The Chemistry of *o*-Phenylenedi-isothiocyanate. Part 3.[1] Studies on the Syntheses of Heterocyclic Compounds

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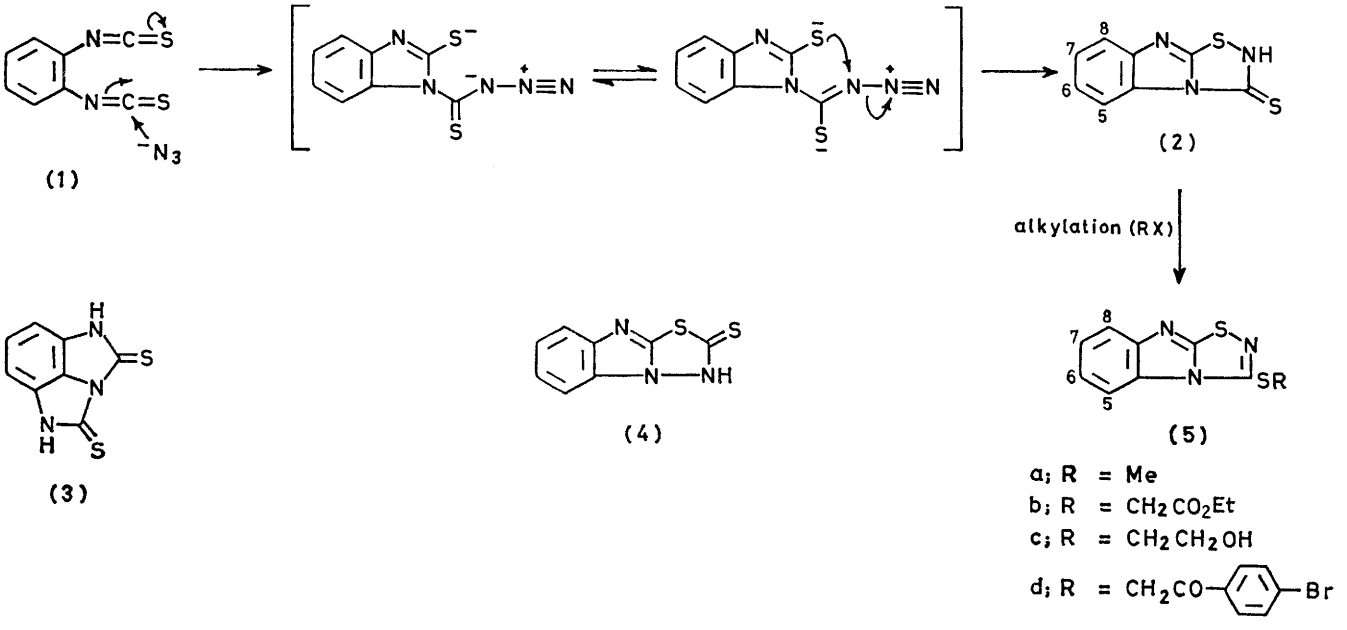
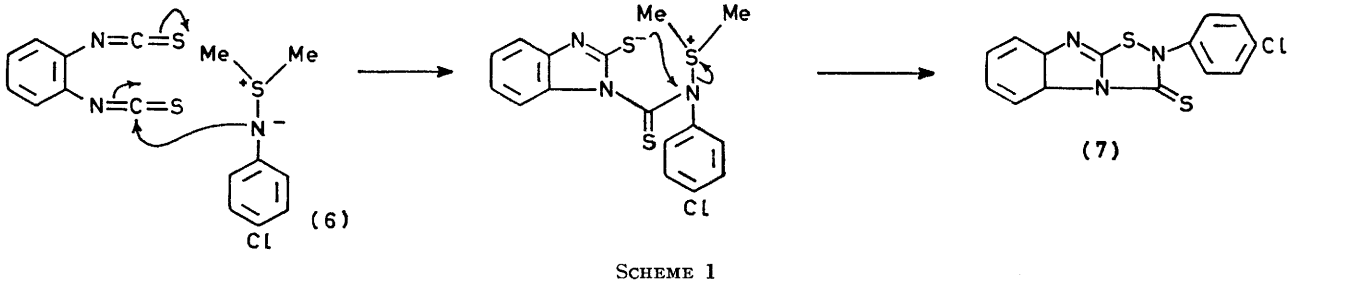
o-Phenylenedi-isothiocyanate (1) reacts with sodium azide to give [1,2,4]thiadiazolo[4,5*a*]benzimidazole-3-thione (2), which undergoes alkylation to the *S*-alkyl derivatives (5a—d). With *N*-(4-chlorophenyl)-*SS*-dimethylsulphimide the di-isothiocyanate (1) yields the corresponding *N*-arylthiadiazolo-derivative (7). Alcohols and thiophenol react with (1) and give alkoxy- or (arylthio)-thiocarbonylbenzimidazolinethiones (9a and b) and (10). The di-isothiocyanate also reacts with chloromethanesulphonamide and yields a dithiadiazepine *S*-dioxide (13) along with benzimidazolyl disulphide (12).

THIS paper describes a number of miscellaneous reactions of *o*-phenylene di-isothiocyanate. It supplements the earlier work on simple nitrogen nucleophiles, and extends our knowledge of intramolecular ring-closure reactions [2]

of the di-isothiocyanate (1) with sodium azide in aqueous dimethoxyethane gave a product $C_8H_5N_3S_2$ [*m/e* 207 (M^+)] accompanied by loss of nitrogen. The reaction sequence is envisaged as addition of the azide nucleophile





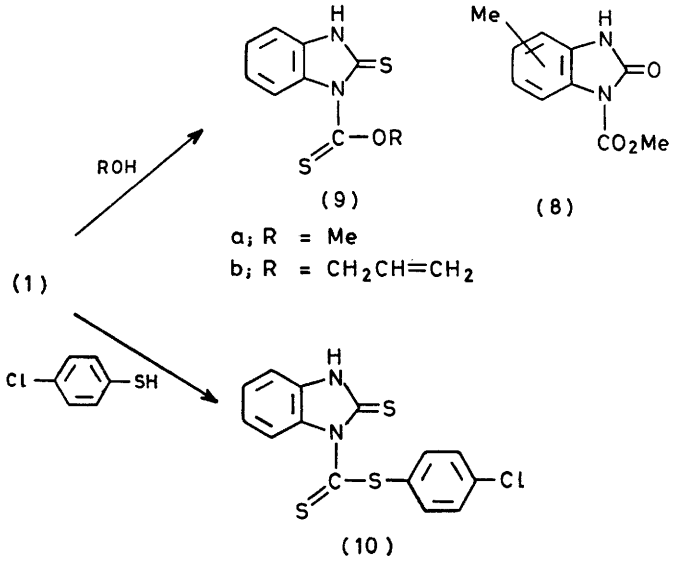
SCHEME 1

brought about by the second neighbouring isothiocyanate group.

RESULTS AND DISCUSSION

Isothiocyanates react with sodium azide to give substituted tetrazolinethiones.[3] We found that treatment to an isothiocyanate radical accompanied by a concerted cyclisation with elimination of nitrogen to yield the thiadiazolobenzimidazolethione (2) (Scheme 1). Two alternative structures [(3) and (4)] could be considered as possibilities for the product, $C_8H_5N_3S_2$. Structure (3) could arise as a result of nitrene formation from the de-

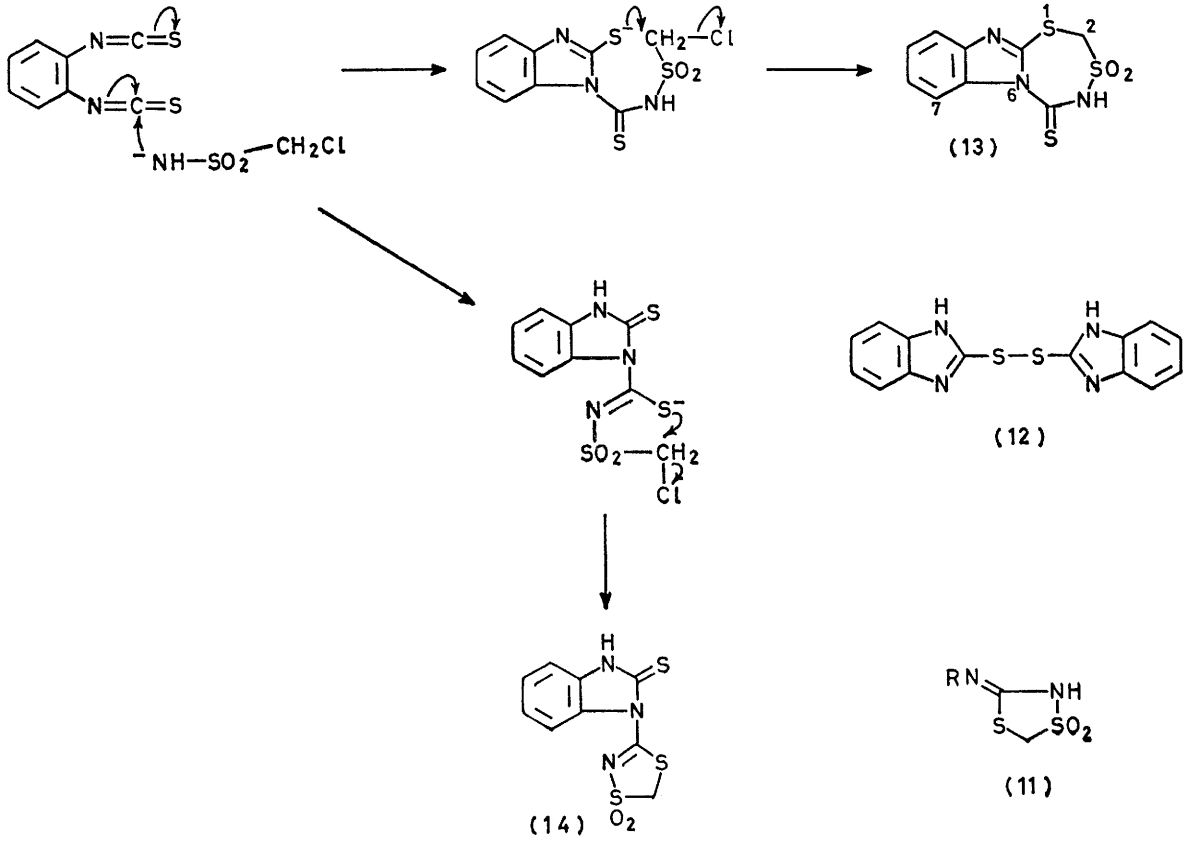
composition of the intermediate thiocarbonylazide, followed by an insertion into the benzenoid nucleus,[4] and structure (4) by a Curtius-type rearrangement



SCHEME 2

followed by ring-closure to the thiadiazolobenzimidazolethione. The n.m.r. spectrum of the compound, $C_8H_5N_3S_2$ showed a downfield aromatic proton at δ 8.85 and three aromatic protons in the range δ 7.7—8.0, thereby eliminating structure (3) which possesses only three aromatic protons. We consider that the deshielding effect of the thiocarbonyl group on the appositely situated proton H-5 is consistent with the assigned formula (2) rather than the isomer (4). The n.m.r. spectrum of an alkylation product of the thione, *e.g.* the methylthio-derivative (5a), showed the proton H-5 now at δ 7.9, with the remainder of the aromatic protons (three) in the range δ 7.4—7.6. It is of interest to compare these results with those which would have been expected from the published chemistry of thiocarbonylazides,[5] where either ring closure takes place to yield thiatriazoles, or recourse is needed to photolysis of the thiatriazole to induce a rearrangement to an isothiocyanate, perhaps by way of a thioacyl azide.[6] The thione (2) was also alkylated with ethyl bromoacetate, 2-bromoethanol, and 4-bromophenacyl bromide, which yielded the *S*-substituted derivatives (5b—d) respectively.

Sulphonium ylides are known to act as nucleophiles;[7] however, no reactions of sulphimides with isothiocyanates appear to have been reported. *N*-(4-Chlorophenyl)-*SS*-dimethylsulphimide (6), prepared according to the method of Claus and Vycudilik,[8] and the diisothiocyanate (1) reacted spontaneously in acetonitrile at room temperature to give, with the elimination of dimethyl sulphide, the thiadiazolobenzimidazolethione (7). The product was probably formed by the mechanism shown in Scheme 1.



SCHEME 3

It has been reported that *o*-tolylene di-isocyanate, when treated with methanol, cyclised to the allophanoyl

derivative (8).[9] We found that the di-isothiocyanate (1) reacted with methanol, allyl alcohol, and *p*-chlorothiophenol to yield three related derivatives, (9a and b) and (10), respectively (Scheme 2).

Zbirovsky and Seifert[10] have shown that the reaction of aromatic and aliphatic isothiocyanates with chloromethanesulphonamide[11] in the presence of an equimolar amount of an alkali-metal hydroxide gave rise to 5-(substituted imino)-1,3,4-dithiazolidine 3,3-dioxides (11). The corresponding reaction of the di-isothiocyanate (1) with chloromethanesulphonamide was therefore tried. We obtained two products in similar yields (20%). The first was the benzimidazolyl disulphide (12) which was identical (m.p. and i.r.) with an authentic sample.[12] The second product analysed for $C_9H_7N_3O_2S_3$ [*m/e* 285 (M^+)] which could be represented by the dithiadiazepine (13) or the 1-substituted benzimidazoline-2-thione (14) (Scheme 3). An n.m.r. study provided the necessary proof of structure (13). The proton H-7, deshielded by the apposite thiocarbonyl group at position 5, was downfield at δ 8.3 and separate from the remainder of the aromatic protons centred at δ 7.3 indicating structure (13) rather than (14).

EXPERIMENTAL

N.m.r. spectra were obtained with a Varian HA 100 spectrometer ($SiMe_4$ internal standard). Mass spectra were measured with a Hitachi RMV 6E or A.E.I. MS9 spectrometer. M.p.s were determined with a Reichert hot-stage apparatus.

[1,2,4]*Thiadiazolo*[4,5-a]*benzimidazole*-3-*thione* (2).—A solution of the di-isothiocyanate (1) (1.74 g, 0.009 mol) in dimethoxyethane (20 ml) was added dropwise to a solution of sodium azide (0.8 g, 0.012 mol) in water–dimethoxyethane (1 : 1) (80 ml). After the initial effervescence had ceased the now cloudy solution was stirred at ambient temperature for 2 h. The solvent was evaporated off and the residue dissolved in water, filtered, then acidified with 2N hydrochloric acid, which precipitated a gelatinous solid. The *product* was filtered, washed with water and vacuum-dried (1.2 g, 64%), m.p. 175 °C (decomp.) (Found: C, 46.5; H, 2.5; N, 20.6. $C_8H_5N_3S_2$ requires C, 46.4; H, 2.4; N, 20.3%); *m/e* 207 (M^+); δ [CF_3CO_2H] 7.7—8.0 (3 H, m, H-6—8), and 8.85 (1 H, m, H-5).

General Method for Alkylation of (2).—3-*Methylthio*-[1,2,4]*thiadiazolo*[4,5-a]*benzimidazole* (5a). The thione (2) (1.5 g, 0.007 mol) was suspended in acetonitrile (15 ml) and a few drops of 2N sodium hydroxide were added to complete dissolution. Iodomethane (1.5 ml, 0.021 mol) was then added dropwise to the stirred solution. A pale yellow solid precipitated out during the addition, and after completion of the addition the mixture was stirred at ambient temperature for 1 h. The solvent was evaporated and the residue triturated with water and filtered off. The crude *product* was crystallised from methanol (0.75 g, 48%), m.p. 146 °C (Found: C, 49.0; H, 3.1; N, 18.6; S, 29.2. $C_9H_7N_3S_2$ requires C, 48.8; H, 3.2; N, 19.0; S, 28.9%); *m/e* 221 (M^+); δ [$(CD_3)_2SO$] 2.85 (3 H, s, Me), 7.4 (2 H, m, H-6, -7), 7.6 (1 H, m, H-8), and 7.9 (1 H, m, H-5).

The following compounds were prepared similarly: *compound* (5b), using 1.5 equiv. of ethyl bromoacetate, 16% yield, m.p. 164 °C (EtOH) (Found: C, 49.3; H, 3.4; N, 14.0; S, 21.5. $C_{12}H_{11}N_3O_2S_2$ requires C, 49.3; H, 3.8; N, 14.3; S, 21.8%); *m/e* 293 (M^+); δ [$CDCl_3$] 1.35 (3 H, t, Me), 4.25 (2 H, s, SCH_2), 4.3 (2 H, q, CO_2CH_2), 7.4 (2 H, m, H-6, -7), and 7.9 (2 H, m, H-5, -8): *compound* (5c), using 1.5 equiv. of 2-bromoethanol, 34% yield, m.p. 153 °C (CH_3CN) (Found: C, 48.1; H, 3.6; N, 16.8; S, 25.3. $C_{10}H_9N_3OS_2$ requires C, 47.8; H, 3.6; N, 16.7; S, 25.5%); *m/e* 251 (M^+); δ [$(CD_3)_2SO$] 3.55 (2 H, m, SCH_2), 3.8 (2 H, m, CH_2O), 5.2 (1 H, t, OH), 7.4 (2 H, m, H-6, -7), 7.8 (1 H, m, H-8), and 8.0 (1 H, m, H-5): *compound* (5d), using 1.5 equiv. of 4-bromophenacyl bromide, 40% yield, m.p. 195 °C (CH_3CN) (Found: C, 47.2; H, 2.4; N, 10.4; S, 15.5. $C_{16}H_{10}BrN_3OS_2$ requires C, 47.5; H, 2.5; N, 10.4; S, 15.8%); *m/e* 403 (M^+); δ [$CDCl_3$] 5.15 (2 H, s, CH_2), 7.6—8.0 (7 H, m, aromatics), and 8.25 (1 H, m, H-5).

2-(4-*Chlorophenyl*)[1,2,4]*thiadiazolo*[4,5-a]*benzimidazole*-3-*thione* (7).—A solution of *N*-(4-chlorophenyl)-*SS*-dimethylsulphimide[8] (1.3 g, 0.007 mol) in acetonitrile (20 ml) was added to a stirred filtered solution of the di-isothiocyanate (1) (1.3 g, 0.007 mol) in acetonitrile (20 ml). The immediate precipitate was filtered off and washed with acetonitrile which yielded the product as cream *needles* (1.3 g, 59%), m.p. 198 °C (Found: C, 52.9; H, 2.5; N, 12.9; S, 20.2. $C_{14}H_8ClN_3S_2$ requires C, 53.0; H, 2.5; N, 13.3; S, 20.1%); *m/e* 317 (M^+); δ [$(CD_3)_2SO$] 7.3 (4 H, q, non-fused aromatics), 7.4 (3 H, m, fused aromatics), and 8.2 (1 H, m, H-5).

O-*Methyl* 2-*Thioxo*-2,3-*dihydrobenzimidazole*-1-*carbothioate* (9a).—A solution of the di-isothiocyanate (1) (2.2 g, 0.01 mol) in methanol (15 ml) was refluxed for 2.5 h, cooled and the crystalline product was filtered off (1.5 g, 61%), m.p. 130—131 °C (40% aqueous MeOH) (Found: C, 48.1; H, 3.6; N, 12.0. $C_9H_8N_2OS_2$ requires C, 48.2; H, 3.6; N, 12.5%). δ [$(CD_3)_2SO$] 4.4 (3 H, s, Me) and 7.2—7.8 (5 H, m, aromatics + NH).

Similarly prepared was (9b) using allyl alcohol, in 60% yield, m.p. 159 °C (cyclohexane) (Found: C, 52.9; H, 3.9; N, 11.1. $C_{11}H_{10}N_2OS_2$ requires C, 52.8; H, 4.0; N, 11.2%); *m/e* 250; δ [$CDCl_3$] 3.75 (2 H, d, OCH_2), 5.35 (2 H, m, $=CH_2$), 6.0 (1 H, m, CH), 7.25 (3 H, m, H-4—6), and 8.2 (1 H, m, H-7).

4-*Chlorophenyl* 2-*Thioxo*-2,3-*dihydrobenzimidazole*-1-*carbodithioate* (10).—A filtered solution of the di-isothiocyanate (1) (0.89 g, 0.004 6 mol) in acetonitrile (15 ml) was added to a solution of 4-chlorothiophenol (0.67 g, 0.004 6 mol) in acetonitrile (10 ml) and the resulting solution was left at ambient temperature for 4 days. The product was then filtered off as orange prismatic *needles* (0.3 g, 20%), m.p. 165—166 °C (Found: C, 49.7; H, 2.6; N, 8.4. $C_{14}H_9ClN_2S_3$ requires C, 50.0; H, 2.6; N, 8.3%); δ [$(CD_3)_2SO$] 7.2 (4 H, m, fused aromatics) and 7.55 (5 H, s, benzenoid aromatics + NH).

5-*Thioxo*-4,5-*dihydro*-2H-*benzimidazo*[1,2-d][1,6,2,4]-*dithiadiazepine* 3,3-*Dioxide* (13).—Chloromethanesulphonamide[11] (2.0 g, 0.015 5 mol) was added to a filtered solution of the di-isothiocyanate (1) (3.0 g, 0.015 5 mol) in acetone (75 ml). Then a solution of sodium hydroxide (0.9 g, 0.023 mol) in water (9 ml) was added dropwise to the stirred solution which darkened, and stirring was continued for 18 h at ambient temperature. The white solid which precipitated was filtered off and washed with acetone to yield the *disulphide* (12) (0.8 g, 18%). The m.p. (230 °C) and i.r. spectrum of the disulphide were identical to those of an authentic sample.[12] The filtrate was acidified with 1N hydrochloric acid and the pink precipitated *product* was filtered off, washed with water, and dried (0.9 g, 20%), m.p. 285—290 °C (Found C, 38.4; H, 2.5; N, 14.6. $C_9H_7N_3$-

O_2S_3 requires C, 38.9; H, 2.5; N, 14.7%), *m/e* 285 (M^+); δ [$(CD_3)_2SO$] 4.8 (2 H, s, CH_2), 7.3 (3 H, m, H-8—10), and 8.3 (1 H, m, H-7).

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