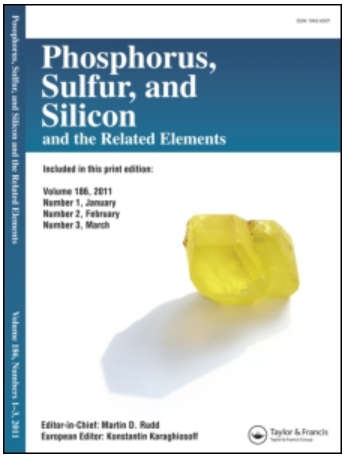

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ON THE SYNTHESIS OF 2-METHYLCHROMENE-4-THIONE AND 2-METHYL-1-THIOCHROMONE

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ON THE SYNTHESIS OF 2-METHYLCHROMENE-4-THIONE AND 2-METHYL-1-THIOCHROMONE

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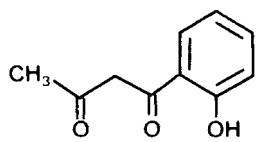
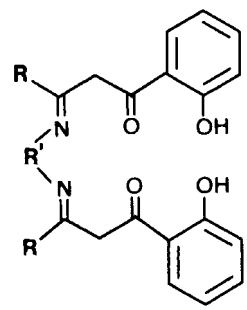
Routes to 2-methylchromene-4-thione and 2-methyl-1-thiochromone from β-ketophenol sources are reported.

1-(2-Hydroxyphenyl)-1,3-butanedione (I) reacts readily with α,ω-alkane-diamines to give Schiff bases, (A, R = CH_3),[1] capable of functioning as compartmental ligands



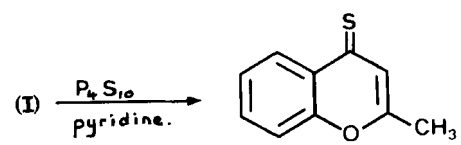
(I)



(A)

for the preparation of mono-, homobi- and heterobi-nuclear metal complexes.[2] During the course of our investigations into the properties of these ligands it was recognized that the introduction of sulphur into the donor sets would offer the opportunity to prepare a wider range of metal complexes. Attempts were made to incorporate sulphur into (I) and related keto-phenols and these led to the facile synthesis of the title compounds.

The reaction of (I) with P_4S_{10} in pyridine led to the isolation of 2-methylchromene-4-thione (II) as red crystals in 75% yield. The ^1H n.m.r. ($CDCl_3$) showed peaks at $\delta = 2.3$ (s, 3H, CH_3); 7.1 (s, 1H, H_3); 7.4 (m, 2H, H_6 and H_8); 7.65 (t, 1H,



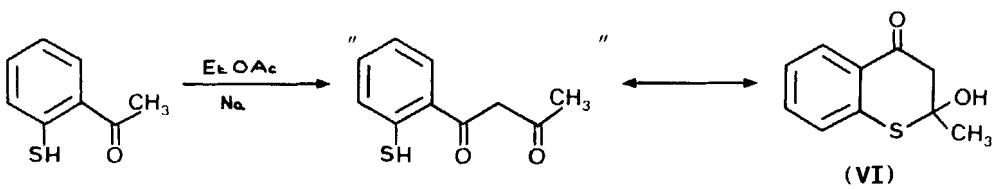
(II)

H_7) and 8.55 (d, 1H, H_5) p.p.m., and the $^{13}C\{^1H\}$ n.m.r. ($CDCl_3$) gave resonances at 19.9 (CH_3); 118.1 (C_8); 123.3 (C_6); 125.8 (C_5); 128.4 (C_7); 129.2 (C_2); 133.8 (C_3); 151.7 (C_{5a}); 157.4 (C_{8a}) and 202.4 (C_4) p.p.m. The formation of this product suggests that either the sulphurization reaction occurs first at the carbonyl next to the

phenolic function of (I) and this is followed by an intramolecular cyclization, in which the —OH group adds across the residual carbonyl with subsequent elimination of water to give (II), or that cyclization occurs first followed by introduction of sulphur into the chromone.

The reaction of 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanedione (III) with P_4S_{10} has been shown[3] to yield two products, 2-(5-phenyl-1,2-dithiolo-3-ylio)phenolate (IV) and 2-phenylchromene-4-thione (V). We have no evidence for the formation of an analogue of (IV) in our reaction.

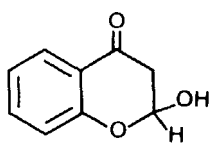
The second approach for introducing sulphur into keto-phenols was based on the preformation of 2-acetothiophenone prior to an extension of the ketone chain. 2-Thioacetophenone was prepared from 2-nitroacetophenone via conversion first to (2-benzylthio)acetophenone using benzyl mercaptan and lithium hydroxide in dimethylformamide according to the procedure of Meth-Cohn and Tarnowski[4] and subsequent removal of the protecting group with aluminum trichloride in benzene.[5] The ^{1}H n.m.r. ($CDCl_3$) showed signals at δ = 2.3 (s, 3H, CH_3); 4.25 (s, 1H, SH); 7.0 (m, 3H, aromatics) and 7.6 (m, H, aromatic) p.p.m. 2-Thioacetophenone was then reacted with ethyl acetate and sodium wire according to the method of Wittig.[6]



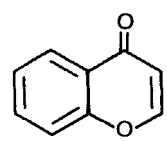
(VI)

The ^{1}H n.m.r. and i.r. spectra of the product from this reaction clearly indicated that the β-diketone had not been isolated but that the compound should be assigned as (VI). No SH stretching frequencies were discerned in the i.r., and the ^{1}H n.m.r. ($CDCl_3$) showed peaks at δ = 1.7 (s, 3H, CH_3); 3.0 (m, 2H, CH_2); 3.5 (s, 1H, OH); 7.15 (m, 2H, H_6 and H_8); 7.35 (t, 1H, H_7) and 8.05 (d, 1H, H_5) p.p.m. An intramolecular cyclization had occurred, the thiol adding across the terminal keto-function. Such processes are well documented and collectively termed ring-chain transformations.[7]

This process had been encountered previously in the synthesis of "1-(2-hydroxyphenyl)-1,3-propanedione" by an analogous route. The ^{1}H n.m.r. of the product clearly shows that (VII) is the isomeric form present.[8,9] Reaction of (VII) with 1,2-diamino ethane gave the acyclic Schiff Base (A, R = H, R^1 = —CH_2CH_2—) as did

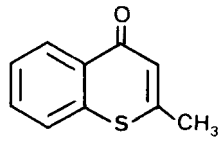


(VII)



(VIII)

also the reaction of the corresponding chromone (VIII) with 1,2-diamino ethane in ethanol.[9] The reaction of 1,2-diamino ethane with (VI) however gave only the product of dehydration, 2-methyl-1-thiochromone (XI). In contrast to (VIII) no Schiff Base formation was detected. The identity of (XI) was confirmed by comparison of the ^{1}H n.m.r., i.r. and mass spectra with those reported in the literature.[10]



(XI)

EXPERIMENTAL

I.r. spectra were measured using a Perkin Elmer 297 instrument on KBr discs. Mass spectra were obtained using a MS 12 spectrometer. ^1H n.m.r. spectra were recorded at 220 MHz using a Perkin Elmer R34 spectrometer. $^{13}C\{^1H\}$ n.m.r. spectra were recorded on a JEOL PFT-100 spectrometer at 25.15 MHz. Microanalyses were carried out by the University of Sheffield Microanalytical Service.

2-Methylchromene-4-thione (II). Phosphorus pentasulphide (5 g) was dissolved in boiling pyridine (100 ml) and a solution of 1-(2-hydroxyphenyl)-1,3-butanedione (4 g) in pyridine (100 ml) was added. The mixture was refluxed for 1 hour and then poured into boiling water (1 *l*). Crystals formed on the surface on cooling and were separated off, dissolved in an equal mixture of benzene and petroleum ether and the red solution chromatographed on alumina. The red fraction, using petroleum ether as an eluant, was evaporated down to give a red-brown compound which gave red needles of 2-methylchromene-4-thione on recrystallization from cyclohexane. The product was identified by spectral comparisons, has $P^+ = 176$, (M = 176), m.p. 96–97°, lit. 96–97,[11] and was obtained in 75% yield.

(2-Benzylthio)acetophenone. Benzyl mercaptan (freshly distilled under N_2) (5 g) and 2-nitroacetophenone (6.65 g) were stirred overnight at room temperature in dimethyl formamide (200 ml) with a three fold excess of LiOH (5 g) present. The deep brown solution was poured into ice (200 g) and stirred until the ice had dissolved. On filtering a light brown solid was isolated which was recrystallized from benzene to give (2-benzylthio)acetophenone in 55% yield. ($P^+ = 242$, M = 242; $C_{15}H_{14}SO$ requires: C, 74.38; H, 5.79; S, 13.22%; found: C, 74.08; H, 6.11; S, 13.43%, ^1H n.m.r. ($CDCl_3$), $\delta = 2.50$ (s, 3H, CH_3); 4.05 (s, 2H, CH_2), 7.25 (m, 9H, ArH) p.p.m.).

2-Thioacetophenone. (2-Benzylthio)acetophenone (4 g) in dry benzene (70 ml) was added dropwise to a stirred suspension of fresh $AlCl_3$ (3.8 g) in dry benzene (30 ml) at 5–10° and under dioxygen-free dinitrogen. The mixture was stirred for 24 hours and then water was added. The product was extracted from the organic layer with aqueous 5% sodium hydroxide. Acidification of the combined alkaline extracts and extraction with ether gave the product as an oil in 81% yield. ($P^+ = 152$, M = 152; C_8H_8OS requires: C, 63.16; H, 5.26; S, 21.05%; found: C, 62.73; H, 5.20; S, 21.12%, ^1H n.m.r. ($CDCl_3$), $\delta = 2.30$ (s, 3H, CH_3); 4.25 (s, 1H, SH), 7.00 (m, 3H, ArH) and 7.60 (m, H, ArH) p.p.m.).)

2,3-Dihydro-2-hydroxy-4H-1-benzothiopyran-4-one, "1-(2-thiophenyl)-1,3-butanedione" (VI). 2-Thioacetophenone (10 g) was added to degassed ethylacetate (40 ml) refluxing over sodium wire (4 g) under dinitrogen. Reflux was maintained for 6 hours and then the flask was cooled. Diethylether (350 ml) was added to give a yellow precipitate which was separated and dissolved in 25% acetic acid. This was then extracted with diethyl ether and the extracts washed with water prior to drying over $MgSO_4$. Removal of the ether gave a brown oil which on standing and cooling overnight gave a white solid. This was washed with cold methanol to give the required product in 20% yield. ($P^+ = 194$, M = 194; $C_{10}H_{10}O_2S$ requires: C, 61.86; H, 5.15; S, 16.49%; found: C, 61.56; H, 5.27; S, 16.46%.)

2-Methyl-1-thiochromone (XI). "1-(2-Thiophenyl)-1,3-butanedione", (0.46 g) was dissolved in warm ethanol (50 ml) under dinitrogen, and to it was added a solution of ethylenediamine (7 ml; made up as 1 g in 100 ml). The mixture was refluxed for 2 hours and the solvent then removed to give a yellow oil. A few drops of ethanol were added and the oil cooled overnight in a refrigerator to give the product as a yellow solid in 60% yield. ($P^+ = 176$, M = 176; $C_{10}H_8SO$ requires: C, 68.18; H, 4.54; S, 18.18; found: C, 68.21; H, 4.65; S, 18.11; ^1H n.m.r. ($CDCl_3$), $\delta = 2.45$ (s, 3H, CH_3); 6.80 (s, 1H, CH), 7.50 (m, 3H, ArH) and 8.50 (m, 1H, ArH) p.p.m.)

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