Reactions of some 1,3-dipolarophiles with 1,2-dithioles and 1,2,4-dithiazoles

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The reactions of 1,2-dithiole-3-thiones and 1,2,4-dithiazole-3-thiones with acetylenic esters provide initial 1,3-dithiole products by 1,3-dipolar additions. 3-Imino-1,2-dithioles react similarly to form thiazoles. Both these initial adducts react further with more acetylenic ester to form spiran type structures. The stereochemistry of these is discussed briefly and applied to their reactivity and spectroscopic properties.

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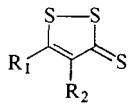
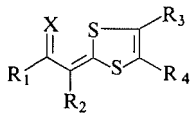
1,2-Dithiole-3-thiones (**1**) have been shown to undergo 1,3-dipolar reactions with activated acetylenes (1–3). The reaction provides 1:1 adducts, formulated as 2-(2-thioacylmethylene)-1,3-dithioles (**2**). Further reaction may provide spirans (**3**) by further 1,4-addition of the activated acetylene with the initially formed adduct. Similarly, 1,2,4-dithiazole-3-thiones (**4**) react with activated acetylenes to give 2-thioacylimino -1,3-dithiole (**5**) initial products (3–5) which may react further with more acetylene to give spiran structures (6) (**6**).



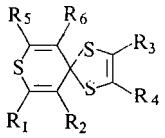
1

a $R_1 = R_2 = Ph$



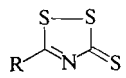
2

a $R_1 = R_2 = Ph, R_3 = R_4 = CO_2Me, X = S$
b $R_1 = R_2 = Ph, R_3 = H, R_4 = CO_2Et, X = S$
c $R_1 = Me, R_2 = H, R_3 = Ph, R_4 = H, X = O$
d $R_1 = R_2 = R_3 = Ph, R_4 = CO_2Et, X = S$



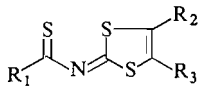
3

a $R_1 = R_2 = Ph, R_3 = R_4 = R_5 = R_6 = CO_2Me$
b $R_1 = R_2 = Ph, R_3 = CO_2Et, R_4 = R_5 = H, R_6 = CO_2Et$
c $R_1 = R_2 = Ph, R_3 = R_4 = CO_2Me, R_5 = H, R_6 = CO_2Et$



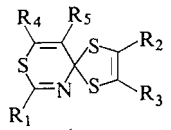
4

a R = Ph



5

a $R_1 = Ph, R_2 = R_3 = CO_2Me$
b $R_1 = Ph, R_2 = R_3 = CF_3$
c $R_1 = Ph, R_2 = H, R_3 = CO_2Et$



6

We were interested in the reactions of some dipolarophilic acetylenes with other such thiones and also with 3-imino-1,2-dithioles (**7***a*,*b*) which might be expected to undergo reactions similarly to the thiones, since partial ionic structures may be also written for these. Behringer reports (7) obtaining adducts by reaction of 5-iminoisothiazoles with dimethyl acetylenedicarboxylate. Probably the reaction of a 3-imino-1,2,4-dithiazole with dimethyl acetylenedicarboxylate (3) proceeds similarly.

4,5-Diphenyl-1,2-dithiole-3-thione (**1***a*) reacted with the three acetylenic esters studied; dimethyl acetylenedicarboxylate, ethyl propiolate, and ethyl phenylpropiolate. The first of these gave first a mono-adduct (**2***a*). The nuclear magnetic resonance (n.m.r.) spectrum of this showed two

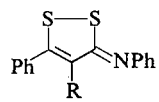
singlets assigned to the methyls of the carbomethoxy groups which are not equivalent in this molecule. It is reported (4) however, that in the related thioacylimino-1,3-dithiole (**5***a*) the two carbomethoxy groups are equivalent. It is also found in 4,5-bistrifluoromethyl-2-thiobenziminо-1,3-dithiole (**5***b*) prepared by reaction of hexafluoro-2-butyne with 5-phenyl-1,2,4-dithiazole-3-thione (**4**) that the two trifluoromethyl groups are equivalent as indicated by n.m.r. It was initially suggested that the equivalence of the methyls was fortuitous, but it now appears more likely that they are in fact equivalent due to ready rotation of the side chain by a means which is not yet clear. Similarly, the n.m.r. spectrum of the ethyl ester (**5***c*) (4) showed the presence of only one carbethoxy group, instead of the two expected if two geometrical isomers had been obtained. Probably the greater electronegativity of the side chain nitrogen in these compounds (**5***a,b,c*) compared to the side chain carbon in compound **2***a* makes the exocyclic double bond acquire more single bond character, permitting free rotation. Such free rotation should be temperature dependent, but even at $-60°$, the n.m.r. spectrum of compound **5***c* indicated that only one compound was present. Further treatment of the mono-adduct (**2***a*) with dimethyl acetylenedicarboxylate provided a di-adduct (**3***a*). The two carbomethoxy groups in the five-membered ring are equivalent in the di-adduct, and this is confirmed by the n.m.r. A small amount of unidentified violet material was also isolated from this reaction.

With ethyl propiolate the thione (**1***a*) gave both mono- and di-adducts. The n.m.r. spectrum of the former (**2***b*) indicated that it was a mixture of two geometrical isomers. This has been previously suggested (8) for a related 1,3-dithiole ketone (**2***c*) and for some other thioacylmethylene-1,3-dithioles (3). These isomers could not be separated. The n.m.r. showed two different singlets at 2.26 τ and 2.13 τ due to the different protons on the five-membered rings of the mono-adducts. A possible mechanism for the 1,3-addition would involve initial β-addition of the thione group to the ethyl propiolate. This is inconsistent with the production of two isomers. Possibly these could interconvert under the conditions of the reaction, but Campaigne (8) has shown that for two such acylmethylene-1,3-dithiole isomers there was no interconversion at 140°.

The n.m.r. spectrum of the di-adduct (**3***b*) obtained was consistent with the presence of two enantiomers, both derived from the geometrical isomers of the mono-adduct. The two protons on the 1,3-dithiole rings absorbed at τ 3.5 and are equivalent in the enantiomers. The carbethoxy group of the thiopyran ring may be α or β to the sulfur atom, depending on the mode of addition of the acetylenic ester to the α,β-unsaturated thioketonic side chain of the initial adduct (**2***b*). Only one singlet for the proton on the thiopyran ring is apparent, hence only one isomer has been formed. Probably the mechanism again involves β-addition of the thione sulfur (from a vinylogous 1,3-dithiole-2-thione) to the acetylenic ester. Even the meribicyclic **6***a*, thiathiophthene system exhibits vinylogous 1,2-dithiole-3-thione properties in its reaction with methyl iodide (9). A 1,4-dipolar mechanism has been proposed (10) for this second addition of acetylenic ester.

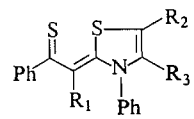
A mixed di-adduct (**3***c*) was prepared by reaction of the mono-adduct (**2***a*) with ethyl propiolate to allow proper assignment of the protons in the different rings of the di-adduct (**3***b*). It demonstrated that the protons on the thiopyran ring of the di-adducts absorb at lower fields than those on the 1,3-dithiole ring.

The reaction of the thione (**1***a*) with ethyl phenylpropiolate provided a mono-adduct (**2***d*) only. Possibly steric hindrance or reduced reactivity of the acetylene made formation of a di-adduct more difficult. Examination of the n.m.r. spectrum again indicated that two geometrical isomers were present.



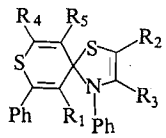
7

a R = H
b R = Ph



8

a R_1 = H,R_2 = R_3 = CO_2Me
b R_1 = Ph,R_2 = R_3 = CO_2Me
c R_1 = H,R_2 = CO_2Et,R_3 = H
d R_1 = H,R_2 = CO_2Et,R_3 = Ph



9

a $R_1 = H, R_2 = R_3 = R_4 = R_5 = CO_2Me$.
b $R_1 = Ph, R_2 = R_3 = R_4 = R_5 = CO_2Me$

Reaction of two 3-phenylimino-1,2-dithioles (**7***a,b*), prepared (11) by reaction of 3-methylthio-1,2-dithiolium salts with aniline, with dimethyl acetylenedicarboxylate gave no mono-adducts (**8**). Instead di-adducts were obtained. These may be formulated as spiran structures (**9***a,b*) respectively which have a thiazole nucleus joined to a thiopyran nucleus. Even when equivalent quantities of reagents were used, no mono-adducts (**8***a, b*) were isolated. Presumably these reacted more rapidly than the starting material with the acetylenic ester. However, Behringer (7) reports obtaining mono-adducts by reaction of isothiazole-3-imines with dimethyl acetylenedicarboxylate. In this case steric interference by phenyl groups on the nitrogen atoms of the side chain of the mono-adduct may hinder reaction with more acetylenic ester.

With the less reactive propiolic and phenylpropiolic esters, only 5-phenyl-3-phenylimino-1,2-dithiole (**7***a*) reacted. Mono-adducts (**8***c,d*) respectively were obtained. The n.m.r. spectrum was inconclusive in deciding whether the products were single compounds or mixtures of two geometrical isomers. Apparently, the ester groups are equivalent in the pairs of geometrical isomers in each case. 4,5-Diphenyl-3-phenylimino-1,2-dithiole (**7***b*) failed to react, probably due to steric hindrance. In these imines (**7***a,b*) the *N*-phenyl group may be "*cis*" or "*trans*" to the sulfur atoms. In the compound (**7***b*) however, steric hindrance by the 4-phenyl group makes the "*cis*" form more likely, and this form would in turn be less susceptible to approach by the acetylenic ester.

Also, the mono-adducts (**8***c,d*) formed may be either thiazole-4- or -5-carboxylic esters. They are formulated as the former since these would be the expected products of initial β-addition to the acetylenic ester.

Experimental

Thin-layer chromatography was performed on "Camag" silica gel type D.S.F. 5, supplied by Mondray Ltd. Development of plates was carried out using benzene with increasing proportions of chloroform and nuclear magnetic resonance spectra were obtained on a Varian model 56/60A spectrometer, in deuteriochloroform solution using tetramethylsilane as an internal standard.

Reaction of 4,5-Diphenyl-1,2-dithiole-3-thione with Dimethyl Acetylenedicarboxylate to form the Mono-adduct (2a)

4,5-Diphenyl-1,2-dithiole-3-thione (12) (381 mg) and dimethyl acetylenedicarboxylate (185 mg) in benzene (60 ml) were stirred together at room temperature for 18 h. The solution was evaporated to give a dark-green solid which was further purified by thin-layer chromatography. Dark-green needles m.p. 158.5–160.5° from chloroform (70%).

Anal. Calcd. for $C_{21}H_{16}O_4S_3$: C, 58.88; H, 3.74; S, 22.43. Found: C, 58.84; H, 3.72; S, 22.24.

Nuclear magnetic resonance 6.19 τ (3H singlet); 6.07 τ (3H singlet); 2.95 τ (5H singlet); 2.79 τ (5H singlet).

Reaction of 4,5-Diphenyl-1,2-dithiole-3-thione with Dimethyl Acetylenedicarboxylate to form the Di-adduct (3a)

4,5-Diphenyl-1,2-dithiole-3-thione (12) (285 mg) and dimethyl acetylenedicarboxylate (282 mg) in benzene (30 ml) were refluxed together for 15 h. The reddish-brown product obtained on evaporation was further purified by thin-layer chromatography. Two bands were obtained. The main product was the di-adduct. Yellow prisms m.p. 111–113° from ethanol (66%).

Anal. Calcd. for $C_{27}H_{22}O_8S_3$: C, 56.84; H, 3.86; S, 16.86. Found: C, 56.96; H, 3.75; S, 16.80.

Nuclear magnetic resonance 6.32 τ (6H singlet); 6.19 τ (3H singlet); 6.13 τ (3H singlet); 3.03–2.70 τ (5H multiplet); 2.77 τ (5H singlet).

A minor product was separated and crystallized from ethanol. Violet powder m.p. 161–163° (10 mg).

Reaction of 4,5-Diphenyl-1,2-dithiole-3-thione with Ethyl Propiolate (2b) and (3b)

The thione (213 mg) and the ester (74 mg) in benzene (50 ml) were refluxed 24 h. After evaporation the crude mixture was treated by thin-layer chromatography to separate the mono- and di-adducts.

Mono-adduct

Brownish-green powder from chloroform (29%) m.p. 175–178°.

Anal. Calcd. for $C_{20}H_{10}O_2S_3$: C, 62.50; H, 4.17; S, 25.00. Found: C, 61.00; H, 4.02; S, 23.89.

Nuclear magnetic resonance 8.72 τ (3H triplet, J = 7.2 c.p.s.); 8.62 τ (3H triplet, J = 7.2 c.p.s.); 5.67 τ (2H quartet, J = 7.2 c.p.s.); 5.57 τ (2H quartet, J = 7.2 c.p.s.); 2.98 τ (5H singlet); 2.80 τ (5H singlet); 2.26 τ (1H singlet); 2.13 τ (1H singlet).

Di-adduct

Yellow prisms from ethanol (70%) m.p. 149–151°.

Anal. Calcd. for $C_{25}H_{22}O_4S_3$: C, 62.24; H, 4.56; S, 19.92. Found: C, 61.98; H, 4.61; S, 19.83.

Nuclear magnetic resonance 8.79 τ (3H triplet, J = 7.0 c.p.s.); 8.69 τ (3H triplet, J = 7.0 c.p.s.); 5.9 τ (2H quartet, J = 7.0 c.p.s.); 5.67 τ (2H quartet, J = 7.0 c.p.s.); 3.50 τ (1H singlet); 2.93 τ (10H singlet); 2.49 τ (1H singlet).

Reaction of Dimethyl 2-(α-phenylthiophenacylidene)-1,3-dithiole-4,5-dicarboxylate with Ethyl Propiolate (3c)

The 1,3-dithiole dicarboxylic ester (151 mg) and ethyl propiolate (51 mg) in benzene (40 ml) were refluxed together for 4 days. The crude product was purified by thin-layer chromatography. Yellow needles from ethanol (62%) m.p. 148–150°.

Anal. Calcd. for $C_{26}H_{22}O_6S_3$: C, 59.32; H, 4.18; S, 18.25. Found: C, 59.12; H, 4.04; S, 18.17.

Nuclear magnetic resonance 8.77 τ (3H triplet, J = 7.0 c.p.s.); 6.38 τ (6H singlet); 5.63 τ (2H quartet, J = 7.0 c.p.s.); 3.02–2.50 τ (10H multiplet); 2.45 τ (1H singlet).

Reaction of 4,5-Diphenyl-1,2-dithiole-3-thione with Ethyl Phenylpropiolate (2d)

The thione (325 mg) and the ester (195 mg) in xylene (25 ml) were refluxed for 24 h. The solvent was removed under reduced pressure, and the crude product recrystallized from ethanol (56%) m.p. 183–185°.

Anal. Calcd. for $C_{26}H_{20}O_2S_3$: C, 67.82; H, 4.35; S, 20.87. Found: C, 67.62; H, 4.30; S, 20.85.

Nuclear magnetic resonance 8.92 τ (3H triplet, J = 7.2 c.p.s.); 8.80 τ (3H triplet, J = 7.2 c.p.s.); 5.90 τ (2H quartet, J = 7.2 c.p.s.); 5.78 τ (2H quartet, J = 7.2 c.p.s.); 3.05–2.53 τ (15H multiplet).

Reaction of 5-Phenyl-3-phenylimino-1,2-dithiole with Dimethyl Acetylenedicarboxylate (9a)

5-Phenyl-3-phenylimino-1,2-dithiole (**11**) (120 mg) and excess dimethyl acetylenedicarboxylate in benzene (50 ml) were refluxed for 18 h. The crude product obtained on evaporation was purified by thin-layer chromatography and crystallized from ethanol, orange prisms m.p. 173–175° (63%).

Anal. Calcd. for $C_{27}H_{23}NO_8S_2$: C, 58.59; H, 4.16; N, 2.53; S, 11.58. Found: C, 58.46; H, 4.10; N, 2.68; S, 11.68.

Nuclear magnetic resonance 6.42 τ (3H singlet); 6.32 τ (3H singlet); 6.20 τ (3H singlet); 6.12 τ (3H singlet); 3.75 τ (1H singlet); 2.83–2.62 τ (5H multiplet); 2.73 τ (5H singlet).

When the reaction was performed with equimolar quantities of reagents, the product was a mixture of di-adduct and unreacted imine.

Reaction of 5-Phenyl-3-phenylimino-1,2-dithiole with Ethyl Propiolate (8c)

The imine (400 mg) and the ethyl propiolate (150 mg) in benzene (20 ml) were refluxed for 18 h. The product obtained on evaporation was purified by thin-layer chromatography and crystallized from ethanol, dark orange needles, m.p. 221–223° (75%).

Anal. Calcd. for $C_{20}H_{17}NO_2S_2$: C, 65.39; H, 4.63; N, 3.82; S, 17.44. Found: C, 65.23; H, 4.66; N, 3.95; S, 17.47.

Nuclear magnetic resonance 8.70 τ (3H triplet, J = 7.2 c.p.s.); 5.83 τ (2H quartet, J = 7.2 c.p.s.); 3.12–2.59 τ (11H multiplet, due to 10 protons on the two benzene rings and one single proton on the thiazole ring); 2.47 τ (1H singlet; proton on side chain).

Reaction of 5-Phenyl-3-phenylimino-1,2-dithiole with Ethyl Phenylpropiolate (8d)

5-Phenyl-3-phenylimino-1,2-dithiole (11) (329 mg) and the ester (200 mg) in xylene (20 ml) were refluxed for 14 h. The solvent was removed under reduced pressure and the yellowish-orange residue was extracted with boiling ethanol (80 ml) to remove unreacted thione, and recrystallized from chloroform. Dark orange needles m.p. 261–263° (64%).

Anal. Calcd. for $C_{26}H_{21}NO_2S_2$: C, 70.43; H, 4.74; N, 3.16; S, 14.45. Found: C, 70.24; H, 4.86; N, 3.26; S, 14.26.

Nuclear magnetic resonance 8.80 τ (3H triplet, J = 7.0 c.p.s.); 5.77 τ (2H quartet, J = 7.0 c.p.s.); 2.97–2.28 τ (16H multiplet, due to 15 protons on the benzene rings and one proton on the thiazole ring).

Reaction of 4,5-Diphenyl-3-phenylimino-1,2-dithiole with Dimethyl Acetylenedicarboxylate (9b)

4,5-Diphenyl-3-phenylimino-1,2-dithiole (11) (330 mg) and the ester (132 mg) in xylene (30 ml) were refluxed for 72 h. The orange residue remaining after removal of the solvent under reduced pressure was recrystallized from ethanol. Yellow prisms m.p. 230–232° (75%).

Anal. Calcd. for $C_{33}H_{27}NO_8S_2$: C, 62.97; H, 4.29; N, 2.33; S, 10.17. Found: C, 62.73; H, 4.47; N, 2.17; S, 10.21.

Nuclear magnetic resonance 6.57–6.37 τ (12H, two main peaks but not properly resolved). 3.05–2.67 τ (15H multiplet, not properly resolved).

Reaction of 4,5-Diphenyl-3-Phenylimino-1,2-dithiole with Ethyl Propiolate

The imine was treated with excess ester in boiling xylene for 1 week. A thin-layer chromatography separation of the mixture indicated only unreacted starting materials.

Reaction of 4,5-Diphenyl-3-phenylimino-1,2-dithiole with Ethyl Phenylpropiolate

The imine was treated with excess ester in boiling xylene for 1 week. A thin-layer chromatography separation of the mixture indicated only unreacted starting materials.

Reaction of 5-Phenyl-1,2,4-dithiazole-3-thione with Hexafluoro-2-butyne (5b)

The thione (500 mg) was heated with excess hexafluoro-2-butyne in benzene (20 ml) in a sealed glass tube at 70° for 7 h. The benzene was evaporated and the product recrystallized from ethanol. Greenish needles m.p. 128–129° (89%).

Anal. Calcd. for $C_{12}H_5F_6NS_3$: C, 38.70; H, 1.30; F, 30.31; N, 13.69; S, 25.52. Found: C, 38.70; H, 1.53; F, 30.47; N, 3.81; S, 25.72.

Nuclear magnetic resonance gave a singlet at +3133 τ.

Low Temperature Nuclear Magnetic Resonance Study of Ethyl 2-Thiobenzimino-1,3-dithiole-4-carboxylate

The ester (4) was examined in saturated deuteriochloroform solution at temperatures to −60°. The absorption of the proton on the 1,3-dithiole ring at 1.98 τ remained a singlet over the temperature range studied.

Acknowledgments

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