3-Hydroxymethylenechroman-4-one

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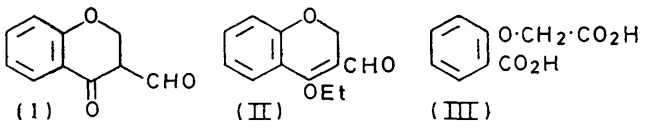
Triethyl orthoformate and boron trifluoride–ether complex convert chroman-4-one into 4-ethoxy-2*H*-chromen-3-carbaldehyde (II), characterised by conversion into *trans*-3-(4-ethoxy-2*H*-chromen-3-yl)-1-phenylprop-2-en-1-one (XIV) and thence into the 2-phenyl-5*H*-pyrano[3,2-*c*][1]benzopyran-1-ylium cation (XV). De-ethylation of (II) with boron trichloride affords a mixture of 3-hydroxymethylenechroman-4-one (XI) and 3-chloromethylchromone, the latter by a ring-substituent exchange reaction. De-ethylation by cold acids gives (XI) only. Hot acids hydrolyse (XI) to chromanone, air oxidises it to (2-carboxyphenoxy)acetic acid, and silica converts it into 2,3-dihydro- 3,3′- methylenebischromen-4-one (XVIII) *via* another ring-substituent exchange reaction followed by an alkylation–hydrolysis sequence. Diazomethane converts (XI) into the 3-methoxymethylene compound (X) which is also obtained by the action of methanol and acid on (II) and therefore represents the thermodynamically stable enol.

We have examined the synthesis and chemistry of 3-formylchroman-4-one (I) (3-hydroxymethylenechroman-4-one) with a view to employing related compounds in syntheses of the fungal metabolites citromycetin [1,2] and fulvic acid.[2,3] Although treatment of chroman-4-one with ethyl formate and base is known to supply the aldehyde (I) directly, we preferred to develop an indirect method which has the advantages of supplying the aldehyde as an enol ether (II) in which the enolic system is protected and in which the heterocyclic ring cannot be opened by Michael elimination.[5,6]

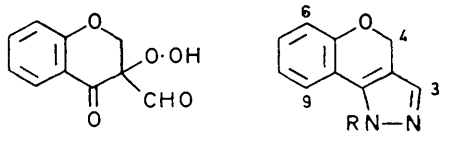
With triethyl orthoformate and boron trifluoride–ether complex, chromanone gave the chromencarbaldehyde (II) in 77% yield, hydrolysis with cold acid then giving an enolic form of (I) nearly quantitatively. This product had the properties described by the earlier workers [4] except that we found it to be sensitive to air, which oxidised it to (2-carboxyphenoxy)acetic acid (III), presumably by way of the peroxide (IV) although after that point several routes seem possible, no one of them being specially advantageous. Notwithstanding the general properties of (I) [solubility in aqueous alkali, colour with ethanolic iron(III) chloride] which are consistent with the

[1] A. Robertson, W. B. Whalley, and J. Yates, *J. Chem. Soc.*, 1951, 2013; J. B. D. Mackenzie, A. Robertson, and W. B. Whalley, *ibid.*, 1950, 2965.
[2] F. M. Dean and D. R. Randall, *J. Chem. Soc.*, 1961, 798.
[3] F. M. Dean, R. A. Eade, R. Moubasher, and A. Robertson, *J. Chem. Soc.*, 1957, 3497.
[4] P. Schenone, G. Bignardi, and S. Morasso, *J. Heterocyclic Chem.*, 1972, **9**, 1341.
[5] M. Padfield and M. L. Tomlinson, *J. Chem. Soc.*, 1950, 2272.
[6] F. M. Dean and K. B. Hindley, *Tetrahedron Letters*, 1972, 1445.

β-dicarbonyl structure, the compound failed to give characteristic heterocyclic condensation products with

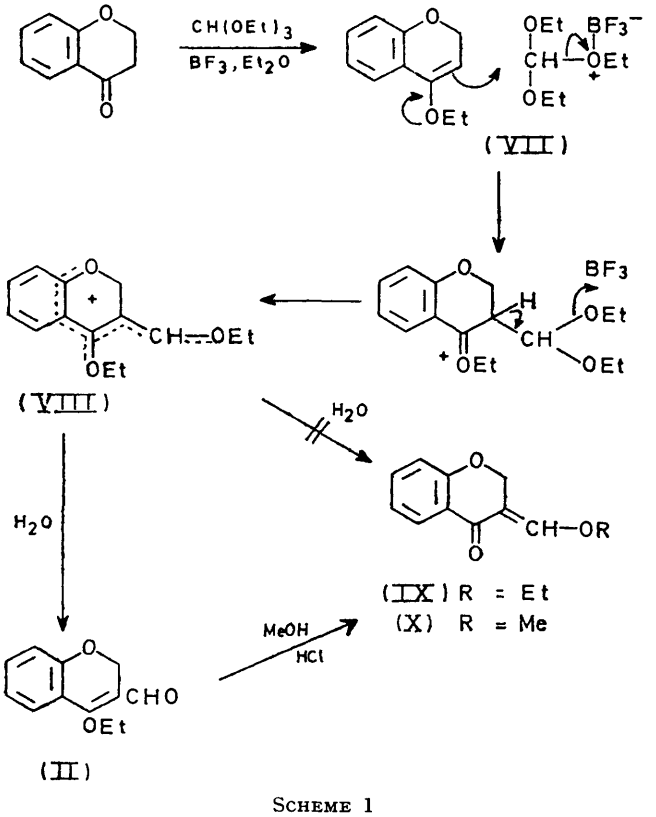


(I) (II) (III)



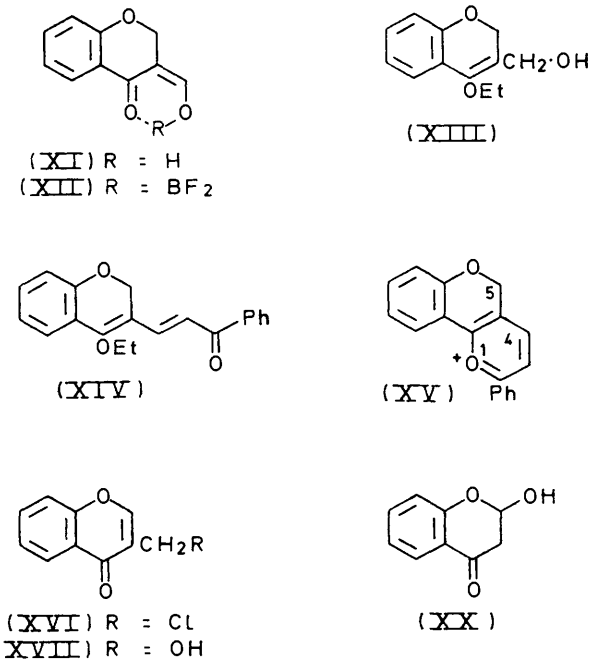
(IV) (V) R = H (VI) R = Ph

malonic or acetoacetic ester or with hydroxylamine; with hydrazine and phenylhydrazine however, the pyrazole derivatives (V) and (VI) (respectively) were formed. The orientations assigned to these are based partly on general grounds and partly on the aromatic proton resonance at τ 2.2 in the n.m.r. spectrum of (V) which is replaced in that of (VI) by one at 3.2. This large shift has to be ascribed to shielding, and models show that only structure (VI) offers a suitable opportunity. In (VI) the phenyl group must lie in a plane perpendicular to the main plane for steric reasons and it will then shield the proton at position 9.



Scheme 1

Generally, orthoester–acid combinations convert ketones into acetals although conversions into enol ethers are also known.[7] On the assumption that chromanone first yields an enol ether, formylation can be initiated as in diagram (VII) (Scheme 1) and should lead to the carbocation (VIII) which is likely to survive until water is added and may be responsible for the red colour of the reaction mixture. Hydrolysis by water is rapid, and gives only the ether (II) because it is under kinetic



(XI) R = H (XII) R = BF_2 (XIII) (XIV) (XV) Ph (XVI) R = Cl (XVII) R = OH (XX)

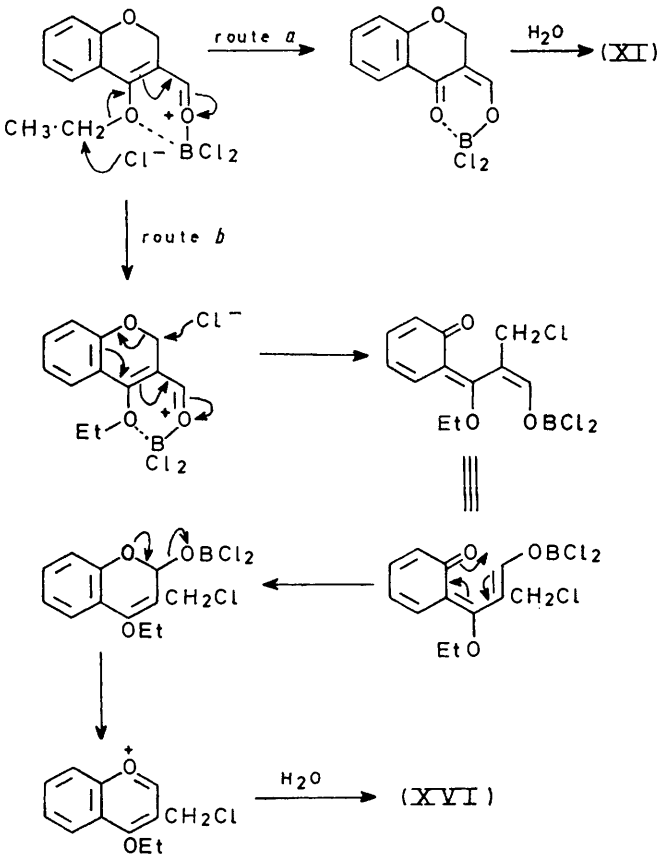
control. That the isomeric ether (IX) is the thermodynamically stable one follows from the selective formation of (X) by methylation of (I) with diazomethane and (more convincingly) from the transformation of (II) into (X) under the influence of acidified methanol, a reagent that would reversibly regenerate carbocations such as (VIII) but with mixed ether groupings. For the same reason we regard 3-formylchromanone as existing almost entirely in the hydroxymethylene form (XI) though the spectroscopic properties such as the resonance at τ −3.45 do not differentiate between this and the alternative enol. The complex (XII) resulting from reaction with methanolic boron trifluoride possesses neither any hydroxylic resonance nor a band appropriate to a formyl proton.

The aldehyde group in (II) was evidenced by an n.m.r. band at τ −0.03 and by the fact that reduction with borohydride gave the alcohol (XIII) which, however, was an oil too unstable for distillation, chromatography, or conversion into esters although its spectroscopic properties leave no doubt as to its structure. The aldehyde group was further characterised by condensing the compound with acetophenone in base to obtain the dienone (XIV) and cyclising this in trifluoroacetic acid to the

[7] A. Serini and H. Köster, *Ber.*, 1938, **71**, 1766; H. H. Inhoffen, *Chem. Ber.*, 1951, **84**, 361; R. Gardi, P. P. Castelli, and A. Ercoli, *Tetrahedron Letters*, 1962, 497.

pyranopyrylium cation (XV) similar to one prepared during degradative studies on citromycetin.[1]

Attempts to dealkylate the ether (II) with boron trichloride [8] did yield the enol (XI) but also produced 3-chloromethylchromone (XVI). The same compound



SCHEME 2

was obtained by chloromethylation of chromone and was characterised by reduction with zinc to 3-methylchromone. A possible origin for the halide was sought in a prototropic shift, converting the enol (XI) into 3-hydroxymethylchromone (XVII) as the first stage, but was abandoned. Known 3-alkylidenechromanones appear not to be susceptible to prototropic shifts in acidic [9] or basic [10] media though elevated temperatures may induce them.[10] In the present case, the enol (XI) was not affected by dry hydrogen chloride nor by boron trichloride, and with hot aqueous acids merely suffered smooth hydrolysis to chromanone. The ether (II) was also stable to dry hydrogen chloride. Thus it appears that (XVI) is formed directly from (II) by the action of boron trichloride. Scheme 2 offers one reasonable sequence. Normally, dealkylation by nucleophilic attack at ethyl by the chloride ion (route *a*) would be the sole reaction. But in route *b* this attack has been transferred to the ring methylene group (route *b*) thus opening the ring and giving the chloromethyl group immediately. The rest of Scheme 2 shows how the desired heterocycle might be built up in stages for each of which there is precise analogy (*e.g.* electrocyclic closure of chromen ring,[11] and nucleophilic displacement in 4-ethoxypyrylium salts [12]). In this Scheme and others like it the carbon atoms at the 2-position and in the 3-substituent exchange places, a phenomenon we find to be common in this area and for which ample evidence has been derived in further work.

Attempts to purify 3-formylchromanone on a silica column fail because a new product is rapidly formed. The same compound also results when the formylchromanone is treated with silica in hot benzene or with sodium acetate in warm acetic acid, and it has been encountered in other (also acid–base) conditions by the earlier workers who have assigned it structure (XVIII) (Scheme 3) on the basis of spectroscopic arguments with which we agree. But we do not accept their view as to the origin of the compound. They offer no evidence and it appeared to us that the properties of (I) would not support the suggested initial aldol condensation, and that the activation at a later stage would not permit the required prototropy. We consider the reaction to constitute another example of ring-substituent switch, induced this time by the acid–base reagents used and leading past 3-hydroxymethylchromone (XVII) to an attack on the enol (XI) which would produce the dimeric system in (XIX). But because non-enolised β-oxo-aldehydes are readily hydrolysed, the reagents employed would at once detach the formyl group giving the observed product (XVIII). In confirmation, a parallel study with acetyl instead of formyl groups has given clear evidence for both the switch and the participation of the alcohol, as well as supplying in good yield an analogue of the key intermediate (XIX).

EXPERIMENTAL

Light petroleum normally refers to the fraction of b.p. 60—80°. I.r. spectra were usually determined for mulls in paraffin; only significant bands are reported. U.v. measurements were made on *ca.* 10^{-4} M-solutions in ethanol. Molecular weights were determined mass spectrometrically.

4-Ethoxy-2H-chromen-3-carbaldehyde (II).—The two-phase mixture of chroman-4-one (2 g), triethyl orthoformate (40 g), and boron trifluoride–ether complex (40 g) slowly turned dark red when stirred vigorously at room temperature for 69 h. The reaction was best protected from moisture but otherwise the access of air was unimportant. The product was stirred into water (300 ml) containing sodium carbonate (anhydrous; 50 g) and after 5 min at pH 8 it was collected into ether (3 × 300 ml), washed with water, dried (Na_2SO_4), and recovered as a red oil which was chromatographed on silica (200 g) from light petroleum and then ether–

[8] F. M. Dean, J. Goodchild, L. E. Houghton, J. A. Martin, R. B. Morton, B. Parton, A. W. Price, and N. Somvichien, *Tetrahedron Letters*, 1966, 4153.

[9] W. H. Perkin, A. Pollard, and R. Robinson, *J. Chem. Soc.*, 1937, 49; C. Tamm. *Arzneim.-Forsch.*, 1972, **22**, 1776.

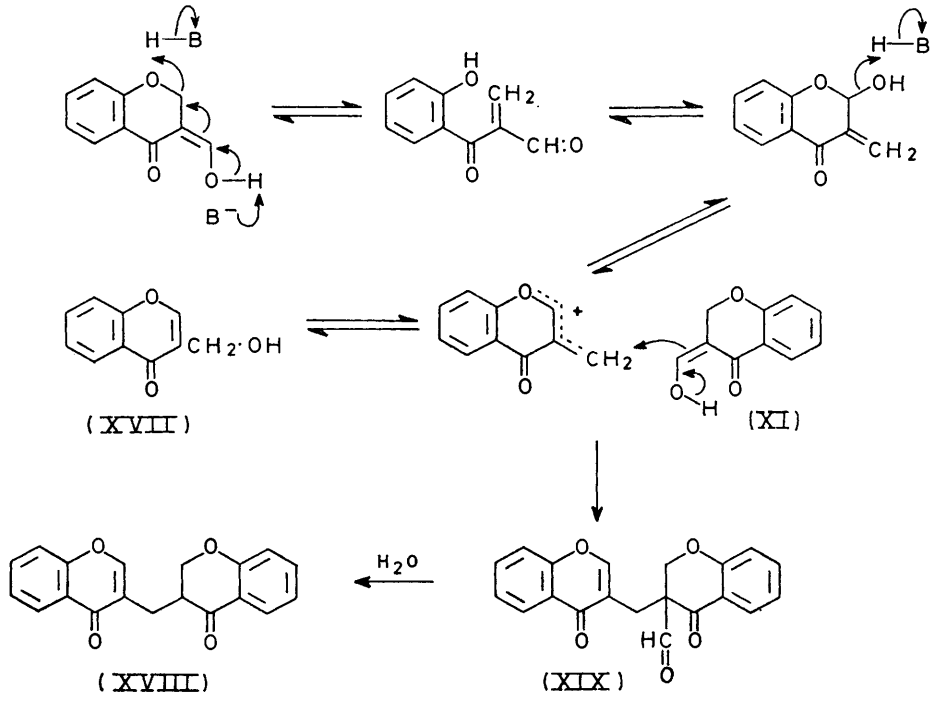
[10] D. H. R. Barton, P. D. Magnus, and J. I. Okogun, *J.C.S. Perkin I*, 1972, 1103.

[11] F. M. Dean, in 'Total Synthesis of Naturally Occurring Oxygen Ring Compounds,' ed. J. ApSimon, Wiley, New York, 1973, p. 467.

[12] R. M. Anber and A. H. Cook, *J. Chem. Soc.*, 1946, 117.

light petroleum (1 : 9). The later fractions contained the *aldehyde* as a yellow oil (2.1 g), crystallisable from light petroleum as pale yellow needles, m.p. 45.5°, $\lambda_{max.}$ 239, 296, and 354 nm (log ε 4.1, 4.1, and 3.9), $\nu_{max.}$ 1 660vw, 1 628, 1 607vs, 1 566, 1 488, 1 274, 1 114, and 833 cm^{-1} (Found: C, 70.7; H, 6.1%; *M*, 204. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9%; *M*, 204).

4-Ethoxy-2H-chromen-3-ylmethanol (XIII).—After 15 min, the red mixture of sodium borohydride (90 mg) and (II) (300 mg) in ethanol (15 ml) was poured into brine (100 ml). The product was isolated by means of ether (3 × 50 ml) as a pale yellow oil (279 mg) behaving as a single substance in chromatographic tests but rapidly deteriorating, especially when warmed, so that elemental analyses and mass spectroscopic results appeared to be variable and not meaningful. For i.r. and n.m.r. spectroscopic examination, solutions of the oil in ether were repeatedly diluted with tetrachloromethane and concentrated under vacuum without the



SCHEME 3

TABLE 1

N.m.r. spectra [a] of chromen and chromanone derivatives (at 100 MHz)

Compound	Solvent	Assignments [b] $CH_3{\cdot}CH_2$ or $CH_3{\cdot}O$	CH_2Cl CH_2OH, or $MeCH_2O$	CH_2O (in ring)	O·CH:C, CH:O, or CH:N	OH [c] or NH [c]	ArH with *o*-CO	Other ArH (all m)
(XI)	CCl_4			5.25 (s)	2.40 (s)	−3.45 (s)	2.20 (dd) (1.5, 6.5)	2.1—3.3
(XII)	$CDCl_3$			5.01 (s)	2.04 [d]		2.04 (dd) (2, 8)	2.3—2.5 (1 H), 2.8—3.1 (2 H)
(X)	CCl_4	6.09 (s)		5.06 (d) (2)	2.73 (q) (2)		2.17 (dd) (1.5, 8)	2.6—3.2
(IX)	CCl_4	8.56 (t) (6.5)	5.84 (q) (6.5)	5.13 (s)	−0.3 (s)			2.4—3.3
(IX) (Me for Et)	$CDCl_3$	6.00 (s)		5.07 (s)	−0.03 (s)			2.4—3.3
(XIII)	CCl_4	8.70 (t) (7.0)	6.25 (q) (7.0) 5.80 (s)	5.28		7.56 (s)		2.8—3.4
(XIV) [e]	CCl_4	8.56 (t) (7.0)	6.00 (q) (7.0)	5.01 (s)			2.0—2.2 (3 H, m)	2.5—3.3 (10 H)
(V)	Me_2CO			4.67 (s)	2.45 (s)	1.88br	2.29 (dd)	2.7—3.2
(VI)	Me_2CO			4.69 (s)	2.47 [f] (s)		*g*	2.7—3.3 (4 H); 2.47 (5 H)
(XVI)	$CDCl_3$		5.45 (s)		1.85 (s)		1.82 (dd) (2, 8.5)	2.1—2.8

[a] With tetramethylsilane as internal standard; τ values. [b] Numbers in parentheses are coupling constants (Hz). Relative proton counts agree with assignments throughout but are given where necessary to avoid ambiguity. [c] Signals removed by contact with D_2O. [d] In acetone, this signal shifts to τ 1.6 and can then be seen to be broadened by long-range effects. [e] Also τ 3.32 (d, *J* 16 Hz, CH:C*H*·C:O). [f] Overlaid by aromatic resonances. [g] See text.

application of heat until the n.m.r. spectrum indicated that a single solute was in hand. The substance had $\nu_{max.}$ (film) 3 380 (OH), 2 850, 2 900, 2 950 (CH), 1 664 (vinyl ether), 1 605, 1 578, 1 491, 1 325, 1 250, 1 097, 775, and 770 cm^{-1}.

trans-3-(4-*Ethoxy*-2H-*chromen*-3-*yl*)-1-*phenylprop*-2-*en*-1-*one* (XIV).—Sodium hydroxide (10 g) was dissolved in water (50 ml) and ethanol (50 ml). The solution (6 ml) was mixed with acetophenone (freshly redistilled; 250 mg) and 4-ethoxy[1]-benzopyran-3-carbaldehyde (300 mg) at 0 °C and during 75 min a yellow solid separated. The mixture was poured into water and the product isolated by means of ether and purified from ethanol giving the *chromen* as tiny yellow needles (337 mg), m.p. 70.5—71°, $\nu_{max.}$ 1 656, 1 617, 1 600, and 1 577 cm^{-1} (C:O, C:C and aromatic) (Found: C, 78.15; N, 6.0%; *M*, 306. $C_{20}H_{18}O_3$ requires C, 78.4; H, 5.9%; *M* 306).

2-*Phenyl*-5H-*pyrano*[3,2-c][1]*benzopyran*-1-*ylium Perchlorate* (XV).—After 15 min the dark maroon solution of the chromenylpropenone (XIV) (100 mg) in trifluoroacetic acid (0.2 ml) was treated with perchloric acid (72% aqueous solution; 2 ml) followed by water (0.1 ml). The precipitate was washed with water and purified from acetone–light petroleum to give the *perchlorate* as orange needles (55 mg), m.p. 236°, $\lambda_{max.}$ 216, 258, and 382 nm (log ε 4.15, 4.06, and 4.14) (Found: C, 60.0; H, 3.8. $C_{18}H_{13}ClO_6$ requires C, 59.9; H, 3.6%), *m/e* 261 ($C_{19}H_{13}O_2$). In the i.r. spectrum there appeared to be no carbonyl absorption, but individual bands could not be assigned except for a broad one at 1 099 cm^{-1} corresponding to the perchlorate anion. The n.m.r. spectrum ($CF_3{\cdot}CO_2H$) consisted of a two-proton singlet at τ 4.41 (ring CH_2) and complex multiplets between 1.3 and 2.9 corresponding to eleven aromatic protons, a doublet at τ 1.40 (*J* 8 Hz) being the only clear feature and considered to originate from the pyrylium proton at position 4.

4-*Methoxy*-2H-*chromen*-3-*carbaldehyde* (II; Me for Et).—Interaction of chromanone (1.5 g) and boron trifluoride–ether complex (30 g) with trimethyl orthoformate (30 g) was conducted as for the ethyl ester and after chromatography the product formed a yellow-orange oil (0.97 g) which could be finally purified by vacuum distillation or by three crystallisations from ether–light petroleum induced by cooling with solid carbon dioxide. So obtained, the *chromen* formed cream-coloured needles, m.p. 71—72°, $\lambda_{max.}$ 238, 297, and 356 nm (log ε 4.13, 4.09, and 3.90), $\nu_{max.}$ 1 658, 1 633, 1 606, 1 575, 1 498, 1 349, 1 100, 969, and 766 cm^{-1} (Found: C, 69.65; H, 5.35%; *M*, 190. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%; *M*, 190).

3-*Formylchroman*-4-*one* (I); 3-*Hydroxymethylenechroman*-4-*one* (XI).—(i) The 4-ethoxychromen (II) (500 mg) in recently redistilled tetrahydrofuran (100 ml) was treated with 3M-hydrochloric acid (20 ml) at room temperature for 3 h, and the product was isolated by diluting the solution with water and extracting it with ether. Thus obtained, the *chromanone* formed a yellowish oil (417 mg), $\nu_{max.}$ (film) 3 050, 2 900, 2 840 (CH), 2 600—3 700br (hydrogen bonded OH), 1 650 and 1 610 cm^{-1} (enone and vinyl ether) (Found: *M*, 176.0471. $C_{10}H_8O_3$ requires *M*, 176.0473). This compound imparted an intense brown colour to ethanolic iron(III) chloride.

(ii) During 3 h the dark solution formed by dissolving the 4-ethoxychromen (II) (500 mg) in boron trifluoride–methanol complex (*d* 1.22; 5 ml) deposited crystals. The mixture was poured into water and left for 1 h to allow displacement of the boron and the product was collected into ether, purified by transferring it into aqueous sodium hydrogen carbonate and then back into ether, and recovered in the usual manner. Thus obtained, 3-formylchromanone formed a yellowish oil (383 mg) identical with a sample prepared as in (i).

Pure material was better secured by means of the intermediate boron complex. Instead of adding the mixture to water, it was diluted with methanol (1 ml) and the crystals were collected, washed with a little methanol and then ether, and crystallised from ethyl acetate–light petroleum giving the boron difluoride complex (XII) as golden plates (301 mg), m.p. 142—143.5°, $\nu_{max.}$ 1 596, 1 566, 1 520, 1 480, 1 320, 1 292, 1 277, 1 040, 770, and 763 cm^{-1} (Found: C, 53,55; H, 3.3. $C_{10}H_7BF_2O_3$ requires C, 53.6; H, 3.15%), *m/e* 224 and 223 (M^+), 205 and 204 (M^+ − F), and 196 and 195 (M^+ − CO), with appropriate metastable peaks. The same complex was obtained from 3-formylchromanone itself and boron trifluoride in methanol and affords the best means of characterising this enol. Decomposed with water, the complex readily supplies 3-hydroxymethylenechromanone, which can be isolated with ether in the usual way as an oil chromatographically pure without further manipulation.

Oxidation of 3-*Formylchroman*-4-*one*.—A solution of the chromanone in ether or benzene left in air for a few weeks gradually deposited brown, amorphous material which was filtered off. Evaporation of the solvent then gave a gum from which a little ether washed out a reddish impurity leaving a white, strongly acidic solid which, when crystallised from water gave (2-carboxyphenoxy)acetic acid (III) as parallelipipeds, m.p. 189—191°, τ(acetone) 5.02 (2 H, s, $ArOCH_2CO_2H$), 1.9—3.0 (4 H, mm, ArH), and 0.10br (2 H, s, CO_2H), *M*, 196 ($C_9H_8O_5$), identical with a synthetic specimen,[13] m.p. 192.5—194° (lit.,[13] 187—188°).

3-*Methoxymethylenechroman*-4-*one* (X).—(i) The 4-ethoxychromen (II) (200 mg) was stirred in methanol (40 ml) containing N-hydrochloric acid (1 drop) until reaction was complete (*ca.* 42 h). After addition of water (100 ml) the product was extracted into ether and washed with aqueous sodium hydrogen carbonate and then water, dried (Na_2SO_4), and recovered by evaporation. The yellowish oily residue was purified on a silica column (6 g) by elution first with light petroleum, then with ether–light petroleum [(1 : 19) which removed a small amount of a non-identified, bright yellow impurity], and finally with ether–light petroleum (1 : 9) which supplied the *methoxymethylenechromanone* as an oil (164 mg) crystallising from ether–light petroleum (b.p. 40—60°) as white needles, m.p. 52—53°, $\lambda_{max.}$ 223, 286, and 336 nm (log ε 4.10, 4.08, and 3.81), $\nu_{max.}$ 1 676 (C:O), 1 613vbr (aromatic and vinyl ether), 1 466, 1 340, 1 250, 1 032, 1 002, and 761 cm^{-1} (Found: C, 69.2; H, 5.3%; *M*, 190. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%; *M*, 190). The compound appears to be remarkably easily hydrolysed, and even the solid deteriorates within 1 day; a colour is imparted to iron-(III) salts in ethanol during the first 10 min and gradually intensifies.

(ii) 3-Formylchromanone (337 mg) in ether (20 ml) was treated with an excess of ethereal diazomethane (dried by repeated treatment with potassium hydroxide pellets) during 35 min at room temperature. The remaining diazomethane was destroyed with acetic acid and the ethereal solution washed with water; the solvent was removed *in vacuo* leaving a brownish oil from which the impurities could not be removed readily. It appeared best to dissolve the oil in the minimum amount of ether, add a larger volume of light petroleum, and chill the solution in ethanol–solid carbon dioxide. A solid appeared which was subjected to the

[13] A. Robertson, *J. Chem. Soc.*, 1932, 1380.

same procedure twice again, after which it crystallised fairly readily from pentane giving the 3-methoxymethylenechromanone as tiny crystals (56 mg), m.p. and mixed m.p. 52°, further identified spectroscopically.

1,4-*Dihydro*[1]*benzopyrano*[4,3-c]*pyrazole* (V).—A mixture of 3-formylchromanone (230 mg) with hydrazine hydrochloride (260 mg) and ethanol (10 ml) was warmed while water was added until dissolution was complete. After 19 h at room temperature, the solution was diluted with water, neutralised with aqueous hydrogen carbonate, and extracted with ether. The extract supplied an orange oil which solidified and was then purified by elution with ether from a silica column followed by sublimation at 0.01 mmHg (for analytical purposes) or recrystallisation (for general purposes) from ether–light petroleum giving the *pyrazole* as small prisms (176 mg), m.p. 162°, $\nu_{max.}$ 3 110 (NH), 1 615, 1 594, 1 568, 1 478, and 1 468 cm^{-1} (benzenoid and pyrazole) (Found: C, 70.0; H, 4.8; N, 16.05%; *M*, 172. $C_{10}H_8N_2O$ requires C, 69.75; H, 4.7; N, 16.3%; *M*, 172).

1-*Phenyl*-1,4-*dihydro*[1]*benzopyrano*[4,3-c]*pyrazole* (VI).—Prepared in the same manner as the foregoing pyrazole but from freshly recrystallised phenylhydrazinium chloride instead of hydrazine, this *pyrazole* separated from ethanol as small prisms (91%), m.p. 140—141°, devoid of i.r. absorption near 3 100 cm^{-1} but tending to retain solvents and sublimed for analytical purposes (Found: C, 77.6; H, 4.9; N, 11.4%; *M*, 248. $C_{16}H_{12}N_2O$ requires C, 77.4; H, 4.9; N, 11.3%; *M*, 248).

2,3-*Dihydro*-3,3′-*methylenebischromen*-4-*one* (XVIII).—(i) 3-Formylchromanone (125 mg) and silica gel (1 g) were heated together in refluxing methanol for 20 min. The silica was removed and washed with methanol, and the combined methanolic solutions were concentrated to a solid that crystallised from methanol or benzene–light petroleum to give the bischromenone as plates (88 mg), m.p. 115.5—116.5° $\lambda_{max.}$ 233, 248, and 307 nm (log ε 4.19, 4.21, 3.98), $\nu_{max.}$ 1 682 (chromanone C:O), 1 635 (chromone), 1 611, 1 577, and 1 489 cm^{-1}; τ ($CDCl_3$) 7.5—6.5 (3 H, mm, ABC system in CH_2·CHC:O), 6.0—5.2 (2 H, mm, ArO·CH·CH), 3.2—1.8 (8 H, mm, ArH), and 2.1 (1 H, s, O·CH:C) (Found: C, 74.3; H, 4.7%; *M*, 306. Calc. for $C_{19}H_{14}O_4$: C, 74.45; H, 4.60%; *M*, 306).

(ii) 3-Formylchromanone (125 mg) was heated with sodium acetate (2.5 g) in a refluxing mixture of acetic acid (10 ml) and water (40 ml) for 3 h. The product was isolated by dilution with water and collected into chloroform, purified on a silica column with elution by ether–petroleum (1 : 4), and crystallised from benzene–light petroleum (charcoal) to give the bischromenone as needles (85 mg), m.p. 116°, identical with a sample prepared as in (i).

3-*Chloromethylchromone* (XVI).—(i) 4-Ethoxy-2*H*-chromen-3-carbaldehyde (750 mg) in dichloromethane (50 ml) was cooled by means of solid carbon dioxide in acetone and similarly cooled boron trichloride (15 g) was added. The dark red mixture was stirred in the cold for 45 min and then poured into saturated, aqueous sodium acetate (300 ml). When the colour of the complex had faded the organic layer was separated and the aqueous layer extracted once with fresh dichloromethane; the combined organic solutions were washed with water, dried ($MgSO_4$), and concentrated to a yellow oil (696 mg) which was diluted with ether and extracted with aqueous sodium hydrogen carbonate. From the extract, acidification liberated 3-formylchromanone (311 mg), isolated as described above; from the ether was obtained 3-*chloromethylchromone*, which separated from methanol or ether–hexane as plates (355 mg), m.p. 108.5—109°, $\lambda_{max.}$ 236, 298, and 304 nm (log ε 4.03, 3.81, and 3.81), $\nu_{max.}$ 1 650, 1 615, 1 575, 1 472 cm^{-1} (Found: C, 61.9; H, 3.8. $C_{10}H_7ClO_2$ requires C, 61.7; H, 3.6%), *m/e* 196 and 194 (M^+), and 159 ($M^+ - Cl$).

Other experiments showed that strict exclusion of water (*e.g.* use of flame-dried apparatus, distillation of solvents from calcium hydride) had little effect upon the outcome of the demethylation.

(ii) The interaction of 2′-hydroxyacetophenone (7 g), ethyl formate (30 ml), and powdered sodium (3 g) in ether (70 ml) gave a salt from which hydrochloric acid liberated a solid as reported by previous workers [14] but described as 2′-hydroxybenzoylacetaldehyde. Purification of this from benzene–light petroleum gave what is clearly the isomeric 2-*hydroxychroman*-4-*one* (XX) as needles (3.5 g), m.p. 97—97.5°, $\nu_{max.}$ 3 380 (OH), 1 667 (C:O), 1 610, 1 580, and 1 477 cm^{-1} (Found: C, 65.7; H, 4.9%; *M*, 164. $C_9H_8O_3$ requires C, 65.85; H, 4.91%; *M*, 164). The revised structure rests upon the slow colouration when a sample is added to iron(III) chloride in ethanol and upon the n.m.r. spectrum with second-order analysis for the ABX spin system formed by the protons at positions 2 and 3: τ 7.01, 7.13, and 4.15 (J_{AB} 16.5, J_{AX} 3.43, J_{BX} 4.78 Hz). Other resonances appeared at 5.97 (1 H, s, OH), 2.16 (1 H, dd, *J* 2 and 8 Hz, H-5), and 2.5—3.2 (3 H, mm, other ArH).

From this compound chromone was obtained as reported.[14] For the chloromethylation,[15] chromone (1 g) and paraformaldehyde (3 g) in acetic acid (16 ml) and water (4 ml) were kept at 90 °C while being saturated by gaseous hydrogen chloride (*ca.* 15 min). After another 27 h, paraformaldehyde (2 g) was again added and after a total of 96 h the reaction was terminated notwithstanding chromatographic evidence for starting material. The cooled mixture in ether was washed 8 times with water, dried, filtered, and evaporated leaving an oil that gradually solidified. This solid was freed from chromone by chromatography on silica from ether–light petroleum (1 : 9) and the product then crystallised from methanol or ether–hexane as plates (601 mg), m.p. 109—110°, identical with a sample from (i).

Reduction of 3-chloromethylchromone (400 mg) by zinc powder (800 mg) in acetic acid (13 ml) and water (2 ml) at 60 °C during 35 min gave 3-methylchromone, which crystallised from ether–light petroleum as tiny needles (231 mg), m.p. 69—69.5° (lit.,[16] 68°), $\nu_{max.}$ 1 643, 1 614, 1 573, and 1 488 cm^{-1}, τ ($CDCl_3$) 8.0 (d, *J* 1 Hz, CH_3), 2.31 (q, *J* 1 Hz, O·CH:), 1.82 (dd, *J* 2.8 Hz H-5), and 2.4—2.9 (mm, other ArH).

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