Thallium(III) Nitrate Oxidation of Chromens: *cis*-Dihydroxylation and Dialkoxylation

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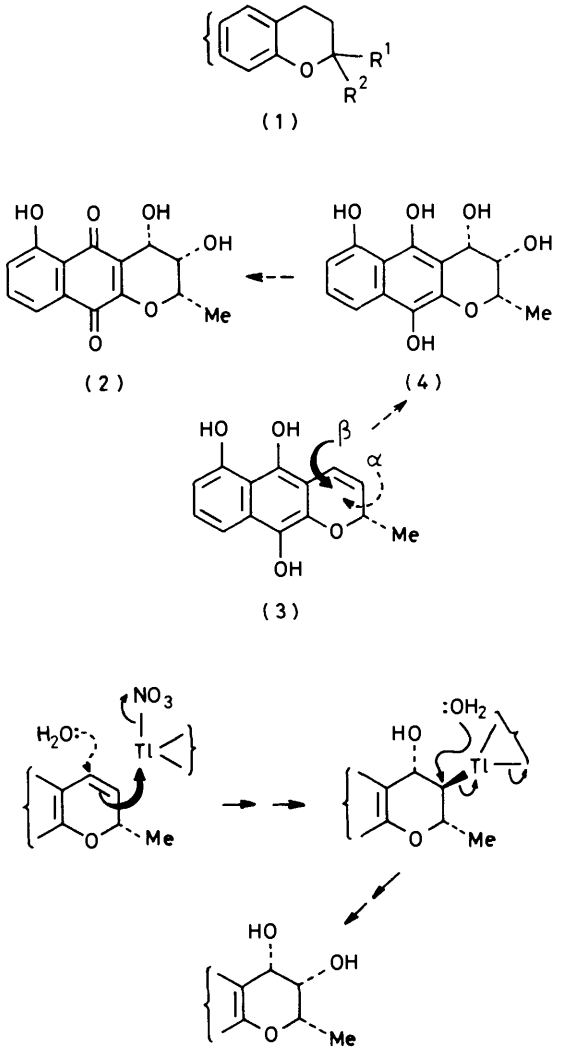
The oxidation of the chromens (6) and (10) with thallium(III) nitrate is described. In the case of the 2-methyl-2*H*-chromen (6) oxidation in aqueous dioxan gave a single *cis*-1,2-diol (7), unexpectedly arising from initial thalliation *syn* to the 2-methyl. The product stereochemistry was determined by single-crystal *X*-ray analysis, using direct methods. Rationalisation is proposed. With the 2,2-dimethylchromen (10), oxidation in methanol gave only the *cis*-dimethoxychroman (11); similar reactions were observed in other hydroxylic solvents. In ethane-1,2-diol the fused dioxan (18) was obtained, but in poor yield.

The chroman ring system (1) at various oxidation levels, is a frequent component of natural product structures. One major group is biogenetically derived from terpene-phenol union, possessing 2,2-dialkylated structures (1; R^1 = Me, R^2 = Me or prenyl). 2*H*-Chromans are also known, *e.g.* (1; R^1 = H, R^2 = aryl or alkyl). We have developed synthetic methods [1] for construction of 2,2-dialkyl and 2-alkyl-2*H*-chrom-3-en systems by annelation of suitable phenols, and complementary methods are available.[2] We looked to expand the scope of such syntheses through oxidation of chrom-3-ens to natural mono- and dioxy-compounds, and set out to investigate a route to cryptosporin [3] (2), an antibacterial metabolite of *Cryptosporium pinicola* (Linder), with an all *cis*-trisubstituted chroman ring.

Previous work suggests that an intermediate chromen (3) could be obtained from condensation of 1,3,4,8-tetrahydroxynaphthalene with crotonaldehyde dimethyl acetal in pyridine; [1d] dinydroxylation of (3), to yield (4), followed by oxidation, would complete synthesis of (2). However, *cis*-dihydroxylation of (3) from the *more hindered* α-face is needed in such a sequence. We argued that a thallium(III) initiated dihydroxylation could meet this requirement, since initial thalliation might be confined to the less hindered β-face. The desired *cis*-α-dihydroxylation would be accomplished as shown in Scheme 1.

Dihydroxylation and dimethoxylation of double bonds using thallium(III) salts in acidic water or methanol have been reported before,[4] and may accompany the widely studied rearrangement reaction [4,5] or supersede it if carbon migration is unfavourable. The stereochemistry has been worked out in a few cases but is substrate, anion, and solvent dependent.[6] However in one case [6d] using steroidal olefins, thallium(III)-catalysed dihydroxylation led to net *cis*-addition from the most hindered face. Since thallium(III) oxidation neither of chromens nor close relatives had been investigated at the outset of this work, and since thallium-induced ring contraction would also have had synthetic potential (*e.g.* in anisoxide [7] synthesis), we chose to study two model systems. In this paper we report the oxythalliation of chromens (6) and (10): the reactions were not high-yielding,† but yielded only *cis*-diols, or *cis*-diol ethers. Reaction with 2*H*-chromen (6) was stereospecific, but not in the sense predicted above, and control of the reaction is discussed.

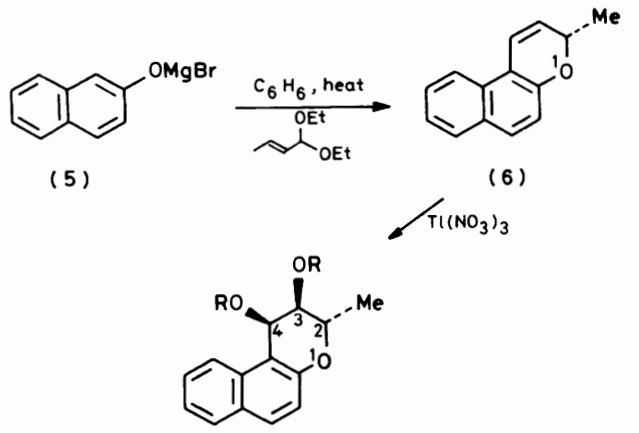
To provide a model 2*H*-chromen, 2-naphthyloxymagnesium bromide (5) was refluxed in benzene with crotonaldehyde diethyl acetal, furnishing [1d] the desired chromen (6) with



Scheme 1.

† Conditions were not optimised for any reaction reported here.

^{1}H n.m.r. data appropriate to a 3-chromen rather than a 2-chromen, *viz.* τ 3.20 (4-H), 4.53dd (3-H), 5.15 m (2-H), and 8.60 d (2-Me). Chromen (6) was then treated with thallium(III) nitrate in aqueous dioxan, to afford the single glycol (7). ^{1}H N.m.r. measurements indicate, with $J_{2,3}$ 10, $J_{3,4}$ 4 Hz, that the stereo-



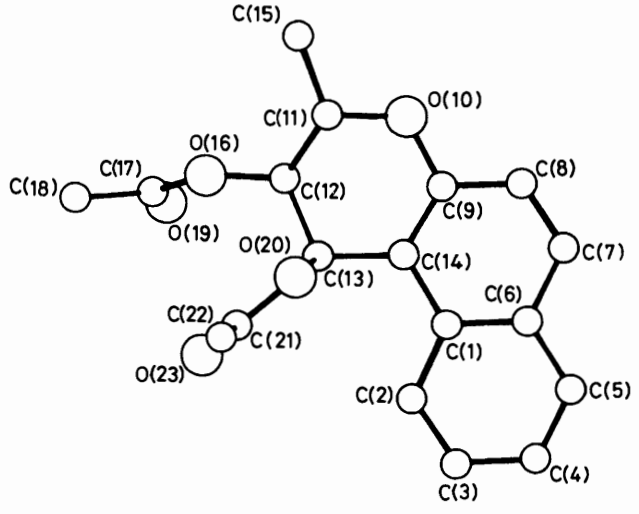


Figure. General view of the structure with crystallographic numbering

chemistry shown in (7) is probable. However because of the uncertainties in this system over conformational preferences and the effect of oxygens on J_{vic}, a single-crystal *X*-ray diffraction study of the diacetate (8) was undertaken. The diacetate (8) formed needles from ethanol, m.p. 129—131 °C.

The structure was determined by *X*-ray crystallography with refinement converging at *R* 4.57% over 1 640 independent observed reflections. The structure and stereochemistry are shown in the Figure which also indicates the crystallographic numbering scheme adopted. Bond lengths and bond angles are displayed in Tables 1 and 2 together with their standard deviations. These show no significant deviations from their normal values. The localised double bonds in the naphthalene section are clearly indicated as expected. The torsion angles about the bonds in the lactone ring are revealed in Table 3. These clearly indicate that the ring adopts the expected half-chair conformation. They also confirm the relative stereochemistry of the substituents to this ring with the acetyl groups *cis* to each other and *trans* to the methyl group, as shown in (8).

The yield of (7), after chromatography and crystallisation, was not high (25%); however, chromatographic (and mass spectral) examination of the total crude material extractable from the aqueous phase, both before and after acetylation, revealed no traces of stereoisomeric diols or their diacetates. The balance of organic material was polar, dark tar. Dihydroxylation of the double bond is thus stereoselective if not stereospecific, for the β-face of the chromen. This is the same

Table 1. Bond lengths (Å)

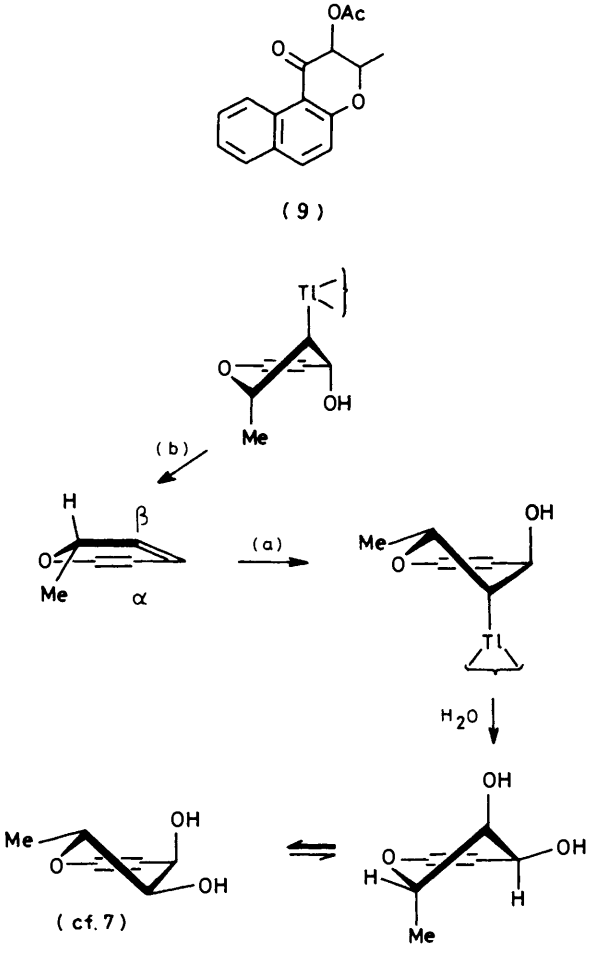
C(1)–C(2)	1.414(4)
C(1)–C(6)	1.411(4)
C(1)–C(14)	1.428(4)
C(2)–C(3)	1.364(5)
C(3)–C(4)	1.393(6)
C(4)–C(5)	1.354(5)
C(5)–C(6)	1.409(4)
C(6)–C(7)	1.420(4)
C(7)–C(8)	1.347(4)
C(8)–C(9)	1.402(4)
C(9)–C(10)	1.371(3)
C(9)–C(14)	1.364(4)
O(10)–C(11)	1.436(3)
C(11)–C(12)	1.516(4)
C(11)–C(15)	1.502(5)
C(12)–C(13)	1.513(4)
C(12)–O(16)	1.446(3)
C(13)–C(14)	1.492(4)
C(13)–O(20)	1.466(3)
O(16)–C(17)	1.338(4)
C(17)–C(18)	1.487(5)
C(17)–O(19)	1.181(4)
O(20)–C(21)	1.343(4)
C(21)–C(22)	1.488(5)
C(21)–O(23)	1.195(4)

Table 2. Bond angles (°)

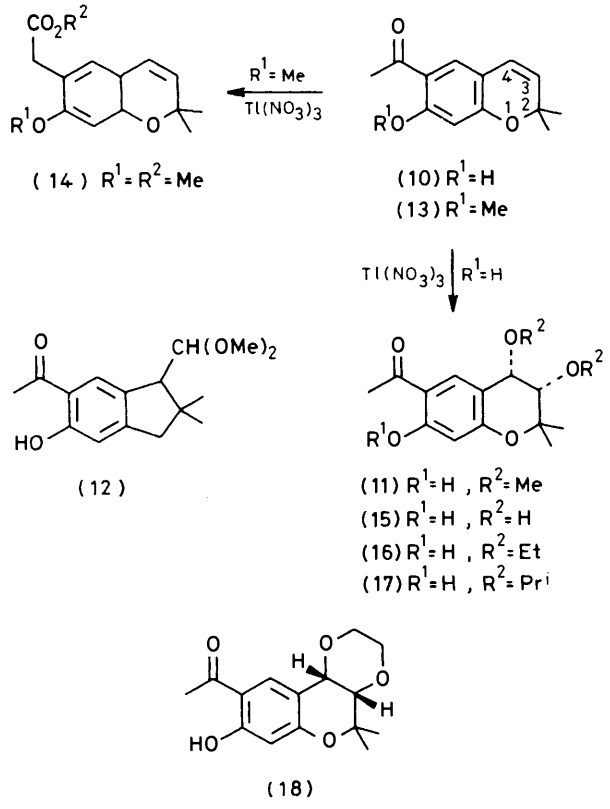
C(2)–C(1)–C(6)	117.7(3)
C(2)–C(1)–C(14)	122.9(3)
C(6)–C(1)–C(14)	119.4(3)
C(1)–C(2)–C(3)	120.5(4)
C(2)–C(3)–C(4)	121.2(4)
C(3)–C(4)–C(5)	119.9(4)
C(4)–C(5)–C(6)	120.5(4)
C(1)–C(6)–C(5)	120.1(3)
C(1)–C(6)–C(7)	118.8(3)
C(5)–C(6)–C(7)	121.1(3)
C(6)–C(7)–C(8)	121.0(3)
C(7)–C(8)–C(9)	119.9(3)
C(8)–C(9)–O(10)	114.6(3)
C(8)–C(9)–C(14)	122.0(3)
O(10)–C(9)–C(14)	123.4(3)
C(9)–O(10)–C(11)	117.2(2)
O(10)–C(11)–C(12)	107.5(2)
O(10)–C(11)–C(15)	106.2(3)
C(12)–C(11)–C(15)	114.2(3)
C(11)–C(12)–C(13)	111.6(2)
C(11)–C(12)–O(16)	107.8(2)
C(13)–C(12)–O(16)	109.3(2)
C(12)–C(13)–C(14)	110.8(2)
C(12)–C(13)–O(20)	108.1(2)
C(14)–C(13)–O(20)	107.1(2)
C(1)–C(14)–C(9)	118.8(3)
C(1)–C(14)–C(13)	120.8(3)
C(9)–C(14)–C(13)	120.4(3)
C(12)–O(16)–C(17)	117.8(2)
O(16)–C(17)–C(18)	111.9(3)
O(16)–C(17)–O(19)	122.9(3)
C(18)–C(17)–O(19)	125.1(3)
C(13)–O(20)–C(21)	118.1(2)
O(20)–C(21)–C(22)	110.4(3)
O(20)–C(21)–O(23)	123.7(3)
C(22)–C(21)–O(23)	125.8(3)

Table 3. Selected torsion angles (°)

C(14)–C(9)–O(10)–C(11)	19.0
C(9)–O(10)–C(11)–C(12)	−48.0
O(10)–C(11)–C(12)–C(13)	61.5
C(11)–C(12)–C(13)–C(14)	−44.7
C(12)–C(13)–C(14)–C(9)	14.4
C(13)–C(14)–C(9)–O(10)	−0.6
C(9)–O(10)–C(11)–C(15)	−170.6
O(10)–C(11)–C(12)–O(16)	−178.4
C(15)–C(11)–C(12)–O(16)	−60.9
C(15)–C(11)–C(12)–C(13)	179.1
C(11)–C(12)–C(13)–O(20)	72.4
O(16)–C(12)–C(13)–O(20)	−46.7
O(16)–C(12)–C(13)–C(14)	−163.8
O(20)–C(13)–C(14)–C(9)	−103.3



Scheme 2.



Scheme 3.

stereochemistry expected from oxidation with *e.g.* osmium tetraoxide. Accordingly, chromen (6) was treated with this reagent and the whole reaction product acetylated. The above diacetate (8) was isolated. A search for minor stereoisomers was again undertaken, but the ketoacetate (9) (3%) was the only other product isolated.

The osmium tetroxide reaction thus shows preference for β-face approach. However the oxythalliation reaction indicates initial thallium(III) approach in the α-sense: simple steric factors do not therefore control the reaction. Conformational factors presumably supervene, and Scheme 2 shows a possible explanation. Thalliation at C-3 is likely, to enable the benzylic C-4 to adopt carbocationic character, with *trans*-addition of water to C-4. Varying degrees of concertedness or of carbocation bridging could be accommodated. β-Face thalliation leads (path b) to a half-chair ring with an unfavourable 1,3-diaxial CH_3–OH interaction, whereas the observed α-approach (path a) avoids any such interactions. Replacement of thallium by water must follow with inversion, to give the observed stereochemistry.

The potential of this reaction for *cis*-dihydroxylation/dialkoxylation was then examined using the polyfunctional 2,2-dimethylchromen (10). This compound was prepared from 2,4-dihydroxyacetophenone by condensation with 3-hydroxy-3-methylbutanal diethyl acetal in pyridine.[1a] Oxidation of (10) with thallium(III) nitrate in methanol afforded the 3,4-dimethoxychroman (11) in fair yield (50%). ^{1}H N.m.r. data (see Experimental section) support gross structure (11) or, less plausibly, the ring-contracted isomer (12). However mass spectroscopic information uphold (11) (Scheme 3) showing the retro-aldol cleavage characteristic of chromans, but not the $(MeO)_2\overset{+}{C}H$ (mass 75) and $M - 75$ ions expected for the alternative (12). The *cis*-stereochemistry shown was indicated by $J_{3,4}$ 1.5 Hz, within the range of *ax-eq* vicinal proton couplings, but inappropriate for the 1,2-diaxial *trans* hydrogen arrangement.

Thus in the chromen (10), thallium(III) oxidation of the ethylenic link was faster than that of the methyl ketone or the phenolic nucleus, and such a reaction might be useful in synthesis of *cis*-3,4-dioxychromans (*e.g. cis*-khellalactone [8]). In contrast, oxidation of the *O*-methyl chromen (13) afforded the substituted methylphenyl acetate (14), whose structure follows from ^{1}H n.m.r. data (Experimental section). Thus, where the carbonyl group is not chelated to an *o*-hydroxy-group, oxidative rearrangement of the methyl ketone is preferred

to oxidative addition at the double bond. Chelation presumably stabilises the keto-form with respect to the enol.

Oxidation of the chromen (10) with thallic nitrate in aqueous dioxan, ethanol, and isopropyl alcohol afforded the corresponding *cis*-dihydroxy-, diethoxy-, and di-isopropoxychromans (15), (16), and (17), while in ethylene glycol the *cis*-fused 1,4-dioxan (18) was obtained. This is an interesting new way of preparing such fused heterocycles, but the yield was very poor (10%).

In a recent paper dealing with thallium trinitrate–methanol induced rearrangement of 2,2-dimethylchromenochalcones, Nógrádi and co-workers [9] observed products both of ring contraction and of non-stereospecific dimethoxylation. The chromens in this work were differently substituted from those in the present investigation, and the reaction is clearly dependent on substrate structure.

Experimental

*2-Methyl-2H-naphtho[2,1-b]pyran.**—2-Naphthol (6.8 g) in dry ether (75 cm^3) was added dropwise to ethylmagnesium bromide [from magnesium (1.13 g) and ethyl bromide (9.4 cm^3)] in dry ether (50 cm^3). The ether was then evaporated under reduced pressure. The residual solid was dissolved in benzene (100 cm^3) and refluxed for 4 h with 1,1-diethoxybut-2-ene (6.8 g). The mixture was then diluted with ether and washed successively with 1M-hydrochloric acid, 1M-sodium hydroxide, and water, before being dried. Evaporation of the solvents gave an oil which after chromatography on a dry silica column (cyclohexane–benzene, 4 : 1) gave the *title compound* (6) as an oil (42%) (Found: C, 85.5; H, 6.3%; M^+, 196.087. $C_{14}H_{12}O$ requires C, 85.7; H, 6.1%; *M*, 196.089); τ($CDCl_3$) 2.16—3.00 (6 H, m, ArH), 3.20 (1 H, d, *J* 12 Hz, ArC*H*), 4.53 (1 H, dd, *J* 3, 12 Hz, ArCH=C*H*), 5.15 (1 H, m, C*H*Me), and 8.60 (3 H, d, *J* 7 Hz, Me); $\lambda_{max.}$ (EtOH) 242 nm (4.61); $\nu_{max.}$ (film) 3 100, 2 975, 1 630, 1 590, 1 460, 1 080, 1 040, 1 020, 950, and 810 cm^{-1}.

3,4-Dihydroxy-2-methyl-2H-naphtho[2,1-b]pyran.—To 2-methyl-2*H*-naphtho[2,1-*b*]pyran (975 mg, 2.4 mmol) in dioxan (25 cm^3) at room temperature was added, dropwise with stirring, thallium(III) nitrate (1.164 g, 2.4 mmol) in 20% nitric acid (15 cm^3). Addition was completed in 10 min when a black precipitate had formed. Stirring of the mixture was continued for 1 h, after which it was diluted with water and extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate and water and then dried. Evaporation of the solvent yielded a brown oil which was purified by p.l.c. (0.8 mm silica plates, ether–hexane, 4 : 1) to give the *title compound* (130 mg, 23%), m.p. 204—206 °C (Found: C, 73.1; H, 6.2%; M^+, 230.095. $C_{14}H_{14}O_3$ requires C, 73.05; H, 6.1%; *M*, 230.094); τ[(CD_3)SO] 1.98—3.20 (6 H, m, ArH), 4.80 (1 H, br, OH), 4.96 (1 H, d, *J* 4 Hz, ArC*H*), 5.04br (1 H, O*H*), 5.77 (1 H, m, C*H*Me), (6.45 1 H, dd, *J* 4, *J* 10 Hz, ArCHC*H*), and 8.60 (3 H, d, *J* 7 Hz, Me); $\lambda_{max.}$ (EtOH) 250 (4.60), 271 nm (4.56); $\nu_{max.}$(KBr) 3 050br, 3 000, 1 630, 1 615, 1 590, 1 510, 1 070, 960, 860, 760, and 740 cm^{-1}.

3,4-Diacetoxy-2-methyl-2H-naphtho[2,1-b]pyran.—(*a*) The diol (7) (150 mg), acetic anhydride (2 cm^3), and pyridine (2 cm^3) were heated on steam for 2 h. The mixture was then poured onto ice, and extracted with ether. The extracts were washed (aqueous sodium hydrogen carbonate, dilute hydrochloric acid, and water), dried, and evaporated to yield the *title compound* (160 mg, 66%), m.p. 129—131 °C (from ethanol) (Found: M^+ 314.114. $C_{18}H_{18}O_5$ requires *M*, 314.115); τ($CDCl_3$) 2.34—3.00 (6 H, m, ArH), 3.21 (1 H, d, *J* 4 Hz, ArC*H*), 4.93 (1 H, dd, *J* 4, 10 Hz, ArCHC*H*), 5.54 (1 H, m, C*H*Me), 7.95 (6 H, s, 2 × Ac), and 8.57 (3 H, d, *J* 7 Hz, Me); $\lambda_{max.}$(EtOH) 229 (4.63), 276 (4.55), and 288 nm (4.54); $\nu_{max.}$ (KBr), 2 950, 2 900, 1 730, 1 620, 1 600, 1 510, 1 050, 1 010, 960, 940, 900, 810, and 760 cm^{-1}.

(*b*) The naphthopyran (6) (99 mg) in dioxan (20 cm^3) was treated with osmium tetraoxide (100 mg), with stirring, for 4 h. Sodium metabisulphite (0.22 g) in water (5 cm^3) and pyridine (3 cm^3) was added, and the mixture was filtered. The organic products were extracted from the filtrate with ether, and acetylated in the above manner to yield the title compound (16 mg, 10%) after chromatography and crystallisation, with ^{1}H n.m.r. and i.r. spectra indistinguishable from those of the above sample. The only other product detectable in t.l.c. was the *acetoxypyranone* (9) (3 mg, 2.5%) (Found: M^+, 270.088. $C_{16}H_{14}O_4$ requires *M*, 270.089); τ($CDCl_3$) 2.34—3.00 (6 H, m, ArH), 4.49 (1 H, d, *J* 4 Hz, C*H*OAc), 5.52 (1 H, m, C*H*Me), 7.92 (3 H, s, Ac), and 8.57 (3 H, d, *J* 7 Hz, Me).

Oxythalliation of 6-Acetyl-5-hydroxy-2,2-dimethylchromen.—Thallium(III) nitrate (0.97 g, 2 mmol) in a protic solvent (25 cm^3) was added dropwise to a stirred solution of the title chromen [1a] (0.45 g, 2 mmol) in the same solvent (25 cm^3), and perchloric acid (1 cm^3) added. The mixture was stirred overnight, and then diluted with water and extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate and water, dried, and evaporated. In this way, using methanol as solvent, was obtained an oil which after chromatography on a silica column (benzene–ethyl acetate, 3 : 1) yielded the *dimethoxychroman* (11) (280 mg, 50%), m.p. 139—141 °C (from hexane) (Found: C, 64.75; H, 7.25. $C_{15}H_{20}O_5$ requires C, 64.3; H, 7.2%); $\lambda_{max.}$ (EtOH) 287 (3.92) and 320 nm (3.96); $\nu_{max.}$ (mull) 1 620 cm^{-1}; τ — 3.6 (1 H, s, OH), 2.27 (1 H, d, *J* 9 Hz, 7-H), 3.50 (1 H, d, 8-H), 5.47 (1 H, d, *J* 2.5 Hz, 4-H), 6.3 and 6.4 (both 3 H, s, OMe), 6.6 (1 H, d, *J* 2.5 Hz, 3-H), 7.42 (3 H, s, Ac), and 8.50 and 8.55 (both 3 H, s, CMe_2). In aqueous dioxan the *3,4-dihydroxychroman* (15) (65 mg, 12%) was obtained, m.p. 116—118 °C from hexane (Found: C, 62.15; H, 6.45. $C_{13}H_{16}O_5$ requires C, 61.9; H, 6.4%); $\lambda_{max.}$ 290 (3.98) and 320 nm (3.95); $\nu_{max.}$ 3 410 and 1 610 cm^{-1}; τ — 4.01 (1 H, s, ArOH), 2.32 (1 H, d, *J* 9 Hz, 7-H), 3.47 (1 H, d, *J* 9 Hz, 8 H), 5.05 (1 H, d, *J* 4.8 Hz, 4-H), 4.7 (1 H, OH), 6.17 (1 H, d, *J* 4.8 Hz, 3-H), 6.8 (1 H, OH), 7.42 (3 H, s, Ac), and 8.52 and 8.75 (both 3 H, s, CMe_2).

Using ethanol in the reaction an oil was obtained which was chromatographed on a silica column (benzene), to yield the *3,4-diethoxychroman* (16) (95 mg, 15%), m.p. 83—85 °C (from hexane) (Found: C, 66.5; H, 8.0. $C_{17}H_{24}O_5$ requires C, 66.2; H, 7.85%); $\lambda_{max.}$ (EtOH) 286 (4.11) and 320 nm (3.95); $\nu_{max.}$ (mull) 1 620 cm^{-1}; τ($CDCl_3$) — 3.65 (1 H, s, OH), 2.25 (1 H, d, *J* 9 Hz, 7-H), 3.45 (1 H, d, *J* 9 Hz, 8-H), 5.35 (1 H, d, *J* 2.3 Hz, 4-H), 6.10 and 6.25 (both 2 H, q, *J* 8 Hz, OCH_2), 6.45 (1 H, d, 3-H), 7.45 (3 H, s, Ac), 8.45 and 8.50 (both 3 H, s, CMe_2), and 8.72 and 8.75 (both 3 H, t, *J* 8 Hz, Me). Employing isopropyl alcohol as reaction medium led to the isolation (silica column, benzene–ethyl acetate, 3 : 1) of the *3,4-di-isopropoxychroman* (17) (50 mg, 8%), m.p. 86—88 °C (from hexane) (Found: C, 67.5; H, 8.35 $C_{19}H_{28}O_5$ requires C, 67.8; H, 8.4%); $\lambda_{max.}$ (EtOH) 287 (4.17) and 329 nm (4.02); $\nu_{max.}$ (mull) 1 620 cm^{-1}; τ($CDCl_3$) —3.63 (1 H, s, OH), 2.25 (1 H, d, *J* 9 Hz, 7-H), 3.47 (1 H, d, 8-H), 5.35 (1 H, d, *J* 1.5 Hz, 4-H), 6.00 (2 H, m, OCH), 6.45 (1 H, d, 3-H), 7.45 (3 H, s, Ac), 8.42 and 8.45 (both 3 H, s, CMe_2), and 8.8 (6 H, $CHMe_2$).

Finally, with ethylene glycol, the *5H-p-dioxino[2,3-c][1]-benzopyran* (18) (50 mg, 10%), m.p. 78—81 °C (from hexane), was obtained (silica column, benzene–ethyl acetate, 9 : 1)

* The numbering in cipher (7) is used throughout to retain consistency with (10) and related pyrans.

Table 4. Atomic co-ordinates

Atom	x/a	y/b	z/c
C(1)	0.016 4(2)	0.543 9(4)	0.130 9(2)
C(2)	0.032 5(3)	0.717 2(5)	0.163 3(2)
C(3)	−0.045 4(4)	0.804 6(6)	0.180 7(2)
C(4)	−0.142 1(3)	0.725 5(6)	0.168 6(2)
C(5)	−0.161 2(3)	0.561 2(6)	0.135 9(2)
C(6)	−0.083 4(2)	0.468 0(4)	0.115 4(2)
C(7)	−0.102 8(3)	0.296 2(5)	0.080 3(2)
C(8)	−0.026 4(2)	0.203 6(5)	0.065 2(2)
C(9)	0.074 3(2)	0.275 9(4)	0.085 2(2)
O(10)	0.146 4(1)	0.166 6(3)	0.070 3(1)
C(11)	0.255 4(2)	0.208 8(4)	0.111 9(2)
C(12)	0.268 7(2)	0.402 6(4)	0.097 4(2)
C(13)	0.205 0(2)	0.515 5(4)	0.136 1(2)
C(14)	0.096 9(2)	0.442 8(4)	0.115 9(2)
C(15)	0.315 5(3)	0.089 4(6)	0.073 8(4)
O(16)	0.378 9(1)	0.444 8(3)	0.137 1(1)
C(17)	0.420 0(2)	0.563 1(5)	0.098 4(2)
C(18)	0.529 0(3)	0.612 2(7)	0.151 9(4)
O(19)	0.372 1(2)	0.625 2(4)	0.031 3(2)
O(20)	0.255 6(2)	0.511 0(3)	0.229 2(1)
C(21)	0.315 3(2)	0.648 5(5)	0.267 6(2)
C(22)	0.363 0(4)	0.617 8(7)	0.361 1(2)
O(23)	0.327 5(2)	0.776 0(4)	0.230 3(2)
H(2)	0.100(2)	0.771(4)	0.174(2)
H(3)	−0.035(3)	0.914(6)	0.203(2)
H(4)	−0.196(3)	0.778(6)	0.182(2)
H(5)	−0.229(3)	0.508(5)	0.125(2)
H(7)	−0.175(3)	0.254(4)	0.066(2)
H(8)	−0.041(2)	0.090(4)	0.043(2)
H(11)	0.274(2)	0.187(4)	0.174(2)
H(12)	0.247(2)	0.427(3)	0.036(2)
H(13)	0.203(2)	0.643(4)	0.118(2)
H(15A)	0.391(3)	0.103(5)	0.101(2)
H(15B)	0.300(3)	−0.025(6)	0.083(3)
H(15C)	0.300(4)	0.114(7)	0.012(4)
H(18A)	0.567(3)	0.525(6)	0.187(3)
H(18B)	0.562(3)	0.671(6)	0.116(3)
H(18C)	0.521(5)	0.696(10)	0.181(4)
H(22A)	0.389(4)	0.717(7)	0.385(3)
H(22B)	0.422(4)	0.525(7)	0.375(3)
H(22C)	0.319(4)	0.552(7)	0.384(3)

(Found: C, 64.7; H, 6.65. $C_{15}H_{18}O_5$ requires C, 64.75; H, 6.5%); $\lambda_{max.}$ 284 (3.90) and 320 nm (3.74); $\nu_{max.}$ 1 620 cm^{-1}; $\tau(CDCl_3)$ — 3.78 (1 H, s, OH), 2.17 (1 H, d, *J* 9 Hz, 7-H), 3.42 (1 H, d, 8-H), 4.82 (1 H, d, *J* 3 Hz, 4-H), 6.22 (1 H, d, 3-H), 6.15 (4 H, m, OCH_2CH_2O), 7.35 (3 H, s, Ac), and 8.45 and 8.72 (both 3 H, s, CMe_2).

6-Acetyl-5-methoxy-2,2-dimethylchromen.—The phenolic chromen (10) (5 g) in acetone (50 cm^3) was refluxed with methyl iodide (20 cm^3) over anhydrous potassium carbonate (10 g) for 24 h. On dilution with water the *methyl ether* (13) (5 g, 94%) crystallised out, m.p. 39—41 °C (Found: C, 72.15; H, 6.95. $C_{14}H_{16}O_3$ requires C, 72.35; H, 6.95%). The methyl ether (13) was treated with thallium(III) nitrate in methanol as described above. The product was chromatographed on silica (benzene) to yield the methyl ester (14), as an oil (Found: M^+, 262.121 $C_{15}H_{18}O_4$ requires *M*, 262.120), $\nu_{max.}$ (film) 1 750, 1 640, and 1 610 cm^{-1}; $\tau(CDCl_3)$ 2.77 (1 H, d, *J* 9 Hz, 7-H), 3.32 (2 H, d, *J* 9 Hz, 4-H, 8-H), 4.25 (1 H, d, *J* 9 Hz, 3-H), 6.15 (3 H, s, ArOMe), 6.20 (3 H, s, CO_2Me), 6.32 (2 H, s, $ArCH_2$), and 8.52 (6 H, s, CMe_2).

* For details of the Supplementary publications scheme see Instructions for Authors (1983), *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

Crystallographic Experimental.—Crystal data. $C_{18}H_{18}O_5$, *M* = 314.3, Monoclinic, *a* = 13.568(2), *b* = 7.615(1), *c* = 16.688(2) Å, β = 110.25(2)°, *U* = 1 618.6 Å^3, *Z* = 4, D_c = 1.29 g cm^{-3}, *F*(000) = 664, space group $P2_1/c$ uniquely from systematic absences, Mo-K_α radiation, λ = 0.71069 Å, μ(Mo-K_α) = 1.02 cm^{-1}.

The space group and preliminary cell parameters were determined photographically. For intensity measurement a crystal of approximate dimensions 0.5 × 0.25 × 0.1 mm^3 was mounted on a Hilger Y290 diffractometer. Accurate lattice parameters were obtained by least-squares refinement of 23 reflections measured on the diffractometer. Intensity data were collected with Mo-K_α radiation using an ω—2θ scan for 1° ≤ θ ≤ 25°. A total of 2 846 independent reflections was measured of which 1 640 had $I \geq 3\sigma(I)$ and were considered observed. The data were corrected for Lorentz and polarisation factors, but no absorption corrections were made. Data reduction and subsequent crystallographic calculations were performed using the 'Crystals' system of programs.

The structure was solved by direct methods using the Multan program. 230 Reflections with $E > 1.7$ were used. The *E* map based on the best set of phases revealed the positions of all 23 non-hydrogen atoms among the largest peaks in the map. Full-matrix isotropic least-squares refinement of these positions gave a value for *R* of 13.4%. Refinement was continued with anisotropic thermal parameters. A difference map was then calculated which clearly revealed the positions of all 18 hydrogen atoms as the largest features. The hydrogen atoms were then included in the least-squares refinement with isotropic vibrations. Analysis of the agreement between F_o and F_c suggested the adoption of a weighting scheme based on a Chebyshev polynominal. Refinement finally converged at a final *R* value of 4.57% after 17 cycles. A final difference map showed no peaks or depressions >0.2 e Å^{-3}. Final atomic co-ordinates are listed in Table 4, temperature factors and observed and calculated structure factors are listed in Supplementary Publication No. 23532 (17 pp.).*

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