Some Reactions of Vinylene Di-isothiocyanate

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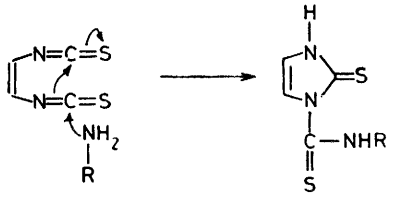
Vinylene di-isothiocyanate (1) reacts readily with some nucleophiles (*p*-chloroaniline, cyclohexylamine, morpholine, isoquinoline, 6,7-dimethoxy-3,4-dihydroisoquinoline, triethylamine, and sodium azide) to yield substituted thiocarbonylimidazoline derivatives of a similar structure to those products formed from the corresponding *o*-phenylene di-isothiocyanate. Different products in which the ratio of nucleophile to di-isothiocyanate was 2 : 1 were obtained from *N*-methylaniline, phenylhydrazine, and ethanol.

PREVIOUSLY we have described the synthesis of vinylene di-isothiocyanate (1) from the reaction of thiophosgene and base on imidazole.[1] We now describe some reactions of the di-isothiocyanate (see Scheme on next page).

Primary amines, as exemplified by *p*-chloroaniline and cyclohexylamine, reacted on a 1 : 1 basis and rapidly formed the (substituted thiocarbonyl)imidazoline-2-thiones [(2) and (3)] respectively, presumably by the mechanism shown.



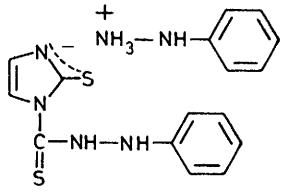
We found that the product (2) from *p*-chloroaniline underwent some decomposition to *p*-chlorophenyl isothiocyanate and imidazoline-2-thione, in dimethyl sulphoxide solution during the ^{1}H n.m.r. determination. The corresponding dithione (3) from cyclohexylamine was stable under similar conditions. The dithione (2) on methylation gave a dimethyl derivative (4), the structure of which was assigned as being di-*S*-methyl on the basis of ^{1}H and ^{13}C n.m.r. data.

The ^{13}C n.m.r. chemical shifts (from $SiMe_4$) in dimethyl sulphoxide for the unambiguous NMe derivative from methylaniline are shown in (5) (see also later) with the Me at δ 45.4. The dimethyl derivative (4) shows the two Me signals (solvent $CDCl_3$), upfield, as a singlet at δ 15.8.

Jackman and Jen [2] have shown the ^{13}C chemical shifts of certain NMe derivatives of 2-aminothiazines to be in the region of δ 39 for NMe. The chemical shifts for C=S in (5) were found at δ 160.3 and 178.6, whereas in the dimethylated derivative (4) they were found upfield at δ 144.8 and 149.5, demonstrating the conversion to =C–SMe. This latter value compares very favourably with the C-2 shift of δ 152 found by Jackman and Jen [2] for the phenyliminotetrahydro-1,3-thiazine (6). Similarly the value of the C-2 chemical shift of the thioimidazole (7) at δ 161.3 moves upfield on *S*-methylation to δ 141.7 for (8).[3]

In the ^{1}H n.m.r. of (5), (9),[4] and (10) [4] the chemical shift of the NMe protons is found at δ 3.7, 3.87, and 3.9, respectively, whilst the methyl protons of (11) [4] are found upfield at δ 2.75, and of (12) [4] at δ 2.28 and 2.78. The methylated product from (2) has methyls at δ 2.3 and 2.5, which we thus consider to be both S–Me as indicated in structure (4).

Secondary amines, exemplified by morpholine and *N*-methylaniline reacted in different ways. Morpholine gave the expected 1 : 1 product (13); however, *N*-methylaniline was unusual in that the initial product was a 2 : 1 adduct, the bis(thiourea) (14) which lost methylaniline on heating to form the bis(thione) (5). It is noteworthy that *o*-phenylene di-isothiocyanate under similar conditions gives only the 1 : 1 product.[4] Indeed, we were never able to isolate any 2 : 1 dithione products from the aromatic di-isothiocyanate and a wide variety of nucleophiles. Phenylhydrazine and also ethanol reacted with the di-isothiocyanate to give the 2 : 1 thioamide (15) and thioester (16) products, respectively. The thioamide (15) was stable to solution in cold aqueous alkali and reprecipitated on neutralisation with aqueous mineral acid; therefore the isomeric salt structure (17) may be discounted.

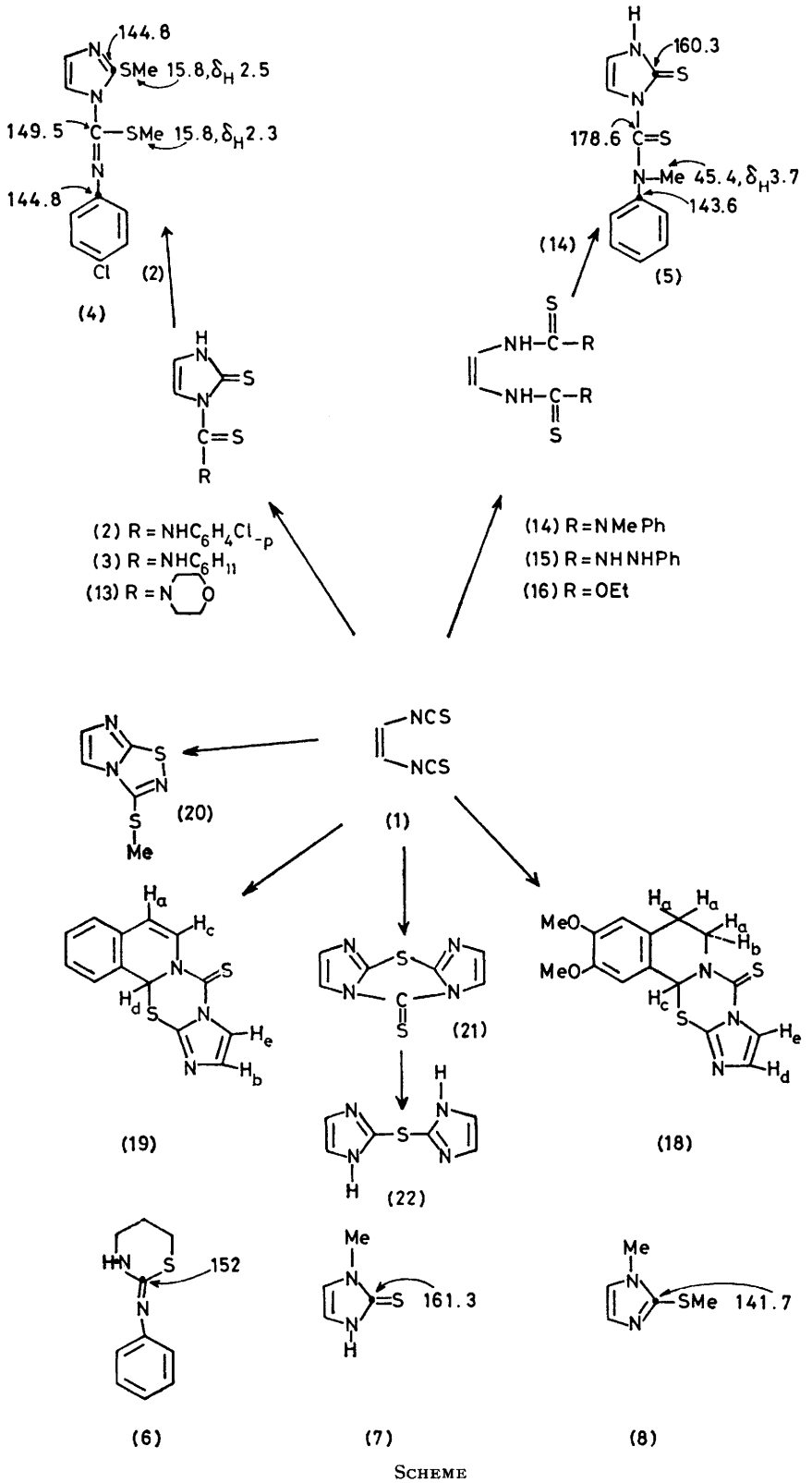


(17)

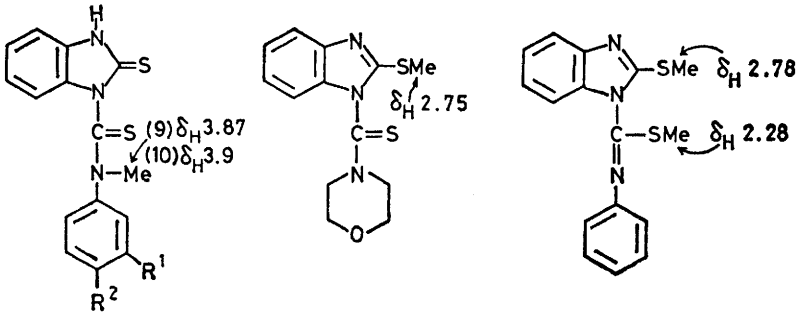
6,7-Dimethoxy-3,4-dihydroisoquinoline and isoquinoline both reacted in like manner with the di-isothiocyanate (1) to yield the tetracycles (18) and (19) respectively. These results are in keeping with the earlier observations on *o*-phenylene di-isothiocyanate.[4]

Loss of nitrogen occurred when sodium azide and the di-isothiocyanate (1) were allowed to react at room temperature in aqueous dimethoxyethane and gave, after methylation, the imidazothiadiazole (20). A similar type of reaction has been found to take place with *o*-phenylene di-isothiocyanate.[5]

We have previously shown that the di-isothiocyanate (1) and *o*-phenylene di-isothiocyanate [6] behaved in a


144.8
SMe 15.8, δH 2.5
149.5
SMe 15.8, δH 2.3
144.8
Cl
(4)
(2)
(2) R = NHC6H4Cl-p
(3) R = NHC6H11
(13) R = N O
160.3
178.6
N–Me 45.4, δH 3.7
143.6
(14)
(5)
(14) R = NMePh
(15) R = NHNHPh
(16) R = OEt
(20)
(1)
(19)
(21)
(18)
(22)
152
161.3
(6)
(7)
(8)

SCHEME



(9) R^1 = H, R^2 = NO_2
(10) R^1 = NO_2, R^2 = H

(11)

(12)

similar manner with triethylamine. The tricyclic thione (21) formed from (1) underwent ring-fission with warm acid or base to yield the novel sulphide (22).

EXPERIMENTAL

For general experimental details see ref. 1.

(1-*Morpholinothiocarbonyl*)-4-*imidazoline*-2-*thione* (13).—A dichloromethane solution of vinylene di-isothiocyanate (1) was evaporated to leave a red oil (3.6 g, 0.025 mol) which was taken up in ether (50 ml) and filtered dropwise into a magnetically stirred solution of morpholine (2.5 g, 0.029 mol) in ether (30 ml) at room temperature. After 6 h the product (4.3 g, 75%) as *buff microprisms*, m.p. 250 °C, was collected, washed with ether, and dried (Found: C, 41.9; H, 4.8; N, 18.0; S, 28.1. $C_8H_{11}N_3OS_2$ requires C, 41.9; H, 4.8; N, 18.3; S, 27.9%); δ [$(CD_3)_2SO$] 2.9—4.4 (8 H, m, morpholine), 7.0 (1 H, d, =CH), and 7.1 (1 H, d, =CH); *m/e* 229 (M^+).

Similarly prepared was 1-[(4-*chlorophenylamino*)*thiocarbonyl*]-4-*imidazoline*-2-*thione* (2) in 63% yield. The precipitated product was filtered off after 16 h, m.p. 225 °C (decomp.) (Found: C, 44.2; H, 3.1; N, 15.4; S, 24.0. $C_{10}H_8ClN_3S_2$ requires C, 44.5; H, 3.0; N, 15.6; S, 23.8%); δ [$(CD_3)_2SO$] 7.15 (1 H, br s, =CH) 7.3—7.9 (4 H, m, aromatics), and 8.1 (1 H, br s, =CH) with decomposition products imidazole-2-thione [δ 6.8 (2 H, s)] and 4-chlorophenyl isothiocyanate [δ 7.45 (4 H, s)] present.

Also similarly prepared was [(1-*cyclohexylamino*)*thiocarbonyl*]-4-*imidazoline*-2-*thione* (3) in 71% yield. The product was obtained on evaporation of the filtrate after stirring for 48 h (a trace of precipitated co-product was found to be imidazole-2-thione, m.p. and i.r. identical to those of authentic material [7]); m.p. 138—140 °C (Found: C, 50.2; H, 6.4; N, 17.3; S, 26.4. $C_{10}H_{15}N_3S_2$ requires C, 49.8; H, 6.2; N, 17.4; S, 26.5%); δ [$(CD_3)_2SO$] 1.2—2.1 (10 H, m, cyclohexyl-CH_2), 4.2 (1 H, m, cyclohexyl-CH), 7.1 (1 H, d, =CH), 8.1 (1 H, d, =CH), and 13.0 (2 H, m, NH); *m/e* 241 (M^+).

N-(4-*Chlorophenyl*)*methylthio*-(2-*methylthioimidazolyl*) *methanimine* (4).—The dithione (2) (1.6 g, 0.006 mol) was dissolved in acetonitrile (90 ml) and 1N sodium hydroxide solution (12 ml, 0.012 mol) at 5 °C. Methyl iodide (0.75 ml, 0.012 mol) was added dropwise with stirring and the mixture allowed to warm to room temperature. After 3 h the mixture was evaporated, the oily residue partitioned between chloroform and water, and the organic phase dried ($MgSO_4$) and evaporated. Chromatography of the crude oil (1.5 g) on silica gel with diethyl ether as eluant gave the *azomethine* (4) as a yellow oil (1.0 g, 57%) (Found: C, 48.4; H, 3.7; N, 13.9; S, 20.9; $C_{12}H_{12}ClN_3S_2$ requires C, 48.4; H, 4.0; N, 14.1; S, 21.5%); δ [$(CD_3)_2SO$] 2.3 (3 H, s, imidazolyl-SMe), 2.5 (3 H, s, SMe), 6.8—7.5 (4 H, m, aromatic), 7.05 (1 H, d, =CH), and 7.6 (1 H, br s, =CH); *m/e* 297 (M^+).

3,3′-*Vinylenebis*-(1-*methyl*-1-*phenylthiourea*) (14).—A solution of (1) (1.1 g, 0.007 7 mol) in ether (20 ml) was filtered dropwise into a solution of *N*-methylaniline (1.7 ml, 0.016 mol) in ether (30 ml) at room temperature and the mixture stirred magnetically for 5 h. The precipitate was filtered off and washed with ether to yield the *bisthiourea* (14) (1.9 g, 68%) as pale cream prismatic needles, m.p. 115—120 °C, resolidifies then decomp. 240 °C (Found: C, 60.5; H, 5.7; N, 15.6. $C_{18}H_{20}N_4S_2$ requires C, 60.65; H, 5.65; N, 15.7%); δ [$CDCl_3$ + CD_3OD] 3.55 (6 H, s, Me), 6.4 (2 H, s, −CH=CH−), and 7—7.55 (10 H, m, aromatic).

Recrystallisation of the bisthiourea (14) from toluene yielded pale cream plates of 1-[(N-*methylanilino*)*thiocarbonyl*]-4-*imidazoline*-2-*thione* (5), m.p. 243—245 °C (decomp.) (Found: C, 52.6; H, 4.7; N, 16.5; S, 25.4. $C_{11}H_{11}N_3S_2$ requires C, 53.0; H, 4.4; N, 16.9; S, 25.7%); δ [$(CD_3)_2SO$] 3.7 (3 H, s, Me) and 6.7—7.5 (7 H, m, −CH=CH− and aromatic); *m/e* 249 (M^+).

OO′-*Diethyl* NN′-*vinylenebis*(*thiocarbamate*) (16).—Vinylene di-isothiocyanate (0.2 g, 0.001 4 mol) was dissolved in ethyl alcohol (10 ml) and left at room temperature 15 days. Evaporation left a red gum which was triturated well with portions of ether. The ether on evaporation left a gum which crystallised from light petroleum (b.p. 60—80 °C) to give the *bisthiocarbamate* as prisms (0.14 g, 42%), m.p. 75—77 °C (Found: C, 41.2; H, 6.1; N, 11.9; S, 27.3. $C_8H_{14}N_2O_2S_2$ requires C, 41.0; H, 6.0; N, 12.0; S, 27.4%); δ [$(CD_3)_2SO$] 1.25 (6 H, t, Me), 4.4 (4 H, q, CH_2), 6.4 (2 H, s, −CH=CH−), and 10.5 (2 H, s, NH); *m/e* 234 (M^+).

4,4′-*Vinylenebis*-(1-*phenylthiosemicarbazide*) (15).—Vinylene di-isothiocyanate (1) (0.9 g, 0.006 3 mol) in ether (20 ml) was filtered into a solution of phenylhydrazine (1.25 ml, 0.012 mol) in ether (50 ml) with stirring at room temperature. After 10 min the microcrystalline *bis*(*thiosemicarbazide*) was collected (1.5 g, 66%), m.p. 135—137 °C (Found: C, 53.3; H, 5.3; N, 23.6; S, 17.8. $C_{16}H_{18}N_6S_2$ requires C, 53.6; N, 5.02; N, 23.5; S, 17.9%); δ [$(CD_3)_2SO$] 6.3—7.6 (10 H, m, aromatic) and 6.56 (2 H, s, CH=CH).

3-*Methylthioimidazo*[1,2-d][1,2,4]*thiadiazole* (20).—A solution of vinylene di-isothiocyanate (5.9 g, 0.041 mol) in dimethoxyethane (40 ml) was filtered into a stirred solution of sodium azide (4.0 g, 0.062 mol) in dimethoxyethane (40 ml) and water (40 ml) at 5 °C. After 16 h at room

temperature the reaction mixture was filtered, methyl iodide (4 ml, 0.064 mol) added, and stirring continued a further 4 h. Dimethoxyethane was evaporated *in vacuo* and water (40 ml) added. The product was collected, washed with water, dried, and purified by sublimation at 80 °C and 0.1 Torr to give the *imidazothiadiazole* (20) as pale yellow prisms (3.8 g, 53%) (Found: C, 34.9; H, 2.8; N, 24.3; S, 37.2. $C_5H_5N_3S_2$ requires C, 35.1; H, 2.9; N, 24.5; S, 37.4%); δ [$(CD_3)_2SO$] 2.8 (3 H, s, Me), 7.4 (1 H, d, =CH), and 7.9 (1 H, d, =CH); *m/e* 171 (M^+).

10,11-*Dimethoxy*-8,12b-*dihydroimidazo*[1,2:3′,2′][1,3,5]-*thiadiazino*[2,3-a]*isoquinoline*-5(6H)-*thione* (18).—A solution of vinylene di-isothiocyanate (2.3 g, 0.016 mol) in ether (50 ml) was filtered into a stirred solution of 3,4-dihydro-6,7-dimethoxyisoquinoline (3.25 g, 0.017 mol) in ether (50 ml). After 1 h the precipitate was collected and washed with ether. Recrystallisation from toluene gave the *product* as pale cream prisms (4.0 g, 74%), m.p. 199—200 °C (Found: C, 54.1; H, 4.6; N, 12.4. $C_{15}H_{15}N_3O_2S_2$ requires C, 54.05; N, 4.5; N, 12.6%); δ [$(CD_3)_2SO$] 2.9—3.6 (3 H, m, H_a), 3.75 (3 H, s, OMe), 3.82 (3 H, s, OMe), 4.9—5.2 (1 H, m, H_b), 6.8 (1 H, s, aromatic), 6.95 (1 H, s, aromatic), 7.04 (1 H, s, H_c), 7.05 (1 H, d, H_d), and 8.0 (1 H, d, H_e); *m/e* 333 (M^+).

Imidazo[1,2:3′,2′][1,3,5]*thiadiazino*[2,3-a]*isoquinoline*-5(12bH)-*thione* (19).—A solution of vinylene di-isothiocyanate (0.9 g, 0.006 3 mol) in ether (20 ml) was filtered into a stirred solution of isoquinoline (0.74 ml, 0.063 mol) in ether (30 ml) at room temperature. After 20 min the precipitate was collected and washed with ether to give the *product* as needles (1.3 g, 76%), m.p. 156—158 °C (Found: C, 57.3; H, 3.1; N, 15.2; S, 23.4. $C_{13}H_9N_3S_2$ requires C, 57.56; H, 3.3; N, 15.5; S, 23.6%); δ [$(CD_3)_2SO$] 6.35 (1 H, d, H_a), 7.1 (1 H, d, H_b), 7.3—7.5 (4 H, m, aromatic), 7.55 (1 H, d, H_c), 7.8 (1 H, s, H_d), and 8.05 (1 H, d, H_e); *m/e* 271 (M^+).

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