Enamino Ketones as Precursors of Functionalised 2*H*-Thiopyrans and Thiopyrano[2,3-*c*]- and [3,2-*b*]-benzothiopyrans

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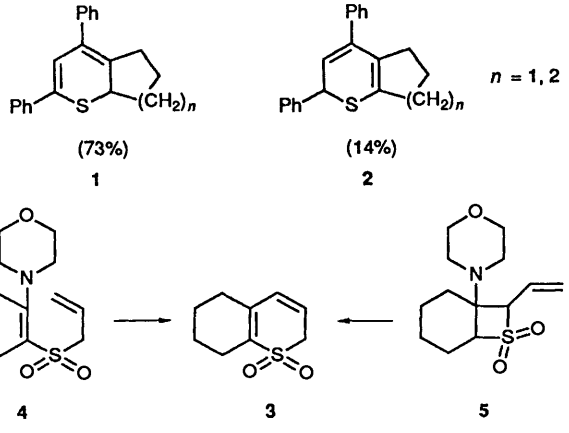
Oxo enamino ketones obtained by treating active methylene compounds with *N,N*-dimethylformamide dimethyl acetal yield novel 2*H*-thiopyrans in a regioselective one pot thionation–[4 + 2]-cycloaddition sequence. Application of similar methodology to thiochroman-3-ones affords novel thiopyrano[2,3-*c*][1]benzothiopyrans and the [3,2-*b*] isomers.

Both 2*H*- and 4*H*-thiopyrans are relatively unstable,[1] decomposing in air at low temperature,[2] but the stability of 2*H*-thiopyrans is considerably improved by substitution and annulation.[3]

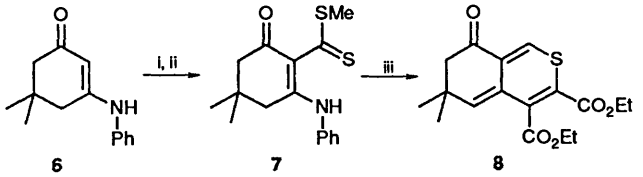
Although the reduction of thiopyrylium salts with complex metal hydrides invariably affords mixtures of the isomeric 2*H*- and 4*H*-thiopyrans,[1] this procedure has been used to obtain the simple isomeric reduced annulated 2*H*-thiopyrans **1** and **2**.[4] The



sulfones **3** have been obtained by the regioselective ring closure and subsequent acidic hydrolysis of 2-allylsulfonyl-1-morpholinocyclohexene **4**[5] and by the isomerisation of the 2-vinylthietane 1,1-dioxide **5**.[6]

Hetero Diels–Alder reactions of enamino thiones with α,β-unsaturated aldehydes, ketones,[7] esters,[8] amides[9] and nitriles,[10] nitroalkenes,[11] ketenes[12] and alkynes[13] have been widely exploited in recent years as a fruitful route to functionalised 2*H*-thiopyrans.

Recently, Tominaga *et al.* have reported the synthesis of the 6*H*-[2]benzothiopyran **8** by cycloaddition of dimethyl acetylenedicarboxylate with the heterodiene **7**, derived from the



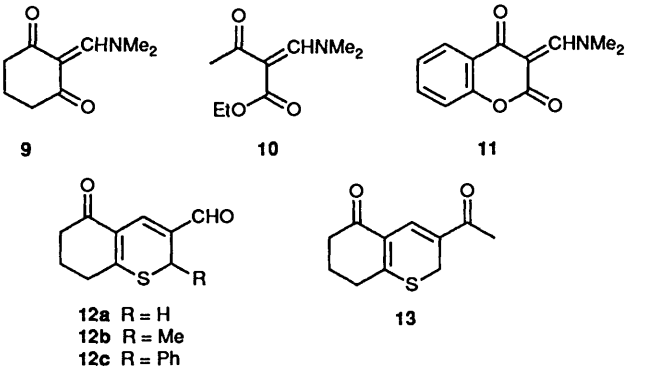
Reagents and conditions: i, CS_2, NaOH; ii, Me_2SO_4; iii, DMAD, heat

enamino ketone **6** by treatment with carbon disulfide under basic conditions and subsequent methylation.[14]

We now report a regioselective synthesis of some tetrahydro-2*H*-[1]benzothiopyrans utilising a one pot thionation–hetero Diels–Alder cycloaddition reaction sequence of oxo enamino ketones. The generality of this procedure has been extended to include the formation of some highly functionalised 2*H*-thiopyrans and a fused thiopyranobenzopyranone. Furthermore, enamino ketones derived from thiochroman-3-ones behave similarly and give access to novel benzologues of thiopyranothiopyrans.

Results and Discussion

It is well established that formamide acetals react with active methylene functions to produce substituted enamines.[15] Treatment of cyclohexane-1,3-dione with *N,N*-dimethylformamide dimethyl acetal (DMFDMA) according to the published procedure[16] gave the enamino dione **9**. Using a similar



procedure, ethyl 2-(dimethylaminomethylene)-3-oxobutanoate **10**[16] was obtained from ethyl 3-oxobutanoate. The ^{1}H NMR spectrum of **10** displayed an exceptionally broad signal for the dimethylamino function at δ 3.01, which was resolved into a singlet at 50 °C as a result of increased free rotation of the NMe_2 group. Other workers have isolated this enamino keto ester as a mixture of the *E*- and *Z*-isomers,[17] but in our hands there was no evidence of two isomers.

Addition of an excess of DMFDMA to 4-hydroxycoumarin and refluxing the dark orange solution resulted in the formation of 3-(dimethylaminomethylene)[1]benzopyran-2,4-dione **11**. In contrast to **10**, the *N*-methyl groups appear as two distinct signals in the ^{1}H NMR spectrum at δ 3.38 and 3.45 suggesting that the NMe_2 function is in a fixed configuration. This feature compares favourably with the simpler cyclic analogue **9** where two signals are similarly observed for the NMe_2 group. The alkenyl proton absorbs at δ 8.35, an identical shift to that observed for 3-(*Z*)-(cyclohexylaminomethylene)chroman-2,4-dione compared with δ 8.55 for the *E*-isomer, and thus suggesting that the stereochemistry of **11** is also *Z*.[18] The ^{13}C NMR spectrum of **11** displays two lowfield signals at δ 177.8 and 162.7 assigned to the benzylic (C-4) and lactone (C-2) carbonyl groups, respectively.

Preliminary attempts to effect the thionation of the enamino ketones with Lawesson's reagent[19] using dimethoxyethane as solvent according to the procedure described by Walter and Proll[20] were only moderately successful. TLC examination of the reaction mixture indicated that a considerable proportion of the enamino ketone remained unchanged. However, a much improved conversion into the enamino thione was achieved in benzene as described by Lawesson and co-workers.[21]

Disappointingly, attempts to isolate the enamino thiones by column chromatography failed. In some cases maroon solids were isolated, the ^{1}H NMR spectra of which suggested that the product was probably polymeric. Therefore, when the thionation reaction was judged to be complete by TLC, the dienophile was added to the reaction mixture, allowing the cycloaddition to occur *in situ* and obviating the need to isolate the enamino thione. It is well established that [4 + 2]-cycloaddition reactions of enamino thiones are extremely rapid and complete conversion into products in under 10 min is not uncommon.[13,22]

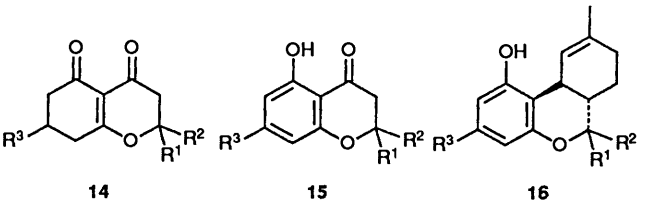
The one pot thionation–cycloaddition of the enamino dione **9** using Lawesson's reagent and, in the first instance, acrolein as the dienophile was achieved in benzene[21] and gave 5-oxo-5,6,7,8-tetrahydro-2*H*-[1]benzothiopyran-3-carbaldehyde **12a**. The cycloaddition is accompanied by the elimination of dimethylamine to afford the extended conjugated system, a common occurrence during cycloadditions of simple enamino thiones,[7] although in some instances the elimination necessitates a separate acid-catalysed operation.[11]

The methyl and phenyl analogues **12b** and **12c** were similarly obtained using crotonaldehyde and cinnamaldehyde respectively as the dienophilic components, although the latter required warming to 40 °C for 30 min to ensure complete reaction of the oxo enamino thione. Similarly, methyl vinyl ketone gave the annulated thiopyran **13**. However, no thiopyrans could be isolated from the reaction mixtures when ethyl cinnamate, β-nitrostyrene, phenyl vinyl sulfone or acrylonitrile were employed as dienophiles.

The ^{1}H NMR spectra of **12a, b, c** all display a lowfield signal at approximately δ 9.6 assigned to the aldehyde proton. The olefinic proton (4-H) appears as a singlet at δ 7.52 in **12a** and **12b** shifted downfield as a consequence of its proximity to the anisotropic aldehyde function. In **12c**, the additional downfield shift of 4-H to δ 7.82 is associated with the phenyl substituent. 2-H Appears as a singlet at δ 3.69 in **12a**, as a quartet at δ 4.12 in **12b** because of the adjacent methyl group and in **12c** as a singlet at δ 5.26 since it is benzylic. The unsymmetrical substitution at C-2 in **12b** and **12c** confers diastereotopic properties on the cycloalkyl protons which results in a complex multiplet for each proton. The ^{13}C NMR spectra of **12a, b, c** display two lowfield carbonyl signals within the narrow range δ 191.2–191.5. In the first instance, these signals can be assigned by comparison of their relative intensities which relate to the relaxation time of the carbon nuclei. The quaternary carbonyl carbon affords a less intense signal than does the tertiary carbon of the aldehyde function and resonates marginally further downfield in all three cases. These inferences were confirmed by the fully coupled ^{13}C NMR spectra in which the more intense upfield signal appears as a doublet with $^1J_{CH}$ 165 Hz, expected for the aldehyde carbon. C-4, conjugated with the aldehyde group, resonates in the region δ 137.3–139.5 with $^1J_{CH}$ in the range 96–105 Hz and C-8a appears as a singlet around δ 165.

The ^{1}H and ^{13}C NMR spectra of **13** closely resemble those of the thiopyrans **12**. 2-H Appears as a singlet at δ 3.67 and 4-H at δ 7.62, but C-4 is shifted marginally upfield to δ 131.5. Two lowfield signals at δ 196.8 and 191.8 are assigned to the acetyl and the 5-carbonyl carbons, respectively.

5-Hydroxychroman-4-ones **15** are useful precursors of

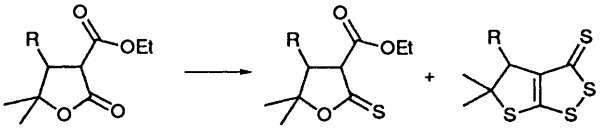


14 **15** **16**

cannabinoids[23] **16** and are accessible by the aromatisation of the reduced benzopyrans **14** using 10% Pd–C in cyclohexene.[24] The tetrahydro-2*H*-[1]benzothiopyrans **12** and **13** are therefore potential sources of 5-hydroxythiochromanones and thiocannabinoids. Such a route would obviate the need for the relatively expensive and evil-smelling 3-methoxythiophenol and, furthermore, would avoid contamination by the 7-hydroxy isomer.[25] Disappointingly, the dehydrogenation of **12** or **13** could not be achieved with Pd–C, DDQ or *o*-chloranil under a variety of conditions. In all cases the tetrahydrobenzothiopyrans were recovered unchanged.

The carbonyl groups of the enamino dione **9** are identical and hence only one thiopyran can result from the thionation–cycloaddition sequence irrespective of the site of thionation. However, the enaminones **10** and **11** are unsymmetrically substituted and the reaction sequence may lead to the formation of two isomeric thiopyrans.

Shabana *et al.* have shown that *N*- and *C*-acetyl groups may be selectively thionated in the presence of ester functions on treatment with Lawesson's reagent in 1,2-dimethoxyethane at room temperature.[26] Similarly, Scheibye *et al.* have observed the selective thionation of the lactone carbonyl group in compounds **17**, although relatively high temperatures (refluxing

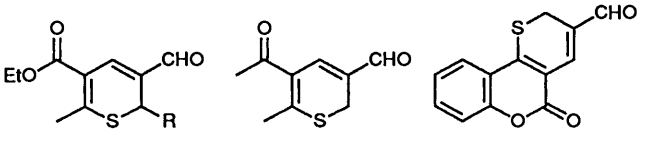


17 **18** **19**

xylene or toluene) and long reaction times (6–8 h) were required. Interestingly some of the bicyclic compound **19** was also formed though at the expense of the thionolactone **18**.[27]

When the enamino keto ester **10** was thionated and treated with acrolein, a single 2*H*-thiopyran was obtained exclusively, as shown by chromatography and spectroscopic measurements. The ^{13}C NMR spectrum of the product displayed a relatively intense lowfield signal at δ 190.6 of an aldehyde group, whilst a less intense signal at δ 163.7 was assigned to the ester function. The olefinic carbon (C-4) resonates at δ 143.7 in the range expected from the spectrum of **12**. The former two chemical shifts confirm the structure of the product as **20a** and affirm that the thionation occurred at the more electrophilic ketonic carbonyl group. For the alternative isomer **21**, in addition to the absence of the ester signal, a second lowfield ^{13}C signal in the range δ 185–195 would have been expected because of the presence of the acetyl function.

The IR spectrum of this 2*H*-thiopyran **20a** further corroborates the structure, since two well resolved, intense



20a R = H
20b R = Ph

21 **22**

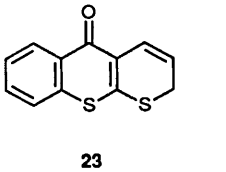
carbonyl stretching bands are present at 1710 and 1663 cm^{-1}, typical of the α,β-unsaturated ester and aldehyde groups, respectively. The ^1H NMR spectrum of **20a** displayed signals at δ 9.58, 7.45 and 3.56 which are assigned to the aldehyde, olefinic (4-H) and methylenic ($S-CH_2$) protons respectively, in common with the spectra of 2*H*-thiopyrans **12** and **13**.

Repetition of the reaction using cinnamaldehyde as the dienophile resulted in the exclusive formation of the 2*H*-thiopyran **20b**, which had comparable spectral data with **20a**.

The synthesis and physiological properties of coumarins with a 3:4 fused ring system have attracted attention in recent years.[28] Application of the thionation–cycloaddition sequence to the chromandione **11** using acrolein as the dienophile afforded the thiopyrano[3,2-*c*][1]benzopyranone **22**. The ^{13}C NMR spectrum displayed a lowfield aldehyde signal at δ 190.3 and the lactone carbonyl was assigned to the signal at δ 158.9 which compares favourably with the analogous signal at δ 162.7 in the precursor **11**. The olefinic carbon (C-4) resonates at δ 140.3. The IR-spectrum of **22** exhibits α,β-unsaturated lactone and aldehyde carbonyl stretching bands at 1728 and 1657 cm^{-1}, respectively.

Thiopyranothiopyrans have attracted considerable interest from a theoretical and synthetic viewpoint. Much of the work in this area has sought to prepare novel compounds which are of potential value as donors for organic conductors, as sensitisers, dyes, photoconductors and electrophoretic pigments.[29a–d]

There are six possible modes of fusion of two thiopyran units. Only the [3,4-*b*]- and [4,3-*c*]-isomers have been obtained as the simple bicyclic systems,[29a] but benzologues of the [2,3-*b*] and [3,2-*b*] systems have additionally been reported. The linear benzologue **23** of the former system results from alkylation of



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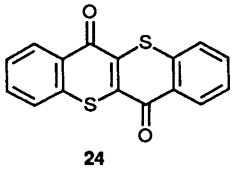

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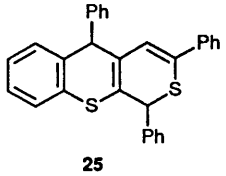

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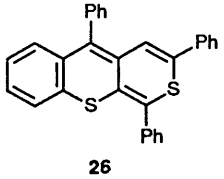


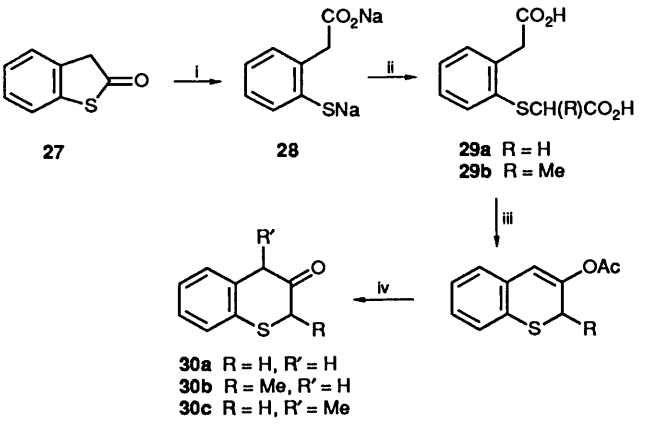
26

4-hydroxybenzothiopyran-2-thione with prop-2-ynyl bromide and a subsequent thio-Claisen rearrangement.[30] The linear dibenzologue **24** of the latter system has been derived from thiochroman-4-one by enamine methodology[29c] and a monobenzologue, prepared from isothiochroman-4-one, has been utilised in the synthesis of some thiasteroids.[31] Fused derivatives of thiopyrano[4,3-*c*]thiopyran, the thiachrysenes, have been obtained using hetero Diels–Alder chemistry.[32]

The only reported benzologue of thiopyrano[3,4-*b*]thiopyran is **25**, which was obtained from thiochromone-3-carbaldehyde *via* a sequence initiated by condensation with dibenzyl sulfoxide.[33] The derived fully conjugated compound **26** possesses donor properties[29b] and is slightly anti-aromatic in accord with calculations.[34]

By analogy with the above syntheses of thiopyrans, benzothiopyrans and thiopyranobenzopyranones, the use of thiochroman-3-ones as a source of enamino ketones should provide an entry to thiopyranobenzothiopyran ring systems.

Thiochroman-3-one **30a** and the 2-methyl analogue **30b** were obtained by the sequence outlined in Scheme 1. Hydroboration–oxidation of benzo[*b*]thiophene gave benzo-



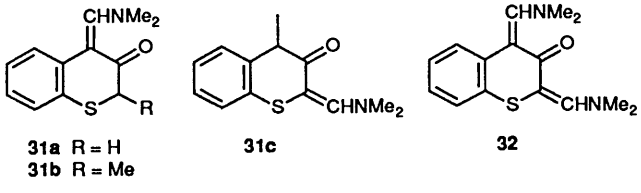
27 **28** **29a** R = H, **29b** R = Me

30a R = H, R' = H
30b R = Me, R' = H
30c R = H, R' = Me

Scheme 1 *Reagents and conditions:* i, NaOH; ii, $ClCH(R)CO_2H$, EtOH, heat, 2 h; iii, Ac_2O, heat, 15 min; iv, H_3O^+, heat, 45 min

[*b*]thiophene-2(3*H*)-one **27** in high yield,[35] nucleophilic ring opening of which gave the disodium salt of 2-mercaptophenylacetic acid **28**. Direct treatment with a chloroacetic acid in refluxing ethanol afforded the diacids **29a, b**, without the need to isolate 2-mercaptophenylacetic acid, which is prone to disulfide formation and cyclisation to thioxindole.[36] Investigation revealed that acidification of the dianion **28**, even under carefully controlled conditions, resulted in the isolation of 2-mercaptophenylacetic acid contaminated with approximately 17% of the disulfide, as measured by ^1H NMR spectroscopy. The diacids **29a, b** were transformed to the thiochroman-3-ones **30a, b** in a two step sequence initiated by cyclisation to the enol-acetate. The final stage was accomplished more readily than described by Clark and McKinnon.[36] 4-Methylthiochroman-3-one **30c** was obtained by methylation of 3-pyrrolidino-2*H*-thiochromene obtained from thiochroman-3-one and pyrrolidine by standard methodology.[36]

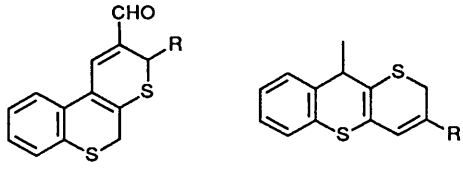
Treatment of thiochroman-3-one **30a** with an excess of DMFDMA at moderate temperatures gave the enamino ketone **31a** together with a small amount of the bis-enamino



31a R = H
31b R = Me

31c

32



33a R = H
33b R = Me
33c R = Ph

34a R = CHO
34b R = CHNNHPh

ketone **32**. This latter compound could be obtained exclusively by heating the reaction mixture under reflux in toluene for 1 h. The site of dimethylaminomethylenation was apparent from the ^1H NMR spectrum of **31a**, which displayed a singlet at δ 3.26, characteristic of the SCH_2 function inferring preferential reaction at the benzylic (C-4) site (*cf.* thiochroman-3-one: SCH_2 δ 3.31 and 4-CH_2 δ 3.72). Formation of the alternative mono-dimethylaminomethylenated product was not observed. The preferred site of attack is in accord with the established direction of enolisation in both chroman-3-ones and the thio

analogues. Similarly, with secondary amines the 3-amino-2*H*-(thio)chromenes are formed exclusively.[36,37]

When the 2-position of thiochroman-3-one was blocked as in **30b**, the enamino ketone **31b** was readily formed and 2-(dimethylaminomethylene)-4-methylthiochroman-3-one **31c** was similarly obtained from **30c**, although a slightly longer reaction time was required.

Addition of acrolein to the thionation reaction mixture from **31a** resulted in the rapid consumption of the enamino thione and the formation of an intense yellow component. Elution of the reaction mixture from silica gave 3*H*,5*H*-thiopyrano[2,3-*c*]-[1]benzothiopyran-2-carbaldehyde **33a**, a novel ring system. The ^{1}H NMR spectrum of this compound displayed distinct singlets at δ 3.51 and 3.69, each accounting for 2 protons and assigned to the 5- and 3-methylene protons, respectively. The aldehyde proton appears as a lowfield singlet at δ 9.64 and the olefinic proton (1-H) is shifted downfield as a consequence of its proximity to the anisotropic aldehyde function and appears as a singlet at δ 7.19 in the centre of a complex aromatic multiplet at δ 7.15–7.34.

Application of the reaction to crotonaldehyde and cinnamaldehyde afforded the methyl and phenyl substituted analogues **33b** and **33c**, respectively, though again, the reaction with cinnamaldehyde had to be warmed to effect complete reaction.

The ^{1}H and ^{13}C NMR spectra of these fused heterocycles display some interesting features. The unsymmetrical substitution at C-3 in **33b** confers diastereotopic properties on the protons at the 5-position, which appear as an AB system with doublets at δ 3.22 and 3.80, J_{AB} 15.9 Hz. The corresponding protons in the 3-phenyl derivative **33c** are observed at δ 3.18 and 3.74. In the methyl analogue **33b**, 3-H appears as a quartet at δ 4.12, but the corresponding proton in **33c** resonates at δ 5.25 since it is benzylic. In compound **33a**, the aldehyde carbon exhibits a lowfield signal at δ 190.7 in the ^{13}C NMR spectrum. The methine carbon (C-1) conjugated with the aldehyde group resonates at δ 143.3. The two methylene carbons adjacent to the sulfur heteroatoms give rise to signals at δ 22.4 and 30.1 assigned to C-3 and C-5, respectively. The signal for C-3 is shifted to δ 30.6 and is isochronous with C-5 in the methyl analogue **33b**, but C-3 resonates at δ 38.5 in **33c** reflecting its benzylic character. The remaining aromatic and olefinic carbons appear within the range δ 123–141.

The linear thiopyrano[3,2-*b*][1]benzothiopyran **34a** was obtained by an identical procedure from **31c** and acrolein, but could not be obtained in a pure form by either column chromatography or recrystallisation. It was therefore characterised as its phenylhydrazone derivative **34b**.

The formation of both linear and angular thiopyranobenzothiopyran isomers further illustrates the potential of this facile thionation–cycloaddition procedure. The enamino ketones **31a,b,c** may also find application in the synthesis of other fused heterocyclic systems derived from thiochroman-3-ones.

Experimental

M.p.s were determined in capillary tubes and are uncorrected. Distillations were performed using a Kugelrohr (Buchi GKR-50 Glass Tube Oven) and all b.p.s quoted relate to the oven temperature at which the distillation commenced. IR spectra were recorded on a Mattson–Polaris Fourier Transform spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Brucker WM250 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, 40–60 m, activated) according to the published procedure.[38]

2-Dimethylaminomethylenecyclohexane-1,3-dione **9** was prepared according to the procedure described by Schenone *et al.*[39] and thiochroman-3-one, 2-methylthiochroman-3-one and 4-methylthiochroman-3-one had identical physical and spectroscopic properties to those reported in the literature.[36]

Ethyl 2-(*Dimethylaminomethylene*)-3-*oxobutanoate*[16] **10**.—*N*,*N*-Dimethylformamide dimethyl acetal (0.125 mol) was added in a single portion to ethyl 3-oxobutanoate (50 mmol). The stirred solution was refluxed for 1 h, diluted with brine (200 cm^3) and extracted with ethyl acetate (5 × 50 cm^3). The combined organic extracts were washed with water (3 × 75 cm^3), dried (Na_2SO_4) and evaporated to afford the *enamino ketoester* (56%), b.p. 105 °C at 5 × 10^{-2} mmHg, as an orange oil, ν_{max}(neat)/cm^{-1} 1692 and 1659, δ_H (295 K) 1.29 (3 H, t, *J* 7.2, CH_3), 2.30 (3 H, s, CH_3), 3.01 (6 H, br s, NMe_2), 4.19 (2 H, q, *J* 7.2, CH_2) and 7.65 (1 H, s, alkenyl-H); δ_H (323 K) 3.01 (6 H, s, NMe_2).

The following compounds were prepared in a similar manner:

3-(*Dimethylaminomethylene*)[1]*benzopyran*-2,4-*dione* **11** (66.5%). M.p. 142.0–142.5 °C, from 4-hydroxycoumarin, as pale orange crystals from ethyl acetate and methanol, ν_{max}(Nujol)/cm^{-1} 1710 and 1640; δ_H 3.38 (3 H, s, CH_3), 3.45 (3 H, s, CH_3), 7.13–7.19 (2 H, m, Ar-H), 7.43–7.49 (1 H, m, Ar-H), 7.95 (1 H, dd, *J* 7.9 and 2.0, 5-H) and 8.35 (1 H, s, alkenyl-H); δ_C 45.1 (CH_3), 49.0 (CH_3), 96.4 (C-3), 116.7, 123.5, 126.1, 133.6 (Ar-CH), 121.0 (C-4a), 154.5 (C-8a), 162.7 (C-2), 164.3 (alkenyl-CH) and 177.8 (C-4) (Found: C, 66.2; H, 5.0; N, 6.2. $C_{12}H_{11}NO_3$ requires C, 66.3; H, 5.1; N, 6.4%).

4-(*Dimethylaminomethylene*)*thiochroman*-3-*one* **31a** (76%). M.p. 127.0–128.0 °C, from thiochroman-3-one after 30 min at 40 °C as bright yellow needles from ethyl acetate and hexane ν_{max}(Nujol)/cm^{-1} 1644, δ_H 2.95 (6 H, br s, NMe_2), 3.26 (2 H, s, 2-H), 6.87 (1 H, dd, *J* 8.1 and 1.2, Ar-H), 6.97–7.16 (2 H, m, Ar-H), 7.38 (1 H, dd, *J* 8.0 and 1.1, Ar-H) and 7.86 (1 H, br s, alkenyl-H) (Found: C, 65.7; H, 6.05; N, 6.4; S, 14.7. $C_{12}H_{13}NOS$ requires C, 65.7; H, 6.0; N, 6.4; S, 14.6%).

The use of an excess of DMFDMA and refluxing in toluene for 1 h prior to work-up yielded 2,4-*bis*(*dimethylaminomethylene*)*thiochroman*-3-*one* **32** (63%), m.p. 212.0–214.0 °C as lime green needles from ethyl acetate; ν_{max}(Nujol)/cm^{-1} 1631; δ_H 2.88 (6 H, s, 4-NMe_2), 3.19 (6 H, s, 2-NMe_2), 6.84–6.99 (2 H, m, Ar-H), 7.10–7.28 (2 H, m, Ar-H), 7.50 (1 H, s, 2-alkenyl-H) and 7.72 (1 H, s, 4-alkenyl-H) (Found: C, 65.6; H, 6.6; N, 10.2; S, 11.6. $C_{15}H_{18}N_2OS$ requires C, 65.6; H, 6.6; N, 10.2; S, 11.7%).

4-(*Dimethylaminomethylene*)-2-*methylthiochroman*-3-*one* **31b** (71%). M.p. 102.0–103.5 °C, as bright yellow needles from hexane; ν_{max}(Nujol)/cm^{-1} 1641; δ_H 1.34 (3 H, d, *J* 7.1, 2-Me), 3.00 (6 H, br s, NMe_2), 3.34 (1 H, q, *J* 7.1, 2-H), 6.86 (1 H, dd, *J* 7.9 and 1.1, Ar-H), 6.96–7.18 (2 H, m, Ar-H), 7.36 (1 H, dd, *J* 8.0 and 1.3, Ar-H) and 7.82 (1 H, br s, alkenyl-H) (Found: C, 66.8; H, 6.5; N, 6.0; S, 13.6. $C_{13}H_{15}NOS$ requires C, 66.9; H, 6.5; N, 6.0; S, 13.7%).

2-(*Dimethylaminomethylene*)-4-*methylthiochroman*-3-*one* **31c** (69%). M.p. 119.5–121.0 °C, as bright yellow needles from hexane, ν_{max}(Nujol)/cm^{-1} 1644; δ_H 1.57 (3 H, d, *J* 6.7, 4-Me), 3.23 (6 H, br s, NMe_2), 3.60 (1 H, q, *J* 6.8, 4-H), 7.15–7.24 (3 H, m, Ar-H), 7.38 (1 H, dd, *J* 7.7 and 0.9, Ar-H) and 7.62 (1 H, s, alkenyl-H) (Found: C, 66.7; H, 6.5; N, 6.0; S, 13.8. $C_{13}H_{15}NOS$ requires C, 66.9; H, 6.5; N, 6.0; S, 13.7%).

General Method for the One Pot Thionation–Cycloaddition Reaction.—Lawesson's reagent (4.9 mmol) was added in a single portion to a stirred solution of the oxo enamino ketone (9.2 mmol) in anhydrous benzene (40 cm^3) maintained at 0 °C. The stirred reaction mixture was allowed to reach room temp. at which it was maintained until TLC examination of the mixture indicated that all of the enamino ketone had been consumed (approximately 2 h). The electrophilic alkene (9.2 mmol) was then added in a single portion to the orange or red reaction

mixture which was stirred at room temp. until the enamino thione had been consumed (*ca.* 10 min). (For the reaction with cinnamaldehyde, the reaction mixture was warmed to 40 °C for 30 min to ensure complete reaction of the enamino thione). The reaction mixture was diluted with water (200 cm^3), extracted with ethyl acetate (5 × 50 cm^3) and the combined, dried (Na_2SO_4) extracts were evaporated to give the crude product which was eluted from silica with 10% ethyl acetate in hexane to afford the thiopyrans which were further purified by recrystallisation or distillation.

The following compounds were prepared by this procedure:

5-*Oxo*-5,6,7,8-*tetrahydro*-2H-[1]*benzothiopyran*-3-*carbaldehyde* **12a** (41%). B.p. 160 °C at 5 × 10^{-2} mmHg, m.p. 64.0–66.0 °C, as a bright yellow solid; ν_{max}(Nujol)/cm^{-1} 1650; δ_H 2.00–2.10 (2 H, m, 7-H), 2.55 (2 H, t, *J* 6.0, 8-H), 2.65 (2 H, t, *J* 6.1, 6-H), 3.69 (2 H, s, 2-H), 7.52 (1 H, s, 4-H) and 9.59 (1 H, s, CHO); δ_C 22.0 (C*–7), 22.7 (C*–2), 31.5 (C–8), 37.4 (C–6), 124.4, 127.1 (2 × C), 139.3 (C–4), 164.7 (C-8a), 191.2 (CHO) and 191.4 (C-5) (Found: C, 61.8; H, 5.2; S, 16.3. $C_{10}H_{10}O_2S$ requires C, 61.8; H, 5.2; S, 16.5%).

2-*Methyl*-5-*oxo*-5,6,7,8-*tetrahydro*-2H-[1]*benzothiopyran*-3-*carbaldehyde* **12b** (53%). M.p. 88.0–89.5 °C, as bright orange needles from light petroleum (b.p. 40–60 °C); ν_{max}(Nujol)/cm^{-1} 1657; δ_H 1.24 (3 H, d, *J* 7.0, 2-Me), 1.99–2.17 (2 H, m, 7-H), 2.52–2.72 (4 H, m, 8-H, 6-H), 4.12 (1 H, q, *J* 7.0, 2-H), 7.52 (1 H, s, 4-H) and 9.58 (1 H, s, CHO); δ_C 22.2 (C*-7), 22.5 (2-Me*), 31.7 (C†-8), 31.8 (C†-2), 37.5 (C-6), 125.8, 130.9 (2 × C), 137.3 (C-4), 164.7 (C-8a), 191.2 (CHO) and 191.5 (C-5) (Found: C, 63.6; H, 5.8; S, 15.2. $C_{11}H_{12}O_2S$ requires C, 63.4; H, 5.8; S, 15.4%).

5-*Oxo*-2-*phenyl*-5,6,7,8-*tetrahydro*-2H-[1]*benzothiopyran*-3-*carbaldehyde* **12c** (64%). M.p. 129.5–131.5 °C, as bright orange needles from ethyl acetate and hexane; ν_{max}(Nujol)/cm^{-1} 1658; δ_H 2.00–2.13 (2 H, m, 7-H), 2.53–2.65 (4 H, m, 8-H, 6-H), 5.26 (1 H, s, 2-H), 7.16–7.31 (5 H, m, Ar-H), 7.82 (1 H, s, 4-H) and 9.65 (1 H, s, CHO); δ_C 22.1 (C-7), 31.5 (C-8), 37.5 (C-6), 39.9 (C-2), 125.6–128.6 (7 × C), 139.5 (C-4), 141.1 (1 × C), 164.5 (C-8a), 191.2 (CHO) and 191.4 (C-5) (Found: C, 70.9; H, 5.2; S, 11.9. $C_{16}H_{13}O_2S$ requires C, 71.1; H, 5.2; S, 11.9%).

3-*Acetyl*-7,8-*dihydro*-2H,6H-[1]*benzothiopyran*-5-*one* **13** (46%). B.p. 170 °C at 5 × 10^{-2} mmHg, m.p. 83.0–84.5 °C, as a bright orange solid; ν_{max}(Nujol)/cm^{-1} 1679; δ_H 1.99–2.06 (2 H, m, 7-H), 2.39 (3 H, s, Me), 2.52 (2 H, t, *J* 6.1, 8-H), 2.63 (2 H, t, *J* 6.2, 6-H), 3.67 (2 H, s, 2-H) and 7.62 (1 H, s, 4-H); δ_C 22.1, 23.6, 25.2, 31.4, 37.5 (5 × C), 123.2, 127.5 (2 × C), 131.5 (C-4), 165.7 (C-8), 191.8 (C-5) and 196.8 (COMe) (Found: C, 63.1; H, 5.7; S, 15.4. $C_{11}H_{12}O_2S$ requires C, 63.4; H, 5.8; S, 15.4%).

Ethyl 3-*formyl*-6-*methyl*-2H-*thiopyran*-5-*carboxylate* **20a** (63%). B.p. 115 °C at 5 × 10^{-2} mmHg, m.p. 45.5–46.5 °C, as a bright yellow solid; ν_{max}(Nujol)/cm^{-1} 1710 and 1663; δ_H 1.34 (3 H, t, *J* 7.0, Me), 2.48 (3 H, s, 6-Me), 3.56 (2 H, s, 2-H), 4.27 (2 H, q, *J* 7.0, CH_2), 7.45 (1 H, s, 4-H) and 9.58 (1 H, s, CHO); δ_C 14.2 (Me), 22.5 (Me-6), 23.2 (C-2), 60.7 (CH_2), 120.9 (C*-3), 123.0 (C*-5), 143.7 (C-4), 162.6 (C-6), 163.7 (CO_2Et) and 190.6 (CHO) (Found: C, 56.6; H, 5.9; S, 14.9. $C_{10}H_{12}O_3S$ requires C, 56.6; H, 5.7; S, 15.1%).

Ethyl 3-*formyl*-6-*methyl*-2-*phenyl*-2H-*thiopyran*-5-*carboxylate* **20b** (56%). B.p. 190 °C at 5 × 10^{-2} mmHg, as a viscous dark orange oil; ν_{max}(neat)/cm^{-1} 1710 and 1659; δ_H 1.37 (3 H, t, *J* 7.0, Me), 2.42 (3 H, s, 6-Me), 4.29 (2 H, q, *J* 7.0, CH_2), 5.19 (1 H, s, 2-H), 7.19–7.28 (5 H, m, Ar-H), 7.71 (1 H, s, 4-H) and 9.64 (1 H, s, CHO); δ_C 14.3 (Me), 23.2 (Me-6), 39.4 (C-2), 60.9 (CH_2), 119.2 (C*-3), 127.0 (C*-5), 126.7–140.9 (6 × Ar-C), 142.8 (C-4), 159.9 (C-6), 163.8 (CO_2Et) and 191.0 (CHO) (Found: C, 66.5; H, 5.6; S, 11.4. $C_{16}H_{16}O_3S$ requires C, 66.6; H, 5.6; S, 11.1%).

5-*Oxo*-2H,5H-*thiopyrano*[3,2-c][1]*benzopyran*-3-*carbaldehyde* **22** (73%). M.p. 195–204 °C (decomp.) as bright orange needles from ethyl acetate and hexane, ν_{max}(Nujol)/cm^{-1} 1728 and 1657; δ_H 3.86 (2 H, s, 2-H), 7.31–7.44 (2 H, m, Ar-H), 7.59–7.65 (1 H, m, Ar-H), 7.69 (1 H, s, 4-H), 7.81 (1 H, dd, *J* 7.8 and 1.9, Ar-H) and 9.70 (1 H, s, CHO); δ_C 21.5 (C-2), 116.3 (C-3), 117.4 (Ar-CH), 117.7 (C-4a), 124.8 (Ar-CH), 125.4 (Ar-CH), 127.0 (Ar-C), 133.8 (Ar-CH), 140.3 (C-4), 152.0 (C-10b), 155.3 (C-6a), 158.9 (C-5) and 190.3 (CHO) (Found: C, 64.1; H, 3.3; S, 13.3. $C_{13}H_8O_3S$ requires C, 63.9; H, 3.3; S, 13.1%).

3H,5H-*Thiopyrano*[2,3-c][1]*benzothiopyran*-2-*carbaldehyde* **33a** (38%). M.p. 145.5–147.5 °C, as bright yellow needles from ethyl acetate and hexane; ν_{max}(Nujol)/cm^{-1} 1640; δ_H 3.51 (2 H, s, 5-H), 3.69 (2 H, s, 3-H), 7.15–7.34 (5 H, m, 4-Ar-H, 1-H) and 9.64 (1 H, s, CHO); δ_C 22.4 (C-3), 30.1 (C-5), 123.9, 126.4, 127.3, 127.8 (4 Ar-CH), 126.2, 127.6, 131.4, 133.4, 139.2 (5 × C), 143.3 (C-1) and 190.7 (CHO) (Found: C, 63.3; H, 4.0; S, 26.2. $C_{13}H_{10}OS_2$ requires C, 63.4; H, 4.1; S, 26.1%).

3-*Methyl*-3H,5H-*thiopyrano*[2,3-c][1]*benzothiopyran*-2-*carbaldehyde* **33b** (43%). M.p. 124.0–126.0 °C, as bright orange needles from hexane; ν_{max}(Nujol)/cm^{-1} 1679; δ_H 1.27 (3 H, d, *J* 6.8, 3-Me), 3.22 (1 H, d, *J* 15.9, 5-H), 3.80 (1 H, d, *J* 15.9, 5-H), 4.12 (1 H, q, *J* 6.8, 3-H), 7.16–7.35 (5 H, m, 4 Ar-H, 1-H) and 9.63 (1 H, s, CHO); δ_C 21.0 (CH_3-3), 30.6 (C-3, C-5), 123.9, 126.4, 127.2, 127.8 (4 Ar-CH) 128.5, 131.4, 132.7, 133.4, 136.2 (5 × C), 141.0 (C-1) and 190.8 (CHO) (Found: C, 64.8; H, 4.7; S, 24.6. $C_{14}H_{12}OS_2$ requires C, 64.6; H, 4.7; S, 24.6%).

3-*Phenyl*-3H,5H-*thiopyrano*[2,3-c][1]*benzothiopyran*-2-*carbaldehyde* **33c** (56%). M.p. 106.5–108.5 °C, as bright yellow needles from hexane; ν_{max}(Nujol)/cm^{-1} 1692; δ_H 3.18 (1 H, d, *J* 16.1, 5-H), 3.74 (1 H, d, *J* 16.1, 5-H), 5.25 (1 H, s, 3-H), 7.16–7.43 (10 H, m, 9 Ar-H, 1-H) and 9.72 (1 H, s, CHO); δ_C 30.4 (C-5), 38.5 (C-3), 123.9–140.6 (15 × C), 142.3 (C-1) and 190.8 (CHO) (Found: C, 71.1; H, 4.4; S, 19.9. $C_{19}H_{14}OS_2$ requires C, 70.8; H, 4.4; S, 19.9%).

10-*Methyl*-2H,10H-*thiopyrano*[3,2-b][1]*benzothiopyran*-3-*carbaldehyde Phenylhydrazone* **34b**.—A solution of crude **34a**, obtained by the aforementioned procedure from **30c** (estimated 1.8 mmol) in ethanol (20 cm^3) containing phenylhydrazine (2.2 mmol) was refluxed for 30 min. The precipitate which formed on cooling the solution was collected, washed with a little ice cold ethanol and recrystallised from ethanol to afford the *phenylhydrazone* (32%), m.p. 148.0–154.0 °C (decomp.), as pale yellow needles; δ_H 1.42 (3 H, d, *J* 7.0, 10-Me), 3.60 (1 H, q, *J* 7.0, 10-H), 3.81 (1 H, d, *J* 14.8, 2-H), 3.99 (1 H, d, *J* 14.8, 2-H), 6.06 (1 H, s, 4-H), 6.83–7.34 (10 H, m, 9 Ar-H, NH) and 7.39 (1 H, s, azomethine-H); δ_C 18.4 (CH_3-10), 24.9 (C-2), 43.2 (C-10), 112.6 (C-4), 115–137 (15 × C) and 144.0 (CHN) (Found: C, 68.4; H, 5.1; N, 8.0; S, 18.5. $C_{20}H_{18}N_2S_2$ requires C, 68.5; H, 5.2; N, 8.0; S, 18.3%).

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*·† *Note:* ^{13}C NMR spectroscopic assignments followed by † or * are tentative assignments only and may be reversed.

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