.r. spectra. Yields of these reactions, and of subsequent Vilsmeier reactions, are recorded in Table 1.

When the C-6 blocked bromo compound (**1c**) [prepared from (**3a**) by debromination with zinc] was treated under Vilsmeier conditions the reaction was slower, giving chlorocarbaldehyde (**4c**) as the minor and (**5c**) as the major product. Prolonged heating of (**5c**) (48 h) under the same conditions gave a quantitative recovery of starting material. Analogous results were obtained with the corresponding 6-methoxychromanone (**1d**).

The 7-methoxy activated chlorochromenes might reasonably have been expected to be intermediates in the formation of the chlorocarbaldehydes[5] but these results indicate that this is not so and that the chlorocarbaldehydes arise entirely from a

Table 1. Products and yields of Vilsmeier reactions

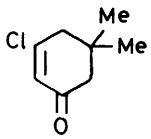
Substrate	4-Chloro-chromene (%)	3-Carbald-ehyde (%)
(**1a**)	(**5a**) (92)	(**4a**) (8)
(**1a**)*	(**5b**) (83)	(**4b**) (9)
(**1c**)	(**5c**) (88)	(**4c**) (12)
(**1d**)	(**5d**) (98)	(**4d**) (2)
(**5c**)*	(**5c**) (100)	
(**5d**)*	(**5d**) (99)	
7-Methoxy-2-methyl-chroman-4-one	4-Chloro-7-meth-oxy-2-methyl-chromene (95)	

* Prolonged reaction

precursor of the chlorochromenes, presumably an enolic derivative.

4-Chloro 3-carbaldehydes have been obtained from many C-2 unsubstituted chroman-4-ones[6] but one 2-methyl group is sufficient to block 3-formylation since 7-methoxy-2-methylchroman-4-one[7] also gave the 4-chlorochromene in high yield. Similarly the related Mannich reaction[8,9] and Vilsmeier 3-formylation of chromenes[10,11] is prevented by C-2 substitution.

The Vilsmeier reagent is highly solvated in the mildly polar solvents normally used[12] and is, therefore, particularly susceptible to steric effects. Steric hindrance is not the only factor involved however, since dimedone, a similarly β-dimethylated diketone, reacts to give the three products (**6**) (**7**), and (**8**) in equal quantities.[13] As found in the present work, the dichlorodiene was not a precursor of the aldehydes.



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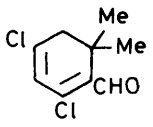

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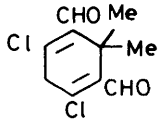
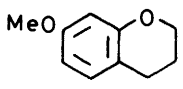


(8)

Electronic factors are also known to be important in Vilsmeier reactions. Thus, whilst 2,2-dimethyl-2*H*-chromene failed to react, the introduction of a 7-methoxy group allowed 6-formylation to take place under normal conditions.[11] Conversely, the introduction of electron-withdrawing groups inhibits both the Vilsmeier and Mannich reactions; 6-nitrochroman-4-one, for example, completely fails to undergo the Mannich reaction.[8] Aromatic formylation at C-6 of the activated chroman (**9**) has also been reported.[14] In contrast, 8-methoxy-2,2,6-trimethylchromene (**10**) failed to undergo formylation.[11] This example shows again the interplay of electronic and steric factors.



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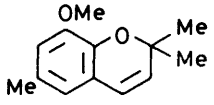
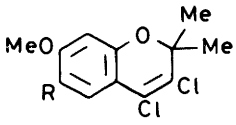


(10)

In an attempt to simplify the preparation of the chlorochromenes, the chromanone (**1a**) was treated with phosphorus pentachloride in boiling ether. No reaction ensued but the use of boiling carbon tetrachloride as solvent afforded the known 3,4-dichlorochromene (**11a**)[15] (98%). Conditions could not be found under which only the 4-chlorochromene was obtained.

There is some evidence[16] that 4-chloro-7-methoxy-2,2-dimethyl-2*H*-chromene (**5a**) acts as a synergist when used in conjunction with certain pyrethroid insectides. In view of the similar activities of the 6-amino and 6-nitro-7-methoxy-2,2-dimethyl-2*H*-chromenes previously described,[3] we undertook to synthesise the 4-chloro derivatives (**5e**) and (**5f**).

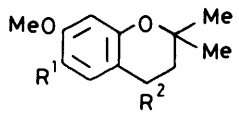


(11)

a; R = H

b; R = NO_2

6-Nitro Derivatives.—As expected from consideration of the literature, reaction of the nitrochromanone (**1b**) with the Vilsmeier reagent was completely inhibited by the 6-nitro group. The nitrochromanone was also unaffected by phosphorus pentachloride. The evident reduced basicity of the carbonyl oxygen atom of the nitrochromanone led us to consider that the 4-chlorochroman (**12a**) might have a sufficiently unreactive chlorine atom to allow its dehydrogenation to (**5e**) with dichlorodicyanobenzoquinone (DDQ). In the absence of a 6-nitro group, 4-chloro-7-methoxychromans are extremely labile so that 7-methoxy-2,2-dimethylchroman (**12b**) was readily obtained by hydrogenation/hydrogenolysis of either the chromanone (**1a**) or the chlorochromene (**5a**). The chroman (**12b**) was nitrated and benzylic chlorination of the resultant 6-nitrochroman (**12c**) attempted.



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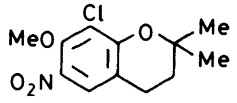


(13)

a; R^1 = NO_2, R^2 = Cl

b; R^1 = H, R^2 = H

c; R^1 = NO_2, R^2 = H

d; R^1 = NO_2, R^2 = OH

e; R^1 = NO_2, R^2 = OEt

No reaction occurred when the nitrochroman was boiled under reflux in carbon tetrachloride containing sulphuryl chloride and a little benzoyl peroxide[17] whilst the use of chlorine gave the 8-chlorochroman (**13**). This structure was deduced from the ^{1}H n.m.r. spectrum which showed just one singlet, at δ 7.65, in the aromatic region. In the unchlorinated nitrochroman (**12c**), singlets appeared at δ 6.27 and 7.56, ascribed to 8-H and 5-H respectively. Side-chain halogenation usually predominates at higher (*ca.* 180 °C) temperatures[18] but the nitrochroman (**12c**) rapidly darkened at temperatures over 100 °C.

The 4-chloronitrochroman was eventually obtained by the simultaneous addition of thionyl chloride and pyridine to a solution of the nitrochromanol[3] (**12d**) in dichloromethane at 0 °C. Despite the stabilisation afforded by the nitro group the chlorochroman (**12a**) lost hydrogen chloride too rapidly for dehydrogenation to occur; treatment with ethanol caused solvolysis to the 4-ethoxychroman (**12e**).

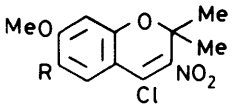
We had not initially attempted direct nitration of the chlorochromene (**5a**) because of the anticipated problem of regioselectivity, the formation of the 3,4-dichlorochromene (**11a**) with phosphorus pentachloride suggesting that nitration at C-3 might predominate. The sensitivity of chromenes towards acids dictated the use of non-acidic reagents so we first used cupric nitrate-acetic anhydride as the nitrating agent since even trimethylsilylarenes have been nitrated without protodesilylation in this medium.[19]

When 1 equiv. of cupric nitrate was used, the 3-nitro-and 3,6-dinitrochlorochromenes (**14a**) and (**14b**) were obtained but 6-mononitrated material was present only as the 3,4-dichloro derivative (**11b**) (see Table 2 for details of this and subsequent nitrations). The structures of these products were evident from ^{1}H n.m.r. spectroscopy; in particular, the position of the higher field singlet at δ 7.87 for (**11b**) showed the nitro group to occupy the 6-position. This compound was identical with that prepared by chlorination of the 6-nitrochlorochromene (**5e**). The 3,6-

Table 2. Products and yields of nitrations of the 4-chlorochromene (**1a**)

Reagent	% Yields 3-NO_2	6-NO_2	3,6-$(NO_2)_2$	Other
1 equiv. $Cu(NO_3)_2$/AA*	16	23[a]	30	
xs $Cu(NO_3)_2$/AA[b]			90	
1 equiv. $Cu(NO_3)_2/Hg^{++}$/AA			45	SM*, 52
$AgNO_3/CCl_4$/silica		30[c]	38[c]	
Transfer nitration	10[c]	46		(**11a**), 26
				(**15d**), 10
				SM, 5
1 equiv. NH_4NO_3/TFFA*		89		
		6[a]		
				(**15c**), 30
1 equiv. NH_4NO_3/AA[d]	9			(**15d**), 35
	3			SM, 16
1 equiv. NH_4NO_3/excess Cu^{++}/AA	34	19[a]		(**15c**), 17
	6			(**15d**), 6
$Pr^iONO_2/AlCl_3$		9(17[e])	28	Dimers
Pr^iONO_2/BF_3		15[a]		(**11a**), 20
				Dimers

* AA = acetic anhydride, TFFA = trifluoroacetic anhydride, SM = starting material. *a* As 3,4-dichloro compound; *b*, Forcing conditions; *c*, As chroman-4-one; *d*, Alone or in acetonitrile; *e* At −60 °C



(**14**)

a; R = H

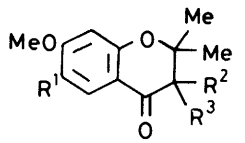
b; R = NO_2

c; R = Br

dinitrochlorochromene (**14b**) could be obtained in 90% yield under forcing conditions. The possibility that the 3,4-dichloronitrochromene (**11b**) might be converted into the 3,6-dinitrochlorochromene (**14b**) by nitrodechlorination was disproved by subjecting the dichloronitrochromene to the same reaction conditions; no dinitrochlorochromene could be detected by mass spectrometry of the crude product. Any oxidation leading to the production of Cl^+, necessary in order to rationalise the formation of the dichloro compound (**11b**), must therefore be significant only when the rate of direct nitration is relatively slow.

An attempt to prevent nitration at C-3 by complexation with mercuric ions (which have only a weak affinity for oxygen) was successful only to the extent that formation of the 3-nitrochlorochromene (**14a**) was inhibited. The formation of the dinitrochlorochromene (**14b**) suggests that 6-nitration results in much weaker binding of mercuric ions and allows subsequent 3-nitration to occur. A related attempt to inhibit reaction at C-3 was made by nitrating the chlorochromene with carbon tetrachloride and silver nitrate adsorbed on silica gel.[20] The only nitrated materials isolated were the chroman-4-ones (**15a**) and (**15b**) indicating that hydrolysis had occurred. The system was not investigated further.

The effects of the steric demands of the Vilsmeier reaction suggested that the use of a bulky nitrating reagent might provide an alternative strategy for preventing attack at C-3. We therefore used transfer nitration with 2,6-dimethyl-1-nitropyridinium tetrafluoroborate[21] and obtained the required 6-nitrochlorochromene (**5e**) in 46% yield. That the success of this strategy was only moderate led us to reconsider acyl nitrate reagents. The more reactive trifluoroacetyl nitrate,[22] used to reduce the extent of side-reactions, afforded the 6-nitrochlorochromene (**11b**) in 89% yield, no 3-nitration being observed.



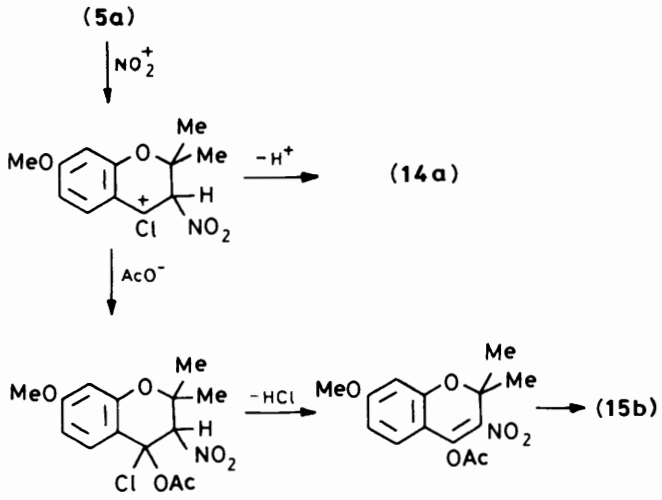
(**15**)

	R^1	R^2	R^3
a;	NO_2	NO_2	H
b;	H	H	NO_2
c;	H	Cl	Cl
d;	H	H	Cl

Large variations in isomer distribution occur when the nitration of strongly activated arenes is carried out in acetic anhydride.[23] In acidic media *para*-substitution is favoured, whilst with metal nitrates there is a pronounced tendency for *ortho*-substitution. This '*ortho*' effect has been explained in terms of co-ordination of the acyl nitrate to the activating group;[24] in acidic solution protonation competes with and prevents such co-ordination and additionally causes steric hindrance at the *ortho* position. Whilst doubt has been cast on the importance of this mechanism in the control of *ortho-para* ratios,[25] it nevertheless led us to consider that the cupric counterion may also inhibit any '*ortho*' effect by co-ordinating to the 7-methoxy group of the chlorochromene (**5a**). Control experiments showed that the absence of cupric ions did have an effect on the course of the reaction and in order to delineate the possible role of the counterion we nitrated the chlorochromene (**5a**) with 1 equiv. of ammonium nitrate in acetic anhydride containing a large excess of cupric chloride. Our expectations were realised in that the yield of 3-nitrated material was doubled whilst that of 6-nitrated material was reduced. We also nitrated the chlorochromene (**5a**) with isopropyl nitrate and Lewis acids in dichloromethane.[26,27] There were differences in the products formed when aluminium trichloride or boron trifluoride was

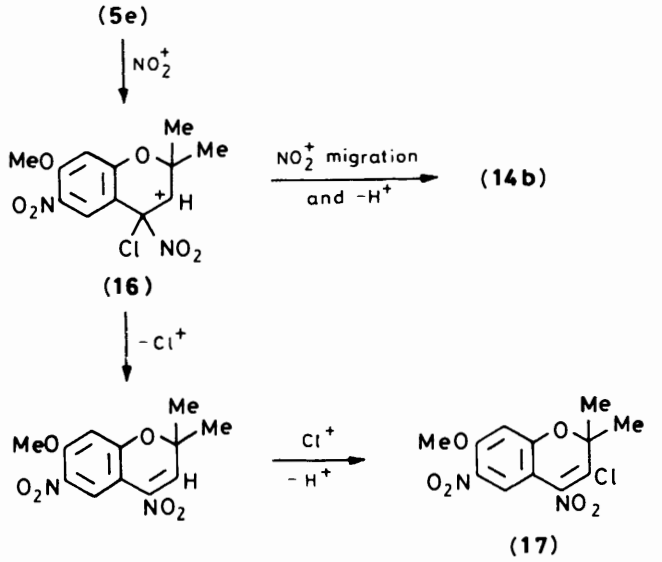
used but both led to the formation of variously nitrated and chlorinated dimers as shown by mass spectrometry.

In most of these nitrations, side-products containing a second chlorine substituent were produced. The most likely mechanism for the generation of the required Cl^+ species is shown in Scheme 1; oxidation of the hydrogen chloride liberated could



Mechanism of nitration leading to elimination of hydrogen chloride which is then oxidised to a Cl^+ species

Scheme 1.



Possible mechanism of nitration involving nitrodechlorination

Scheme 2.

lead to chlorine or to nitryl chloride, for example, which is known to generate dichloro species from alkenes.[28] Alternatively, the positive chlorine could arise by nitrodehalogenation as indicated in Scheme 2, attack at C-4 being more plausible on the less polarised 6-nitrochlorochromene (**5e**) to form the intermediate (**16**). We consider this mechanism to be unlikely since nitrodehalogenation usually requires *ortho para*-directing activation, and nitrodechlorination is rare.[29] Moreover no 4-nitrochromenes had been isolated whereas 3-nitrochromanones (Scheme 1) had. Nevertheless this possibility leads to the consideration that the dinitrochlorochromene may not have the structure (**14b**) but the alternative structure (**17**). Although the chemical shift of 5-H at δ 8.11, compared with δ 7.93 for the 6-nitrochlorochromene (**5e**), does not support structure (**17**) we sought additional proof of structure (**14b**).

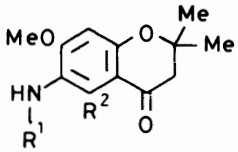
U.v. spectroscopy confirmed that the nitro group in compound (**14a**) is conjugated with the 7-methoxy group since the highest absorption band shifts from 318sh nm in the starting material (**5a**) to 382 nm in (**14a**). (Compare styrene, 282 nm; 4-methoxystyrene, 292 nm; β-nitrostyrene, 309 nm; 3-nitrostyrene, 316 nm; 4-methoxy-β-nitrostyrene, 347 nm, and 3-nitro-β-nitrostyrene, 271 nm).[30] A similar shift from 326sh to 388 nm was observed for the 6-bromo analogues (**5c**) and (**14c**). The position of this band was essentially the same (346—350 nm) for both the 6-nitro (**5e**) and 3,6-dinitro (**14b**) chlorochromenes because of competitive conjugation and was thus inconclusive evidence. Structure (**14b**) was, therefore, established by nitration of the 3-nitrochlorochromene (**14a**) to afford the dinitrochlorochromene (**14b**) in theoretical yield.

Nitration of the chlorochromene (**5a**) is clearly highly dependent on the nitrating medium. Such regioselectivity as has been achieved suggests that the exploitation of a metal ion '*ortho*' effect may be of value in controlling regioselectivity in non-acidic systems and that further study is desirable.

6-Amino Derivatives.—The 6-nitrochromene (**5e**) could not be reduced with sulphurated sodium borohydride[31] but hydrogenation of the 6-nitrochromanone (**1b**) afforded the aminochromanone (**18a**) in theoretical yield, no reduction of the carbonyl group taking place even on continued hydrogenation. The action of the Vilsmeier reagent (3 equiv.) on the unprotected amine gave the *N*-formylchromanone (**18b**) as the major product, the formylamino group being sufficiently deactivating to inhibit chlorochromene formation. Only 4% of the *N*-formylchlorochromene was formed and prolonged reaction times merely decreased the yield of recovered starting material.

When the amino group was protected with an ethoxycarbonyl group, the Vilsmeier reagent afforded the chlorochromene derivative (**19a**) in good yield (80%). The 6-aminochlorochromene (**5f**) was obtained from this derivative by alkaline hydrolysis; hydrolysis under acidic conditions gave the aminochromanone (**18a**).

The 6-nitrochromanone (**1b**) could also be reduced to the amine with stannous chloride in hydrochloric acid. A by-product (7%) of this reaction was the 6-amino-5-chlorochromanone (**18c**) formed by nucleophilic attack by chloride ion on the protonated hydroxylamine intermediate.[32] The yield of the 5-chloro derivative was raised to 68% by the standard



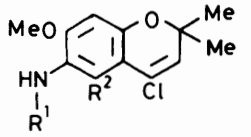
(**18**)

a; $R^1 = R^2 = H$

b; $R^1 = CHO$, $R^2 = H$

c; $R^1 = H$, $R^2 = Cl$

d; $R^1 = CO_2Et$, $R^2 = Cl$



(**19**)

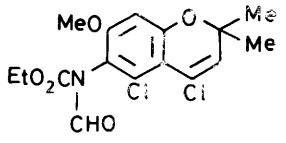
a; $R^1 = CO_2Et$, $R^2 = H$

b; $R^1 = CO_2Et$, $R^2 = Cl$

c; $R^1 = H$, $R^2 = Cl$

technique of using ethanol as co-solvent. The position of the chlorine, expected to be *ortho* to the amino group from mechanistic considerations, was established by the presence of a singlet at δ 6.29 in the ^1H n.m.r. spectrum. The original aminochromanone (**18a**) showed signals at δ 7.10 and 6.27 ascribed to C-5 and C-8 respectively.

The *N*-ethoxycarbonyl derivative (**18d**) of the 5-chlorochro-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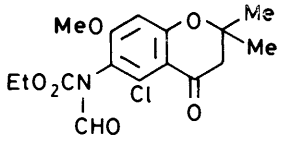
(21)

manone afforded the 4-chlorochromene (**19b**) to only a minor extent (13%), although the *N*-formyl-chlorochromene (**20**) was also isolated (8%). The major product was the *N*-formyl-chromanone (**21**), obtained in 53% yield. We attribute this behaviour to the reduced conjugation of the nitrogen lone-pair with the aromatic ring which is enforced by the two *ortho* substituents in (**18d**). Alkaline hydrolysis of the 4-chloro-chromenes (**19b**) and (**20**) afforded the aminochlorochromene (**19c**).

The 4-chlorochromenes described here are of potential synthetic value since, being vinylogous enol ethers, they are hydrolysed under acidic conditions to the corresponding chromanones. The more reactive 4-chlorochromenes are hydrolysed rapidiy, and those possessing electron withdrawing groups (6-nitro, 6-formyl) are resistant. We have shown that electrophilic substitution of the chlorochromenes can be carried out with some selectivity and it follows that these derivatives, as chromanone equivalents, may allow the difficulties encountered with chromanones to be circumvented. The scope of such reactions is under investigation.

Experimental

M.p.s are uncorrected. I.r. spectra were recorded on a Hilger and Watts Infrascan. U.v. spectra were determined with a Perkin-Elmer Model 137 spectrometer. Routine (60 MHz) n.m.r. spectra were obtained on a Varian EM 360 or Perkin-Elmer R24 machine with tetramethylsilane as internal standard and 300 MHz spectra on a Brüker WM 300 WB spectrometer. Mass spectra were obtained on a MS9 instrument. Homogeneity of non-crystalline compounds was established by t.l.c. in at least three solvent systems of differing polarities. Ether refers to diethyl ether. Light petroleum refers to that fraction with b.p. 40—60 °C.

3,3,6-*Tribromo*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**3a**).—7-Methoxy-2,2-dimethylchroman-4-one (0.421 g, 2.04 mmol) in carbon tetrachloride (20 ml) was treated dropwise with bromine (1.10 g, 6.15 mmol) in carbon tetrachloride (20 ml) and the resultant solution was allowed to stand overnight. The solution was then filtered through a short column of alumina and the solvent removed. Chromatography of the resultant red gum on silica gel afforded the title tribromochromanone (**3a**) (0.897 g, 100%) as colourless *needles*, m.p. 161—162 °C (chloroform–light petroleum); $\nu_{max.}$(KBr) 1 697, 1 604, and 1 570 cm^{-1}; $\lambda_{max.}$(EtOH) 215 (ε 26 400 dm^3 mol^{-1} cm^{-1}), 236 (18 800), 281 (14 150), and 333 nm (8 400); δ(CCl_4) 1.74 (6 H, s), 3.90 (3 H, s), 6.33 (1 H, s), and 7.99 (1 H, s) (Found: C, 32.65; H, 2.35%; M^+, 439.8265. $C_{12}H_{11}Br_3O_3$ requires C, 32.54; H, 2.50%; *M*, 439.8259).

6-*Bromo*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**1c**).—The above tribromochromanone (0.89 g, 2.00 mmol) was stirred overnight at room temperature in ether (30 ml) containing water and acetic acid (each 2 drops) and an excess of zinc powder (0.30 g, 4.6 mmol). The mixture was filtered through a short column of alumina and the solvent removed. The resultant homogeneous (t.l.c.) oil (0.567 g, 100%) was the title monobromochromanone, (**1c**) obtained as colourless needles, m.p. 86—90 °C → prisms, m.p. 97 °C (light petroleum) (lit.,[33] m.p. 96—97 °C); $\nu_{max.}$(KBr) 1 673, 1 600, and 1 565 cm^{-1}; $\lambda_{max.}$(EtOH) 221 (ε 16 750 dm^3 mol^{-1} cm^{-1}), 238 (16 000), 269 (11 000), and 324 nm (4 900); δ(CCl_4) 1.38 (6 H, s), 2.50 (2 H, s), 3.80 (3 H, s), 6.21 (1 H, s), and 7.71 (1 H, s) (Found: C, 50.45; H, 4.5%; M^+, 284.0060. Calc. for $C_{12}H_{13}BrO_3$: C, 50.54; H, 4.59%; *M*, 284.0048).

7-*Methoxy*-2,2-*dimethyl*-3,3,6-*trinitrochroman*-4-*one* (**3b**).—7-Methoxy-2,2-dimethylchroman-4-one (**1a**) (1.50 g, 7.28 mmol) in acetic anhydride (10 ml) was treated with finely ground cupric nitrate trihydrate (3.0 g, 12.4 mmol) and the mixture stirred overnight at 100 °C. The dark solution was poured into water (100 ml) and stirred for 30 min. The precipitate was collected by filtration, dissolved in chloroform and passed through a short column of alumina. Removal of the solvent left a pale yellow solid which afforded the trinitrochromanone (**3b**) (2.2 g, 89%) as pale yellow *needles*, m.p. 147—148 °C (ethanol); $\nu_{max.}$(KBr) 1 716, 1 703sh, 1 621, and 1 567 cm^{-1}; $\lambda_{max.}$(EtOH) 218 (ε 15 100 dm^3 mol^{-1} cm^{-1}), 263 (17 500), 238sh, (15 200), and 321 nm (6 600); δ($CDCl_3$) 1.89 (6 H, s), 4.07 (3 H, s), 6.70 (1 H, s), and 8.63 (1 H, s) (Found: C, 42.0; H, 3.1; N, 12.1%; M^+, 341.0512. $C_{12}H_{11}N_3O_9$ requires C, 42.24; H, 3.25; N, 12.31%; *M*, 341.0495).

General Procedure for Reaction of Chromanones and 4-*Chlorochromenes with the Vilsmeier Reagent*.—Phosphorus oxychloride (0.454 ml, 5.0 mmol) and dry dimethylformamide (0.387 ml, 5.0 mmol) were added to dry solvent (dichloromethane, carbon tetrachloride, or trichloroethylene, 20 ml) and the solution stirred at room temperature for 10 min. A solution of the chromanone or chlorochromene (3.33 mmol) in the same solvent (20 ml) was added, and the solution was boiled under reflux until starting material had disappeared (t.l.c.). The mixture was allowed to cool and then poured onto saturated aqueous sodium acetate (20 ml). The lower layer was removed and the aqueous layer extracted twice with dichloromethane (20 ml). The combined extracts were washed with water, dried ($MgSO_4$), and evaporated to give a yellow oil which was subjected to silica-gel chromatography. The chlorochromene was eluted first, any 4-chlorochromene-3-carbaldehyde being then eluted as a bright yellow, highly fluorescent band.

If the 4-chlorochromene-3-carbaldehyde is not required, the sodium acetate work-up can be omitted and the concentrated reaction mixture merely passed through silica gel in dichloromethane. The following 4-chlorochromenes and 4-chlorochromene-3-carbaldehydes were thus obtained.

4-*Chloro*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene* (**5a**). A homogeneous (t.l.c.) colourless *oil* (92%); $\nu_{max.}$(film) 1 633 and 1 615 cm^{-1}; $\lambda_{max.}$(EtOH) 218 (ε 16 000 dm^3 mol^{-1} cm^{-1}), 232sh (12 000), 275 (4 800), 285 (4 700), 309 (4 900), and 318sh (4 200); δ($CDCl_3$) 1.40 (6 H, s), 3.69 (3 H, s), 5.53 (1 H, s), 6.30 (1 H, d, *J* 2 Hz), 6.48 (1 H, dd, *J* 8 and 2 Hz), and 7.28 (1 H, d, *J* 8 Hz) (Found: M^+, 224.0606. $C_{12}H_{13}ClO_2$ requires *M*, 224.0604).

4-*Chloro*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene*-3-*carbaldehyde* (**4a**). A homogeneous (t.l.c.) bright yellow *oil* (8%); $\nu_{max.}$($CHCl_3$) 1 666, 1 615, 1 596, and 1 588 cm^{-1}; δ($CDCl_3$) 1.56 (6 H, s), 3.71 (3 H, s), 6.12 (1 H, d, *J* 2 Hz), 6.33 (1 H, dd, *J* 8 and 2 Hz), 7.34 (1 H, d, *J* 8 Hz), and 9.91 (1 H, s) (Found: M^+, 252.0568. $C_{13}H_{13}ClO_3$ requires *M*, 252.0553). The DNP was obtained as crimson needles, m.p. 246—247 °C (ethanol) (Found: C, 52.8; H, 3.9; N, 13.0%; M^+ 432.0847. $C_{19}H_{17}N_4ClO_6$ requires C, 52.72; H, 3.96; N, 12.95%; *M*, 432.0836).

6-*Bromo*-4-*chloro*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene* (**5c**). Colourless *needles* (88%) m.p. 107—108 °C (aq. ethanol); $\nu_{max.}$(KBr) 1 630, 1 614sh, and 1 605 cm^{-1}; $\lambda_{max.}$(EtOH) 226 (ε 28 550 dm^3 mol^{-1} cm^{-1}), 232sh (26 700), 240sh (20 670), 276 (14 040), 287sh (11 570), 315 (7 100), and 326sh nm (5 860); δ($CDCl_3$) 1.39 (6 H, s), 3.74 (3 H, s), 5.43 (1 H, s), 6.17 (1 H, s), and

7.32 (1 H, s) (Found: C, 47.35; H, 3.85%; M^+, 301.9722. $C_{12}H_{12}BrClO_2$ requires C, 47.47; H, 3.99% M, 301.9709).

6-Bromo-4-chloro-7-methoxy-2,2-dimethyl-2H-chromene-3-carbaldehyde (**4c**). Yellow *plates* (12%), m.p. 126—127 °C (ethanol); $\nu_{max.}$(KBr) 1 670, 1 600, 1 587, and 1 541 cm^{-1}; $\lambda_{max.}$(EtOH) 209 (ε 8 800 dm^3 mol^{-1} cm^{-1}), 257sh (9 700), 263 (10 600), 302sh (3 950), 311 (4 650), and 377 nm (5 500); δ($CDCl_3$) 1.57 (6 H, s), 3.83 (3 H, s), 6.20 (1 H, s), 7.60 (1 H, s), and 10.01 (1 H, s) (Found: C, 47.1; H, 3.5%; M^+ 329.9658. $C_{13}H_{12}BrClO_3$ requires C, 47.08; H, 3.65%; M, 329.9661).

4-Chloro-6,7-dimethoxy-2,2-dimethyl-2H-chromene (**5d**). Colourless *needles* (98%), m.p. 62—63 °C (ethanol); $\nu_{max.}$(KBr) 1 628, 1 613, and 1 574 cm^{-1}; $\lambda_{max.}$(EtOH) 217 (ε 16 300 dm^3 mol^{-1} cm^{-1}), 231 (19 850), 276 (3 250), 280sh (2 750), 328 (7 350), and 345sh nm (3 500); δ($CDCl_3$) 1.41 (6 H, s) 3.78 (3 H, s), 5.49 (1 H, s), 6.25 (1 H, s), and 6.80 (1 H, s) (Found: C, 61.3; H, 6.0%; M^+, 254.0742. $C_{13}H_{15}ClO_3$ requires C, 61.30; H, 5.94%; M, 254.0710.

4-Chloro-6,7-dimethoxy-2,2-dimethyl-2H-chromene-3-carbaldehyde (**4d**) A bright yellow homogeneous *oil* (2%); δ($CDCl_3$, 300 MHz/FT) 1.62 (6 H, s), 3.87 (6 H, s), 3.90 (3 H, s), 6.40 (1 H, s), 7.12 (1 H, s), and 10.18 (1 H, s) (Found: M^+, 282.0665. $C_{14}H_{15}ClO_4$ requires M, 282.0659).

4-Chloro-7-methoxy-2-methyl-2H-chromene. A colourless homogeneous (t.l.c.) *oil* (88%); $\nu_{max.}$(film) 1 615, 1 570, and 1 500 cm^{-1}; $\lambda_{max.}$(EtOH) 218 (ε 19 000 dm^3 mol^{-1} cm^{-1}), 228 (17 000), 273 (8 300), 281sh (7 600), and 308 nm (7 900); δ($CDCl_3$) 1.39 (3 H, d, J 6 Hz), 3.75 (3 H, s), 5.00 (H, dq, J 6 and 3 Hz), 5.62 (1 H, d, J 3 Hz), 6.40—6.50 (2 H, m), and 7.30 (1 H, d, J 9 Hz) (Found: M^+, 210.0438. $C_{11}H_{11}ClO_2$ requires M, 210.0448).

Extended Reaction with the Vilsmeier Reagent.—(*a*) *With 7-methoxy-2,2-dimethylchroman-4-one* (**1a**). The above chromanone was boiled with an excess of the Vilsmeier reagent in trichloroethylene for 36 h. Work-up and chromatography on silica gel (light petroleum-dichloromethane) afforded two components.

The first was *4-chloro-6-formyl-7-methoxy-2,2-dimethyl-2H-chromene* (**5b**) (83%), colourless needles, m.p. 119—120 °C (aq. ethanol); $\nu_{max.}$(KBr) 1 672, 1 631, 1 613, and 1 510 cm^{-1}; $\lambda_{max.}$(EtOH) 219sh (ε 13 650 dm^3 mol^{-1} cm^{-1}), 255 (32 400), 307sh (5 100), and 342 nm (7 300); δ($CDCl_3$) 1.62 (6 H, s), 3.98 (3 H, s), 5.74 (1 H, s), 6.43 (1 H, s), 7.92 (1 H, s), and 10.23 (1 H, s) (Found: C, 61.75; H, 5.15%; M^+, 252.0553. $C_{12}H_{13}ClO_3$ requires C, 61.79; H, 5.18%; M, 252.0553).

The second was *4-chloro-3,6-diformyl-7-methoxy-2,2-dimethyl-2H-chromene* (**4b**) (9%), yellow prisms, m.p. 140—141 °C (aq. ethanol); $\nu_{max.}$($CHCl_3$) 1 677 and 1 605 cm^{-1}; $\lambda_{max.}$(EtOH) 206sh (ε 2 050 dm^3 mol^{-1} cm^{-1}), 230 (4 000), 274 (9 700), and 356 nm (3 850); δ($CDCl_3$) 1.62 (6 H, s), 3.86 (3 H, s), 6.26 (1 H, s), 8.02 (1 H, s), 9.97 (1 H, s), and 10.05 (1 H, s) (Found: C, 59.8; H, 4.75%; M^+, 280.0507. $C_{14}H_{13}ClO_4$ requires C, 59.90; H, 4.67%; M, 280.0502).

(*b*) Extended treatment of the chlorochromenes (**5c**) and (**5d**) (56 h) did not lead to reaction, starting material being recovered unchanged (t.l.c., n.m.r., and u.v.). The chlorochromene (**5a**) afforded only the 6-formyl derivative (**5b**). 7-Methoxy-2,2-dimethyl-6-nitrochroman-4-one (**1b**) did not react and was recovered unchanged (t.l.c., n.m.r.).

The Action of Phosphorus Pentachloride on Chromanones.—(*a*) The chromanone (**1a**) (0.314 g, 1.5 mmol) in dry ether (20 ml) was treated with phosphorus pentachloride (0.32 g, 1.5 mmol) and the mixture stirred at 20 °C. After 2 h no reaction had occurred (t.l.c., n.m.r.).

(*b*) The experiment was repeated using carbon tetrachloride as the solvent. The mixture was boiled under reflux for 4 h then concentrated and chromatographed on silica gel (benzene as eluant) to give 3,4-dichloro-7-methoxy-2,2-dimethyl-*2H*-chromene[15] (**11a**) (0.386 g, 98%) as a homogeneous (t.l.c.) oil; δ($CDCl_3$) 1.56 (6 H, s), 3.76 (3 H, s), 6.36 (1 H, d, J 2 Hz), 6.43 (1 H, dd, J 8 and 2 Hz), and 7.31 (1 H, d, J 8 Hz) (Found: M^+, 258.0232. Calc. for $C_{12}H_{18}Cl_2O_2$: M, 258.0214).

(*c*) The experiment was repeated at several temperatures below the boiling point of carbon tetrachloride. No conditions could be found which led to formation of the 4-chlorochromene (**7**) without further chlorination.

(*d*) The nitrochromanone (**1b**) (0.320 g, 1.27 mmol) and phosphorus pentachloride (0.33 g, 1.3 mmol) in carbon tetrachloride (20 ml) were boiled under reflux for 15 h. After chromatography on alumina (carbon tetrachloride as eluant) a brown residue was obtained which was essentially starting material (t.l.c., n.m.r. and mass spectrometry).

7-Methoxy-2,2-dimethylchroman (**12b**).[14]—A solution of the chlorochromene (**7**) (1.20 g, 5.36 mmol) in ethanol (50 ml) was hydrogenated at room temperature over platinum. When 1 equiv. of hydrogen had been absorbed, n.m.r. spectroscopy showed the presence of starting material (43%), 7-methoxy-2,2-dimethylchroman (**12b**) (49%), and a little 4-chlorochroman (8%). Further hydrogenation gave the chroman (**12b**) as a homogeneous (t.l.c.) oil (100%); $\lambda_{max.}$(EtOH) 230 (ε 6 200 dm^3 mol^{-1} cm^{-1}), 286 (5 500), and 291 nm (5 000); δ($CDCl_3$) 1.30 (6 H, s), 1.71 (2 H, t, J 7 Hz), 2.66 (2 H, t, J 7 Hz), 3.70 (3 H, s), 6.27 (1 H, d, J 2 Hz), 6.30 (1 H, dd, J 8 and 2 Hz), and 6.85 (1 H, d, J 8 Hz) (M^+, 192. Calc. for $C_{12}H_{16}O_2$: M, 192).

7-Methoxy-2,2-dimethyl-6-nitrochroman (**12c**).—Finely ground cupric nitrate trihydrate (2.23 g) was added over 20 min to a solution of the chroman (**12b**) (1.47 g, 7.65 mmol) in acetic anhydride (20 ml) at 50 °C. The mixture was stirred at 60 °C for a further 1 h and then poured into water (200 ml) and stirred for 30 min. The aqueous layer was decanted leaving a black oil which was washed with water (2 × 50 ml), decanted, dissolved in chloroform, dried ($MgSO_4$), and passed through a short alumina column before being chromatographed on silica gel (chloroform as eluant) to yield the pale yellow title *nitrochroman* (**12c**) (1.44 g, 80%), m.p. 91—92 °C (from ethanol); $\nu_{max.}$(KBr) 1 625, 1 570, and 1 510 cm^{-1}; δ($CDCl_3$) 1.32 (6 H, s), 1.80 (2 H, t, J 6 Hz), 2.74 (2 H, t, J, 6 Hz), 3.80 (3 H, s), 6.27 (1 H, s), and 7.56 (1 H, s) (Found: C, 60.8; H, 6.55; N, 6.0%; M^+ 237.1019. $C_{12}H_{15}NO_4$ requires C, 60.75; H, 6.37; N, 5.91%; M, 237.1001).

Chlorination of the Nitrochroman (**12c**).—(*a*) *With sulphuryl chloride.* The nitrochroman (0.05 g, 0.21 mmol) and benzoyl peroxide (0.002 g) in carbon tetrachloride (10 ml) were treated with sulphuryl chloride (0.03 g, 0.22 mmol) and the mixture boiled under reflux for 2 h. No change was detected by t.l.c. or n.m.r.

(*b*) *With chlorine.* A solution of the nitrochroman (**12c**) (0.06 g, 2.5 mmol) in carbon tetrachloride (10 ml) containing a trace of benzoyl peroxide was treated with an excess of chlorine and left at 60 °C overnight. Removal of the solvent followed by chromatography on silica gel (chloroform as eluant) afforded *8-chloro-7-methoxy-2,2-dimethyl-6-nitrochroman* (**13**) (0.05 g, 84%), pale yellow crystals, m.p. 59—60 °C (from light petroleum); δ($CDCl_3$) 1.41 (6 H, s), 1.90 (2 H, t, J 6 Hz), 2.87 (2 H, t, J 6 Hz), 4.00 (3 H, s), and 7.65 (1 H, s) (Found: M^+, 271.0620. $C_{12}H_{14}ClNO_4$ requires M, 271.0611).

4-Chloro-7-methoxy-2,2-dimethyl-6-nitrochroman (**12a**).—To a stirred solution of the nitrochromanol (**12d**) (0.1 g, 0.395 mmol) in dry dichloromethane (10 ml) at 0 °C were added dropwise both dry pyridine (0.027 ml, 0.395 mmol) and thionyl chloride (0.042 ml, 0.395 mmol), each in dry dichloromethane (1 ml). Stirring was continued for 1 h at 20 °C and the solution then washed rapidly with ice-water, dried ($MgSO_4$), and

evaporated at 20 °C to afford crude product (0.066 g, 66%) as a solid which lost hydrogen chloride, both with time and on attempted silica-gel chromatography. Recrystallisation from dry, light petroleum–dichloromethane (charcoal) gave pure 4-*chloro*-7-*methoxy*-2,2-*dimethyl*-6-*nitrochroman* (**12a**), m.p. 122—123 °C; $\nu_{max.}$(KBr) 1 628, 1 615, and 1 517 cm^{-1}; $\lambda_{max.}$ (light petroleum) 227 (ε 11 900 dm^3 mol^{-1} cm^{-1}), 272 (5 400), and 313 nm (4 000); δ($CDCl_3$) 1.36 (3 H, s), 1.56 (3 H, s), 2.32 (2 H, m), 3.91 (3 H, s), 5.21 (1 H, m, 4-H), 6.43 (1 H, s), and 8.20 (1 H, s) (Found: C, 53.3; H, 5.1; N, 5.05%; M^+, 271.060 20. $C_{12}H_{14}ClNO_4$ requires C, 53.04; H, 5.19; N, 5.16%; *M*, 271.0611).

4-*Ethoxy*-7-*methoxy*-2,2-*dimethyl*-6-*nitrochroman* (**12e**).—A solution of the chlorochroman (**12a**) in absolute ethanol was warmed to 60 °C and on cooling yielded the title ethoxychroman in theoretical yield as pale yellow *needles*, m.p. 79—80 °C; $\nu_{max.}$(KBr) 1 622, 1 570, and 1 510 cm^{-1}; $\lambda_{max.}$(EtOH) 210 (ε 14 300 dm^3 mol^{-1} cm^{-1}), 220 (15 450), 245 (8 850), 288 (6 200), and 333 nm (7 450); δ($CDCl_3$) 1.23 (3 H, t), 1.34 (3 H, s), 1.42 (3 H, s), 1.93 (2 H, m), 3.20 (2 H, q), 4.33 (1 H, m), 6.25 (1 H, s), and 7.60 (1 H, s) (Found: C, 59.75; H, 6.8; N, 5.0%; M^+, 281.1288. $C_{14}H_{19}NO_5$ requires C, 60.75; H, 6.75; N, 5.06%; *M*, 281.1263).

Attempted Dehydrogenation of the 4-*Chlorochroman* (**12a**).—To the chlorochroman (**12a**) (0.08 g, 0.295 mmol) in dry benzene (10 ml) was added DDQ (0.067 g, 0.295 mmol) and the mixture was stirred at room temperature for 2 h. Filtration of the dark solution gave a mixture of starting material and the nitrochromene (*ca.* 1:1 by n.m.r., compared with authentic material). No chlorochromene was detected by n.m.r. or mass spectrometry.

Nitration of the 4-*Chlorochromene* (**5a**).—(a) *With cupric nitrate (1 equiv.) in acetic anhydride.* A solution of the chlorochromene (**5a**) (0.225 g, 1.0 mmol) in acetic anhydride (5 ml) was stirred with a suspension of cupric nitrate trihydrate (0.120 g, 0.5 mmol) in acetic anhydride (5 ml) at 0 °C for 1 h and then allowed to reach room temperature overnight. The mixture was poured into ice–water (50 ml) and stirred for 1 h and then extracted with dichloromethane. The organic layer was washed with water (2 × 10 ml) and aqueous sodium hydrogen carbonate (2 × 10 ml), dried ($MgSO_4$), and evaporated to afford a yellow oil which was chromatographed on silica gel (light petroleum–dichloromethane as eluant) to give three components.

The first component was 4-*chloro*-7-*methoxy*-2,2-*dimethyl*-3-*nitro*-2H-*chromene* (**14a**) (0.032 g, 16%), bright yellow needles, m.p. 80—81 °C (from ethanol), $\nu_{max.}$(KBr) 1 633sh, 1 615, 1 537sh, 1 523, and 1 508 cm^{-1}; $\lambda_{max.}$(EtOH) 212 (ε 23 500 dm^3 mol^{-1} cm^{-1}), 262 (6 350), 288 (6 000), 316 (4 900), and 382 nm (4 150); δ($CDCl_3$) 1.59 (6 H, s), 3.70 (3 H, s), 6.24 (1 H, d, *J* 2 Hz), 6.39 (1 H, dd, *J* 8 and 2 Hz), and 7.27 (1 H, d, *J* 8 Hz) (Found: C, 53.6; H, 4.5; N, 5.3%; M^+, 269.0467. $C_{12}H_{12}ClNO_4$ requires C, 53.44; H, 4.49; N, 5.19%; *M*, 269.0455).

The second component was 3,4-*dichloro*-7-*methoxy*-2,2-*dimethyl*-6-*nitro*-2H-*chromene* (**11b**) (0.070 g, 23%), pale yellow needles (darkening in light), m.p. 104—105 °C (from ethanol); $\lambda_{max.}$(EtOH) 231 (ε 20 250 dm^3 mol^{-1} cm^{-1}), 269 (20 000), 302sh (7 950), and 350 nm (4 500); δ($CDCl_3$) 1.57 (6 H, s), 3.85 (3 H, s), 6.39 (1 H, s), and 7.86 (1 H, s) (Found: C, 47.45; H, 3.6; N, 4.7%; M^+, 303.0086. $C_{12}H_{11}Cl_2NO_4$ requires C, 47.39; H, 3.65; N, 4.61%; *M*, 303.0065). Identical material was prepared by chlorination of the 6-nitrochlorochromene (**5e**), see later.

The third component was 4-*chloro*-7-*methoxy*-2,2-*dimethyl*-3,6-*dinitro*-2H-*chromene* (**14b**) (0.095 g, 30%), deep yellow plates, m.p. 110—111 °C (ethanol); $\nu_{max.}$(KBr) 1 615 and 1 562 cm^{-1}; $\lambda_{max.}$(EtOH) 234 (ε 15 450 dm^3 mol^{-1} cm^{-1}), 263 (1 685), and 346 nm (6 300); δ($CDCl_3$) 1.69 (6 H, s), 4.00 (3 H, s), 6.57 (1 H, s), and 8.11 (1 H, s) (Found: C, 45.8; H, 3.3; N, 8.75%; M^+, 314.0307. $C_{12}H_{11}ClN_2O_6$ requires C, 45.80; H, 3.50; N, 8.90%; *M*, 314.0306).

(b) *With cupric nitrate (excess) in acetic anhydride.* A solution of the chlorochromene (**5a**) (0.530 g, 2.366 mmol) in acetic anhydride (5 ml) was added to a suspension of cupric nitrate trihydrate (1.05 g, 4.34 mmol) in acetic anhydride (2 ml) and the mixture was stirred at 60 °C for 2 h. Work-up as before, followed by chromatography, yielded the 3,6-dinitro-chlorochromene (**14b**) (0.673 g, 90%).

(c) *In the presence of mercuric chloride.* The chlorochromene (**5a**) (0.18 g, 0.8 mmol) and mercuric chloride (0.217 g, 0.8 mmol) were stirred in ethyl acetate (10 ml) until a clear solution was obtained. Acetic anhydride (10 ml) was added and the ethyl acetate removed by evaporation. The resultant clear solution was treated with cupric nitrate trihydrate (0.098 g, 0.4 mmol) and the mixture stirred at 20 °C overnight. Work-up and chromatography afforded starting material (0.093 g, 52%) and the 3,6-dinitrochlorochromene (**14b**) (0.113 g, 45%), (by t.l.c., n.m.r. and mass spectrometry).

(d) *With carbon tetrachloride and silver nitrate on silica gel.* Silver nitrate was adsorbed onto silica gel as described by Gordon.[20] An excess of the treated silica (*ca.* 5 g) was covered with carbon tetrachloride and the mixture allowed to stand at room temperature for 20 min. The chlorochromene (**5a**) (0.07 g, 0.31 mmol) in carbon tetrachloride (5 ml) was then added and the mixture left in the dark at room temperature for 18 h. Organic material was washed from the silica with dichloromethane and solvents removed to give a yellow oil which was chromatographed on silica gel (dichloromethane as eluant) to give two fractions.

The first fraction consisted of 7-*methoxy*-2,2-*dimethyl*-3,6-*dinitrochroman*-4-*one* (**15a**) (0.033 g, 38%) as a pale yellow homogeneous (t.l.c.) gum; $\nu_{max.}$(film) 1 698, 1 618, and 1 560 cm^{-1}; δ($CDCl_3$) 1.54 (3 H, s), 1.63 (3 H, s), 3.98 (3 H, s), 4.98 (1 H, s), 6.47 (1 H, s), and 8.27 (1 H, s), (Found: M^+, 296.0657. $C_{12}H_{12}N_2O_7$ requires *M*, 296.0643).

The second fraction was 7-*methoxy*-2,2-*dimethyl*-6-*nitrochroman*-4-*one* (**1b**) (0.028, 30%) (by t.l.c., n.m.r. and mass spectrometry with authentic material).

(e) *By transfer nitration.* Nitronium tetrafluoroborate (0.323 g, 1.70 mmol) was stirred at 0 °C in dry acetonitrile (2 ml) whilst dry 2,6-lutidine (2,6-dimethylpyridine) (0.197 ml, 1.70 mmol) in dry acetonitrile (2 ml) was added over 10 min. The mixture was stirred for a further 15 min and then a solution of chlorochromene (**5a**) (0.380 g, 1.70 mmol) in dry acetonitrile (2 ml) was added over 30 min. Removal of the solvent from the yellow solution left a black oil which was chromatographed on silica gel (light petroleum–dichloromethane, 1:1, as eluant). From the column was eluted 3,4-dichloro-7-methoxy-2,2-dimethyl-2*H*-chromene (**11a**) (0.114 g, 26%), identical (t.l.c., n.m.r. and mass spectrometry) with material obtained earlier. The main product was 4-*chloro*-7-*methoxy*-2,2-*dimethyl*-6-*nitro*-2H-*chromene* (**5e**) (0.210 g, 46%), pale yellow needles, m.p. 172—173 °C (from ethanol); $\nu_{max.}$(KBr) 1 638sh, 1 625, 1 565, 1 519, and 1 511sh cm^{-1}; $\lambda_{max.}$(EtOH) 227 (ε 16 500 dm^3 mol^{-1} cm^{-1}), 233sh (15 000), 262 (13 950), 303sh (4 050), and 350 nm (3 900); δ($CDCl_3$) 1.46 (6 H, s), 3.86 (3 H, s), 5.67 (1 H, s), 6.36 (1 H, s), and 7.93 (1 H, s) (Found: C, 53.6; H, 4.5; N, 5.1%; M^+, 269.0448. $C_{12}H_{12}ClNO_4$ requires C, 53.44; H, 4.49; N, 5.19%; *M*, 269.0455).

Also eluted was a mixture of a little 3-chlorochromanone (**15d**) and 3-nitrochromanone (**15b**) (each *ca.* 10%) as suggested by mass spectrometry (*m/z* 240/242 and 251) and n.m.r. [δ 1.53 and 1.60 (each 3 H, s), 3.79 (3 H, s), 4.24 (1 H, s), 6.2—6.7 (2 H, two sets of dd and d), and 7.6—7.8 (two sets of d, *J* 8 Hz)].

(f) *With ammonium nitrate and trifluoroacetic anhydride.* Chlorochromene (**5a**) (0.276 g, 1.23 mmol) in dry acetonitrile (10

ml) was stirred at −15 °C and trifluoroacetic anhydride (2 ml) added. Finely ground ammonium nitrate (0.100 g, 1.24 mmol) was added in one lot and the mixture stirred at −15 °C for 1 h and then allowed to reach room temperature over 30 min. The product was concentrated and chromatographed on silica gel (light petroleum–dichloromethane, 1:1, as eluant).

From the column was eluted 4-chloro-7-methoxy-2,2-dimethyl-6-nitro-2*H*-chromene (**5e**) (0.291 g, 89%), identical (t.l.c. and n.m.r.) with material obtained earlier. Also eluted was 3,4-dichloro-7-methoxy-2,2-dimethyl-6-nitro-2*H*-chromene (**11b**) (0.023 g, 6%) identical (t.l.c., n.m.r.) with material previously obtained. Mass spectrometry of the residual material revealed a little trinitrochromene (*m/z* 325) and un-nitrated dichlorochromene (*m/z* 240).

(g) *With ammonium nitrate and acetic anhydride in the presence of an excess of cupric ions.* Anhydrous cupric chloride (2.55 g, 18.9 mmol) was stirred in acetic anhydride (10 ml) at 100 °C for 15 min and the mixture allowed to cool. Chlorochromene (**5a**) (0.423 g, 1.89 mmol) was added and then finely ground ammonium nitrate (0.151 g, 1.89 mmol) was added over 30 min. The suspension was left at 5 °C overnight and then worked up in the usual way. Chromatography on silica gel (light petroleum–dichloromethane, 1:1, as eluant) afforded the 3-nitrochlorochromene (**14a**) (0.130 g, 34%) and 3,4-dichloro-6-nitrochromene (**11b**) (0.108 g, 19%). Also eluted were 3,3-*dichloro*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**15c**) (0.090 g, 17%); δ 1.62 (6 H, s), 3.77 (3 H, s), 6.29 (1 H, d, *J* 2 Hz), 6.54 (1 H, dd, *J* 8 and 2 Hz), and 7.73 (1 H, d, *J* 8 Hz) (Found: M^+, 274.0199. $C_{12}H_{12}Cl_2O_3$ requires *M*, 274.0163) and a mixture of 3-chloro-7-methoxy-2,2-dimethylchroman-4-one (**15d**) and 7-methoxy-2,2-dimethyl-3-nitrochroman-4-one (**15b**) (tog. 0.051 g, 13%) as described earlier.

(h) *With ammonium nitrate and acetic anhydride.* Chlorochromene (**5a**) (0.140 g, 0.625 mmol) in acetic anhydride (3 ml) was stirred at room temperature with finely ground ammonium nitrate (0.050 g, 0.625 mmol) for 20 h. Work-up gave material which n.m.r. revealed to contain *ca.* 10% of the 3-nitrochlorochromene (**14a**), eluted from a silica gel column (0.015 g, 9%). N.m.r. and m.s. revealed the residual material to contain chloro- (**15d**), dichloro- (**15c**), and nitro chromanone (**15b**). When the reaction was repeated with acetonitrile (10 ml) as solvent essentially the same result was obtained.

(i) *With isopropyl nitrate and Lewis acids.* Aluminium trichloride (0.072 g, 0.54 mmol) was crushed under dry dichloromethane (10 ml) and isopropyl nitrate (0.052 ml, 0.54 mmol) added. The mixture was stirred at room temperature until a clear solution was obtained (30 min). Chlorochromene (**5a**) (0.121 g, 0.54 mmol) in dry dichloromethane (5 ml) was added in one lot and the resultant dark blue-black solution stirred for 30 min. The solution was filtered through silica gel, concentrated, and then chromatographed on silica gel (light petroleum–dichloromethane) to give 6-nitrochlorochromene (**5e**) (0.013 g, 9%) and 3,6-dinitrochlorochromene (**14b**) (0.048 g, 28%). Mass spectrometry of the remaining material revealed the presence of a little 3,4-dichloronitrochromene (**11b**) as well as trinitrated material (*m/z* 325) and various chlorinated and nitrated dimers (*m/z* 412 and above). When the reaction was run at −60 °C the yield of 6-nitrochlorochromene was raised to 17%.

When the aluminium chloride was replaced by boron trifluoride–ether, a cleaner reaction ensued and chromatography of the product gave the 3,4-dichlorochromene (**11a**) (20%) and dichloronitrochromene (**11b**) (15%) as major components. The remaining material was again a complex mixture of dimers.

Nitration of the 3,4-*Dichloro*-6-*nitrochromene* (**11b**).—The dichloronitrochromene (0.049 g, 0.2 mmol) was nitrated with an excess of cupric nitrate trihydrate (0.240 g, 1.0 mmol) in acetic anhydride (2 ml) at 60 °C for 2 h. Work-up afforded a yellow oil which by t.l.c. and mass spectrometry was shown to contain no dinitrochlorochromene (*m/z* 314). It consisted mainly of starting material (*m/z* 303) together with materials (*m/z* 319 and 285) which were presumed to be the 3,3-dichloro- and 3-chloronitrochromanones, respectively.

Nitration of the 3-*Nitrochlorochromene* (**14a**).—The 3-nitrochlorochromene (0.040 g, 0.15 mmol) was nitrated with an excess of cupric nitrate trihydrate (0.120 g, 0.5 mmol) in acetic anhydride (2 ml) at 60 °C for 2 h. Work-up afforded a yellow oil which t.l.c., n.m.r., and mass spectrometry showed to be the 3,6-dinitrochlorochromene (**14b**) (100%).

6-*Bromo*-4-*chloro*-7-*methoxy*-2,2-*dimethyl*-3-*nitro*-2H-*chromene* (**14c**).—6-Bromo-4-chlorochromene (**5c**) (0.183 g, 0.600 mmol) in acetonitrile (5 ml) and trifluoroacetic anhydride (1 ml) was stirred with ammonium nitrate (0.048 g, 0.600 mmol). After 30 min the solvents were removed by evaporation and the residue filtered through silica gel in light petroleum–dichloromethane (1:1). The leading bright yellow band was collected and afforded the title bromochloronitrochromene (**14c**) (0.160 g, 76%) as pale yellow *needles*, m.p. 153—154 °C (from ethanol); $\nu_{max.}$(KBr) 1 601, 1 511, and 1 493 cm^{-1}; $\lambda_{max.}$(EtOH), 219 (ε 19 950 $dm^3\ mol^{-1}\ cm^{-1}$), 237sh (8 300), 246sh (7 250), 262 (7 050), 290sh (2 800), 319 (2 550), and 388 nm (2 300); δ($CDCl_3$) 1.61 (6 H, s), 3.82 (3 H, s), 6.32 (1 H, s), and 7.53 (1 H, s) (Found: C, 41.35; H, 3.1; N, 3.95%; M^+, 346.9593. $C_{12}H_{11}BrClNO_4$ requires C, 41.34; H, 3.18; N, 4.02%; *M*, 346.9560).

Hydrogenation of 6-*Nitrochromanone* (**1b**).—The nitrochromanone (**1b**) (10.0 g, 40 mmol) in ethyl acetate (160 ml) was hydrogenated at room temperature and atmospheric pressure over platinum (3—4 h). Filtration through Hi-Flo and evaporation of the solvent afforded 6-*amino*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**18a**) (8.0 g, 99%), colourless plates, m.p. 103—104 °C (from light petroleum–dichloromethane); $\nu_{max.}$(KBr) 3 450, 3 370, 1 672, 1 623, 1 595, 1 520, and 1 500 cm^{-1}; $\lambda_{max.}$(EtOH) 217 (ε 12 600 $dm^3\ mol^{-1}\ cm^{-1}$), 246 (16 000), 276 (7 200), and 346 nm (3 800); δ($CDCl_3$) 1.35 (6 H, s), 2.56 (2 H, s), 3.84 (5 H, br s), 6.17 (1 H, s), and 7.07 (1 H, s) (addition of deuterium oxide caused the signal at δ 3.84 to reduce to a sharp singlet, 3 H) (Found: C, 64.95; H, 6.75; N, 6.5%; M^+, 221.1063. $C_{12}H_{15}NO_3$ requires C, 65.14; H, 6.83; N, 6.33%; *M*, 221.1052).

6-*Formamido*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**18b**).—The aminochromanone (**18a**) (0.248 g, 1.12 mmol) was subjected to the usual Vilsmeier procedure. Chromatography of the crude product on silica gel (chloroform and ether as eluants) gave starting material (0.063 g, 20%) and the title chromanone (**18b**) (0.197 g, 70%) as colourless *needles*, m.p. 188—189 °C (from chloroform–carbon tetrachloride or aq. alcohol); $\nu_{max.}$($CHCl_3$) 1 697 and 1 677sh cm^{-1}; δ($CDCl_3$) 1.44 (6 H, s), 2.70 (2 H, s), 3.90 (3 H, s), 6.40 (1 H, s), 7.64 (1 H, br s, N*H*), 7.31 and 8.58 (tog. 1 H, dd, rotameric NC*H*O), and 8.68 (1 H, s); δ[$(CD_3)_2SO$] 1.45 (6 H, s), 2.73 (2 H, s), 2.73 (2 H, s), 4.00 (3 H, s), 6.70 (1 H, s), 8.37 (1 H, d, *J* 2 Hz), 8.56 (1 H, s), and 9.70 (1 H, br s) (irradiation at δ 9.70 caused the signal at 8.37 to collapse to a singlet) (Found: C, 62.55; H, 6.1; N, 5.7%; M^+, 249.1021. $C_{13}H_{15}NO_4$ requires C, 62.64; H, 6.07; N, 5.62%; *M*, 249.1001).

This *N*-formyl derivative could also be prepared by boiling the aminochromanone under reflux in 98% formic acid containing 1.05 equiv. of acetic anhydride. Removal of the formic acid by distillation with toluene afforded the derivative as described above. Material recrystallised from chlorinated solvents rapidly turned black but material recrystallised from aqueous solvent was stable over several months. The same effect

was observed with the other *N*-formyl or ethoxycarbonyl derivatives described below.

4-*Chloro*-6-*formamido*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene*.—The *N*-formylchromanone (**18b**) (0.568 g, 2.29 mmol) was subjected to the usual Vilsmeier formylation for 4 h (trichloroethene). Work-up and chromatography on silica gel (chloroform and ether as eluants) gave starting material (80%) and a small quantity (0.022 g, 4%) of the title chlorochromene as a homogeneous (t.l.c.) *gum*, δ[$(CD_3)_2SO$] 1.40 (6 H, s), 3.78 (3 H, s), 5.90 (1 H, s), 6.62 (1 H, s), 8.23 (1 H, s), 8.27 (1 H, d, *J* 2 Hz, C*HO*), and 9.58 (1 H, br s, N*H*) (irradiation at δ 9.58 caused the doublet at 8.27 to collapse to a singlet). This material was unstable, rapidly darkening in air, and a satisfactory mass spectrum could not be obtained. Longer reaction times did not afford more of this material but merely decreased the yield of recovered starting material.

6-*Ethoxycarbonylamino*-7-*methoxy*-2,2-*dimethylchroman*-4-*one*.—The aminochromanone (10.6 g; 47.9 mmol) was dissolved in chloroform. Pyridine (4.15 g, 52 mmol) was added, followed by the dropwise addition of ethyl chloroformate (5.61 g, 52 mmol). The mixture was stirred at room temperature for 24 h. Work-up afforded the title chromanone (11.0 g, 87%), as colourless *needles*, m.p. 150—152 °C (ether–dichloromethane); $\nu_{max.}$(KBr) 3 340, 1 705, 1 677, 1 623, and 1 593 cm^{-1}; $\lambda_{max.}$(EtOH) 207 (ε 7 900 dm^3 mol^{-1} cm^{-1}), 223 (13 475), 243 (25 050), 270 (12 300), and 335 nm (4 850); δ($CDCl_3$) 1.27 (3 H, t), 1.42 (6 H, s), 2.67 (2 H, s), 3.89 (3 H, s), 4.24 (2 H, q), 6.35 (1 H, s), 6.89 (1 H, br s), and 8.37 (1 H, s) (Found: C, 61.50; H, 6.5; N, 4.85%; M^+ 293.1255. $C_{15}H_{19}NO_5$ requires C, 61.41; H, 6.53; N, 4.77%; *M*, 293.1263).

4-*Chloro*-6-*ethoxycarbonylamino*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene* (**19a**).—The ethoxycarbonylaminochromanone (2.0 g, 6.82 mmol) was subjected to Vilsmeier formylation in dichloromethane. After 24 h work-up, followed by chromatography on silica gel (ether as eluant), gave the title chlorochromene (1.68 g, 79%), colourless *needles*, m.p. 63—65 °C (from aq. ethanol); $\nu_{max.}$(KBr) 3 440, 1 730, 1 620, 1 590, and 1 520 cm^{-1}; $\lambda_{max.}$(EtOH) 211 (ε 11 825 dm^3 mol^{-1} cm^{-1}), 237 (26 400), 277 (4 200), 289sh (3 575), and 324 nm (5 750); δ($CDCl_3$) 1.33 (3 H, t), 1.43 (6 H, s), 3.80 (3 H, s), 4.20 (2 H, q), 5.56 (1 H, s), 6.31 (1 H, s), 6.86 (1 H, br s, N*H*), and 8.15 (1 H, s) (Found: C, 57.65; H, 5.65; N, 4.45%; M^+, 311.0951. $C_{15}H_{18}ClNO_4$ requires C, 57.78; H, 5.81; N, 4.49%; *M*, 311.0924).

6-*Amino*-4-*chloro*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene* (**5f**).—The chlorochromene (**19a**) (1.0 g, 3.21 mmol) was treated with ethanolic sodium hydroxide (20%; 20 ml) and the mixture boiled under reflux for 3 h in an atmosphere of nitrogen. Water (150 ml) was added and the mixture was extracted with ether, dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel (dichloromethane as eluant) to give the title aminochlorochromene (**5f**) (0.55 g, 72%) as a homogeneous (t.l.c.) colourless *oil*; $\nu_{max.}$(film) 3 442, 3 370, 1 623, 1 600, and 1 580 cm^{-1}; δ($CDCl_3$) 1.37 (6 H, s), 3.38 (2 H, br s, NH_2), 3.73 (3 H, s), 5.47 (1 H, s), 6.23 (1 H, s), and 6.60 (1 H, s) (addition of deuterium oxide caused the signal at δ 3.38 to disappear) (Found: M^+, 239.0732. $C_{12}H_{14}ClNO_2$ requires *M*, 239.0713).

6-*Amino*-5-*chloro*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**18c**).—A mixture of stannous chloride dihydrate (4.29 g, 19.0 mmol), the nitrochromanone (**1b**) (1.25 g, 4.98 mmol) and concentrated hydrochloric acid (10 ml) was warmed gently to initiate a vigorous reaction. When the initial reaction had subsided, ethanol (10 ml) was added and the mixture boiled under reflux for 1 h and then poured into water. The aqueous solution was washed with ether, made alkaline (pH 12) with concentrated aqueous sodium hydroxide and extracted with ether (4 × 30 ml). Evaporation of the dried (Na_2SO_4 and $NaHCO_3$) extract afforded a yellow gum which was chromatographed on silica gel (ether as eluant) to give the aminochromanone (0.967 g, 88%) described above and the title aminochlorochromanone (**18c**) (0.081 g, 7%), colourless *needles*, m.p. 106—107 °C (from light petroleum); $\nu_{max.}$(KBr) 3 475, 3 380, 1 670, 1 615, 1 580, and 1 562 cm^{-1}; $\lambda_{max.}$(EtOH) 219 (ε 9 700 dm^3 mol^{-1} cm^{-1}), 248 (14 650), 277 (6 625), and 358 nm (3 450); δ($CDCl_3$) 1.38 (6 H, s), 2.68 (2 H, s), 3.89 (3 H, br s, O*Me* and NH_2), and 6.29 (1 H, s) (addition of deuterium oxide caused the signal at δ 3.89 to reduce to a sharp singlet, 3 H) (Found: C, 56.75; H, 5.5; N, 5.45% M^+, 255.0684. $C_{12}H_{14}ClNO_3$ requires C, 56.36; H, 5.52; N, 5.48%; *M*, 255.0662).

When the reaction was repeated with ethanol as a co-solvent (100 ml) present initially the 5-chloro derivative (**18c**) was obtained in 68% yield.

5-*Chloro*-6-*ethoxycarbonylamino*-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**18d**).—The aminochromanone (**18c**) (12.4 g, 51.7 mmol) and pyridine (4.4 g, 56.9 mmol) in chloroform (30 ml) were treated dropwise with ethyl chloroformate (6.145 g, 56.9 mmol) and the resultant mixture was stirred at room temperature for 24 h under a calcium chloride tube. It was then washed with water, dilute hydrochloric acid, and water. The dried ($MgSO_4$) organic phase was separated and filtered through a short alumina column (with chloroform) to yield the title ethoxycarbonylaminochromanone (**18d**) (16.0 g, 92%) as colourless *needles*, m.p. 122 °C (ether); $\nu_{max.}$(KBr) 3 430, 1 725, 1 681, 1 603, and 1 560 cm^{-1}; $\lambda_{max.}$(EtOH) 238 (ε 10 450 dm^3 mol^{-1} cm^{-1}), 253 (18 500), 264 (17 400), 299 (10 500), and 345 nm (3 650); δ($CDCl_3$) 1.33 (3 H, t), 1.44 (6 H, s), 2.73 (2 H, s), 3.86 (3 H, s), 4.20 (2 H, q), and 5.90 (1 H, s) (Found: C, 55.05; H, 5.5; N, 4.25%; *M*, 327.061. $C_{15}H_{18}ClNO_5$ requires C, 54.96; H, 5.53; N, 4.27%; *M*, 327.0873).

Reaction of the 6-*Ethoxycarbonylaminochromanone* (**18d**) *with the Vilsmeier Reagent*.—The chromanone (**18d**) (2.0 g, 6.12 mmol) was subjected to the Vilsmeier reaction in boiling dichloromethane for 56 h. Work-up afforded a gum which on silica-gel chromatography gave three products.

The first was 5-*chloro*-6-(*ethoxycarbonylformamido*)-7-*methoxy*-2,2-*dimethylchroman*-4-*one* (**21**) (1.2 g, 53%), colourless needles, m.p. 145—146 °C (from ethanol); $\nu_{max.}$(KBr) 1 742, 1 718, 1 687, 1 600, and 1 555 cm^{-1}; $\lambda_{max.}$(EtOH) 211 (ε 14 150 dm^3 mol^{-1} cm^{-1}) 227 (24 650), 238 (18 300), 272 (11 900), and 315 nm (2 070); δ($CDCl_3$) 1.30 (3 H, t), 1.46 (6 H, s), 2.73 (2 H, s), 3.80 (3 H, s), 4.30 (2 H, q), 6.37 (1 H, s) (Found: C, 54.2; H, 5.0; N, 3.9%; M^+, 355.0864. $C_{16}H_{18}ClNO_6$ requires C, 54.01; H, 5.09; N, 3.93%; *M*, 355.0823).

The second component was 4,5-*dichloro*-6-(*ethoxycarbonylformamido*)-7-*methoxy*-2,2-*dimethyl*-2H-*chromene* (**20**) (0.20 g, 8.5%), colourless needles, m.p. 88—91 °C (from light petroleum); $\nu_{max.}$(KBr) 1 745—1 735, 1 718, 1 623, 1 603, and 1 557 cm^{-1}; $\lambda_{max.}$(EtOH) 228 (ε 8 400 dm^3 mol^{-1} cm^{-1}), 237 (21 550), 246 (15 300), 275 (6 525), 284 (5 775), 310 (5 775), and 318 nm (5 600); δ($CDCl_3$) 1.27 (3 H, t), 1.42 (6 H, s), 3.73 (3 H, s), 4.31 (2 H, q), 5.67 (1 H, s), 6.30 (1 H, s) and 9.23 (1 H, s) (Found: C, 51.2; H, 4.5; N, 3.7%; M^+, 373.0494. $C_{16}H_{17}Cl_2NO_5$ requires C, 51.35; H, 4.58; N, 3.74%; *M*, 373.0484).

The third component was 4,5-*dichloro*-6-*ethoxycarbonylamino*-7-*methoxy*-2,2-*dimethyl*-2H-*chromene* (**19b**) (0.28 g, 13%), m.p. 97—98 °C (from light petroleum); $\nu_{max.}$(KBr) 3 240, 1 703, 1 613, 1 565, and 1 523 cm^{-1}; $\lambda_{max.}$(EtOH) 229 (ε 23 800 dm^3 mol^{-1} cm^{-1}), 238sh (23 100), 246sh (18 975), 275 (7 600), 285sh (6 900), and 315 nm (6 900); δ($CDCl_3$) 1.28 (3 H, t), 1.40 (6 H, s), 3.76 (3 H, s), 4.16 (2 H, q), 5.73 (1 H, s), 5.91 (1 H, br s, NH), and

6.36 (1 H, s) (Found: C, 52.05; H, 4.9; N, 3.95%; M^+, 345.0559. $C_{15}H_{17}Cl_2NO_4$ requires C, 52.03; H, 4.94; N, 4.04%; M, 345.0535).

6-Amino-4,5-dichloro-7-methoxy-2,2-dimethyl-2H-chromene (**19c**).—The chlorochromene (**19b**) (0.10 g, 0.29 mmol) was boiled under reflux in an atmosphere of nitrogen with ethanolic sodium hydroxide (20%; 10 ml) for 2 h. Water (50 ml) was added and the mixture was extracted with ether, dried ($MgSO_4$) and evaporated to afford a gum which on silica-gel chromatography (dichloromethane as eluant) afforded the title aminochromene (**19c**) as a homogeneous (t.l.c.) *oil* (0.056 g, 71%), $\nu_{max.}$(film) 3 480, 3 390, 1 613, 1 587, and 1 560 cm^{-1}; $\delta(CDCl_3)$ 1.36 (6 H, s), 3.83 (5 H, br s, OMe and NH_2), 5.74 (1 H, s), and 6.38 (1 H, s) (addition of deuterium oxide caused the signal at δ 3.83 to reduce to a sharp singlet, 3 H) (Found: M^+, 273.0339. $C_{12}H_{13}Cl_2NO_2$ requires M, 273.0323).

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