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Synthesis and Reactivity of Some 4-Bromo- 2*H*-Chromenes and 2*H*-Thiochromenes

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Abstract: A facile synthesis of 4-bromo- 2*H*-chromenes and 2*H*-thiochromenes and of 1-bromo-3,4-dihydronaphthalene from the corresponding ketones and PBr_3 is described. In some instances, significant quantities of the phosphonic acids (3) are isolated. Conversion of the bromo compounds to the lithio derivatives provides access to a wide range of novel 4-substituted 2*H*-chromenes and 2*H*-thiochromenes.

Introduction

The 2,2-disubstituted 2*H*-[1]benzopyran unit occurs in a variety of plant species[1] and the recent isolation of macrocyclic chromenes from *Smenospongia* sp. indicates an even wider natural occurrence.[2] An upsurge of interest in the system followed the discovery of the anti-juvenile hormone activity exhibited by 7-methoxy- and 6,7-dimethoxy-2,2-dimethylchromenes, the precocenes.[3] The photochromic[4] and thermochromic[5] activity of various spirobenzopyrans[6] has been known for some time, but only recently has the value of simpler benzopyran derivatives as photochromes been recognised.[7] Our interest in benzopyran chemistry has been extended to include the sulfur analogues and covers both their pharmacological and hi-tech uses. We have recently focussed our attention on the value of both heterocyclic systems as synthetic reagents, notably in the formation of heterofused pyrans and thiopyrans[8] and in the synthesis of thiorotenoid derivatives.[9] We now report a convenient route to 4-bromo- 2*H*-[1]benzopyrans and 2*H*-[1]benzothiopyrans and discuss their use in the formation of novel 4-substituted chromenes and thiochromenes.

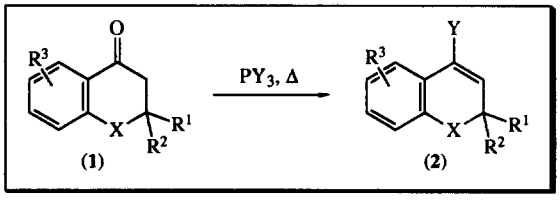
A survey of the literature revealed that these compounds were available by a multistep sequence from chroman-4-ones involving reduction to the chroman-4-ol and dehydration to afford the 2*H*-chromene. Subsequent addition of bromine and elimination of HBr from the *trans*-3,4-dibromochroman using alkoxide gives the 4-bromochromenes.[10] Alternatively, thermal cyclisation of γ-bromopropargylphenyl ethers affords mixtures of 3- and 4-bromochromenes by a Claisen rearrangement.[11] The above methods are not readily applicable to the sulfur analogues. The reaction of base with 3,4-dibromothiochromans is known to result in ring contraction of the thiopyran ring to a substituted benzothiophene,[12] whilst the alternative thio-Claisen rearrangement of thiopropargyl ethers suffers from a competitive thiopropynylic rearrangement.[13] Brown *et al.* have obtained a range of 4-chlorochromenes by Vilsmeier-Haack formylation of chroman-4-ones,[14a] but only

one bromo derivative, 4-bromo-7-methoxy-2,2-dimethylchromene, was reported which required the initial preparation of $POBr_3$.[14b] More recently, Hungarian workers have communicated an expedient route to 4-halo-2*H*-chromenes from chroman-4-ones and phosphorus trihalides.[15]

Discussion

This last approach appeared particularly attractive because of the ready availability of chroman-4-ones (1) using the Kabbe synthesis[16] from which the 4-bromochromenes can be obtained in a single step. Unfortunately, we could not reproduce the literature method, isolating instead intractable tars which yielded only small quantities of the 4-bromochromenes (ca. 5 %) after column chromatography. However, 4-bromochromenes (2) were obtained in good yield by refluxing the chromanones with PBr_3 for 30-90 minutes (Table 1), a drastic reduction from the 8-12 hours advocated.[15]

Furthermore, 4-bromo-2*H*-thiochromene (2j) was produced in good yield without the formation of any ring contracted products by refluxing 2,2-dimethylthiochroman-4-one in PBr_3. Unfortunately, the corresponding 4-bromo-2*H*-thiochromene 1,1-dioxide (2k) could not be obtained from the thiochroman-4-one 1,1-dioxide even after prolonged reflux. This lack of reactivity is probably a consequence of the electron withdrawing sulfone function which deactivates the 4-carbonyl function to attack by the PBr_3. No attempt was made to investigate the reaction between 2,2-dimethylthiochroman-4-one 1-oxide with PBr_3 since the reduction of sulfoxides to sulfides with phosphorus trihalides is well documented.[17] Application of this methodology to the homocyclic analogue, 1-tetralone, provided 1-bromo-3,4-dihydronaphthalene (2l) in satisfactory yield.

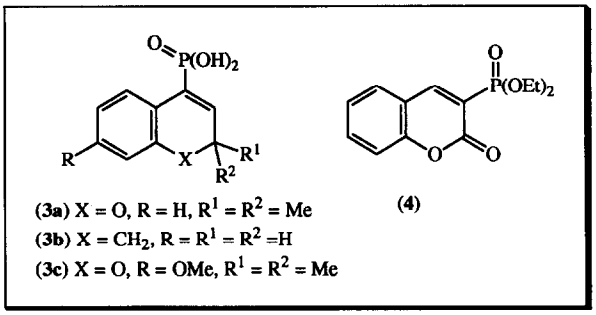


(1) (2)

The crude reaction product from 2,2-dimethylchroman-4-one and PBr_3 appeared as an off white sticky solid rather than a mobile yellow oil typical of chromenes. This solid was collected by vacuum filtration and washed well with 1% diethyl ether in light petroleum (b.p. 40-60 °C) and the washings were evaporated to yield crude 4-bromo-2,2-dimethyl-2*H*-chromene as a pale yellow oil which was initially purified by column chromatography. The remaining solid was recrystallised from ethyl acetate and hexane. The ^1H NMR spectrum of this solid (3a) displayed a singlet at δ 1.29 accounting for 6 protons and assigned to the geminal methyl group at C-2, a doublet at δ 6.37 accounting for 1 proton with a coupling constant of 20.2 Hz, four distinct signals in the range δ 6.45 - δ 7.57 integrating for a total of 4 protons with a pattern typical of the aromatic unit of a chromene and a broad singlet at δ 8.62 integrating for two protons. This latter signal disappeared when the sample was shaken with D_2O.

The magnitude of the coupling constant suggests that a phosphorus atom has been incorporated into the 2,2-dimethylchromene unit and this feature was confirmed by a ^{31}P NMR spectrum which displayed a singlet at δ 15.1. This chemical shift compares favourably with those of aryl phosphonic acids and esters which normally absorb in the range δ 0 - δ 25.[18]

These data for (3a) and those obtained for diethyl coumarin-3-phosphonate (4), prepared by either $TiCl_4$-pyridine catalysed condensation of triethyl phosphonoacetate and salicylaldehyde[19a] or by liquid/liquid phase transfer promoted condensation between *O*-acetylsalicylaldehyde and triethyl phosphonoacetate,[19b] show some close similarities. In particular, the *cis*-$^3J_{PH}$ coupling constant of 18 Hz for (4) and the ^{31}P NMR chemical shift of the phosphorus atom in (4) and several analogues (δ 5.12 - δ 21.84) show good agreement.



(3a) X = O, R = H, $R^1 = R^2$ = Me
(3b) X = CH_2, R = $R^1 = R^2$ =H
(3c) X = O, R = OMe, $R^1 = R^2$ = Me

(4)

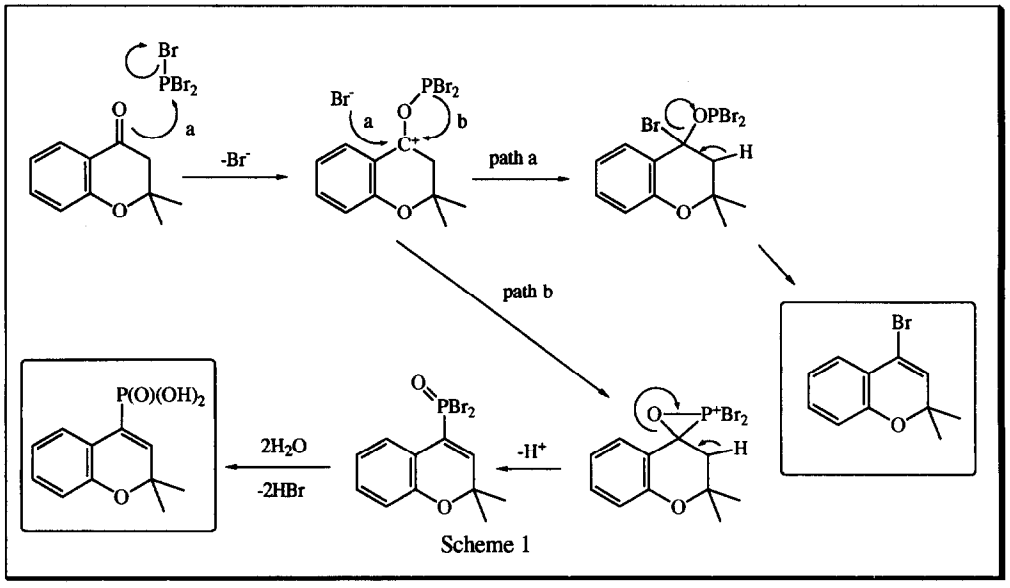
The ^{13}C NMR spectrum of (3a) corroborates the incorporation of the phosphorus function since the carbon directly bonded to the phosphorus atom gives rise to a doublet at δ 125.5 with J = 184.7 Hz, the large coupling constant being typical for $^1J_{PC}$.[20] Additionally, P-C coupling is observed for the signals at δ 74.8 (J 14.7 Hz) (C-2), 117.9 (J 11.2 Hz), 140.6 (J 5.8 Hz), 152.0 (J 10.1 Hz) and associated with C-2, C-3, C-4a and C-8a, although only the first of these can be unequivocally assigned by comparison of the chemical shift of C-2 with that of other 2*H*-chromenes and chroman-4-ones.[21]

The infrared spectrum of compound (3a) displays a broad band centred at 2650 cm^{-1} appertaining to the $P(OH)_2$ function and a weak band at 1260 cm^{-1} which is assigned to a P=O stretch.[22] The electron impact mass spectrum gives *m/z* 240 (18%), 225 (100%) and 207 (85%) and then multiple fragmentation. The major peaks relate to M^+, (M - CH_3) (base peak) and subsequent loss of water, respectively. It is noteworthy that fragmentation involving the loss of a methyl group is common to 2,2-dimethyl- chromene and chroman-4-one analogues.[23]

Similar phosphonic acids (3b) and (3c) were isolated from 1-tetralone with PBr_3 and from 2,2-dimethyl-7-methoxychroman-4-one with PCl_3 respectively and have comparable spectroscopic parameters to (3a). Interestingly, the mass spectrum of (3b), derived from 1-tetralone, gives peaks at *m/z* 210 (12%) for M^+ and at *m/z* 128 (100%) for $C_{10}H_8^+$ presumably by aromatisation through loss of 2H together with loss of the phosphorus function. Coupling between H-2 and the 3-methylene protons in the ^1H NMR spectrum of (3b) confirms the regiospecific formation of the benzylic phosphonic acid. The ^1H NMR spectrum of (3c) displays long range coupling between the phosphorus atom and H-8 with $^5J_{PH}$ = 1.8 Hz. Long range coupling between H-4 and H-8 has been observed for some substituted 2*H*-chromenes.[24]

Tlc examination of the crude products from reactions of several substituted chromanones with PBr_3 revealed that in addition to the fast running 4-bromochromene and unreacted chroman-4-one, a polar material remained on the base line even when the polarity of the eluent was increased. Attempts to induce the crude reaction mixtures to solidify by addition of light petroleum (b.p. 40-60 °C) and ether were unsuccessful. Elution of the reaction mixtures from silica gave the 4-bromochromene and the chroman-4-one, but the polar material, probably the 4-phosphonic acid, could not be eluted from the column.

The ^{1}H NMR spectra of the 2,2-disubstituted 4-bromochromenes obtained in this work are very similar, with H-3 appearing as a singlet in the range δ 5.98-6.08 with the exception of (2g) where the presence of the 2-phenyl substituent causes a downfield shift to δ 6.37. H-3 is similarly deshielded in the sulfur analogue (2j) and resonates at δ 6.28. Benzannulation has no great influence on the chemical shift of H-3 *viz.* δ 6.07, δ 6.04 and δ 6.15 for (2h), (2i) and (2p) respectively. The aromatic protons absorb in the range δ 6.7-7.5, with H-5, *peri* to the 4-halogen substituent, being the furthest downfield of the aromatic signals at ~δ 7.4 (2a-g). 5,6-Benzannulation has a marked effect on the chemical shift of this *peri* proton which resonates at δ 8.79. A similar feature obtains in the simple dialkyl chroman-4-ones where H-5 routinely absorbs at ~δ 8.0 but at δ 9.4 for the corresponding proton in the 5,6-benzologue, shifted further downfield in comparison with the bromo compounds because of the greater deshielding effect of the *peri* carbonyl group.



Scheme 1

The 4-bromochromene and the phosphonic acid are considered to arise from a common intermediate formed by nucleophilic attack of the chromanone on PBr_3 (Scheme 1). Attack of bromide ion at the carbocation centre is followed by elimination of $HOPBr_2$ and leads to the chromene (path a). Coordination of the phosphorus to the cationic site affords the 4-phosphonic acid (path b).

Refluxing 2,2-dimethylchroman-4-one in PCl_3 did not give the 4-chloro compound, but the 7-methoxy derivative was converted into the 4-chlorochromene (2r) together with some of the phosphonic acid (3c) on refluxing in PCl_3 for 9h. In the latter example, conjugation between the 7-methoxy substituent and the carbonyl function increases the nucleophilicity of the carbonyl oxygen atom, promoting attack at the electrophilic phosphorus atom. Whilst the P atom in PCl_3 is more electrophilic than that in PBr_3, other factors such as the leaving group ability and the nucleophilic power of the halides point to higher reactivity for PBr_3 in this type of reaction. The weaker strength of the P-Br bond (274 KJmol^{-1}) compared with that of the P-Cl bond (331 KJmol^{-1})[25] and the greater release of steric strain associated with displacement of bromide ion in step 1 of

the proposed mechanism are also contributory features. Attempts to obtain a 4-iodochromene using PI_3 were unsuccessful.

Table 1 Experimental Data for the Preparation of 4-Halo-2*H*-chromenes.

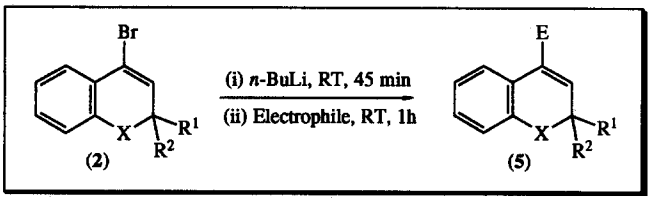
	X	Y	R^1	R^2	R^3	Time (min)	Yield (%)	^{1}H NMR 3-H (ppm)
2a	O	Br	Me	Me	H	40	67	6.02
2b	O	Br	Me	Et	H	30	75	5.98
2c	O	Br	Me	*i*-Pr	H	30	69	6.04
2d	O	Br	Me	*n*-Bu	H	45	71	5.99
2e	O	Br	-$(CH_2)_5$-		H	40	82	6.05
2f	O	Br	-$(CH_2)_6$-		H	35	60	6.08
2g	O	Br	Me	Ph	H	45	67	6.37
2h	O	Br	Me	Me	7,8-Benzo	60	28	6.07
2i	O	Br	-$(CH_2)_5$-		7,8-Benzo	65	33	6.04
2j	S	Br	Me	Me	H	40	71	6.28
2k	SO_2	Br	Me	Me	H	600	0	-
2l	CH_2	Br	H	H	H	70	44	6.49†
2m	O	Br	H	*i*-Pr	H	60	0	-
2n	O	Br	H	*i*-Pr	H	120	49‡	6.12
2o	O	Cl	Me	Me	H	600	0	-
2p	O	Br	Me	Me	5,6-Benzo	90	59	6.15
2q	O	I	Me	Me	7-OMe	600	0	-
2r	O	Cl	Me	Me	7-OMe	540	65	5.63
2s	O	Br	H	H	H	105	37‡	6.16

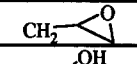
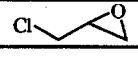
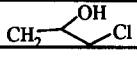
Footnotes: † Chemical shift of corresponding proton (H-2).
‡ Reaction mixture maintained at 90 °C.

The selective generation of alkenyl lithium reagents by the metal-halogen exchange reaction of *n*-butyllithium with either a bromo- or an iodo-alkene is of considerable value in organic synthesis.[26] Addition of *n*-butyllithium to a stirred solution of a 4-bromochromene in ether at room temperature and under N_2 affords the 4-chromenyl lithium in high yield after ~ 45 minutes. These lithiochromenes have been quenched with a range of electrophiles to afford a range of novel chromene-4-carboxylic acids, chromene-4-carbaldehydes and 4-aroylchromenes (5) in good to excellent yield (Table 2). The use of *N,N*-dimethylcarbamoyl chloride as the

electrophile yielded the dichromenyl ketone (5f) and in a similar manner, acetic anhydride gave the 1,1-disubstituted ethene (5r). Chlorotrimethylsilane, diphenyl disulfide and 4-methoxybenzaldehyde all gave the expected products. Epichlorohydrin apparently underwent attack at two of the electrophilic centres since both (5d) and (5e) were isolated from the reaction.

Table 2 Experimental Data for the Preparation of 4-Substituted-2*H*-chromenes.

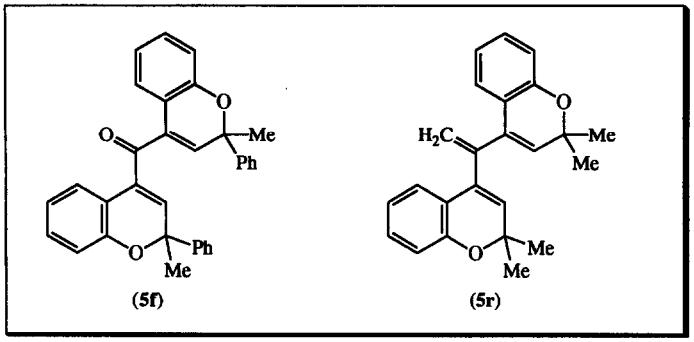


	R^1	R^2	X	Electrophile	E	Yield	^{1}H NMR (ppm)	
						%	3-H	5-H
5a	Me	Me	O	Me_3SiCl	Me_3Si	25	5.86	7.20
5b	Me	Me	O	$(PhS)_2$	PhS	27	5.92	7.41
5c	Me	Me	O	4-$MeOC_6H_4CHO$	4-$MeOC_6H_4CHOH$	39	5.88	¶
5d	Me	Me	O			41	5.57	¶
5e	Me	Me	O			30	5.55	¶
5f	Me	Ph	O	Me_2NCOCl	§	24	6.47	7.61
5g	Me	Me	O	2-FC_6H_4CN	2-FC_6H_4CO	54	5.74	¶
5h	Me	Me	O	PhCN	PhCO	77	5.95	7.91
5i	Me	Me	O	2-$MeOC_6H_4CN$	2-$MeOC_6H_4CO$	62	5.99	7.64
5j	Me	Me	S	(2,4-diMeO)C_6H_3CN	(2,4-diMeO)C_6H_3CO	61	6.14	7.35
5k	-$(CH_2)_5$-		O	(2,4-diMeO)C_6H_3CN	(2,4-diMeO)C_6H_3CO	66	5.94	7.35
5l	Me	Me	O	CO_2	COOH	93	6.88	8.04
5m	Me	Ph	O	CO_2	COOH	83	7.24	8.02
5n	Me	*i*-Pr	O	CO_2	COOH	91	6.90	8.04
5o	Me	Me	O	Me_2NCHO	CHO	74	6.44	8.21
5p	Me	Et	O	Me_2NCHO	CHO	87	6.43	8.24
5q	H	*i*-Pr	O	Me_2NCHO	CHO	63	6.61	8.19
5r	Me	Me	O	Ac_2O	*	38	5.63	7.30

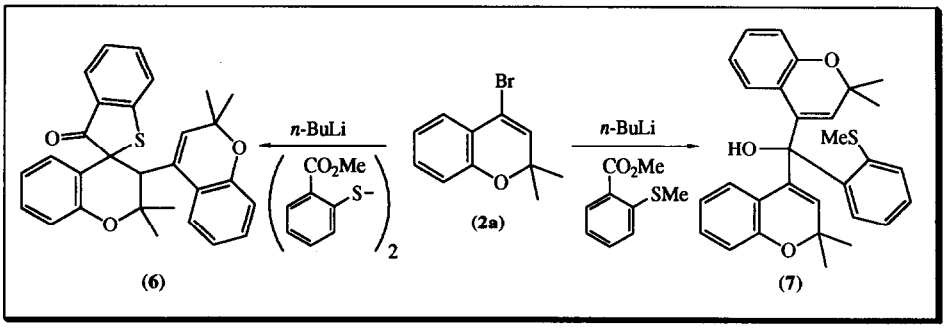
Footnotes: ¶ H-5 not distinct from other aromatic protons.

§ See stucture (5f).

* See structure (5r).



Attempts to obtain 2,2-dimethyl-4-[2-(methylthio)benzoyl]-2*H*-chromene by reacting the anion generated from (2a) with an equimolar amount of methyl (2-methylthio)benzoate failed and instead the major product was characterised as bis(2,2-dimethyl-4-chromenyl)-2-methylthiophenylmethanol (7), irrespective of the mode of addition of the reagents. Similarly, quenching the anion from (2a) with the lithium salt of methyl 2-mercaptobenzoate did not give 2,2-dimethyl-4-(2-mercaptobenzoyl)-2*H*-chromene. The major product was 2,2-dimethylchromene, though a small amount of the spiro fused heterocycle (6) was identified, which was possibly derived from a disulfide impurity in the methyl 2-mercaptobenzoate. The formation of (6) is envisaged to proceed through acylation of the anion with di(2-methoxycarbonylphenyl) disulfide. Spirocyclisation ensues by conjugate addition of the 4-chromenyl lithium to the intermediate 4-acylchromene and elimination of a thiolate ion.



Experimental

Melting points were determined in capillary tubes and are uncorrected. Distillations were performed using a Kugelrohr (Buchi GKR-50 Glass Tube Oven) and all boiling points quoted relate to the oven temperature at which the distillation commenced. Fourier Transform infrared spectra were recorded on a Mattson Polaris spectrophotometer. ^1H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker WM 250 instrument for solutions in $CDCl_3$ unless stated otherwise, *J* values are given in Hz. Flash chromatographic separations were performed on Crossfields Sorbsil C60 silica gel (M.P.D. 60Å, 40-60μ, activated) according to the published procedure.[27] 2,2-Dimethylthiochroman-4-one was prepared according to the literature procedure.[28]

Synthesis of Chroman-4-ones.

Chroman-4-ones were prepared from the 2'-hydroxyacetophenone by reaction with a carbonyl compound in the presence of pyrrolidine.[16] The following new chroman-4-ones were prepared by this method.

(i) **2-Methyl-2-isopropylchroman-4-one** (56%) as a pale yellow oil, b.p. 130 °C at 0.3 mmHg; ν_{max} (neat)/cm^{-1} 1680; δ_H (60 MHz) 1.00 (6H, d, CH(C<u>H</u>$_3$)$_2$), 1.25 (3H, s, 2-Me), 2.10 (1H, sept., C<u>H</u>(CH$_3$)$_2$), 2.65 (2H, ABq, 3-H), 6.70-7.90 (4H, m, Ar-H); (Found: C, 76.4; H, 7.9. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%).

(ii) **2-*n*-Butyl-2-methylchroman-4-one** (62%) as a pale yellow oil, b.p. 125-130 °C at 0.5 mbar; ν_{max} (neat)/cm^{-1} 1678; δ_H (60 MHz) 0.89 (3H, m, CH$_3$), 1.40 (3H, s, 2-CH$_3$), 1.26-2.01 (6H, m, -(CH$_2$)$_3$-), 2.69 (2H, ABq, 3-H), 6.76-7.86 (4H, m, Ar-H); (Found: C, 76.9; H, 8.1. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%).

(iii) **Spiro[7,8-benzochroman-2,1'-cyclohexane]-4-one** (68%) as pale yellow plates from ethyl acetate and hexane, m.p. 97.0-98.0 °C; δ_H 1.21-2.34 (10H, m, -(CH$_2$)$_5$-), 2.80 (2H, s, 3-H), 7.05-8.45 (6H, m, Ar-H); (Found: C, 81.4; H, 6.8. $C_{18}H_{18}O_2$ requires C, 81.2; H, 6.8%).

General Procedure for the Preparation of 4-Bromo- and 4-Chloro- 2*H*-chromenes and 2*H*-thiochromenes.

A solution of the chroman-4-one (30 mmol) in phosphorus trihalide (130 mmol) was refluxed for 30-90 min. (see Table 1). The solution was cooled and cautiously poured onto crushed ice (300g). The resulting aqueous solution was extracted with ethyl acetate (5 x 50 cm^3) and the combined extracts were washed with water (2 x 50 cm^3), dried (Na_2SO_4) and evaporated to afford either an off white semi-solid or a mobile yellow oil.

In the former case, the semi-solid was suspended in 1% diethyl ether in light petroleum (b.p. 40-60 °C), collected by filtration and washed well with light petroleum (b.p. 40-60 °C) to give the crude 2*H*-chromene-4-phosphonic acid (3) which was then recrystallised. Evaporation of the filtrate gave a mobile pale yellow oil.

This oil or that obtained directly, was eluted from silica with 7.5 % ethyl acetate in hexane to afford the pure 4-bromo-2*H*-chromene (2) and a small amount of the unreacted chroman-4-one.

The following compounds were obtained by this protocol:

(i) 2,2-Dimethylchroman-4-one gave **2,2-dimethyl-2*H*-chromene-4-phosphonic acid (3a)** (31%) as colourless needles from ethyl acetate and hexane, m.p. 219.0-224.5 °C (decomp.); ν_{max} (Nujol) cm^{-1} 2650(br), 1449, 1260, 1210; δ_H 1.29 (6H, s, 2-Me), 6.37 (1H, d, *J* 20.2, 3-H), 6.45 (1H, dd, *J* 8.1, 1.5, 8-H), 6.73 (1H, m, 6-H), 6.99 (1H, m, 7-H), 7.57 (1H, dd, *J* 8.0, 1.4, 5-H), 8.62 (2H, bs, 2 x OH(variable)); δ_C 26.6 (2 x C), 74.8 (d, *J* 14.7), 116.3, 117.9 (d, *J* 11.2), 120.6, 125.5 (d, *J* 184.7), 126.4, 129.2, 140.6 (d, *J* 5.8), 152.0 (d, *J* 10.1); δ_P 15.1; δ_P (D_2O,NaOH) 10.9; (Found: M$^+$, 240.0552; C, 54.9; H, 5.4; P, 13.0.$C_{11}H_{13}O_4P$ requires M$^+$, 240.0551(5); C, 55.0; H, 5.5; P, 12.9 %); and **4-bromo-2,2-dimethyl-2*H*-chromene (2a)**

(67%) as a colourless oil, b.p. 90 °C at 0.5 mbar; δ_H 1.47 (6H, s, 2-Me), 6.02 (1H, s, 3-H), 6.81 (1H, d, *J* 8.2, 8-H), 6.94 (1H, m, 6-H), 7.17 (1H, m, 7-H), 7.43 (1H, dd, *J* 8.2, 1.3, 5-H); δ_C 27.6 (2 x C), 78.3, 116.4, 117.0, 120.6, 121.0, 126.8, 130.5, 131.8, 153.0 (Found: C, 55.3; H, 4.4; Br, 33.2. $C_{11}H_{11}BrO$ requires C, 55.3; H, 4.6; Br, 33.4 %).

(ii) 2-Ethyl-2-methylchroman-4-one gave **4-bromo-2-ethyl-2-methyl-2*H*-chromene (2b)** (75%) as a colourless oil, b.p. 145 °C at 0.5 mbar; δ_H 1.01 (3H, t, *J* 7.1, $CH_2\underline{CH_3}$), 1.42 (3H, s, 2-Me), 1.74 (2H, q, *J* 7.1, $\underline{CH_2}CH_3$), 5.98 (1H, s, 3-H), 6.80 (1H, d, *J* 8.1, 8-H), 6.93 (1H, m, 6-H), 7.20 (1H, m, 7-H), 7.43 (1H, dd, *J* 8.1, 1.4, 5-H); δ_C 8.15, 25.5, 33.7, 81.1, 116.2, 117.2, 120.5, 120.8, 126.8, 130.5, 130.9, 153.3 (Found: C, 56.7; H, 5.1; Br, 31.4. $C_{12}H_{13}BrO$ requires C, 56.9; H, 5.2; Br, 31.6 %).

(iii) 2-Methyl-2-isopropylchroman-4-one gave **4-bromo-2-methyl-2-isopropyl-2*H*-chromene (2c)** (69%) as a colourless oil, b.p. 120 °C at 0.5 mbar; δ_H 1.00 (6H, d, *J* 6.8, $CH(\underline{CH_3})_2$), 1.39 (3H, s, 2-Me), 2.03 (1H, m, $\underline{CH}(CH_3)_2$), 6.04 (1H, s, 3-H), 6.79 (1H, d, *J* 8.1, 8-H), 6.93 (1H, m, 6-H), 7.20 (1H, m, 7-H), 7.42 (1H, dd, *J* 8.0, 1.3, 5-H); δ_C 17.0 (2 x C), 22.7, 37.1, 83.4, 116.1, 117.0, 120.6, 120.7, 126.8, 130.1, 130.5, 153.4 (Found: C, 58.5; H, 5.7; Br, 29.8. $C_{13}H_{15}BrO$ requires C, 58.4; H, 5.7; Br, 29.9 %).

(iv) 2-*n*-Butyl-2-methylchroman-4-one gave **4-bromo-2-*n*-butyl-2-methyl-2*H*-chromene (2d)** (71%) as a colourless oil, b.p. 110 °C at 0.6 mbar; δ_H 0.93 (3H, t, *J* 7.2, $2\text{-}(CH_2)_3\underline{CH_3}$), 1.42 (4H, m, $2\text{-}CH_2(\underline{CH_2})_2CH_3$), 1.46 (3H, s, 2-Me), 1.78 (2H, m, $2\text{-}\underline{CH_2}(CH_2)_2CH_3$), 5.99 (1H, s, 3-H), 6.78 (1H, dd, *J* 8.1, 1.3, 8-H), 6.93 (1H, m, 6-H), 7.21 (1H, m, 7-H), 7.41 (1H, dd, *J* 8.0, 1.3, 5-H); δ_C 13.9, 22.9, 25.9, 26.0, 40.8, 80.9, 116.2, 117.0, 120.5, 120.8, 126.8, 130.5, 131.2, 153.3 (Found: C, 59.9; H, 6.2; Br, 28.3. $C_{14}H_{17}BrO$ requires C, 59.8; H, 6.1; Br, 28.4 %).

(v) Spiro[chroman-2,1'-cyclohexane]-4-one gave **4-bromo-2*H*-spiro[chromen-2,1'-cyclohexane]**[15] **(2e)** (82%) as a colourless oil, b.p. 115 °C at 0.6 mbar; δ_H 1.49-1.99 (10H, m, cyclohexane ring), 6.05 (1H, s, 3-H), 6.83 (1H, d, *J* 8.1, 8-H), 6.92 (1H, m, 6-H), 7.19 (1H, m, 7-H), 7.41 (1H, dd, J 8.1, 1.3, 5-H); δ_C 21.3 (2 x C), 25.1, 35.6 (2 x C), 79.1, 116.4, 117.3, 121.0, 121.5, 126.8, 130.3, 131.6, 152.9.

(vi) Spiro[chroman-2,1'-cycloheptane]-4-one gave **4-bromo-2*H*-spiro[chromen-2,1'-cycloheptane] (2f)** (60%) as a colourless oil, b.p. 125 °C at 0.6 mbar; δ_H 1.40-2.18 (12H, m, cycloheptane ring), 6.08 (1H, s, 3-H), 6.81 (1H, d, *J* 8.2, 8-H), 6.93 (1H, m, 6-H), 7.19 (1H, m, 7-H), 7.40 (1H, dd, *J* 8.1, 1.1, 5-H); δ_C 21.5 (2 x C), 29.3 (2 x C), 39.0 (2 x C), 83.7, 116.4, 116.6, 120.9, 121.2, 126.7, 130.3, 132.5, 152.9 (Found: C, 61.3; H, 5.8; Br, 27.1. $C_{15}H_{17}BrO$ requires C, 61.4; H, 5.9; Br, 27.3 %).

(vii) 2-Methyl-2-phenylchroman-4-one gave **4-bromo-2-methyl-2-phenyl-2*H*-chromene (2g)** (67%) as a viscous colourless oil, b.p. 160 °C at 0.5 mbar; δ_H 1.83 (3H, s, 2-Me), 6.37 (1H, s, 3-H), 6.90-6.89 (2H, m, Ar-H), 7.19-7.54 (2H, m, Ar-H); δ_C 29.1, 80.9, 116.4, 117.9, 118.3, 120.7, 121.3, 125.1, 127.0, 127.6, 127.9, 128.3, 130.7, 130.8, 144.6, 152.9 (Found: C, 63.9 ; H, 4.3; Br, 26.7. $C_{16}H_{13}BrO$ requires C, 63.8; H, 4.4; Br, 26.5 %).

(viii) 7,8-Benzo-2,2-dimethylchroman-4-one gave **7,8-benzo-4-bromo-2,2-dimethyl-2*H*-chromene (2h)** (28%) as a viscous colourless oil, b.p. 160 °C at 0.4 mbar; δ_H 1.59 (6H, s, 2-Me), 6.07 (1H, s, 3-H), 7.43-7.54 (3H, m, Ar-H), 7.64 (1H, d, *J* 7.8, Ar-H), 7.80 (1H, m, Ar-H), 8.27 (1H, m, Ar-H); δ_C 27.5 (2 x C), 79.1, 114.8, 117.6, 120.2, 122.4, 123.9, 124.7, 125.7, 127.0, 127.6, 130.0, 135.0, 143.9 (Found: C, 62.0; H, 4.5; Br, 27.3. $C_{15}H_{13}BrO$ requires C, 62.3; H, 4.5; Br, 27.6 %).

(ix) Spiro[7,8-benzochroman-2,1'-cyclohexane]-4-one gave **4-bromo-2*H*-spiro[7,8-benzochromen-2,1'-cyclohexane] (2g)** (33%) as colourless crystals from hexane and ethyl acetate, m.p. 114.0-116.0 °C; δ_H 1.54-2.22 (10H, m, cyclohexane ring), 6.04 (1H, s, 3-H), 7.41-7.61 (4H, m, Ar-H), 7.79 (1H, m, Ar-H), 8.29 (1H, m, Ar-H); δ_C 21.1 (2 x C), 25.2, 35.5 (2 x C), 80.1, 115.5, 117.9, 120.1, 122.3, 124.0, 124.8, 125.7, 126.9, 127.6, 130.0, 135.0, 148.7 (Found: C, 65.8; H, 5.2; Br, 24.2. $C_{18}H_{17}BrO$ requires C, 65.7; H, 5.2; Br, 24.3 %).

(x) 2,2-Dimethylthiochroman-4-one gave **4-bromo-2,2-dimethyl-2*H*-thiochromene (2h)** (71%) as a colourless oil, b.p. 120 °C at 0.5 mbar; δ_H 1.43 (6H, s, 2-Me), 6.28 (1H, s, 3-H), 7.20 (3H, m, 8-H, 7-H, 6-H), 7.69 (1H, dd, *J* 8.0, 1.1, 5-H); δ_C 29.0 (2 x C), 43.1, 121.1, 125.6, 127.4, 128.8, 128.9, 130.7, 132.9, 136.3 (Found: C, 51.6; H, 4.2; Br, 31.0; S, 12.7. $C_{11}H_{11}BrS$ requires C, 51.7; H, 4.3; Br, 31.3; S, 12.6 %).

(xi) 1-Tetralone gave **3,4-dihydronaphthalene-1-phosphonic acid (3b)** (39%) as colourless crystals from methanol, ethyl acetate and hexane, m.p. 230.5-232.0 °C (decomp.); ν_{max} (Nujol) cm^{-1} 2640(br), 1435, 1250; δ_H (D_2O, NaOH), 2.28 (2H, m, 3-H), 2.70 (2H, m, 4-H), 6.79 (1H, dt, *J* 18.0, 7.2, 2-H), 7.19-7.26 (3H, m, 5-H, 6-H, 7-H), 7.87 (1H, d, *J* 8.4, 8-H); δ_C ($CDCl_3$) 22.7 (d, *J* 13.8), 29.8, 125.7, 126.6 (d, *J*, 18.4), 129.3, 130.3, (d, *J* 188.9), 130.7 (d, *J* 12.6), 134.9 (d, *J* 6.7), 136.6, 140.7 (d, *J* 8.9); δ_P (D_2O, NaOH) 9.67 (Found: M^+, 210.0446; C, 57.0; H, 5.3; P, 14.7. $C_{10}H_{11}O_3P$ requires M^+, 210.0445(8); C, 57.1; H, 5.3; P, 14.8 %) and **1-bromo-3,4-dihydronaphthalene (2l)** (44%) as a pale yellow oil, b.p. 75 °C at 0.5 mbar [Lit. b.p. 81-84 °C at 0.44 torr[29]; δ_H 2.41 (2H, m, 3-CH_2), 2.88 (2H, t, *J* 6.8, 4-CH_2), 6.49 (1H, t, *J* 4.9, 2-H), 7.16-7.92 (4H, m, Ar-H).

(xii) 2-Isopropylchroman-4-one gave **4-bromo-2-isopropyl-2*H*-chromene (2n)** (49%) as a colourless oil which gradually darkened on exposure to air at room temperature, b.p. 130 °C at 0.5 mbar; δ_H 1.05 (3H, d, *J* 6.9, Me), 1.08 (3H, d, *J* 7.0, Me), 2.07 (1H, m, 2-C<u>H</u>$(CH_3)_2$), 4.65 (1H, dd, *J* 3.8, 6.4, 2-H), 6.12 (1H, d, *J* 3.8, 3-H), 6.83 (1H, dd, *J* 8.1, 1.3, 8-H), 6.94 (1H, m, 6-H), 7.19 (1H, m, 7-H), 7.44 (1H, dd, *J* 8.0, 1.3, 5-H); δ_C 17.7, 17.8, 33.2, 81.7, 115.7, 118.3, 121.1, 121.4, 125.9, 126.9, 130.6, 154.2. Satisfactory elemental analysis could not be obtained for this compound.

(xiii) 5,6-Benzo-2,2-dimethylchroman-4-one gave **5,6-benzo-4-bromo-2,2-dimethyl-2*H*-chromene (2p)** (59%) as a pale yellow oil b.p. 150 °C at 0.2 mbar; δ_H 1.50 (6H, s, 2-Me), 6.15 (1H, s, 3-H), 7.12 (1H, d, *J* 8.1, 10-H), 7.39 (1H, m, Ar-H), 7.55 (1H, m, Ar-H), 7.78 (2H, m, Ar-H), 8.79 (1H, d, *J* 8.0, 5-H); δ_C 26.0 (2 x C), 78.0, 114.4, 114.5, 118.2, 123.7, 125.3, 125.6, 128.5, 129.9, 130.0, 131.7, 133.1, 153.0 (Found: C, 62.1; H,4.5 ; Br, 27.5. $C_{15}H_{13}BrO$ requires C, 62.3; H, 4.5; Br, 27.6 %).

(xiv) 2,2-Dimethyl-7-methoxychroman-4-one[3] and PCl_3 gave **2,2-dimethyl-7-methoxy-2*H*-chromene-4-phosphonic acid (3c)** (21%) as colourless needles from methanol, ethyl acetate and hexane, m.p. 235.0-241.0 °C (decomp.); ν_{max} (Nujol) cm^{-1} 2645(br), 1450, 1255, 1210; δ_H (D_2O, NaOH), 1.45 (6H, s, 2-Me), 3.83, s, 7-OMe), 6.22 (1H, d, *J* 17.7, 3-H), 6.50 (1H, dd, *J* 1.8, 1.2, 8-H), 6.67 (1H, dd, *J* 8.1, 1.2, 6-H), 7.71 (1H, d, *J* 8.1, 5-H); δ_C (DMSO-d_6) 30.7 (2 x C), 59.2, 79.4 (d, *J*, 14.1), 106.0, 110.6, 116.9 (d, *J* 10.1), 129.7 (d, *J* 181.1), 131.6, 139.7 (d, *J* 6.8), 156.5 (d, *J* 9.4), 163.1; δ_P (D_2O, NaOH) 7.66 (Found: M^+, 270.066; C, 53.4; H, 5.6; P, 11.4.$C_{12}H_{15}O_5P$ requires M^+, 270.065(7); C, 53.3; H, 5.6; P, 11.4 %) and **4-chloro-2,2-dimethyl-7-methoxy-2*H*-chromene[14] (2r)** (48%) as a colourless oil, b.p. 150 °C at 0.5 mbar; δ_H 1.47 (6H, s, 2-Me), 3.79 (3H, s, MeO), 5.62 (1H, s, 3-H), 6.39 (1H, d, *J* 1.2, 8-H), 6.49 (1H, dd, *J* 8.1, 1.2, 6-H), 7.34 (1H, d, *J* 8.1, 5-H); δ_C 27.8 (2 x C), 56.3, 78.1, 102.0, 106.8, 113.3, 124.4, 125.3, 126.7, 154.5, 161.8.

(xv) Chroman-4-one gave **4-bromo-2*H*-chromene (2s)** (37%) as a pale yellow oil after elution from silica which rapidly darkened at room temperature and was not distilled; δ_H 4.81 (2H, d, *J* 4.0, 2-H), 6.16 (1H, t, *J* 4.0, 3-H), 6.16 (1H, dd, *J* 8.1, 1.2, 8-H), 6.98 (1H, m, 6-H), 7.20 (1H, m, 7-H), 7.42 (1H, dd, *J* 8.1, 1.3, 5-H); δ_C 66.7, 115.8, 118.1, 121.6, 121.9, 123.5, 127.0, 130.6, 154.4. Satisfactory elemental analysis could not be obtained for this compound.

Preparation of 4-Substituted-2*H*-chromenes.

To a stirred solution of the 4-bromo-2*H*-chromene (15 mmol) in anhydrous ether (40 cm^3) at room temperature and under N_2, *n*-butyllithium (15 mmol, 2.5M in hexanes) was added *via* syringe in a single portion. The resulting pale orange solution was stirred at RT for 45 min., whereupon the electrophile (15 mmol) was added in a single portion. The resulting pale yellow solution was stirred at RT for 1h, poured into water (200 cm^3) and extracted with ethyl acetate (4 x 50 cm^3). The combined extracts were washed with water (2 x 50 cm^3), dried (Na_2SO_4) and evaporated to give the crude product. Subsequent elution from silica with ethyl acetate in hexane [percentage EtOAc in hexane, solvent system A = 5%; B = 10%; C = 15%, D = 20%] gave a small amount of the respective 2*H*-chromene, resulting from protonation of some of the unreacted anion, together with a small amount of the unreacted electrophile and the desired product. Further purification was affected by either distillation or recrystallisation to give the following compounds.

(i) Quenching the anion generated from (**2a**) with *N,N*-dimethylformamide gave **2,2-dimethyl-2*H*-chromene-4-carbaldehyde (5o)** [solvent system B] (74%) as a colourless oil, b.p. 90 °C at 0.6 mbar; ν_{max} (neat)/cm^{-1} 1693; δ_H 1.51 (6H, s, 2-Me), 6.44 (1H, s, 3-H), 6.85-6.98 (2H, m, 8-H, 6-H), 7.20 (1H, m, 7-H), 8.21 (1H, dd, *J* 8.2, 1.3, 5-H), 9.65 (1H, s, CHO); δ_C 26.7 (2 x C), 75.7, 116.9, 117.0, 121.2, 125.8, 130.4, 131.8, 150.0, 152.5, 191.2 (Found: C, 76.9; H, 6.5. $C_{12}H_{12}O_2$ requires C, 76.6; H, 6.4 %).

(ii) Quenching the anion generated from (**2b**) with *N,N*-dimethylformamide gave **2-ethyl-2-methyl-2*H*-chromene-4-carbaldehyde (5p)** [solvent system D] (87%) as a colourless oil, b.p. 120 °C at 0.6 mbar; ν_{max} (neat)/cm^{-1} 1694; δ_H 1.01 (3H, t, *J* 7.1, 2-$CH_2\underline{CH_3}$), 1.46 (3H, s, 2-Me), 1.82 (2H, q, *J* 7.1, 2-$\underline{CH_2}CH_3$), 6.43 (1H, s, 3-H), 6.89-6.97 (2H, m, 8-H, 6-H), 7.21 (1H, m, 7-H), 8.24 (1H, dd, *J* 8.2, 1.4, 5-H), 9.64

(1H, s, CHO); δ_C 8.06, 24.5, 32.9, 78.4, 116.7, 116.9, 121.0, 125.7, 130.4, 132.4, 149.4, 152.8, 191.1 (Found: C, 77.1; H, 7.0. $C_{13}H_{14}O_2$ requires C, 77.2; H, 7.0 %).

(iii) Quenching the anion generated from (**2n**) with *N,N*-dimethylformamide gave **2-isopropyl-2*H*-chromene-4-carbaldehyde** (**5q**) [solvent system B] (63%) as a pale yellow oil b.p. 120 °C at 0.6 mbar; ν_{max} (neat)/cm^{-1} 1693; δ_H 1.07 (3H, d, *J* 6.5, 2-CH(C<u>H</u>$_3$)$_2$), 1.09 (3H, d, *J* 6.5, 2-CH(C<u>H</u>$_3$)$_2$), 2.14 (1H, m, 2-C<u>H</u>(CH$_3$)$_2$), 4.77 (1H, dd, *J* 3.9, 6.4, 2-H), 6.61 (1H, d, *J* 4.0, 3-H), 6.93 (2H, m, Ar-H), 7.22 (1H, m, Ar-H), 8.19 (1H, dd, *J* 8.3, 2.0, 5-H), 9.69 (1H, s, C<u>H</u>O); δ_C 17.9 (2 x C), 32.7, 79.5, 116.1, 117.7, 121.2, 125.8, 130.4, 133.9, 144.4, 153.5, 190.8 (Found: C, 77.2; H, 6.9. $C_{13}H_{14}O_2$ requires C, 77.2; H, 7.0%).

(iv) Quenching the anion generated from (**2a**) with 2-methoxybenzonitrile gave **2,2-dimethyl-4-(2-methoxybenzoyl)-2*H*-chromene** (**5i**) [solvent system D] (62%) as colourless needles from hexane and ethyl acetate, m.p. 70.5-71.5 °C; ν_{max} (Nujol)/cm^{-1} 1659; δ_H 1.46 (6H, s, 2-Me), 3.73 (3H, 2'-OMe), 5.99 (1H, s, 3-H), 6.87-7.01 (3H, m, Ar-H), 7.05 (1H, m, Ar-H), 7.18 (1H, m, Ar-H), 7.46-7.56 (2H, m, Ar-H), 7.64 (1H, dd, *J* 8.2, 1.4, 5-H); δ_C, 26.8 (2 x C), 55.5, 75.3, 111.7, 116.9, 119.0, 120.5, 120.9, 125.8, 128.8, 129.6, 130.5, 132.9, 134.1, 138.0, 152.8, 158.1, 195.3 (Found: C, 77.7; H, 6.2. $C_{19}H_{18}O_3$ requires C, 77.5; H, 6.2 %).

(v) Quenching the anion generated from (**2e**) with 2,4-dimethoxybenzonitrile gave **4-(2,4-dimethoxybenzoyl)-2*H*-spiro[chromen-2,1'-cyclohexane]** (**5k**) [solvent system B] (66%) as colourless crystals from hexane and ethyl acetate m.p. 109.5-110.5 °C; ν_{max} (Nujol)/cm^{-1} 1664; δ_H 1.46-1.99 (10H, m, cyclohexane ring), 3.66 (3H, s, 4'-OMe), 3.86 (3H, s, 2'-OMe), 5.94 (1H, s, 3-H), 6.43 (1H, d, *J* 1.5, 3'-H), 6.54 (1H, dd, *J* 8.6, 1.5, 5'-H), 6.80 (1H, m, 6-H), 6.91 (1H, dd, *J* 8.0, 1.0, 8-H), 7.13 (1H, m, 7-H), 7.35 (1H, dd, *J* 8.1, 1.0, 5-H), 7.63 (1H, d, *J* 8.4, 6'-H); δ_C 21.2 (2 x C), 25.2, 34.9 (2 x C), 55.4, 55.5, 76.0, 98.7, 109.4, 116.8, 120.4, 120.7, 121.6, 125.4, 129.3, 133.0, 134.8, 135.4, 152.6, 160.5, 164.3, 194.0 (Found: M$^+$, 364.1675; C, 76.0; H, 6.7. $C_{23}H_{24}O_4$ requires M$^+$, 364.1673; C, 75.9; H, 6.7%).

(vi) Quenching the anion generated from (**2j**) with 2,4-dimethoxybenzonitrile gave **4-(2,4-dimethoxybenzoyl)-2,2-dimethyl-2*H*-thiochromene** (**5j**) [solvent system B] (61%) as colourless needles from hexane and ethyl acetate m.p. 110.0-111.0 °C; ν_{max} (Nujol)/cm^{-1} 1637; δ_H 1.45 (6H, s, 2-Me), 3.55 (3H, s, 4'-OMe), 3.86 (3H, s, 2'-OMe), 6.14 (1H, s, 3-H), 6.33 (1H, d, *J* 1.5, 3'-H), 6.55 (1H, dd, *J* 8.6, 1.5, 5'-H), 6.99 (1H, m, 6-H), 7.17 (2H, m, 7-H,8-H), 7.35 (1H, dd, *J* 8.2, 1.1, 5-H), 7.70 (1H, d, *J* 8.3, 6'-H); δ_C 28.2 (2 x C), 40.5, 55.2, 55.4, 98.5, 105.1, 121.5, 125.0, 126.2, 127.7, 127.8, 130.7, 132.6, 133.2, 137.5, 140.5, 160.6, 164.5, 195.0 (Found: M$^+$, 340.1133; C, 70.7; H, 6.0; S, 9.6. $C_{20}H_{20}O_3S$ requires M$^+$, 340.1133; C, 70.6; H, 5.9; S, 9.4%).

(vii) Quenching the anion generated from (**2a**) with 2-fluorobenzonitrile gave **2,2-dimethyl-4-(2-fluorobenzoyl)-2*H*-chromene** (**5g**) [solvent system D] (54%) as a viscous orange oil which decomposed on distillation; δ_H 1.48 (6H, s, 2-Me), 5.74 (1H, s, 3-H), 6.81-7.07 (2H, m, Ar-H), 7.10-7.21 (3H, m, Ar-H), 7.43 (1H, m, Ar-H), 7.67 (1H, m, Ar-H).

(viii) Quenching the anion generated from (**2a**) with benzonitrile gave **4-benzoyl-2,2-dimethyl-2*H*-chromene (5h)** [solvent system B] (77%) as a viscous yellow oil, 180-190 °C at 0.4 mbar; ν_{max} (Nujol)/cm^{-1} 1663; δ_H 1.53 (6H, s, 2-Me), 5.95 (1H, s, 3-H), 6.86-6.92 (2H, m, Ar-H), 7.18-7.28 (2H, m, Ar-H), 7.48-7.51 (2H, m, Ar-H), 7.60 (1H, m, Ar-H), 7.91 (1H, dd, *J* 8.2, 1.4, 5-H); δ_C 27.2 (2 x C), 75.4, 117.1, 119.1, 121.0, 125.6, 128.5 (2 x C), 129.9, 130.0 (2 x C), 132.8, 133.2, 135.7, 137.2, 152.6, 195.2 (Found: C, 81.9; H, 5.9. $C_{18}H_{16}O_2$ requires C, 81.8; H, 6.1 %).

(ix) Quenching the anion generated from (**2a**) with 1-chloro-2,3-epoxypropane gave two products on elution from silica [solvent system C]: *Fraction 1:* **2,2-dimethyl-4-(2,3-epoxypropyl)-2*H*-chromene (5d)** (41%) as a colourless oil, b.p. 130-135 °C at 0.6 mbar; δ_H 1.44 (3H, s, 2-Me), 1.45 (3H, s, 2-Me), 2.57-2.66 (3H, m, 1'-CH_2, 3'-CH), 2.84 (1H, m, 3'-CH), 3.17 (1H, m, 2'-CH), 5.59 (1H, d, *J* 0.9, 3-H), 6.82-6.91 (2H, m, 8-H, 6-H), 7.12-7.20 (2H, m, 7-H, 5-H); δ_C 27.8, 27.9, 34.1, 47.0, 50.7, 75.6, 116.7, 120.6, 122.0, 123.0, 128.0, 128.6, 129.1, 153.1 (Found: C, 77.4; H, 7.5. $C_{14}H_{16}O_2$ requires C, 77.7; H, 7.5 %). *Fraction 2:* **4-(3-chloro-2-hydroxypropyl)-2,2-dimethyl-2*H*-chromene (5e)** (30%) as a colourless oil, b.p. 160 °C at 0.6 mbar; ν_{max} (neat)/cm^{-1} 3439 (br); δ_H 1.43 (6H, s, 2-Me), 2.36 (1H, d, *J* 4.9, OH), 2.69 (2H, m, 1'-CH_2), 3.62 (2H, m, 3'-CH_2), 4.09 (1H, m, 2'-CH), 5.58 (1H, d, *J* 0.8, 3-H), 6.82-6.94 (2H, m, 8-H, 6-H), 7.13-7.21 (2H, m, 7-H, 5-H); δ_C 27.7 (2 x C), 36.4, 49.4, 69.2, 116.9, 120.7, 121.4, 123.0, 127.6, 129.3, 130.2, 153.2 (Found: C, 66.7; H, 6.9; Cl, 13.9. $C_{14}H_{17}ClO_2$ requires C, 66.5; H, 6.8; Cl, 14.0 %)

(x) Quenching the anion generated from (**2a**) with chlorotrimethylsilane gave **2,2-dimethyl-4-trimethylsilyl-2*H*-chromene (5a)** [solvent system B] (25%) as a mobile pale yellow oil b.p. 80 °C at 0.4 mbar; ν_{max} (neat)/cm^{-1} 1596; δ_H 0.28 (9H, s, 4-$SiMe_3$), 1.41 (6H, s, 2-Me), 5.86 (1H, s, 3-H), 6.81-6.90 (2H, m, 8-H, 6-H), 7.12 (1H, m, 7-H), 7.20 (1H, dd, *J* 8.2, 1.5, 5-H); δ_C -0.86 (3 x C), 27.3 (2 x C), 74.7, 117.0, 120.4, 123.8, 126.7, 128.4, 132.2, 140.3, 152.4 (Found: C, 72.2; H, 8.9. $C_{14}H_{20}OSi$ requires C, 72.4; H, 8.7 %).

(xi) Quenching the anion generated from (**2a**) with diphenyl disulfide gave **2,2-dimethyl-4-phenylthio-2*H*-chromene (5b)** [solvent system A] (27%) as colourless crystals from m.p. 65.5-67.0 °C; ν_{max} (Nujol)/cm^{-1} 1604; δ_H 1.48 (6H, s, 2-Me), 5.92 (1H, s, 3-H), 5.82-5.85 (2H, m, Ar-H), 7.15-7.34 (6H, m, Ar-H), 7.41 (1H, dd, *J* 8.4, 1.5, 5-H) (Found: C, 76.2; H, 6.0; S, 12.1. $C_{17}H_{16}OS$ requires C, 76.1; H, 6.0; S, 11.9 %).

(xii) Quenching the anion generated from (**2a**) with *p*-anisaldehyde gave **4-methoxyphenyl-4-(2,2-dimethyl-2*H*-chromenyl)methanol (5c)** [solvent system D] (39%) as a viscous yellow oil b.p. 175 °C at 0.4 mbar; ν_{max} (Nujol)/cm^{-1} 3426 (br); δ_H 1.51 (6H, s, 2-Me), 2.10 (1H, bs, CHO<u>H</u>), 3.80 (3H, s, 4'-OMe), 5.64 (1H, bs, C<u>H</u>OH), 5.88 (1H, s, 3-H), 6.73-6.91 (4H, m, Ar-H), 6.98-7.35 (2H, m, Ar-H), 7.38 (2H, m, Ar-H); δ_C 27.8, 27.9, 55.2, 72.2, 75.8, 114.1 (2 x C), 116.7, 120.3, 120.4, 123.9, 127.5, 128.4 (2 x C), 128.9, 133.2, 133.8, 159.4 (Found: C, 77.0; H, 6.6. $C_{19}H_{20}O_3$ requires C, 77.0; H, 6.8 %).

(xiii) Quenching the anion generated from (**2g**) with *N,N*-dimethylcarbamoyl chloride gave **di-4-(2-methyl-2-phenyl-2*H*-chromenyl)ketone (5f)** [solvent system B] (24%) as a pale yellow viscous oil b.p. 215 °C at 0.5 mbar; ν_{max} (Nujol)/cm^{-1} 1667; δ_H 1.78 (3H, 2-Me), 1.80 (3H, s, 2-Me), 6.46 (1H, s, 3-H), 6.48 (1H, s, 3-H),

6.92-7.01 (4H, m Ar-H), 7.04-7.44 (12H, m, Ar-H), 7.61 (2H, m, 5-H) (Found: C, 84.1; H, 5.6. $C_{33}H_{26}O_3$ requires C, 84.2; H, 5.6 %).

(xiv) Quenching the anion generated from (**2a**) with acetic anhydride gave **1,1-bis[4-(2,2-dimethyl-2*H*-chromenyl)]ethene (5r)** [solvent system B] (38%) as colourless microcrystals from ethyl acetate and hexane, m.p.89.0-89.5 °C; δ_H 1.39 (12H, s, 2-Me), 5.53 (2H, s, $=CH_2$)#, 5.63 (2H, s, 3-H)#, 6.87 (4H, m, Ar-H), 7.14 (2H, m, Ar-H), 7.30 (2H, m, 5-H); δ_C 27.1, 75.6, 117.0, 120.5, 121.4, 122.5, 125.3, 129.0, 130.0, 133.6, 143.0, 153.4; (Found: M^+, 344.1764; C, 83.5; H, 6.9. $C_{24}H_{24}O_2$ requires M^+, 344.1776; C, 83.7; H, 7.0 %).

assignments may be reversed.

Preparation of 2*H*-Chromene-4-carboxylic Acids

A solution of the 4-chromenyl lithium prepared as above was added to cold (-10 °C) ether saturated with CO_2. This solution was stirred and allowed to warm to room temperature over 30 min. during which, a steady stream of CO_2 gas was passed through the ethereal solution. The resulting pale yellow solution was then stirred at RT for 1h, poured into water (200 cm^3) and washed with ether (2 x 50 cm^3). The aqueous solution was cautiously acidified with conc. HCl and extracted with ethyl acetate (4 x 50 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated to give the crude product which was then recrystallised or distilled.

(i) (**2a**) gave **2,2-dimethyl-2*H*-chromene-4-carboxylic acid (5l)** (93%) as colourless needles from ethyl acetate and hexane, m.p. 135.5-137.0 °C; ν_{max} (Nujol)/cm^{-1} 2618 (br), 1696; δ_H 1.52 (6H, s, 2-Me), 6.88 (1H, s, 3-H), 6.91-7.02 (2H, m, 8-H, 6-H), 7.22 (1H, m, 7-H), 8.04 (1H, dd, *J* 8.0, 1.3, 5-H), 12.20 (1H, bs, CO_2H); δ_C 26.5 (2 x C), 75.3, 117.1, 118.0, 121.2, 124.4, 126.2, 130.0, 142.3, 152.9, 171.2 (Found C, 70.4; H, 5.8. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9 %).

(ii) (**2c**) gave **2-methyl-2-isopropyl-2*H*-chromene-4-carboxylic acid (5n)** (91%) as a viscous colourless oil, b.p. 180 °C at 0.6 mbar; ν_{max} (Nujol)/cm^{-1} 2620 (br), 1694; δ_H 1.06 (6H, m, 2-CH($\underline{CH_3}$)$_2$), 1.41 (3H, s, 2-Me), 2.10 (1H, m, 2-C$\underline{H}$(CH_3)$_2$), 6.87-6.99 (3H, m, 3-H, 8-H, 6-H), 7.23 (1H, m, 7-H), 8.04 (1H, dd, *J* 8.2, 1.4, 5-H), 11.85 (1H, bs, CO_2H); δ_C, 17.0, 17.1, 21.4, 36.1, 80.3, 116.9, 118.0, 120.8, 124.7, 126.1, 129.9, 141.4, 153.1, 171.1 (Found: C, 72.4; H, 7.0. $C_{14}H_{16}O_3$ requires C, 72.4; H, 7.0 %).

(iii) (**2g**) gave **2-methyl-2-phenyl-2*H*-chromene-4-carboxylic acid (5m)** (83%) as colourless needles from ethyl acetate and hexane, m.p. 145.5-147.5 °C; ν_{max} (Nujol)/cm^{-1} 2600 (br), 1690; δ_H 1.88 (3H, s, 2-Me), 6.98-7.05 (2H, m, Ar-H), 7.22-7.41 (6H, m, 3-H, Ar-H), 7.41-7.56 (2H, m, Ar-H), 8.02 (1H, dd, *J* 8.3, 1.5, 5-H), 12.10 (1H, bs, CO_2H); δ_C 28.5, 117.1, 118.0, 121.4, 124.7, 125.1 (2 x C), 126.4, 127.7, 128.5 (2 x C), 130.2, 141.2, 143.9, 153.0, 171.0 (Found: C, 77.0; H, 5.25. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3 %).

Bis(2,2-dimethyl-4-chromenyl)-2-methylthiophenylmethanol (7)

A solution of the chromenyl lithium from (**2a**) (12 mmol) prepared as described earlier was added to a vigorously stirred cold (-10 °C) solution of methyl 2-methylthiobenzoate (15 mmol) in anhydrous ether (40 cm^3). This solution was stirred and allowed to warm to room temperature over 30 min., poured into water (200 cm^3) and extracted with ethyl acetate (5 x 50 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated to give a cream solid which was collected and washed with warm methanol to give the **title methanol** (7) (43%) as a white powder, m.p. 249.5-251.5 °C; ν_{max} (Nujol) cm^{-1} 3435; δ_H 1.32 (3H, s, 2-Me), 1.35 (3H, s, 2-Me), 1.41 (3H, s, 2-Me), 1.44 (3H, s, 2-Me), 2.56 (3H, s, SMe), 4.81 (1H, bs OH), 5.61 (1H, s, 3-H), 5.80 (1H, s, 3-H), 6.72-6.89 (4H, m, Ar-H), 7.10-7.35 (6H, m, Ar-H), 7.59 (1H, d, *J* 8.4, 5-H), 7.80 (1H, d, *J* 8.3, 5-H); δ_C 19.2, 25.9, 26.4, 27.8, 28.0, 75.3, 75.5, 82.6, 116.8 (2 x C), 120.1 (2 x C), 120.3, 126.3, 128.4, 128.7 (2 x C), 128.9, 129.6, 129.7 (2 x C), 132.3, 132.8 (2 x C), 133.0, 136.3, 136.4, 143.8, 153.9 (Found: C, 76.8; H, 6.5; S, 6.7. $C_{30}H_{30}O_3S$ requires C, 76.6; H, 6.4; S, 6.8 %).

2',3'-Dihydro-2',2'-dimethyl-3'-(2,2-dimethyl-2*H*-3-chromenyl)spiro[2*H*-benzo[*b*]thiophene -2,4'(4*H*)-chromene]-3-one (6)

The product from the reaction of lithium 2-methoxycarbonylthiophenoxide (15 mmol) with the anion derived from (2a) was eluted from silica with 10% ethyl acetate in hexane to give (i) 2,2-dimethylchromene[30] (51%) and (ii) the **spiro-fused heterocycle** (**6**) (11%) as colourless microcrystals from ethyl acetate and hexane m.p. 154.5-156.0 °C; ν_{max} (Nujol) cm^{-1} 1876, 1874, 1608; δ_H 1.42 (3H, s, 2-Me), 1.43 (6H, s, 2-Me), 1.54 (3H, s, 2-Me), 3.79 (1H, s, 3-H), 5.91 (1H, s, 3-alkenyl-H), 6.87 (3H, m, Ar-H), 7.07 (1H, m, Ar-H), 7.21 (1H, m, Ar-H), 7.28-7.56 (6H, m, Ar-H), 7.67 (1H, dd, *J* 8.3, 1.4, 5-H), 7.89 (1H, dd, J 8.3, 1.3, 5-H); δ_C 24.8, 25.3, 26.5, 26.7, 61.0, 75.2, 80.4, 116.9, 118.1, 118.4, 118.8, 121.1, 121.2, 126.3, 127.4, 127.8, 129.3, 130.0, 131.0, 131.8, 133.3, 134.8, 135.9, 141.4, 142.9, 152.8, 158.4, 188.1, 195.6 (Found: M^+, 470.155; C, 74.2; H, 5.5; S, 6.9. $C_{30}H_{30}O_3S$ requires M^+, 470.155(1); C, 74.0; H, 5.6; S, 6.8 %).

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