Routes to 3-Aryl-5-phenyl-2-thioacylmethylene-2*H*-1,3,4-thiadiazolenes

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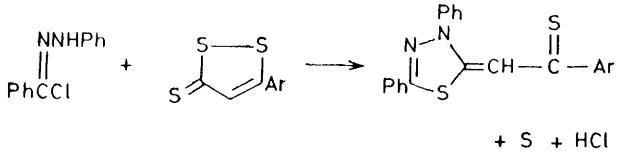
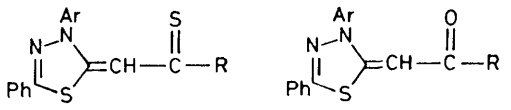
Prospective routes to the above compounds include reaction of an *N'*-arylbenzothiohydrazide or of its *N'*-acetyl derivative with thioacetic acid, when the thioacyl and acyl derivatives are formed, as well as by reaction of the 2-acylmethylene-3-aryl-5-phenyl-2*H*-1,3,4-thiadiazolenes with phosphorus pentasulphide. The ^{1}H n.m.r. and mass spectra of these compounds are discussed.

3,5-DIPHENYL-2-THIOAROYLMETHYLENE-2*H*-1,3,4-THIADIAZOLENES (1; R = aryl) have previously been prepared by reaction of 5-aryl-1,2-dithiole-3-thiones with



N-α-chlorobenzylidene-*N'*-phenylhydrazine in boiling xylene.[1] When treated with mercury(II) acetate, these compounds (1) are converted to the aroyl analogues (2; R = aryl), presumably with concurrent formation of mercury(II) sulphide and acetic anhydride.[2] This transformation could be reversed, *i.e.* (2) could be reconverted to (1), by heating compounds (2) with phosphorus pentasulphide in xylene.



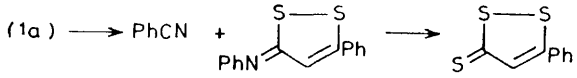
(1) (2)

a; Ar = R = phenyl
b; Ar = 2,4-dibromophenyl, R = methyl
c; Ar = 2,4-dibromophenyl, R = phenyl
d; Ar = phenyl, R = methyl

Compounds of type (2; R = methyl, phenyl) are now readily available from *N'*-arylbenzothiohydrazides and their *N'*-acetyl derivatives,[3] and this has led us to reconsider the phosphorus pentasulphide reaction as a route to compounds (1). We have also identified a direct preparative route to compounds (1) from *N'*-arylbenzothiohydrazides and their *N'*-acetyl derivatives.

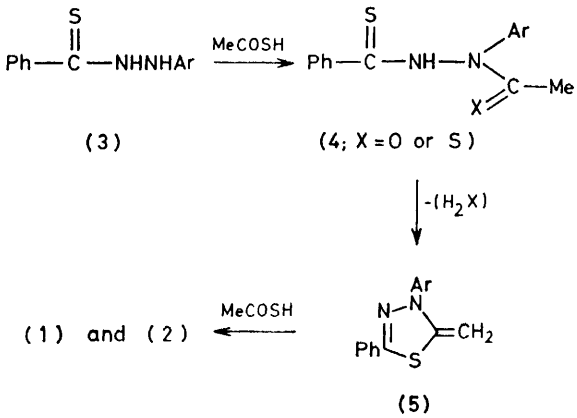
We first re-examined the preparation of (1a) from (2a) and phosphorus pentasulphide in xylene (75 min reflux).[1] As had been noted, this reaction went with the accompanying formation of 5-phenyl-1,2-dithiole-3-thione. The two products could not be satisfactorily separated by chromatography, but a pure sample of (1a), with the reported properties, was obtained by subsequent crystallization. The occurrence of the 1,2-dithiole-3-thione amongst the reaction products, presumably from secondary reaction of (1a) with phosphorus pentasulphide, is tiresome.

On the basis of the work of Maignan and Vialle with a related system,[4] we chose milder conditions (benzene; 15—30 min reflux) for subsequent experiments. Compounds (2b) and (2c) were thus converted into the thiocarbonyl analogues (1b) and (1c) in good yield, and



formation of the 1,2-dithiole-3-thiones was not observed in these circumstances. Compound (1b) could be reconverted to (2b) by reaction with mercury(II) acetate, indicating the generality of the method.

We have also established that (1d) is produced, together with (2d) as a minor product, when *N'*-phenylbenzothiohydrazide is heated with thioacetic acid. Similar reactions are observed with *N'*-2,4-dibromophenylbenzothiohydrazide and with its *N'*-acetyl-derivative, although the relative yields of (1b) are a little lower and of (2b) a little higher than those of (1d) and of (2d) in the previous experiment. The formation of (1) and (2) in these reactions is summarized in Scheme 1.

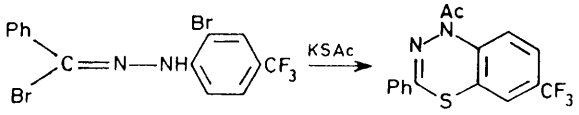


SCHEME 1

This reaction has not been examined in further detail and, while it has been shown for one case that compound (4; X = O) undergoes the reaction, the possible involvement of (4; X = S) as an intermediate in a concurrent reaction has not been excluded. Subsequent formation of (5) follows its proposed formation as an

intermediate in the acetylation of (3) to give (2).[3] Reaction of (5) with thioacetic acid then gives (1) and (2). The apparent preference for thioacetylation is unusual in that thioacetic acid is normally considered as an acetylating agent.[5a]

The formation of (1; R = Me) and smaller amounts of (2) in the reaction of *N'*-acetyl-*N'*-arylbenzothiohydrazides with thioacetic acid is of interest in another connection, namely the formation of by-products in syntheses of 1-acetyl-1*H*-4,1,2-benzothiadiazines from hydrazonoyl halides and sodium or potassium thioacetate. In these reactions, the smell of thioacetic acid



becomes detectable at an early stage and by-products in the reaction usually include the hydrazonoyl sulphide, the *N'*-acetyl-*N'*-arylbenzothiohydrazide, and other unidentified products. Our present findings suggest that compounds (1) and (2; R = Me) may also be formed in these reactions. Indeed, the compound $C_{18}H_{12}BrF_3N_2S_2$, m.p. 191.5—193 °C, isolated as a by-product following synthesis of 1-acetyl-3-phenyl-6-trifluoromethyl-1*H*-4,1,2-benzothiadiazine is very probably (1; R = Me, Ar = 2-bromo-4-trifluoromethylphenyl).[5b]

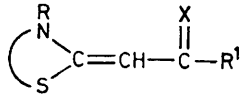
The ^{1}H n.m.r. data for the non-aromatic protons of the thioketones (1) and their oxygen analogues (2) are shown in the Table.

^{1}H N.m.r. data for (1) and (2) (δ from $SiMe_4$)

Compound	Me		H	
(1b)	2.70	Δδ = 0.58	6.60	Δδ = 1.15
(2b)	2.12		5.45	
(1c)			7.03	Δδ = 0.87
(2c)			6.16	
(1d)	2.67	Δδ = 0.5	7.01	Δδ = 0.91
(2d)	2.17		6.10	
(1a)			(7.13—8.03) *	
(2a)			6.70	

* Buried in the aromatic region.

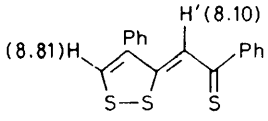
It has been demonstrated[6] that the thiocarbonyl group is much more effective in the deshielding phenomenon than, but exhibits the same co-ordinate susceptibilities as, the carbonyl group, *i.e.* protons in the plane



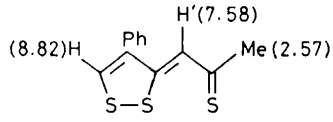
(6; X = S, O)

of the thiocarbonyl group experience deshielding and those above the plane experience shielding. This effect is clearly observed for the thiocarbonyl compounds (2b—d) where, relative to the oxygen analogues, a downfield shift of *ca.* 1 p.p.m. is observed for the olefinic protons and 0.5 p.p.m. for the methyl protons. Unfortunately, although a number of compounds containing the structural unit (6) have been prepared, comparative ^{1}H n.m.r. data do not seem to be readily available.

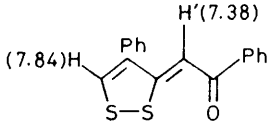
One series of compounds where the chemical shifts resulting from sulphur–oxygen exchange has been examined[7] are the thioxodithioles, (7a) and (7b), and their oxygen analogues (8a) and (8b). The chemical



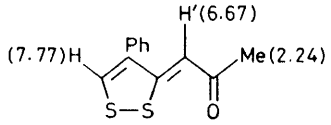
(7a)



(7b)

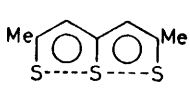


(8a)

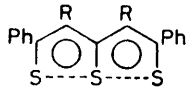


(8b)

shifts of the non-aromatic protons are shown in parentheses and are seen to be of the same order as those observed for the compounds (1) and (2) which we have prepared. This is particularly interesting since the chemical shift differences of the oxygen and sulphur analogues (0.96—1.07 for the olefin proton, H') were regarded as evidence of a greater ring current and aromaticity in the thioxodithioles. It should be noted that the thioxodithioles exhibit a so-called no-bond resonance,[8] the molecules being planar about the central carbon–sulphur bond [*e.g.* (9a)]; the oxygen analogues are thought to exhibit a similar interaction but to a much lesser extent.[7,9]



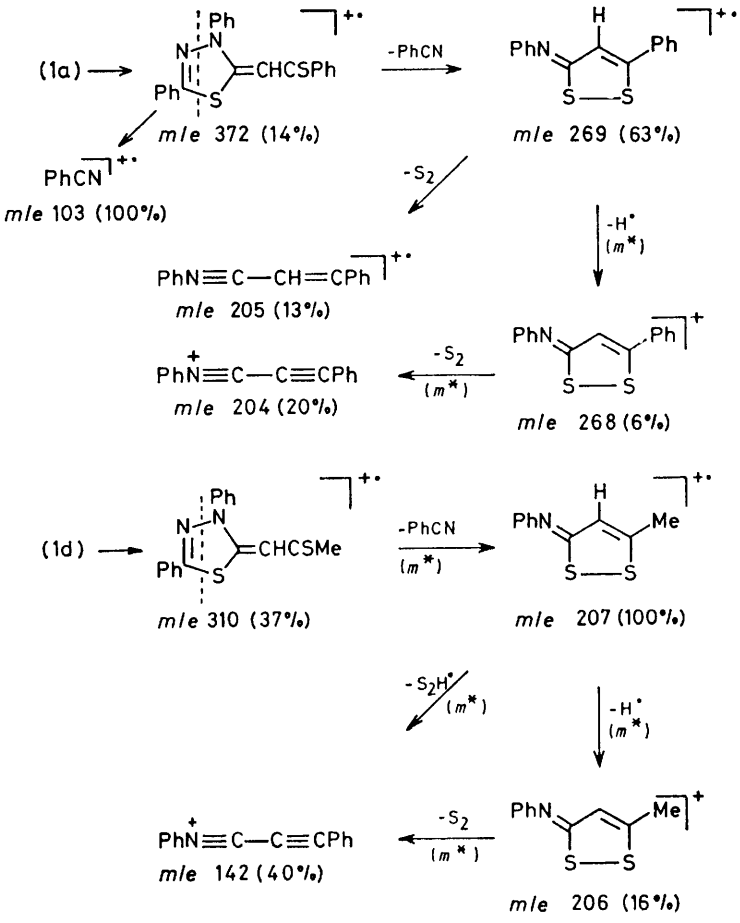
(9a)



(9b)

It is tempting to suggest that a similar effect is being observed for the thiadiazolene analogues (1), but there are insufficient data to support this.

The principal features of mass spectra of the thioketones (1a) and (1d) are summarized in Scheme 2. As can be seen, these spectra are radically different from those of their oxygen analogues.[3] Presumably ionization of the thioketone sulphur occurs and formation of an S–S bond brings about the loss of benzonitrile. The resulting dithiole ion then appears to break down through the loss of S_2 or S_2H (*cf.* ref. 9). A somewhat similar effect has been noted in the mass spectra of compounds (9b),[10] but in that instance the ion $PhC{\equiv}S^+$ was observed.



SCHEME 2

EXPERIMENTAL

Instrumental techniques were as noted in the preceding publication.[3]

Reactions of 2-Acylmethylene-3,5-diaryl-2H-1,3,4-thiadiazolenes (2) *with Phosphorus Pentasulphide.*—(*a*) Compound (2a) [3] (430 mg) in xylene (50 ml) containing phosphorus pentasulphide (2.2 g) was refluxed for 75 min. The hot solution was decanted and the residual solid was extracted with boiling xylene (50 ml). The combined extracts were washed with water (3 × 200 ml), with 5% sodium hydroxide (2 × 200 ml), and again with water (2 × 200 ml). After drying the organic solution (sodium sulphate), the solvent was removed. Column chromatography on silica gel (benzene as eluant) followed by crystallization from ethanol afforded compound (1a) (150 mg, 26%) as short orange needles, m.p. 210—212 °C (lit.,[1] 212 °C); $\nu_{max.}$ 1 525, 1 490, 1 470, 1 445, 1 250, 775, 755, and 680 cm^{-1}; δ 7.13—8.03 (–CH and arom.).

(*b*) Compound (2b) [3] (3.7 g) in dry benzene (70 ml) containing phosphorus pentasulphide (4.4 g) was refluxed for 15 min. The suspension was filtered while hot and the remaining solid was washed with boiling benzene (50 ml). The combined benzene solutions were washed with water (3 × 200 ml), with 5% sodium hydroxide (2 × 300 ml), and again with water until the washings were neutral. Removal of the solvent followed by crystallization from 95% ethanol gave *compound* (1b) (1.8 g, 46%) as yellow needles, m.p. 185—187 °C (Found: C, 43.8; H, 2.6; N, 5.9. $C_{17}H_{12}Br_2N_2S_2$ requires C, 43.6; H, 2.6; N, 6.0%); $\nu_{max.}$ 1 530, 1 495, 1 480, 1 475, 1 275, 1 260, 770, and 765 cm^{-1}; δ 2.70 (s, 3 H, MeC=S), 6.60 (s, 1 H, HC=), and 7.2—8.1 (m, 8 H, arom.); *m/e* 466 (1%, M^+), 387 (100, M^+ – Br, *m** 377), 363 (44, M^+ – PhC), 355 (30, 387 – S), 308 (42, 387 – Br, *m** 244), 298 (42, 363 – S_2H), 284 (17, 363 – Br, *m** 223), and 259 (11, $C_6H_3Br_2CN$).

(*c*) A suspension of compound (2c) [3] (750 mg) and phosphorus pentasulphide (800 mg) in dry benzene (25 ml) was refluxed for 30 min. It was filtered while hot and the remaining solid was extracted with boiling benzene (50 ml). The combined benzene solutions were washed with water (3 × 100 ml), with 5% sodium hydroxide (3 × 100 ml), and again with water (3 × 100 ml). Removal of the solvent followed by crystallization from chloroform–light petroleum (b.p. 30—60 °C) afforded *compound* (1c) (540 mg, 68%) as orange needles, m.p. 224—227 °C (Found: C, 48.8; H, 3.0; N, 5.5. $C_{22}H_{14}Br_2N_2S_2$ requires C, 49.0; H, 2.9; N, 5.7%); $\nu_{max.}$ 1 525, 1 490, 1 480, 1 460, 1 440, 1 260, 860, and 725 cm^{-1}; δ 7.03 (s, 1 H, HC=) and 7.26—8.03 (m, 13 H, arom.); *m/e* 527 (3%, M^+ – H), 449 (38, M^+ – Br, *m** 389), 425 (12, M^+ – PhCN), 417 (5, 449 – S), 370 (5, 449 – Br, *m** 304), 360 (5, 425 – S_2H), 316 (13, 417 – PhC_2H), and 102 (100, PhC_2H).

Reaction of 3-(2,4-Dibromophenyl)-5-phenyl-2-thioacetylmethylene-2H-1,3,4-thiadiazolene (1b) *with Mercury*(II) *Acetate.*—Compound (1b) (1.0 g) in acetic acid (40 ml) con-

taining mercury(II) acetate (750 mg) was refluxed for 5 min. When cool, the solution was poured into water (400 ml) and the precipitate was collected. Column chromatography on silica gel (benzene as eluant) afforded compound (2b) (650 mg, 67%) as dark brown prisms, m.p. 148—152 °C. Successive recrystallizations gave material of m.p. and mixed [3] m.p. 155—157 °C; *m/e* 450 (17%, M^+), 435 (6, M^+ — Me), 408 (3, M^+ — CH_2CO), 371 (100, M^+ — Br), 356 (68, 371 — Me), 329 (43, 371 — CH_2CO), 292 (6, 371 — Br), 250 (30, 292 — CH_2CO).

Reactions with Thioacetic Acid.—(*a*) A suspension of *N'*-acetyl-*N'*-(2,4-dibromophenyl)benzothiohydrazide (2.0 g) in thioacetic acid (10 ml) was stirred at room temperature for 12 h. T.l.c. of the reaction mixture showed only the presence of starting material. The mixture was then refluxed for 45 min. Removal of the excess of solvent under reduced pressure followed by column chromatography on silica gel (benzene as eluant) afforded compound (1b) (1.14 g, 52%), m.p. and mixed m.p. 185—187 °C (from 95% ethanol). Further elution gave compound (2b) (320 mg, 15%), m.p. 150—154 °C (from acetonitrile). Further crystallization of the latter gave material of m.p. and mixed m.p. 155—157 °C.

(*b*) Similar treatment of *N'*-(2,4-dibromophenyl)benzothiohydrazide [11] (5 g) with thioacetic acid (20 ml) afforded compound (1b) (3.6 g, 59%), m.p. and mixed m.p. 185—187 °C, followed by compound (2b) (1.1 g, 24%), m.p. and mixed m.p. 155—157 °C.

(*c*) Similarly, *N'*-phenylbenzothiohydrazide [11] (3.1 g) and thioacetic acid (15 ml) afforded *compound* (1d) (3.24 g, 78%) as orange needles, m.p. 162—163 °C (from ethanol) (Found: C, 65.9; H, 4.6; N, 8.8. $C_{17}H_{14}N_2S_2$ requires C, 65.8; H, 4.6; N, 9.0%); $\nu_{max.}$ 1 525, 1 490, 1 460, 1 270, 1 120, 780, 760, and 690 cm^{-1}; δ 2.67 (s, 3 H, MeC=), 7.01 (s, 1 H, HC=), and 7.48—7.96 (m, 10 H, arom.). Further elution gave compound (2d) (200 mg, 5%), m.p. and mixed [3] m.p. 150—152 °C.

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