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Direct Aromatic *tert*-Butylation during the Synthesis of Thiochroman-4-ones

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Dedicated to Professor C W Rees FRS in celebration of his 65th birthday

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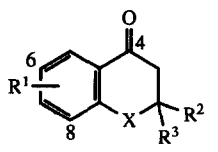
Abstract· The synthesis of thiochroman-4-ones from thiophenols and 3-methylbut-2-enoic acid effected by methane sulphonic acid is accompanied by *tert*-butylation of the aromatic ring 3-Arylthiobutanoic acids, available using β-butyrolactone, are efficiently cyclised in the same manner

The value of chroman-4-ones as precursors of other heterocyclic compounds adequately compensates for their infrequent natural occurrence and has ensured that their chemistry has been extensively studied [1] Of the various routes to chroman-4-ones,[1] their formation by the reaction of phenols with α,β-unsaturated carboxylic acids or their acid chlorides has been widely exploited [2] However, the chromanone (1, X = O) is often formed together with the isomeric dihydrocoumarin (2), which may even be the major product [3] Indeed this feature has resulted in confusion over structural assignments, notably in the days before the application of spectroscopic techniques largely eliminated such errors In the absence of an acidic catalyst which effects heterocyclisation, the α,β-unsaturated ester (3, X = O) can be isolated and subsequently cyclised in a Fries rearrangement [1] Other products which have been noted include (4, X = O) which results from *p*-acylation of the phenol[4] and the ester (5) arising from addition of HCl to the alkenic portion of the α,β-unsaturated ester [5] The influence which substituent, catalyst and reaction conditions have on the product composition has been investigated [3]



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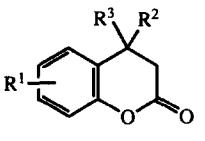

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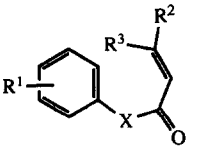

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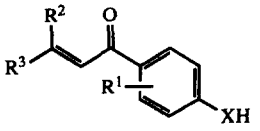

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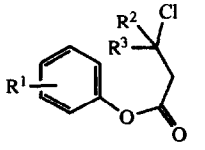

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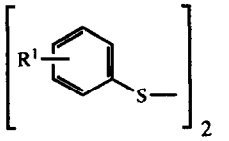


(6)

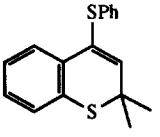
The synthesis of thiochroman-4-ones has been less thoroughly investigated,[6] possibly as a consequence of the limited range of commercially available thiophenols together with their frequently evil odour but also because

of their propensity towards oxidation to the disulphides (6) Previously, the most convenient route to 2,2-dimethylthiochroman-4-ones involved Michael addition of a thiophenol to methyl 3-methylbut-2-enoate, subsequent hydrolysis to the 3-arylthiobutanoic acid and finally cyclodehydration using polyphosphoric acid or sulphuric acid [7,8] The latter report emphasises the need for the hydrolysis of the ester to the acid prior to cyclisation Recently, the use of methanesulphonic acid (MSA) for the direct cyclocondensation of thiophenols with 3-methylbut-2-enoic acid has been advocated,[3,9] largely because of its advantageous handling properties and superior solvent power [10] The intermediacy of the *S*-aryl ester (3, X = S) was demonstrated and *p*-acylation of the thiophenol was also observed [9]

As part of our programme on benzothiopyrans, we required a range of thiochroman-4-ones and we now report some of our findings on their synthesis from thiophenols and α,β-unsaturated acids using MSA as the cyclising medium

Heating thiophenol and 3-methylbut-2-enoic acid in commercial 98% MSA for 3 h at 75 °C gave 2,2-dimethylthiochroman-4-one (1, X = S, R^1 = H, R^2 = R^3 = Me) (69%), diphenyl disulphide (6, R^1 = H) (10%) and the enol thioether (7) (9%)(Table, entry 1) Attempts to prepare (7) from the thiochromanone and thiophenol in MSA failed. The base washings yielded *ca* 5% of a solid, m p 71°C, characterised as 3-methyl-(3-phenylthio)butanoic acid[7] (8) presumably arising from 1,4-addition of thiophenol to the acrylic acid A much larger amount of the disulphide resulted from 2-thionaphthol (Entry 10) but this was reduced by using a longer reaction time and a lower temperature (Entry 11) When the thiophenol contained an electron withdrawing substituent (Entry 13) the reaction was hindered giving the thiochromanone in low yield Clearly the aromatic ring is deactivated towards ring closure by a Friedel-Crafts type mechanism, as is the case with the analogous phenols, and would presumably fail completely with a stronger electron withdrawing substituent [4] As expected, donor groups facilitate the reaction (Entry 9)

In an attempt to reduce disulphide formation and yet maintain a convenient reaction time, 2-methylthiophenol was heated at 80 °C with a 10-fold excess of the acrylic acid (Entry 7) Two major products resulted, the thiochromanone (1, X = S, R^1 = 8-Me, R^2 = R^3= Me) and the unexpected 6-*tert*-butyl derivative (9) Only a small amount of the disulphide was formed



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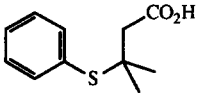

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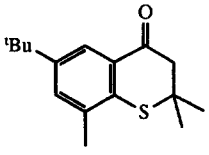


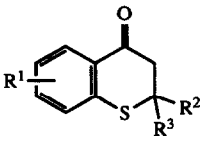
(9)

Formation of the *tert*-butylated product can be attributed to isomerisation of the α,β-unsaturated acid to the β,γ-isomer and subsequent facile decarboxylation to 2-methylpropene A cyclic transition state has been proposed to account for the ready loss of CO_2 [11] Under the acidic reaction conditions, the electron rich aromatic species is attacked by the protonated alkene. Both 2-methylpropene and CO_2 were detected in these reactions

Attempts to extend the *tert*-butylation procedure to other thiocresols yielded only the thiochromanones (Entries 4,5), although notably the *meta*-isomer gave the 2,2,5- and 2,2,7-trimethylthiochroman-4-ones in approximately equal amounts Similar isomer formation is known in chromanone chemistry,[12] but normally the 7-substituted isomer is formed exclusively 2-Aminothiophenol gave no thiochromanone, the major product being 2-

(*tert*-butylthio)aniline.[13] Under the experimental conditions, the amino group will be protonated, deactivating the system to electrophilic attack and hence preventing cyclisation to the thiochromanone

Table Experimental Results for the Preparation of Some Thiochroman-4-ones



	Substituents			Reaction Conditions			Product Yields (%)	
No	R^1	R^2	R^3	Reagent Ratio[a]	Temp (°C)	Time (h)	Ketone (1)	Disulphide (6)
1	H	Me	Me	1 1	75	3	69	10
2	H	Me	Me	1 1	95	3	74	10
3	H	Me	Me	1 1 1	75	3	70	7
4	5-Me	Me	Me	1 2	80	5	36[b]	3
	7-Me	Me	Me				33[b]	
5	6-Me	Me	Me	1 2	80	7	67	8
6	8-Me	Me	Me	1 1 05	70	6	62[c]	5
7	8-Me,6-^{t}Bu	Me	Me	1 10	80	6	41[d]	1
8	6-^{t}Bu	Me	Me	1 1 05	75	4	48	10
9	5,7-Me_2	Me	Me	1 1 1	75	4	89	5
10	5,6-Benzo	Me	Me	1 1 05	80	3	51	22
11	5,6-Benzo	Me	Me	1 1 1	30	22	74	2
12	7,8-Benzo	Me	Me	1 1 1	75	5	34	13
13	6-Cl	Me	Me	1 1 1	75	6	11	20
14	5,6-Benzo	Me	H	1 1 5	75	5	21	15
15	8-Me	Me	H	1 10	75	5	9	17

(a) Ratio of thiophenol to the acrylic acid

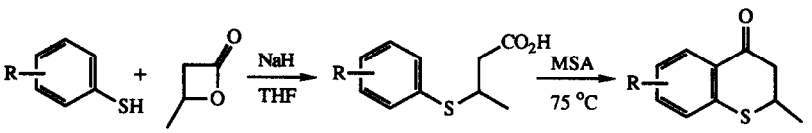
((b) Reaction afforded a mixture of 2,2,5- and 2,2,7-trimethylthiochroman-4-ones

(c) Under these reaction conditions only 8% of the *tert*-butylated product (9) was observed

(d) Approximately 27% of 2,2,8-trimethylthiochroman-4-one was also obtained

There was no evidence of isopropylation when various thiophenols were heated with but-2-enoic acid in MSA and only low yields of 2-methylthiochroman-4-ones (1, X = S, R^2 = H, R^3 = Me) were isolated (Entries 14,15) However, almost quantitative yields resulted from the cyclisation in MSA of 3-arylthiobutanoic acids (Scheme)

derived from the nucleophilic ring opening of β-butyrolactone with sodium thiophenoxides which proceeds via alkyl-oxygen bond fission [14]



Scheme

The ^{1}H NMR spectra of the 2,2-dimethylthiochroman-4-ones are relatively simple and exhibit a singlet for the C-3 methylene function which routinely absorbs in the relatively narrow range δ 2 85-3 00 The C-2 geminal methyl groups are equivalent and give rise to a signal at approximately δ 1 45 H-5, *peri* to the anisotropic carbonyl function absorbs at approximately δ 8 0 for the simple substituted analogues 7,8-Benzannulation shifts the signals for the C-2 methyl substituents and H-5 downfield to δ 1 55 and 8 21, respectively In the 5,6-benzologue, H-10 is heavily deshielded by the carbonyl group and appears at δ 9.29 The ^{1}H NMR spectra of the 2-methylthiochroman-4-ones are more complex than those of their dimethyl counterparts The C-3 protons are non-equivalent because of the unsymmetrical substitution at C-2 and geminal coupling of the order of 16 5 Hz is observed Vicinal *trans*- and *cis*- coupling with H-2 of ~11 Hz and ~3 Hz respectively are also seen and hence a pair of double doublets are observed for these protons at *ca* δ 2 7 and δ 3.0 Published data for the ^{1}H NMR spectra of non-planar six-membered rings indicate that axial-axial coupling constants are of the order of 8-13 Hz and axial-equatorial coupling constants are in the range 3-6 Hz, whilst equatorial-equatorial coupling constants are smaller still [15] From the magnitude of the vicinal coupling constants obtained in this work it appears that the C-2 methyl group occupies a pseudo-equatorial site H-2 appears as a complex multiplet at ~ δ 3 6, deshielded by the adjacent heteroatom The H-5 proton appears furthest downfield in the ^{1}H NMR spectra of the 2-methyl analogues with comparable chemical shifts to those of the dimethyl compounds

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 ^{1}H and ^{13}C NMR spectra were recorded on a Brucker WM 250 instrument for solutions in $CDCl_3$, *J* values are given in Hz Flash chromatographic separations were performed on Crossfields Sorbsil C60 silica gel (M P D 60A, 40-60μ, activated) according to the published procedure [16]

General Method for the Preparation of Thiochroman-4-ones.

A mixture of the thiophenol (0 03mol) and the acrylic acid in methanesulphonic acid (75 cm^3, 98%) was heated until all of the acrylic acid was judged to have reacted by tlc examination of the reaction mixture The cooled reaction mixture was then poured into ice water (400 cm^3) and extracted with ethyl acetate (3 x 50 cm^3) The combined organic extracts were washed with aqueous sodium hydroxide (2M, 3 x 50 cm^3) and then with water (2 x 100 cm^3) Removal of the dried (Na_2SO_4) solvent afforded a dark brown oil which was purified by elution from silica and either recrystallisation or distillation

a) Thiophenol and 3-methylbut-2-enoic acid gave three fractions on elution from silica with 2% ethyl acetate in hexane. (i) **diphenyl disulphide** (10%) m.p 59-61 °C [lit m p 61 °C[17a]], (ii) **2,2-dimethyl-4-(phenylthio)-2*H*-thiochromene** (9%) m p 62-64 °C as colourless crystals after sublimation, δ_H 1 45 (6H, s, 2-Me), 6 40 (1H, s, 3-H), 6 99-7 31 (8H, m, SPh and Ar-H), 7 74 (1H, dd, *J* 7 9, 1 3, 5-H) (Found C, 71 8, H, 5 7, S, 22 4 $C_{17}H_{16}S_2$ requires C, 71 8, H, 5 7, S, 22 5%), (iii) **2,2-dimethylthiochroman-4-one** (74%) m p 65 0-65 5 °C as colourless crystals from light petroleum (b p 30-40 °C) [lit m p 63-65 °C[7]], υ_{max} (Nujol) CO 1679 cm^{-1}, δ_H 1 47 (6H, s, 2-Me), 2 87 (2H, s, 3-H), 7 13-7 43 (3H, m, Ar-H), 8 08 (1H, dd, *J* 8 1, 1 2, 5-H)

The base washings gave **3-methyl-(3-phenylthio)butanoic acid** (~5%) m p 69 5-71 5 °C as colourless crystals from hexane and ethyl acetate [lit. m p 69-71 °C[7]], υ_{max} (Nujol) CO 1699, OH 3050 cm^{-1}, δ_H 1 42 (6H, s, 3-Me), 2 56 (2H, s, 2-H), 7 30-7 39 (3H, m, Ar-H), 7 55-7 59 (2H, m, Ar-H), δ_C 28 5 (3-Me), 46 4 (2-C*), 46.7 (3-C*), 128 7 (2'-C, 6'-C), 129 1 (4'-C), 131 2 (1'-C), 137 6 (3'-C, 5'-C), 176 8 (1-C) C* ^{13}C assignments may be reversed

b) 4-Methylthiophenol and 3-methylbut-2-enoic acid gave on recrystallisation **2,2,6-trimethylthiochroman-4-one** (67%) m p 74 0-75 0 °C as colourless crystals from light petroleum (b p 30-40 °C) [lit m p 74-75 °C[18]], υ_{max} (Nujol) CO 1676 cm^{-1}, δ_H 1 45 (6H, s, 2-Me), 2 32 (3H, s, 6-Me), 2 85 (2H, s, 3-H), 7 13-7 26 (2H, m, Ar-H), 7 91 (1H ,d, *J* 1 4, 5-H)

c) 2-Methylthiophenol and 3-methylbut-2-enoic acid gave two thiochroman-4-ones after elution from silica with 20% diethyl ether in hexane (i) **6-*tert*-butyl-2,2,8-trimethylthiochroman-4-one** (27%) m p 115 0-116 5 °C as colourless crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1672 cm^{-1}, δ_H 1 31 (9H, s, 6-^{t}Bu), 1 47 (6H, s, 2-Me), 2 29 (3H, s, 8-Me), 2 85 (2H, s, 3-H), 7 34 (1H, d, *J* 0 9, 7-H), 8 01 (1H, d, *J* 0 9, 5-H) (Found C, 73 2, H, 8 5, S, 12 4 $C_{16}H_{22}OS$ requires C, 73 2, H, 8 5, S, 12 2%), (ii) **2,2,8-trimethylthiochroman-4-one** (41%) m p 93 5-94 5 °C as colourless crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1682 cm^{-1}, δ_H 1 48 (6H, s, 2-Me), 2 29 (3H, s, 8-Me), 2 86 (2H, s, 3-H), 7 08-7 29 (2H, m, Ar-H), 8 00 (1H,dd, *J* 8 2, 1 9, 5-H) (Found C, 69 8, H, 6 9, S, 15 5 $C_{12}H_{14}OS$ requires C, 69 9, H, 6 9, S, 15 5%)

d) 3-Methylthiophenol and 3-methylbut-2-enoic acid gave two thiochroman-4-ones after elution from silica with 20% diethyl ether in hexane (i) **2,2,5-trimethylthiochroman-4-one** (36%) m p 52 5-53 5 °C as colourless microcrystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1697 cm^{-1}, δ_H 1 45 (6H, s, 2-Me), 2 61(3H, s, 5-Me), 2 87 (2H, s, 3-H), 6 92-7 24 (3H, m, Ar-H) (Found C, 69 6, H, 6 8, S, 15 8 $C_{12}H_{14}OS$ requires C, 69 9, H, 6 9, S, 15 5%), (ii) **2,2,7-trimethylthiochroman-4-one** (33%) m p 82 0-82 5 °C as colourless crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1677 cm^{-1}, δ_H 1 44 (6H, s, 2-Me), 2 26 (3H, s, 7-Me), 2.78 (2H, s, 3-H), 6 89-6 97 (2H, m, Ar-H), 7 91(1H, d, *J* 7 9, 5-H) (Found C, 69 7, H, 6 9, S, 15 5 $C_{12}H_{14}OS$ requires C, 69 9, H, 6 9, S, 15 5%)

e) 4-*tert*-Butylthiophenol and 3-methylbut-2-enoic acid on elution from silica with 1% ethyl acetate in hexane gave **6-*tert*-butyl-2,2-dimethylthiochroman-4-one** (48%) m p 84 5-85 5 °C as colourless crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1679 cm^{-1}, δ_H 1 31 (9H, s, 6-^{t}Bu), 1 46 (6H, s, 2-Me), 2 86 (2H, s, 3-H), 7 14-7 48 (2H, m, Ar-H), 8 12 (1H, d, *J* 8 2, 5-H) (Found C, 72 6, H, 8 2, S, 12 7 $C_{15}H_{20}OS$ requires C, 72 5, H, 8 1, S, 12 9%)

f) 3,5-Dimethylthiophenol and 3-methylbut-2-enoic acid on elution from silica with 20% diethyl ether in hexane gave **2,2,5,7-tetramethylthiochroman-4-one** (89%) b p 105 °C at 0 12 mmHg as a colourless oil, υ_{max} (neat) CO 1672 cm^{-1}, δ_H 1 44 (6H, s, 2-Me), 2 27 (3H, s, 7-Me), 2 59 (3H, s, 5-Me), 2 85 (2H, s, 3-H), 6 76 (1H, d, *J* 1 3, Ar-H), 6 91 (1H, d, *J* 1 3, Ar-H) (Found C, 71 0, H, 7 4, S, 14 7 $C_{13}H_{16}OS$ requires C, 70 9, H, 7 3; S, 14 5%)

g) 4-Chlorothiophenol and 3-methylbut-2-enoic acid on elution from silica with 0 5% ethyl acetate in hexane gave **6-chloro-2,2-dimethylthiochroman-4-one** (11%) m p 60 0-60 5 °C as pale yellow needles from light petroleum (b p. 30-40 °C), υ_{max} (Nujol) CO 1687 cm^{-1}, δ_H 1 46 (6H, s, 2-Me), 2 86 (2H, s, 3-H), 7 16-7 38 (2H, m, Ar-H), 8 06 (1H, d, *J* 1 1, 5-H) (Found C, 58 1, H, 4 7, Cl, 15 5, S, 14 1 $C_{11}H_{11}ClOS$ requires C, 58 3, H, 4 9; Cl, 15 6, S, 14 1%)

h) 2-Thionaphthol and 3-methylbut-2-enoic acid on recrystallisation gave **5,6-benzo-2,2-dimethylthiochroman-4-one** (74%) m p 93 0-93 5 °C as pale brown granular crystals from light petroleum (b p. 40-60 °C), υ_{max} (Nujol) CO 1658 cm^{-1}, δ_H 1 53 (6H, s, 2-Me), 3 00 (2H, s, 3-H), 7 20-7 81 (5H, m, Ar-H), 9 29 (1H, dd, *J* 8.2, 2 2, 5-H) (Found C, 74 4 , H, 5 8 , S, 13 2 $C_{15}H_{14}OS$ requires C, 74 3, H, 5 8, S, 13 2%)

i) 1-Thionaphthol [19] and 3-methylbut-2-enoic acid on elution from silica with 10% diethyl ether in hexane gave **7,8-benzo-2,2-dimethylthiochroman-4-one** (34%) m p 93 5-94 0 °C as bright yellow plates from light petroleum (b.p 30-40 °C), υ_{max} (Nujol) CO 1657 cm^{-1}, δ_H 1 56 (6H, s, 2-Me), 2 96 (2H, s, 3-H), 7 52-8 17 (5H, m, Ar-H), 8.21 (1H, dd, *J* 8 1, 1 9, 5-H) (Found C, 74 2, H, 5 8, S, 13 2 $C_{15}H_{14}OS$ requires C, 74 3, H, 5 8, S, 13 2%)

j) 2-Aminothiophenol and 3-methylbut-2-enoic acid gave two fractions on elution from silica with 20% ethyl acetate in hexane: (i) **2-(*tert*-butylthio)aniline** (58%) b p 147-151 °C at 15 mmHg [lit b p 149 °C at 15 mmHg[13]] as a pale pink oil, δ_H 1 34 (9H, s, ^tBu), 4 40 (2H, bs, NH_2), 6 66-6 78 (2H, m, Ar-H), 7 16 (1H, m, Ar-H), 7 38 (1H, m, Ar-H), (ii) **2-aminodiphenyldisulphide** (21%) m p 92 0-93 5 °C [lit m p 93 0 °C[17b]], δ_H 4 14 (4H, bs, NH_2), 6 55-6 64 (2H, m, Ar-H), 6 69-6 73 (2H, m, Ar-H), 7 12-7 19 (4H, m, Ar-H)

k) 2-Thionaphthol and but-2-enoic acid on recrystallisation gave **5,6-benzo-2-methylthiochroman-4-one** (21%) m p 52 5-53 0 °C as colourless crystals from light petroleum (b p 40-60 °C) and ethyl acetate, υ_{max} (Nujol) CO 1699 cm^{-1}, δ_H 1 49 (3H, d, *J* 6 7, 2-Me), 2 92 (1H, dd, *J* 16 6, 11 3, 3-H), 3 14 (1H, dd, *J* 16 6, 2 9, 3-H), 3 70 (1H, m, 2-H), 7 24-7 80 (5H, m, Ar-H), 9 19 (1H, dd, *J* 8 1, 2 1, 5-H) (Found C, 73 6, H, 5 2, S, 14 0 $C_{14}H_{12}OS$ requires C, 73 6, H, 5 3, S, 14 0%)

l) 2-Methylthiophenol and but-2-enoic acid on elution from silica with 2% ethyl acetate in hexane gave **2,8-dimethylthiochroman-4-one** (9%) m p 53 0-53 5 °C as colourless crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1686 cm^{-1}, δ_H 1 46 (3H, d, *J* 6 8, 2-Me), 2 31 (3H, s, 8-Me), 2 74 (1H, dd, *J* 16 2, 11 1, 3-H), 3 00 (1H, dd, *J* 16 2, 2 7, 3-H), 3 61 (1H, m, 2-H), 7 05-7 30 (2H, m, Ar-H), 7 98 (1H, dd, *J* 8 0, 1 7, 5-H) (Found C, 68 5, H, 6 3, S, 16 4 $C_{11}H_{12}OS$ requires C, 68 7, H, 6 3, S, 16 7%)

General Method for the Preparation of 3-(Arylthio)butanoic Acids.

β-Butyrolactone (0 26 mol) was added in a single portion to a vigorously stirred, cooled solution of the sodium thiophenoxide prepared from sodium hydride (0 25 mol, 60% dispersion in mineral oil) and the thiophenol (0 25 mol) in anhydrous tetrahydrofuran (100 cm^3) The resulting mixture was heated under reflux for 2 hours and after cooling to room temperature the tetrahydrofuran was removed to afford a white solid which was dissolved in water and washed with ethyl acetate (2x50 cm^3) The aqueous phase was cautiously acidified with concentrated hydrochloric acid and extracted with ethyl acetate (4x75 cm^3) The combined extracts were washed with water (2x100 cm^3) Removal of the dried solvent (Na_2SO_4) solvent afforded the butanoic acids which were further purified by bulb-to-bulb distillation

a) **3-(Phenylthio)butanoic acid** (98%) b p 130 °C at $1x10^{-1}$ mmHg as a colourless oil, δ_H 1 37 (3H, d, *J* 6 7, 3-Me), 2 49 (1H, dd, *J* 8 2, 16 0, 2-H), 2 70 (1H, dd, *J* 6 0, 16 0, 2-H), 3 56-3 67 (1H, m, 3-H), 7 25-7 48 (5H, m, Ar-H), 11 42 (1H, bs, OH)

b) **3-(4-Chlorophenylthio)butanoic acid** (99%) b p 175 °C at $5\ 8x10^{-2}$ mmHg as a colourless oil, δ_H 1 34 (3H, d, *J* 6 7, 3-Me), 2 48 (1H, dd, *J* 8 1, 16 1, 2-H), 2 65 (1H, dd, *J* 6 4, 16 1, 2-H), 3 50-3 64 (1H, m, 3-H), 7 25-7 43 (4H, m, Ar-H), 11 30 (1H, bs, OH)

c) **3-(4-Methylphenylthio)butanoic acid** (97%) b p 140 °C at $5\ 0x10^{-2}$ mmHg as a pale yellow oil, δ_H 1 34 (3H, d, *J* 6 7, 3-Me), 2 34 (3H, s, Ar-Me), 2 45 (1H, dd, *J* 8 5, 15 9, 2-H), 2 67 (1H, dd, *J* 6 0, 15 9, 2-H), 3 49-3 57 (1H, m, 3-H), 7 09-7 15 (2H, m, Ar-H), 7 33-7 41 (2H, m, Ar-H), 10 6 (1H, bs, OH)

d) **3-(2-Naphthylthio)butanoic acid** (99%) b p 190 °C at $4\ 6x10^{-2}$ mmHg, m p 64 5-65 5 °C as an off white solid, δ_H 1 40 (3H, d, *J* 6 9, 3-Me), 2 51 (1H, dd, *J* 8 4, 16 0, 2-H), 2 73 (1H, dd, *J* 5 8, 16 0, 2-H), 3 65-3 77 (1H, m, 3-H), 7 43-7 53 (3H, m, Ar-H), 7 77-7 82 (3H, m, Ar-H), 7 93 (1H, m, Ar-H), 10 0 (1H, bs, OH)

General Method for the Preparation of 2-Methylthiochroman-4-ones.

A solution of the 3-(arylthio)butanoic acid (0 015 mol) in methanesulphonic acid (100 cm^3, 98%) was stirred for 30 minutes at 75 °C After cooling, the crude reaction mixture was poured into ice water (500 cm^3) and extracted with ethyl acetate (3x50 cm^3) The combined organic extracts were washed with aqueous sodium hydroxide (2M, 3x50 cm^3) and water (2x100 cm^3) Removal of the dried (Na_2SO_4) solvent afforded a pale yellow oil or solid which was purified by bulb-to-bulb distillation or recrystallisation to yield the 2-methylthiochroman-4-one

a) **2-Methylthiochroman-4-one** (97%) b p 87-89 °C at $6x10^{-2}$ mmHg [lit b p 146-147 °C at 9 mmHg[14]] as a colourless oil, υ_{max} (neat) CO 1667 cm^{-1}, δ_H 1 42 (3H ,d, *J* 6 7, 2-Me), 2 73 (1H, dd, *J* 11 1, 16 5, 3-H), 3 00 (1H, dd, *J* 2 9, 16 5, 3-H), 3 60 (1H, m, 2-H), 7 11-7 40 (3H, m, Ar-H), 8 07(1H, dd, *J* 7 9, 1 7, 5-H)

b) **6-Chloro-2-methylthiochroman-4-one** (92%) m p 60 5-61 0 °C as pale yellow crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1683 cm^{-1}, δ_H 1 42 (3H, d, *J* 6 7, 2-Me), 2 72 (1H, dd, *J* 11 2, 16 6, 3-H), 3 00 (1H, dd, *J* 2 8, 16 6, 3-H), 3 59 (1H, m, 2-H), 7 16-7 34 (2H, m, Ar-H), 8 01 (1H, d, *J* 1 9, 5-H) (Found C, 56 6, H, 4 2, Cl, 16 5, S, 15.0 $C_{10}H_9ClOS$ requires C, 56 4, H, 4 3, Cl, 16 7, S, 15 1%)

c) **2,6-Dimethylthiochroman-4-one** (98%) m p 66 0-66 5 °C as pale yellow crystals from light petroleum (b p 30-40 °C), υ_{max} (Nujol) CO 1679 cm^{-1}, δ_H 1 42 (3H, d, *J* 6 7, 2-Me), 2 33 (3H, s, 6-Me), 2 72 (1H, dd, *J* 11 1, 16.2, 3-H), 2.99 (1H, dd, *J* 2 7, 16 2, 3-H), 3 61 (1H, m, 2-H), 7 19-7 22 (2H, m, Ar-H), 7 91 (1H, d, *J* 1 6, 5-H) (Found. C, 68 7, H, 6 3, S, 16 8 $C_{11}H_{12}OS$ requires C, 68 7, H, 6 3, S, 16 7%)

d) **5,6-Benzo-2-methylthiochroman-4-one** (97%) identical in all aspects to the previously prepared sample

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