Synthesis of Thiazolidine-2,5-dithiones: Characterisation of 4-Substituted Thiazolidinedithiones

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A general method for the synthesis of a series of 4,4-disubstituted thiazolidine-2,5-dithiones (**1**)–(**6**) initially consisted in reactions of α-metallated aralkyl isothiocyanates with carbon disulphide. 4-Monosubstituted thiazolidine-2,5-dithiones (**7**)–(**9**) are very susceptible to oxidation, changing rapidly into their oxidative dimers. The reason for the unexpected methylation of thiazolidine dithiones (**7**)–(**9**) became evident from the results of MNDO calculations.

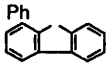
Very little is known about the title compounds, thiazolidine-2,5-dithiones, while considerable information is available on isomeric thiazolidine-2,4-dithiones. Shahak *et al.*[1] studied the reactions of *N,N*-dibenzyl-α-amino acid amides and carbon disulphide in the presence of sodium hydride and isolated thiazolidinedithiones among other products. The yields by this method, however, are fair to poor except for one case. Shahak's method for the title compounds appears to be the only synthetic method currently available but is applicable only to the synthesis of 4-acylthiazolidine-2,5-dithiones. Schaumann[2] reported that 4,4-dimethylthiazolidine-2,5-dithione could be obtained in 45% yield by treatment of the 1:1 adduct of 3-dialkylamino-2,2-dimethyl-2*H*-azirine and carbon disulphide with hydrogen sulphide. The chemical properties of the parent and 4-monosubstituted thiazolidine-2,5-dithiones are apparently unknown.

In our study on the reactions of 1,3-thiazine-2,6-dithiones with thioureas[3] or β-imino nitriles[4] in the presence of sodium 1,1-dimethylpropanolate, it appeared that prior to reactions with these reactants the ring opening of 4-aryl-1,3-thiazine-2,6-dithiones by a base occurs to produce 3-isothiocyanatodithiocinnamate as a reactive intermediate. This in turn reacts with the thioureas and β-imino nitriles to give reaction intermediates, followed by the formation of new heterocyclic products. The possibility thus occurred to us that thiazolidinedithiones may be synthesized from α-metallated alkyl isothiocyanates and carbon disulphide. The carbanions were used for the synthesis of 2-thioxo-oxazolidines.[5,6]

The present study describes a general and simple synthesis of 4,4-disubstituted thiazolidine-2,5-dithiones (**1**)–(**6**) and 4-substituted thiazolidine-2,5-dithiones (**7**)–(**9**) by reactions of carbanions from isothiocyanates bearing one or two α-hydrogens with carbon disulphide. The methylation of 4-substituted thiazolidinedithiones is discussed and the results of MNDO calculations are also presented.

When a mixture of α-methylbenzyl isothiocyanate and carbon disulphide was added dropwise to a stirred suspension of potassium t-butoxide in tetrahydrofuran (THF) under N_2, 4-methyl-4-phenylthiazolidine-2,5-dithione (**1**) was obtained as light orange crystals in high yield. Compounds (**2**)–(**6**) were also synthesized similarly in high yield.

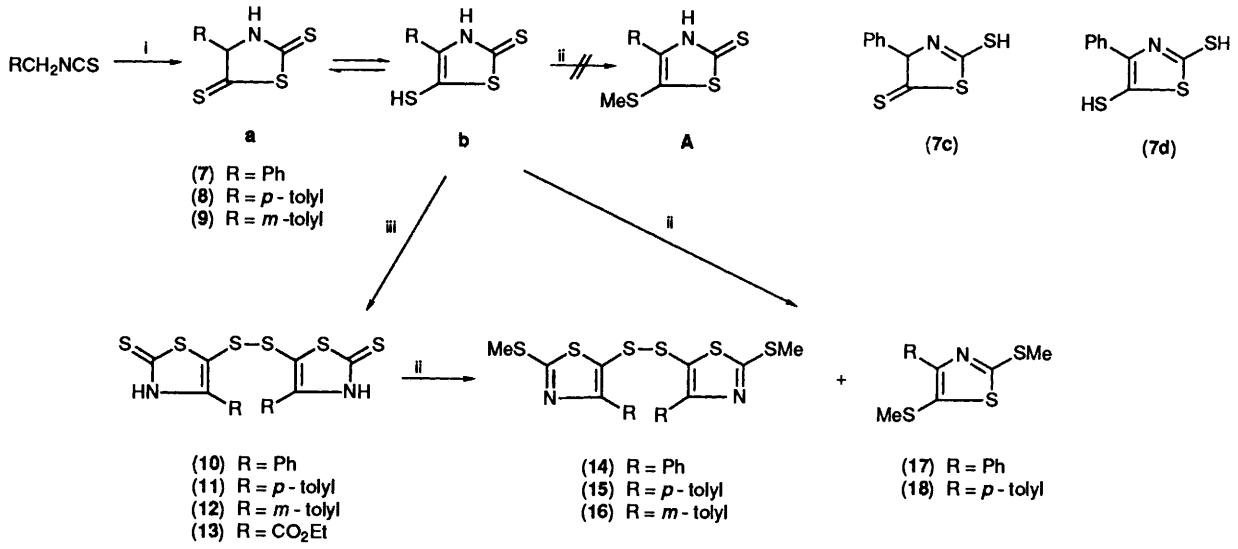
Aliphatic isothiocyanates such as isopropyl isothiocyanate and its alkyl homologues, even when treated as above with lithium 2,2,6,6-tetramethylpiperidide (LiTMP), never reacted with carbon disulphide to give 4,4-dialkylthiazolidine-2,5-dithiones, possibly because α-lithio-(α-alkyl)aliphatic isothiocyanates were not formed. 4-Methoxy-α-methylbenzylisothiocyanate also hardly underwent this reaction. It is known that methyl isothiocyanate is not metallated by potassium t-butoxide and only to a limited extent by LiTMP.[6] In this study, it was not possible to obtain even trace amounts of the expected thiazolidinedithione by reaction of methyl isothiocyanate with carbon disulphide in the presence of LiTMP. In contrast, aralkyl isothiocyanates such as benzyl, 4-methyl-, and 3-methylbenzyl isothiocyanates on treatment with carbon disulphide in the presence of potassium t-butoxide at −78 °C gave the expected 4-arylthiazolidine-2,5-dithiones (**7**)–(**9**) which, immediately following isolation, showed an SH stretching absorption band at *ca.* 2 395 cm^{-1} (KBr). Compounds (**7**)–(**9**) were very susceptible to oxidation since they favoured the enethiol form, and they were changed into oxidative dimers (**10**)–(**13**) on attempted purification by recrystallisation.

(**1**) R^1 = Me, R^2 = Ph
(**2**) R^1 = Me, R^2 = *p*-tolyl
(**3**) R^1 = Me, R^2 = 2-naphthyl
(**4**) R^1 = Et, R^2 = Ph
(**5**) R^1 = R^2 = Ph
(**6**) R^1 = R^2 = 

Reagents: CS_2, $C_4H_9{}^tOK$, THF.

All attempts to obtain 5-methylthiothiazol-2(3*H*)-thiones (**A**) by methylation of compounds (**7**)–(**9**) with methyl iodide in the presence of triethylamine were unsuccessful. Instead, only bis-(2-methylthiothiazol-5-yl) disulphides (**14**)–(**16**), methyl derivatives of compounds (**10**)–(**12**), were obtained (Scheme). In some cases, these methyl derivatives were accompanied by dimethyl derivatives, *viz.* 2,5-bis(methylthio)thiazoles (**17**) and (**18**). Compound (**9**), in spite of our repeated attempts, did not form the 2,5-dimethylthio derivative at all by this methylation reaction, but instead gave compound (**16**) as the sole product.

To explain this abnormal behaviour of compounds (**7**)–(**9**) on methylation, MNDO calculations for compound (**7**) were carried out. Calculations of the heat of formation of 4-phenylthiazolidine-2,5-dithione (**7a**), 5-mercapto-4-phenylthiazole-2(3*H*)-thione (**7b**), 2-mercapto-4-phenylthiazole-5(4*H*)-thione (**7c**), and 2,5-dimercapto-4-phenylthiazole (**7d**) by



Scheme. *Reagents:* i, CS_2, $C_4H_9{}^tOK$, THF; ii, MeI, NEt_3, EtOH; iii, [O].

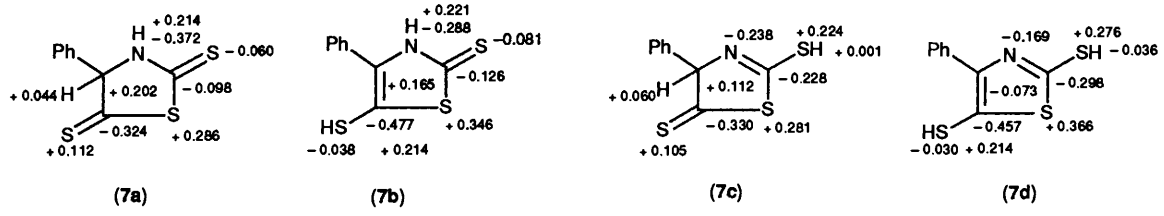
MNDO indicated tautomer (**7d**), in the gas phase, to be the most stable tautomer and (**7b**) to be the second-most stable tautomer, though the energy difference between isomers (**7b**) and (**7d**) is only 16.2 kJ mol^{-1}. It also became evident that the charge distribution of both of mercapto-sulphurs and imino-hydrogen in compounds (**7b**) and (**7d**) is positive, while those of mercapto-hydrogens are all negative. In view of the results of these calculations and their IR spectra and chemical reactions, the predominant structure of compound (**7**) was thus concluded to be 5-mercaptothiazole-2(3*H*)-thione (**7b**) in solution and it also became clear that the mercapto-sulphur of compound (**7b**) is electron deficient. Furthermore, the calculation revealed that 5-mercapto-4-phenylthiazole-2-thiolate anion is the most stable (see Table) and that the tautomer (**7c**) is also negligible because its ΔH_f-value is 49.0 kJ higher than that of tautomer (**7b**). These conclusions and findings are quite consistent with the fact that tautomer (**7b**) is not methylated by methyl iodide under charge control conditions. The charge distribution of the thiocarbonyl-sulphur of compound (**7b**) was only slightly negative (−0.081) but calculation of electron densities showed the highest

Table. Calculated heats of formation of the tautomers of compound (**7**) and their thiolate anions.

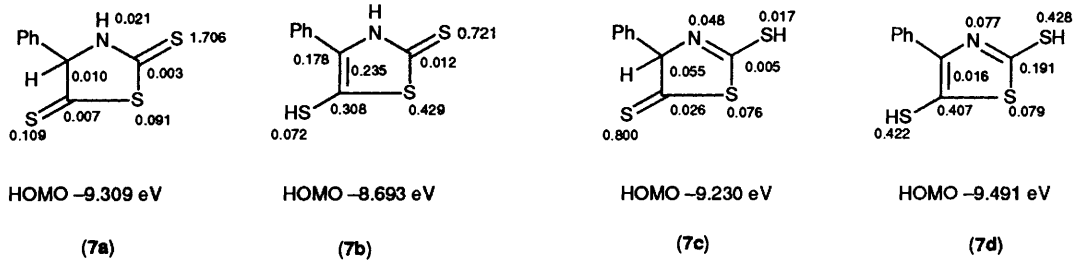
Tautomer	Neutral (kJ mol^{-1})	2-Thiolate anion[a] (kJ mol^{-1})
(**7a**)	317.5	—
(**7b**)	252.4	(84.1)
(**7c**)	301.4	130.5
(**7d**)	236.2	51.4 (54.0)

[a] ΔH_f for 5-thiolate anion are given in parentheses.

Atomic charge distributions



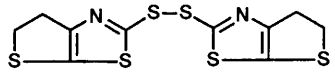
Electron densities of HOMO



MNDO calculations. Atomic charge distributions and electron densities of HOMO

distribution for electron density of the HOMO to be an unshared pair of electrons on the thiocarbonyl-sulphur at the 2-position in (**7a**) (1.706), π-electrons of the thiocarbonyl-sulphur at the 2-position in (**7b**) (0.721), and π-electrons of the thiolate-sulphur in the 2-thiolate anion of (**7d**). These calculation results are also quite consistent with the experimental data.

Allyl isothiocyanate, under the same reaction conditions, gave a large quantity of an unidentified solid containing a small quantity of compound (**19**): it was tentatively assigned as bis-(4,5-dihydrothieno[3,2-*d*]thiazol-2-yl) disulphide from elemental analysis, and IR and mass spectra. Compound (**19**) was insoluble in almost organic solvents but not in hot dimethylacetamide, which gradually decomposes it.



(**19**)

δ-Values in the ^{13}C NMR spectra for thiocarbonyl carbon at the 5-position in compounds (**1**)–(**6**) ranged from δ_C 235–236.3 and were significantly more downfield than those of other thiocarbonyl carbons at the 2-position in the same compounds (**1**)–(**6**) (δ *ca.* 193). Other spectral data for compounds (**1**)–(**6**) showed complete agreement with the proposed structure.

Application of these thiazolidine-2,5-dithiones to the synthesis of fused hetero-ring compounds with various reagents will be reported elsewhere.

Experimental

M.p.s were determined on a YANAGIMOTO micro melting point apparatus and are uncorrected. NMR spectra were determined with a JNM-GX270-FT-NMR spectrometer at 270 MHz with tetramethylsilane as internal standard. IR spectra were determined with a JASCO A-302 spectrophotometer. Electronic spectra were obtained on a Hitachi 557 double-wavelength double-beam spectrophotometer. Mass spectra were determined on a JEOL JMS-DX 300 mass spectrometer.

Materials.—1-Phenylethyl,[7] 1-(2-naphthyl)ethyl,[8] 1-phenylpropyl,[9] 1,1-diphenylmethyl,[10] and fluoren-9-yl[11] isothiocyanates were prepared by Jochims' method.[12] 1-(*p*-Tolyl)ethyl isothiocyanate was previously unknown and was prepared by the usual method[12] for known alkyl isothiocyanates; yield 70% (fractional distillation), b.p. 130 °C/7 mmHg; ν_{max}(KBr) 3 020, 2 970, 2 100vs, 1 522, 1 452, 1 381, 1 340, 1 314s, 1 025, and 816s cm^{-1}; $\delta_H(CDCl_3)$ 7.11 (4 H, *ca.* s, ArH), 4.78 (1 H, q, *J* 7 Hz, 1-H), 2.29 (3 H, s, Ar*Me*), and 1.58 (3 H, d, *J* 7 Hz, 1-Me).

3- And 4-methylbenzyl isothiocyanates[13] were also prepared by the literature procedure.[12]

Preparation of 4,4-*Disubstituted Thiazolidine*-2,5-*dithiones* (**1**)–(**6**).—To a stirred suspension of potassium t-butoxide (6.2 g, 0.055 mol) in THF (90 ml) cooled to −78 °C was added dropwise to a mixture of a 1-arylalkyl isothiocyanate (0.050 mol), carbon disulphide (5.7 g, 0.075 mol), and THF (20 ml). The mixture was kept for 20 min at −78 °C and for an additional 16 h at room temperature. Water (200 ml) and diethyl ether (100 ml) were added to the reaction mixture and the aq. layer was separated, washed twice with diethyl ether, and then any ether remaining in the aq. layer was removed under diminished pressure. A small amount of corresponding thiazolidinedithione which separated out was collected and the aq. layer was acidified (pH *ca.* 1) with 2M-HCl to give a red oil which solidified after a short time. The solid was collected, washed with water, and dried. The above ethereal layer and the ethereal washings were combined, washed with water, dried ($MgSO_4$), and evaporated to dryness to afford some crystals which were collected and washed with hexane to give a thiazolidinedithione. Each thiazolidinedithione was recrystallised to give pure crystals.

4-*Methyl*-4-*phenylthiazolidine*-2,5-*dithione* (**1**). Yield 70%, m.p. 114 °C [from benzene–hexane (1:1)]; ν_{max}(KBr) 3 090, 2 950, 2 830w, 1 500s, 1 448, 1 436, 1 363, 1 338, 1 215, 1 200, 1 125, 1 110, 1 013, and 916 cm^{-1}; λ_{max}(EtOH) 316 (log ε 4.13), 480 (2.13), and 509 nm (1.93); $\delta_H(CDCl_3)$ 13.609 (1 H, br s, NH), 7.5 (5 H, m, Ph), and 2.364 (3 H, s, Me); $\delta_C(CDCl_3)$ 235.44, 193.39, 139.04, 129.06, 125.33, 87.69, and 27.94 (Found: C, 50.1; H, 3.8; N, 6.1; S, 40.0. $C_{10}H_9NS_3$ requires C, 50.2; H, 3.8; N, 5.9; S, 40.2%).

4-*Methyl*-4-(p-*tolyl*)*thiazolidine*-2,5-*dithione* (**2**). Yield 77%, m.p. 131 °C (from benzene); ν_{max}(KBr) 3 070, 2 930, 2 820, 1 508s, 1 446, 1 435, 1 210, 1 188, 1 119s, 1 030s, 955, and 921 cm^{-1}; λ_{max}(EtOH) 270 (4.16), 316 (4.11), 486 (1.73), and 506 nm (1.66); $\delta_H(CDCl_3)$ 9.13 (1 H, br s, NH), 7.32 (2 H, d, *J* 8 Hz, ArH), 7.18 (2 H, d, *J* 8 Hz, ArH), 2.30 (3 H, s, Me), and 2.02 (3 H, s, C_6H_4Me); $\delta_C(CDCl_3)$ 236.08, 193.38, 139.26, 136.35, 129.81, 125.28, 87.62, 28.00, and 21.06 (Found: C, 52.3; H, 4.4; N, 5.7; S, 38.0. $C_{11}H_{11}NS_3$ requires C, 52.1; H, 4.4; N, 5.5; S, 37.9%).

4-*Methyl*-4-(2-*naphthyl*)*thiazolidine*-2,5-*dithione* (**3**). Yield 88%, m.p. 138.5 °C (from benzene); ν_{max}(KBr) 3 080, 2 930, 2 815, 1 600w, 1 500s, 1 451, 1 370, 1 337, 1 272w, 1 183w, 1 111s, 1 020s, 950, and 918 cm^{-1}; λ_{max}(EtOH) 272.5 (4.36) and 310 nm (4.14); $\delta_H(CDCl_3)$ 9.15 (1 H, br s, NH), 7.7 (7 H, m, $C_{10}H_7$), and 2.11 (3 H, s, Me); $\delta_C(CDCl_3)$ 235.50, 193.48, 136.35, 133.12, 132.81, 129.26, 128.50, 127.62, 127.24, 126.92, 124.77, 122.81, 87.76, and 27.97 (Found: C, 58.0; H, 3.9; N, 4.9; S, 33.1. $C_{14}H_{11}NS_3$ requires C, 58.0; H, 3.8; N, 4.8; S, 33.2%).

4-*Ethyl*-4-*phenylthiazolidine*-2,5-*dithione* (**4**). Yield 81%, m.p. 105–106 °C [from benzene–hexane (1:10)]; ν_{max}(KBr) 3 100, 2 950, 2 800w, 1 500s, 1 430, 1 377, 1 338, 1 303, 1 182, 1 123, 1 036, and 999 cm^{-1}; λ_{max}(EtOH) 272 (4.36), 311 (4.14), 488 (1.71), and 150 nm (1.65); $\delta_H(CDCl_3)$ 9.248 (1 H, br s, NH), 7.4 (5 H, m, Ph), 2.631 (1 H, dq, *J* 14.6 and 7.3 Hz, C*H*H), 2.391 (1 H, dq, *J* 14.6 and 7.3 Hz, CH*H*), and 1.057 (3 H, t, *J* 7.3 Hz, Me); $\delta_C(CDCl_3)$ 235.04, 194.70, 138.63, 129.15, 125.51, 91.78, 34.50, and 8.22 (Found: C, 52.0; H, 4.2; N, 5.6; S, 38.2. $C_{11}H_{11}NS_3$ requires C, 52.1; H, 4.4; N, 5.5; S, 37.9%).

4,4-*Diphenylthiazolidine*-2,5-*dithione* (**5**). Yield 97%, m.p. 225–226.5 °C (from EtOH); ν_{max}(KBr) 3 090, 2 940, 2 800w, 1 500s, 1 441, 1 339, 1 181, 1 088, 1 064s, 1 029, and 996 cm^{-1}; λ_{max}(EtOH) 273 (4.23), 324 (4.07), and 506 nm (2.23); $\delta_H[(CD_3)_2SO]$ 12.638 (1 H, br s, NH) and 7.4 (10 H, m, 2 × Ph); $\delta_C[(CD_3)_2SO]$ 236.31, 189.96, 139.66, 129.60, 127.22, 126.45, and 91.78 (Found: C, 59.5; H, 3.5; N, 4.7; S, 31.6. $C_{15}H_{11}NS_3$ requires C, 59.8; H, 3.7; N, 4.7; S, 31.9%).

Fluorene-9-*spiro*-4′-*thiazolidine*-2′,5′-*dithione* (**6**). Yield 32%, m.p. 203.5 °C [from benzene–hexane (1:1)]; ν_{max}(KBr) 3 210, 1 600w, 1 485s, 1 460s, 1 450, 1 319, 1 283, 1 188, 1 185, 1 080s, 1 049, 999, 942, and 900 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 12.079 (1 H, br s, NH), 7.852 (2 H, d, *J* 7.7 Hz, 1- and 8-H), 7.487 (2 H, d, *J* 7.7 Hz, 4- and 5-H), 7.473 (2 H, t, *J* 7.7 Hz, 2- and 7-H), and 7.349 (2 H, d, *J* 7.7 Hz, 3- and 6-H); $\delta_C[(CD_3)_2SO]$ 234.81, 191.98, 139.92, 130.35, 128.84, 123.65, 120.78, and 94.51 (Found: C, 60.5; H, 3.1; N, 4.4; S, 32.2. $C_{15}H_9NS_3$ requires C, 60.2; H, 3.0; N, 4.7; S, 32.1%).

Preparation of 4-*Substituted Thiazolidine*-2,5-*dithiones* (**7a**)–(**9a**) *or their Tautomers* 5-*Mercaptothiazol*-2(3H)-*thiones* (**7b**)–(**9b**).—These compounds (**7**)–(**9**) were also prepared similarly to compounds (**1**)–(**6**) (the same molar ratio of reactants and conditions). To the reaction mixture was added water (100 ml)

and the aq. solution was washed three times with diethyl ether. The ether remaining in the aq. solution was removed under diminished pressure and then the solution was neutralised to separate orange solids, which were collected, and washed successively with water and ethanol. Because of their extreme susceptibility to oxidation, O_2-free water and 2M-HCl, and peroxide-free diethyl ether were used for above work-up procedures. Compounds (**7**)–(**9**) could not be purified. Only IR spectra of compounds (**7**)–(**9**) were determined immediately after separation. From the IR spectra, predominant forms for these compounds are enethiolic 5-mercaptothiazole-2(3*H*)-thiones. Compounds (**7**)–(**9**) are stable thermally and can be stored in sealed tubes in the dark for over five years.

4-*Phenylthiazolidine*-2,5-*dithione* (**7a**) *or* 5-*Mercapto*-4-*phenylthiazole*-2(3H)-*thione* (**7b**). Crude yield 70%, ν_{max}(KBr) 3 050, 2 960, 2 860, 2 720w, 2 395m, 1 580w, 1 550m, 1 494s, 1 460vs, 1 429, 1 330, 1 260, 1 244, 1 072vs, 757vs, 681vs, and 595vs cm^{-1}.

4-(p-*Tolyl*)*thiazolidine*-2,5-*dithione* (**8a**) *or* 5-*mercapto*-4-(p-*tolyl*)*thiazole*-2(3H)-*thione* (**8b**). Crude yield 59%, ν_{max}(KBr) 3 050, 2 850, 2 310w, 1 608, 1 575w, 1 550w, 1 503vs, 1 460vs, 1 439, 1 238, 1 062vs, 815s, 685, and 608vs cm^{-1}.

4-(m-*Tolyl*)*thiazolidine*-2,5-*dithione* (**9a**) *or* 5-*mercapto*-4-(m-*tolyl*)*thiazole*-2(3H)-*thione* (**9b**). Crude yield 62%, ν_{max}(KBr) 2 720w, 2 385, 1 560, 1 459vs, 1 270, 1 091, 1 005, and 782 cm^{-1}.

These crude compounds (**7**)–(**9**) may contain their corresponding oxidative dimers, bis-(4-substituted 2,3-dihydro-2-thioxothiazol-5-yl) disulphides to some extent: re-extraction of crude compounds (**7**)–(**9**) with dilute, O_2-free, aq. sodium hydroxide followed by reneutralisation with distilled, dil. hydrochloric acid (2M) gave rather impure monomers.

Oxidative Dimerisation of Compounds (**7**)–(**9**).—For example, crude compound (**7**) was dissolved in dimethylformamide (DMF)–acetone (1:1) and to this solution was added half its volume of water. Orange crystals which separated out from the solution were collected, washed with acetone–water, and dried ($CaCl_2$) to give *bis*(4-*phenyl*-2-*thioxo*-2,3-*dihydrothiazol*-5-*yl*) *disulphide* (**10**) (80%), m.p. 213–214 °C [from DMF–acetone–water (1:1:1)]; ν_{max}(KBr) 3 045, 2 960, 2 850, 1 550, 1 488, 1 447, 1 428, 1 242, 1 062, and 1 003 cm^{-1}; λ_{max}(EtOH) 311 (4.34) and 407 nm (4.06); δ_H[$(CD_3)_2SO$] 13.656 (2 H, br s, 2 × NH) and 7.41 (10 H, s, 2 × Ph) (Found: C, 48.3; H, 2.8; N, 6.4; S, 42.7. $C_{18}H_{12}N_2S_6$ requires C, 48.2; H, 2.7; N, 6.2; S, 42.9%).

Other oxidative dimers (**11**) and (**12**) were also obtained by a similar procedure.

Bis-[4-(p-*tolyl*)-2-*thioxo*-2,3-*dihydrothiazol*-5-*yl*] *disulphide* (**11**). Yield 80%, m.p. 211.5–212.5 °C [from DMF–acetone–water (1:1:2)]; ν_{max}(KBr) 3 045, 2 955, 2 840, 1 550, 1 485, 1 448s, 1 427s, 1 326, 1 242s, 1 061, 1 022, 1 000, and 910 cm^{-1}; λ_{max}(EtOH) 271 (4.26), 309 (4.28), 349 (4.01), and 407 nm (4.05); δ_H[$(CD_3)_2SO$] 13.68 (2 H, br s, 2 × NH), 7.27 (8 H, s, 2 × C_6H_4, and 2.39 (6 H, s, 2 × Me) (Found: C, 50.5; H, 3.4; N, 6.2; S, 40.1. $C_{20}H_{16}N_2S_6$ requires C, 50.4; H, 3.4; N, 5.9; S, 40.4%).

Bis-[4-(m-*tolyl*)-2-*thioxo*-2,3-*dihydrothiazol*-5-*yl*] *disulphide* (**12**). Yield 62%, m.p. 226–227 °C [from DMF–acetone–water (3:1:3)]; ν_{max}(KBr) 3 045, 2 960, 2 850, 1 550, 1 483, 1 450s, 1 242s, 1 069, and 1 015 cm^{-1}; δ_H[$(CD_3)_2SO$] 13.55 (2 H, br s, 2 × NH), 7.25 (8 H, s, 2 × C_6H_4), and 2.38 (6 H, s, 2 × Me) (Found: C, 50.2; H, 3.5; N, 6.2; S, 40.1. $C_{20}H_{16}N_2S_6$ requires C, 50.4; H, 3.4; N, 5.9; S, 40.4%).

Bis-[4-(*ethoxycarbonyl*)-2-*thioxo*-2,3-*dihydrothiazol*-5-*yl*] *disulphide* (**13**). Compound (**13**) was obtained directly by the reaction of ethyl isothiocyanatoacetate[14] with carbon disulphide. The molar ratio of the reactants, reaction conditions and work-up procedures were similar to those for compounds (**1**)–(**6**). Compound (**13**) was prepared in 33% yield, m.p. 212–213°C [from DMF–acetone–water (1:1:2)]; ν_{max}(KBr) 3 050, 2 980, 2 880, 1 709s, 1 550s, 1 458s, 1 371, 1 332s, 1 288, 1 204, 1 085, and 1 022 cm^{-1}; (Found: C, 32.8; H, 2.8; N, 6.1. $C_{12}H_{12}N_4O_4S_6$ requires C, 32.7; H, 2.8; N, 6.4%).

Methylation of Oxidative Dimers. Formation of Bis-(4-*aryl*-2-*methylthiothiazol*-5-*yl*) *Disulphides* (**14**)–(**16**).—*General procedure.* To a mixture of an oxidative dimer (5 mmol), triethylamine (111 mg, 11 mmol), and ethanol (10 ml) was added methyl iodide (142 mg, 10 mmol). The red colour of the mixture faded away and yellow crystals separated out. A small quantity of water was added carefully to the mixture, then the crystals were collected, washed with water, dried ($CaCl_2$), and recrystallised.

Bis-[2-*methylthio*-4-(*phenyl*)*thiazol*-5-*yl*] *disulphide* (**14**). Pale yellow prisms (80.5%), m.p. 126 °C (from hot EtOH); ν_{max}(KBr) 1 470s, 1 433, 1 388, 1 310, 1 290, 1 267, 1 066, 1 039s, 960, and 903 cm^{-1}; λ_{max}(EtOH) 260 (4.41) and 363 nm (3.98); δ_H ($CDCl_3$) 7.70 (10 H, m, 2 × Ph) and 2.60 (6 H, s, 2 × SMe) (Found: C, 50.4; H, 3.4; N, 5.7; S, 39.9. $C_{20}H_{16}N_2S_6$ requires C, 50.4; H, 3.4; N, 5.9; S, 40.4%).

Bis-[2-*methylthio*-4-(p-*tolyl*)*thiazol*-5-*yl*] *disulphide* (**15**). Pale yellow prisms (65.5%), m.p. 134.0–135.5 °C [from acetone–water (5:1)]; ν_{max}(KBr) 1 609w, 1 500w, 1 470, 1 397, 1 309, 1 288, 1 250, 1 180, 1 110, and 1 032 cm^{-1} (Found: C, 52.8; H, 4.3; N, 5.8; S, 38.1. $C_{22}H_{20}N_2S_6$ requires C, 52.3; H, 4.0; N, 5.6; S, 38.2%).

Bis-[2-*methylthio*-4-(m-*tolyl*)*thiazol*-5-*yl*] *disulphide* (**16**). Golden yellow plates (28%), m.p. 111–112 °C [from EtOH–water (4:1)]; ν_{max}(KBr) 1 600w, 1 500w, 1 469s, 1 429, 1 400s, 1 307, 1 265, 1 207, 1 122, 1 098, 1 040s, 962, and 911 cm^{-1}; λ_{max}(EtOH) 261 (4.34), 296sh (4.01), and 363 nm (3.86) (Found: C, 52.1; H, 4.0; N, 5.7; S, 37.9. $C_{22}H_{20}N_2S_6$ requires C, 52.3; H, 4.0; N, 5.6; S, 38.2%).

Methylation of 4-*Monosubstituted Thiazolidine*-2,5-*dithiones. Formation of* 2,5-*Bis*(*methylthio*)-4-*arylthiazoles* (**17**) *and* (**18**).—For example, a mixture of crude 4-phenylthiazolidine-2,5-dithione (**7**) (1.125 g, 5 mmol), triethylamine (1.01 g, 10 mmol), and methyl iodide (1.50 g, 10.3 mmol) was kept at room temperature for 10 min. To the colourless reaction mixture was added ice (10 g) and the mixture was extracted with methylene dichloride (10 ml × 3). The extracts were combined, dried over magnesium sulphate, and evaporated to separate a pale yellow solid and an oil. The solid was collected, and washed successively with ethanol and hexane to give compound (**14**) (5%).

The above mixture of the oil and washings was evaporated and the remaining oil was distilled *in vacuo* to give 2,5-*bis*(*methylthio*)-4-*phenylthiazole* (**17**) as an oil (63%), b.p. 158 °C/0.11 Torr; ν_{max}(KBr) 3 054, 2 990w, 2 910, 1 600w, 1 577w, 1 503w, 1 468vs, 1 438vs, 1 412s, 1 313, 1 293, 1 265, 1 129, 1 073, 1 055, 1 038vs, 967s, 915w, and 840 cm^{-1} (Found: C, 52.1; H, 4.4; N, 5.4. $C_{11}H_{11}NS_3$ requires C, 52.1; H, 4.4; N, 5.5%).

2,5-*Bis*(*methylthio*)-4-(p-*tolyl*)*thiazole* (**18**). Compound (**18**) was also obtained similarly by distillation of the oily product *in vacuo* from which compound (**15**) (48%) was removed. *Compound* (**18**) was obtained in (32%) yield, b.p. 192 °C/0.22 Torr; ν_{max}(KBr) 3 054w, 3 010, 2 980, 2 915s, 1 606w, 1 568w, 1 519, 1 467vs, 1 428s, 1 410s, 1 312, 1 290, 1 260w, 1 184, 1 129w, 1 113, 1 052, 1 033vs, 963, 848w, and 820vs cm^{-1}; δ_H($CDCl_3$) 7.86 (2 H, d, *J* 9 Hz, ArH), 7.22 (2 H, d, *J* 9 Hz, ArH), 2.68 (3 H, s, Me), 2.38 (3 H, s, C_6H_4*Me*), and 2.37 (3 H, s, SMe); δ_C($CDCl_3$) 165.9, 155.1, 138.1, 129.4, 129.3, 128.8, 128.6, 21.9, 21.3, and 16.3 (Found: C, 53.8; H, 4.2; N, 5.1. $C_{12}H_{13}NS_3$ requires C, 53.9; H, 4.3; N, 5.2%).

Compound (**9**) never formed a 2,5-bis(methylmercapto)

derivative by this methylation reaction, but instead gave compound (**16**) as the sole product in 17% yield.

Bis-(5,6-*dihydrothieno*[3,2-*d*]*thiazol*-2-*yl*) *Disulphide* (**19**).—To a stirred mixture of potassium t-butoxide (6.8 g, 61 mmol) and THF (70 ml) at −78 °C was added dropwise a solution of allyl isothiocyanate (5.0 g, 51 mmol) and carbon disulphide (5.8 g, 76 mmol) in THF (30 ml). The resulting mixture was kept at −78 °C for an additional 30 min, then at room temperature for 20 h. Water (100 ml) was added to the reaction mixture and the aq. layer was washed twice with diethyl ether and was then acidified with 2M-HCl to give a pale yellow solid, which was extracted with 2M-NH_4OH and the combined aq. extracts were saturated with NaCl to precipitate a pale yellow solid, which was dissolved in water. This solution was again acidified with 2M-HCl to give a pale yellow solid, which was collected and recrystallised from hot dimethylacetamide to give *compound* (**19**) as pale yellow crystals (0.88 g, 5%), m.p. >300 °C; ν_{max}(KBr) 3 070, 2 995, 2 870, 1 574, 1 462vs, 1 332, 1 270, 1 091vs, 1 026, 960, and 680 cm^{-1}; *m*/*z* 348 (M^+, 87%) and 174 (M^+/2, 100) (Found: C, 34.5; H, 2.3; N, 7.8; S, 55.5. $C_{10}H_8N_2S_6$ requires C, 34.5; H, 2.3; N, 8.0; S, 55.2%). The NMR spectrum could not be measured because compound (**19**) did not dissolve in any NMR solvent.

Calculations.—Calculations were carried out on Fuji-tsu FACOM M 360 (Josai University) computers by using the MNDO program QCPE #549.[15]

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