Thiopyrano[1]benzothiophens. Synthesis of 1-Phenyl-3*H*-thiopyrano-[3,4-*b*][1]benzothiophen-3-thione 9,9-Dioxide and Related Compounds

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The title compound (3a) was prepared by the reaction of 2-benzoylbenzo[*b*]thiophen-3(2H)-one 1,1-dioxide (1) with tetraphosphorus decasulphide, acetonitrile, and sodium hydrogen carbonate. The structure was confirmed by an alternative synthesis from ethyl 3-benzo[*b*]thienylacetate. The isomeric 4-phenyl-2*H*-thiopyrano[3,2-*b*][1]benzothiophen-2-thione 5,5-dioxide (2a) and a number of analogues of (3a) and (2a) were prepared.

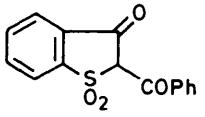
An improved procedure for the thiation of ketones with tetraphosphorus decasulphide, Scheeren's reagent,[1] involves the use of sodium hydrogen carbonate and a polar solvent such as acetonitrile. When 2-benzoylbenzo[*b*]thiophen-3(2*H*)-one 1,1-dioxide (1) was treated with this reagent a red compound, $C_{17}H_{10}O_2S_3$, was obtained. The compound was tentatively assigned as a dithiopyrone (2a) or (3a), either of which could be formed by reaction of the thiated thiophen with the solvent acetonitrile. To distinguish between these structures syntheses of compound (2a) and (3a) were undertaken.

The synthesis of compound (2a) is shown in Scheme 1. An unusual preparation of 2*H*-[1]benzothieno[3,2-*b*]pyran-2-one by the reaction of *o*-mercaptobenzoic acid with pent-2-enedioic acid in concentrated sulphuric acid has been described by Smiles and Hart.[2] An analogous reaction with 3-phenylpent-2-enedioic acid yielded the corresponding 4-phenylpyrone (4b) which was oxidised to the sulphone (2b). Treatment of the sulphone (2b) with sodium sulphide afforded a mixture of the thiopyrone (2c) and a thioacid. The latter, which was not characterised, was cyclised to the thiopyrone (2c) by pyrolysis. Conversion of the thiopyrone (2c) into the dithiopyrone (2a) was achieved using both tetraphosphorus decasulphide, which gave a low yield, and the dimer of (*p*-methoxyphenyl)thionophosphine sulphide, Lawesson's reagent,[3] which gave an improved yield. The dithiopyrone (2a) differed (m.p., i.r. and mass spectra) from that obtained directly from compound (1).

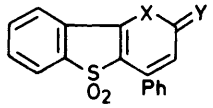
The synthesis of compound (3a) is shown in Scheme 2. There were no examples in the literature of the formation of 3*H*-[1]benzothieno[2,3-*c*]pyrones. However, an analogous indolopyrone had been prepared[4] in 95% yield by the polyphosphoric acid-catalysed reaction of 1-methylindol-3-ylacetic acid and benzoic acid. A similar reaction between ethyl 3-benzo[*b*]thienylacetate and benzoic acid gave the corresponding pyrone (5b) in quantitative yield. Substitution of phenyl dithiobenzoate for the benzoic acid in this reaction afforded the thiopyrone (5c) in low yield. This compound was oxidised to the corresponding sulphone (3c) which, on treatment with tetraphosphorus decasulphide, gave the dithiopyrone (3a). The latter was identical (m.p., i.r. and mass spectra) with that obtained from compound (1).

The formation of compound (3a) from compound (1) presumably proceeds by addition of the thioenol group of the thiated form of (1) (2-thiobenzoyl substituent) to acetonitrile to form an intermediate (6) which can undergo intramolecular condensation followed by thiation or these two steps in reverse order.

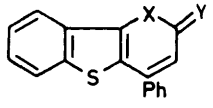
A number of other 1,3-diketones, including 2-benzoylbenzo[*b*]thiophen-3(2*H*)-one, the unoxidised analogue of compound (1), were subjected to treatment with Scheeren's reagent but in each case a complex mixture (t.l.c.) was formed and the reaction was not further examined. The reaction of compound (1) with Scheeren's reagent and propionitrile in place of acetonitrile, however, afforded compound (7) in 50% yield.



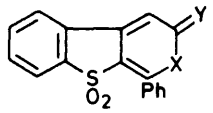
(1)



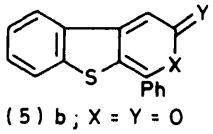
(2) a; X = Y = S
b; X = Y = O
c; X = S, Y = O
d; X = O, Y = S



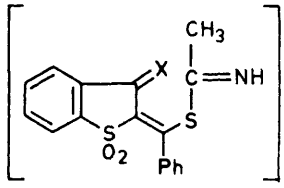
(4) b; X = Y = O
d; X = O, Y = S



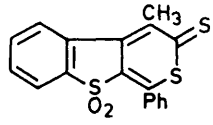
(3) a; X = Y = S
b; X = Y = O
c; X = S, Y = O
d; X = O, Y = S



(5) b; X = Y = O
c; X = S, Y = O
d; X = O, Y = S



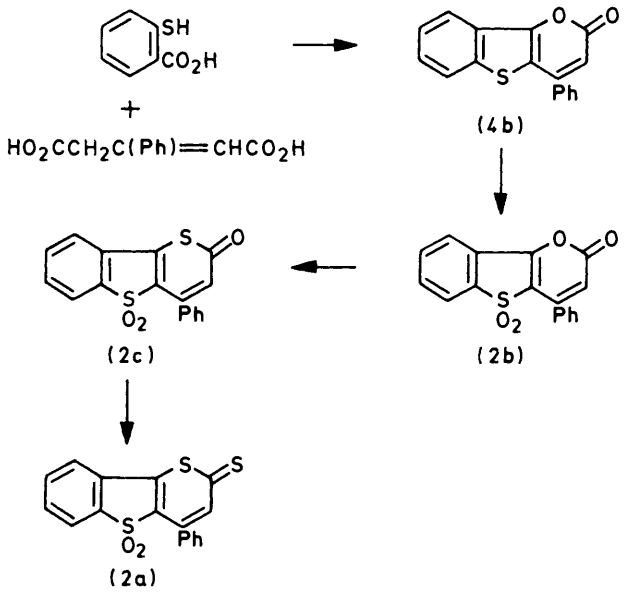
(6) X = O or S



(7)

In the course of this work additional compounds to complete the series (2a—d) and (3a—d) were prepared. Thus compound (3b) was obtained by oxidation of compound (5b). The thioxopyran-sulphones (2d) and (3d) and -thiophenes (4d) and (5d) were prepared from their oxygen analogoues using tetraphosphorus decasulphide.

I.r. and mass spectroscopic data for compounds (2)—(6) are summarised in the Table. In the mass spectra of the dithio compounds (2a), (3a), and (7) the molecular ion is the



Scheme 1.

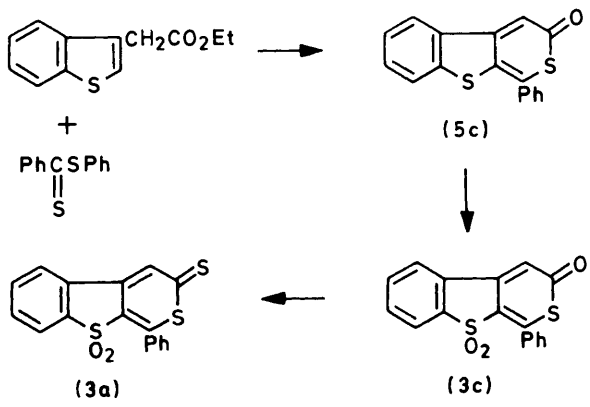
base peak and the major fragmentation is initial loss of C=S. The major fragmentation for the pyrones (2b), (3b), (4b), and (5b) and the thiopyrones (2c), (3c), and (5c) is elimination of C=O. The spectra of the two series differ in that those of the pyrones have abundant molecular ions [the base peak in compounds (3b), (4b), and (5b)] while those of the thiopyrones have molecular ions of low relative intensity (<30%) and base peaks of m/z $M^+ - 28$. The spectra of the thioxopyrans (2d), (3d), (4d), and (5d) show the molecular ion as base peak with an abundant peak at m/z $M^+ - 1$ in the case of compounds (3d) and (5d). The four thioxopyrans undergo fragmentation partially by loss of CS and partially, presumably by isomerisation to the thiopyrones, by loss of CO; loss of SH is significant in the case of compound (4d). A peak at m/z 136 is notable in the spectra of the sulphonylpyrans (2a—d).

Experimental

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded with a Perkin-Elmer 337 spectrophotometer and are reported for KBr discs. P.l.c. (preparative layer chromatography) was carried out on Merck $PF_{254+366}$ silica gel. Reactions with tetraphosphorus decasulphide were worked up by diluting the reaction mixture with chloroform and washing successively with aqueous ammonium sulphide (8% w/v), water, and brine. The organic solution was dried ($MgSO_4$) and concentrated and the residue was purified by p.l.c. in the dark with chloroform as eluant.

1-*Phenyl*-3H-*thiopyrano*[3,4-b][1]*benzothiophen*-3-*thione* 9,9 *Dioxide* (3a).—(a) A mixture of tetraphosphorus decasulphide (10 g) and sodium hydrogen carbonate (1.3 g) in acetonitrile (250 ml) was heated under reflux for 0.5 h. 2-Benzoylbenzo[*b*]thiophen-3(2*H*)-one 1,1-dioxide (1) (2.2 g) was added to the mixture whch was refluxed for a further 2 h. Work-up then afforded the *thiopyran* (3a) which crystalised from chloroform–methanol as deep red needles (1.23 g, 45%), m.p. 213—214 °C.

(b) A mixture of the thiopyran-3-one (3c) (55 mg) and tetraphosphorus decasulphide (182 mg) was refluxed in xylene (10 ml) for 8 h. Work-up yielded the thiopyranthione (44 mg, 76%), identical with that prepared by method (a).



Scheme 2.

4-*Phenyl*-2H-[1]*benzothieno*[3,2-b]*pyran*-2-*one* (4b).—A stirred suspension of 3-phenylpent-2-enedioic acid (6.8 g) and *o*-mercaptobenzoic acid (4.4 g) in concentrated sulphuric acid (50 ml) was heated at 45 °C for 1 h. The solution was poured into water and the resulting precipitate taken up in diethyl ether. The extracts were washed in turn with aqueous sodium hydrogencarbonate (5%) and water, dried ($MgSO_4$), and concentrated. The residue was crystallised from chloroform–methanol to give the *pyrone* (4b) as needles (5.5 g, 60%), m.p. 174—175 °C.

4-*Phenyl*-2H-[1]*benzothieno*[3,2-b]*pyran*-2-*one* 5,5-*Dioxide* (2b).—A solution of the pyranone (4b) (1.3 g) and 28% hydrogen peroxide (7 ml) in a mixture of acetic acid (10 ml) and acetic anhydride (10 ml) was heated until it boiled. On being cooled the solution deposited the *sulphone* (2b) as pale yellow needles (1.13 g, 78%), m.p. 190—192 °C (from ethanol).

4-*Phenyl*-2H-*thiopyrano*[3,2-b][1]*benzothiophen*-2-*one* 5,5-*Dioxide* (2c).—A solution of sodium sulphide (400 mg) and the pyrone (2b) (198 mg) in methanol (10 ml) was refluxed for 5 h. The cooled mixture was diluted with water, acidified with 10% hydrochloric acid, and extracted with chloroform. The extracts were washed in turn with water and brine, dried, and concentrated. P.l.c. of the residual oil with chloroform as eluant afforded, at higher R_F value, the *thiopyrone* (2c) as yellow needles (25 mg, 12%), m.p. 233—234 °C (from ethanol) and, at lower R_F, a yellow compound (134 mg) which, on pyrolysis at 250—270 °C for 10 min, afforded the thiopyran (2c) (115 mg, 55%); total yield 61%.

4-*Phenyl*-2H-*thiopyrano*[3,2-b][1]*benzothiophen*-2-*thione* 5,5-*Dioxide* (2a).—Tetraphosphorus decasulphide (900 mg) was added to a solution of compound (2c) (316 mg) in xylene (20 ml) and the mixture was refluxed for 8 h. Work-up afforded the *dithiopyrone* (2a) (150 mg, 45%) which recrystallised from chloroform–methanol as deep red needles, m.p. 256—259 °C (decomp.).

Thiation of compound (2c) (100 mg) using Lawesson's reagent [3] in refluxing toluene (10 ml) for 3.5 h afforded the dithiopyrone (2a) (79 mg, 76%).

1-*Phenyl*-3H-[1]*benzothieno*[2,3-c]*pyran*-3-*one* (5b).—A mixture of benzoic acid (2.86 g), ethyl 3-benzo[*b*]thienyl acetate [5] (3.76 g), and polyphosphoric acid (60 g) was stirred at 115 °C for 2 h. The mixture was poured onto ice and the resulting yellow precipitate (4.58 g, 97%) was crystallised from ethanol–chloroform to give the *pyrone* as needles, m.p. 211—222 °C (decomp.).

Table. Analytical and spectroscopic data

Compd.	Formula	Found % (Required %) C	H	S	$\nu_{max.}$ (cm^{-1})	*m/z* (relative intensity)
(2a)	$C_{17}H_{10}O_2S_3$ [a]			28.56 (28.09)		342 (M^+, 100%), 298 ($M^+ - 44$, 86)
(2b)	$C_{17}H_{10}O_4S$	65.31 (65.81	3.28 3.23	10.43 10.32)	1 740 (C=O)	310 (M^+, 85%), 282 ($M^+ - 28$, 100)
(2c)	$C_{17}H_{10}O_3S_2$	62.66 (62.56	3.14 3.09	19.88 19.65)	1 620 (C=O)	326 (M^+, 15%), 298 ($M^+ - 28$, 100)
(2d)	$C_{17}H_{10}O_3S_2$	62.04 (62.56	3.09 3.09	19.47 19.65)		326 (M^+, 100%), 298 ($M^+ - 28$, 15), 282 ($M^+ - 44$, 5%), 262 ($M^+ - 64$, 47)
(3a)	$C_{17}H_{10}O_2S_3$	59.86 (59.62	3.00 2.94	27.65 28.09)		342 (M^+, 100%), 298 ($M^+ - 44$, 65)
(3b)	$C_{17}H_{10}O_4S$	65.27 (65.81	3.49 3.23	10.88 10.32)	1 720 (C=O)	310 (M^+, 100%), 282 ($M^+ - 28$, 80)
(3c)	$C_{17}H_{10}O_3S_2$	62.19 (62.56	3.36 3.09	19.64 19.65)	1 625 (C=O)	326 (M^+, 28%), 298 ($M^+ - 28$, 100)
(3d)	$C_{17}H_{10}O_3S_2$	62.26 (62.56	2.81 3.09	19.46 19.65)		326 (M^+, 100%), 325 ($M^+ - 1$, 88), 298 ($M^+ - 28$, 15%), 282 ($M^+ - 44$, 10)
(4b)	$C_{17}H_{10}O_2S$	73.27 (73.36	3.43 3.62	11.24 11.52)	1 710 (C=O)	278 (M^+, 100%), 250 ($M^+ - 28$, 95), 221 ($M^+ - 57$, 58)
(4d)	$C_{17}H_{10}OS_2$	69.85 (69.36	3.07 3.42	22.00 21.78)	1 110 (C=S)	294 (M^+, 100%), 266 ($M^+ - 28$, 10), 261 ($M^+ - 33$, 42), 250 ($M^+ - 44$, 15)
(5b)	$C_{17}H_{10}O_2S$	73.57 (73.36	3.81 3.62	11.81 11.52)	1 710 (C=O)	278 (M^+, 100%), 250 ($M^+ - 28$, 95), 221 ($M^+ - 57$, 76)
(5c)	$C_{17}H_{10}OS_2$	69.36 (69.36	3.38 3.42	21.77 21.78)	1 620 (C=O)	294 (M^+, 25%), 266 ($M^+ - 28$, 100)
(5d)	$C_{17}H_{10}OS_2$	69.17 (69.36	3.40 3.42	22.00 21.78)	1 095 (C=S)	294 (M^+, 100%), 293 ($M^+ - 1$, 70), 266 ($M^+ - 28$, 32), 250 ($M^+ - 44$, 20)
(7)	$C_{18}H_{12}O_2S_3$	60.71 (60.64	3.25 3.39	26.85 26.97)		356 (M^+, 100%), 312 ($M^+ - 44$, 80)

[a] Correct carbon and hydrogen analyses were not obtained; accurate mass analysis agreed with molecular formula $C_{17}H_{10}O_2S_3$.

1-Phenyl-3H-thiopyrano[3,4-b][1]benzothiophen-3-one (5c).—A mixture of ethyl 3-benzo[*b*]thienylacetate (670 mg) and phenyl dithiobenzoate (700 mg) in polyphosphoric acid (12 g) was stirred and heated at 115 °C for 2 h. The mixture was poured onto ice and the resulting precipitate was collected and purified by p.l.c. with chloroform as eluant. The major yellow band yielded the *thiopyran-3-one* (5c) as an orange solid (164 mg, 18.3%) which crystallised from ethanol as needles, m.p. 217—219 °C.

1-Phenyl-3H-thiopyrano[3,4-b][1]benzothiophen-3-one 9,9-Dioxide (3c).—A solution of the thiopyrone (5c) (144 mg) and 28% hydrogen peroxide (1.5 ml) in a mixture of acetic acid (1.5 ml) and acetic anhydride (1.5 ml) was heated slowly until vigorous ebullition occurred. On being cooled the solution deposited pale yellow needles of the title *sulphone* (127 mg, 80%), m.p. 225—227 °C (from ethanol).

4-Methyl-1-phenyl-3H-thiopyrano[3,4-b][1] benzothiophen-3-thione 9,9-Dioxide (7).—A mixture of tetraphosphorus decasulphide (2.0 g) and sodium hydrogencarbonate (0.26 g) in propionitrile (50 ml) was heated under reflux for 30 min. The sulphone (1) (0.43 g) was then added and the mixture was refluxed for a further 2 h. Work-up gave the *dithiopyrone* (7) as deep red needles (290 mg, 54%), m.p. 208—210 °C (decomp.)

1-Phenyl-3H-[1]benzothieno[2,3-c]pyran-3-one 9,9-Dioxide (3b).—Oxidation of the pyrone (5b) (1.3 g) with 28% hydrogen peroxide (7 ml) in a mixture of acetic acid and acetic anhydride (20 ml; 1 : 1) as before gave the *sulphone* (3b) as pale yellow needles (1.24 g, 85%), m.p. 230—231 °C (from chloroform–ethanol).

The Thioxopyrans (2d), (3d), (4d), *and* (5d).—Thiation with tetraphosphorus decasulphide of the pyrones (2b) and (3b) for 8 h in refluxing xylene, and of the pyrones (4b) and (5b) for 6 h in refluxing toluene, afforded the corresponding thioxopyrans (crystallisation from chloroform–methanol): *4-phenyl-2H-[1]benzothieno[3,2-b]pyran-2-thione 5,5-dioxide* (2d) rust-coloured needles (57%), m.p. 198—200 °C; *1-phenyl-3H-[1]benzothieno[2,3-c]pyran-3-thione 9,9-dioxide* (3d), rust-coloured needles (66%), m.p. 245—247 °C; *4-phenyl-2H-[1]benzothieno[3,2-b]pyran-2-thione* (4d), red needles (94%), m.p. 158—159 °C; *1-phenyl-3H-[1]benzothieno[2,3-c]pyran-3-thione* (5d), red needles (74%), m.p. 219—220 °C.

Acknowledgement

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References

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