vic-Iodothiocyanates and Iodoisothiocyanates. Part 5.[1] Reactions of Iodoisothiocyanates with Sulphur Nucleophiles

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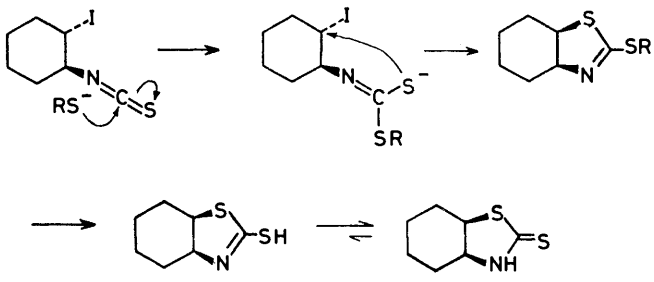
The reactions of *vic*-iodoisothiocyanates with some sulphur nucleophiles to form either 2-sulphur-substituted 2-thiazolines or thiazolidine-2-thiones are reported. The thiazolidine-2-thione (10) is an effective sulphur-transfer agent for the conversion of oxirans into the corresponding thiirans.

In earlier Parts [1,2] we reported the reactions of *vic*-iodoisothiocyanates with oxygen, nitrogen, and carbon nucleophiles. In a continuation of this study we now report reactions of *vic*-iodoisothiocyanates with some sulphur nucleophiles to form 2-sulphur-substituted 2-thiazolines or thiazolidine-2-thiones. The former are important in the field of β-lactam antibiotic synthesis [3] and have also been developed as reagents for the iodomethylation [4] and *trans*-propenylation [5] of alkyl halides *via* their corresponding 2-alkylthiazolinyl-lithium derivatives. Thiazolidine-2-thiones have been used as sulphur-transfer agents in the conversion of oxirans into thiirans.[6,7] Hackler and Balko [8] have recently reported the synthesis of 2-sulphur-substituted 2-thiazolines from the reaction of thiols with 1-chloro-2-isothiocyanatoethane.

Reactions of the readily available substrate, *trans*-1-iodo-2-isothiocyanatocyclohexane (1) with butane- and benzene-thiols (Scheme 1) are summarized in Table 1.



Scheme 1

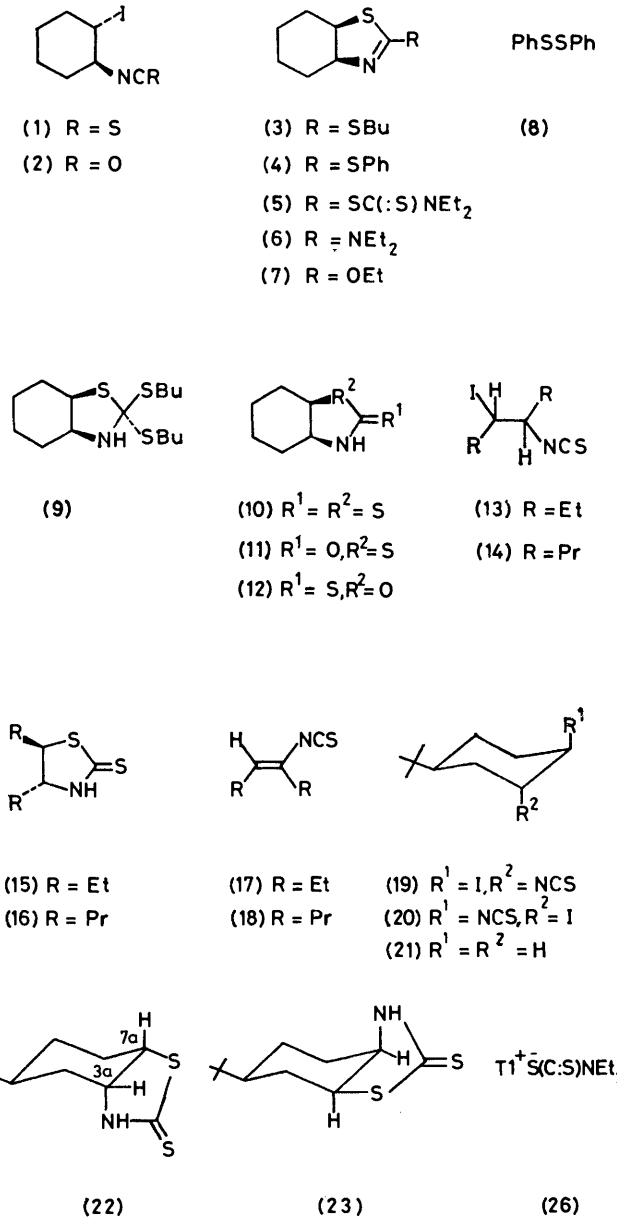
Treatment of (1) with an excess of butanethiol at 20 °C for 92 h gave only a low yield (7%) of the 2-butylthio-2-thiazoline (3). However, with the inclusion of triethylamine to convert the thiol into its thiolate anion,[9] and by carrying out the reaction in tetrahydrofuran, the yield was increased markedly to 72%. A similar reaction with benzenethiol gave 2-phenylthio-2-thiazoline (4) in 79% yield along with a small amount of diphenyl disulphide (8).[10] Reaction of equimolar amounts of the iodoisothiocyanate (1) and butanethiol in benzene

Table 1

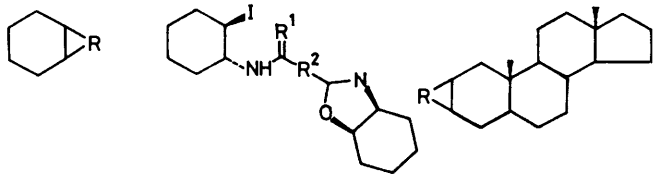
Reactions of compound (1) with sulphur nucleophiles [a]

Reagent [b]	Solvent	Temp. (°C)	Time (h)	Products (%)
BuSH	Et_2O	20	70	(3) 50
				(1) 24
BuSH	THF	66	23	(3) 72
PhSH [c]	THF	66	1	(4) 79
				(8) 5
PhSH	THF	66	17	(4) 43
				(8) 19

[a] Mol. ratio (1) : reagent = 1 : 2. [b] Plus equimolar amount of Et_3N. [c] Under argon.



with aqueous sodium hydroxide in the presence of the phase-transfer catalyst Adogen 464 resulted in an enhanced rate of reaction giving a 41% yield of the product (3) after 20 min, but with a four molar excess of the thiol the yield was reduced to 19% and an appreciable amount (16%) of the 2,2-dibutylthio-2-thiazolidine



(27) R = O (24) R^1 = S, R^2 = O (29) R = α-O
(28) R = S (25) R^1 = O, R^2 = S (30) R = β-S

(9) was also formed (*cf.* ref. 11). In the absence of the phase-transfer catalyst the latter reaction slowly but cleanly afforded (3) (56%). However, starting material still remained after 63 h. The stereochemistry of each of the compounds (3) and (4) followed from the 4-H,5-H coupling constants of *ca.* 7 and 6 Hz in their ^{1}H n.m.r. spectra which were in agreement with those for similar protons in *cis*-2-thiazolines (7.4 Hz) but not for *trans*-2-thiazolines (3.9 Hz).[12,13]

Reactions in which the hydrosulphide anion was used as the nucleophile in the presence of a phase-transfer catalyst are summarized in Table 2 (*cf.* ref. 14). No reactions occurred in the absence of the phase-transfer

TABLE 2

Reactions of *vic*-iodoisothiocyanates with hydrosulphide anion [a,b]

Compound	Time (min)	Product	Yield (%) [c]
(1)	30	(10) [15]	62
(13)	30	(15) [12]	49
		(17)	Trace
(14)	60	(16)	48
		(18)	15
(19), (20) [d]	30	(22)	33
		(23)	24

[a] Mol. ratio substrate : $Na_2S{\cdot}9H_2O$ = 1 : 5. [b] In $CHCl_3$–H_2O at 20 °C with Adogen 464. [c] Isolated from p.l.c. [d] 5 : 4 mol. ratio.

catalyst. I.r.[12] and ^{1}H n.m.r. analysis indicated that, as expected,[16] the products existed as the thiazolidine-2-thiones and not as the tautomeric 2-thiazoline-2-thiols. The absence of the ene-thiol tautomer was attested by the lack of thiol proton absorption in either the ^{1}H n.m.r. (δ 8—9) or i.r. spectra (2 550—2 600 cm^{-1}).[17] The stereochemistry of the 4,5-dipropyl-substituted 2-thiazolidine-2-thione (16) followed from comparison of its 4-H, 5-H coupling constant (*J ca.* 4.5 Hz) in the ^{1}H n.m.r. spectrum with that (*J* 4.2 Hz) of compound (15) of known *trans*-stereochemistry.[12] Formation of compounds (15) and (16) was accompanied by the elimination of hydrogen iodide to give low yields of the corresponding (*E*)-vinyl isothiocyanates (17) and (18).

Although the regioisomers (19) and (20) [2] could not be separated by multiple elution p.l.c., reaction of the mixture of isomers with hydrosulphide anion gave thiones (22) and (23) which were readily separated. In the ^{1}H n.m.r. spectra of both (22) and (23) (Experimental) the 7a-H signals occurred as a well resolved doublet of doublet of doublets from which coupling constants of the *vic*-methine protons were determined by first order analysis as 8.3 and 8.5 Hz, respectively, thereby indicating that these protons were *cis* to each other and therefore that the compounds were regioisomers. The stereochemistry of each isomer was defined from an examination of the substituent chemical shift effects in the ^{13}C n.m.r. spectra, using the spectrum of t-butylcyclohexane (21) [18] as the reference. The ring junction carbon atoms of each isomer show large deshielding effects (Table 3) which are due to the combined α- and β-effects exerted on C-3a and -7a by the nitrogen and sulphur atoms of the thiazolidine-2-thione ring. The relative orientation of the t-butyl groups as *trans* and *cis* with respect to the thiazolidine-2-thione ring in the isomers (22) and (23) was determined by comparison of the total substituent chemical shift effects on C-5 in (22) and C-6 in (23). In particular, a γ_{gauche} effect (−7.8 p.p.m.) could be correlated unambiguously with the isomer (22) bearing an axial nitrogen atom on C-3a; the isomer (23) had a smaller substituent chemical shift effect (−2.8 p.p.m.) for C-6 due to the γ_{trans} effect of the C-7a equatorial sulphur atom. These unequivocal structural assignments for the bicyclic heterocycles (22) and (23) provide chemical confirmation of our earlier [2] spectral assignment of both regio- and stereo-chemistry to the precursor *vic-trans*-iodoisothiocyanates (19) and (20).

Treatment of the *vic*-iodoisocyanate (2) with hydrosulphide anion as for the *vic*-iodoisothiocyanates, gave

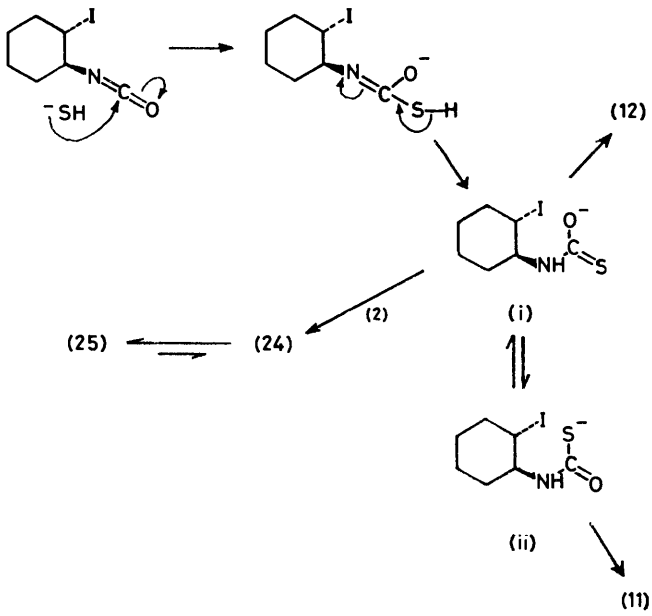
TABLE 3

^{13}C N.m.r. chemical shifts

Position relative to			(22)		(23)		
C	3-NH	1-S	Chemical shift	Total shift effect [a]	Chemical shift	Total shift effect [a]	Operative substituents
2			200.7		201.5		
3a	α	β	64.9	+37.1	63.2	+36.0	(α + β)
4	β	γ	31.7	+3.5	32.6	+4.8	(β + γ_{trans})
5	γ	δ	41.1	−7.8	21.2	−7.0	(γ_{gauche})
6	δ	γ	25.2	−3.0	46.1	−2.8	(γ_{trans})
7	γ	β	28.3	+0.5	27.7	−0.5	(β + γ_{gauche})
7a	β	α	49.5	+22.3	50.8	+23.0	(α + β)

[a] Relative to equivalent carbon in t-butylcyclohexane.

the thiazolidin-2-one (11) [1] (9%), the oxazolidine-2-thione (12) (3%), and the thioxo- and thiol-carbamates (24) (4%) and (25) (4%). The isomers (11) and (12) arise from an equilibrium mixture of the carbamate anions (i) and (ii) (Scheme 2). The thioxocarbamate (24) arises from reaction of the anion of the iodothioxocarbamate (i) with the iodoisocyanate (2) while the isomeric iodothiolcarbamate (25) then arises by a Newman–Kwart thioxo–thiolo rearrangement.[19]



SCHEME 2

In an attempt to use diethyl dithiocarbamate anion as a nucleophile, the iodoisothiocyanate (1) was also treated with diethylcarbamoyldithioato-*SS*-thallium (26).[20] Reaction in chloroform under reflux for 45 h gave none of the expected dithiocarbamate ester (5) but instead afforded an 86% yield of the *NN*-diethylamino-2-thiazoline (6) whose structure was confirmed by an independent synthesis from the iodoisothiocyanate (1) and diethylamine (*cf.* ref. 2). Thus, in the formation of (6) carbon disulphide was expelled either from the thallium salt (26) by its preferential reaction with chloroform to liberate diethylamine (*cf.* ref. 21), or from the 2-thiazoline (5) following nucleophilic attack by the intact diethyl dithiocarbamate anion. Since the compound (6) was also formed in 21% yield when the reaction was carried out in the aprotic solvent carbon tetrachloride, the latter pathway is favoured. There is precedent for loss of carbon disulphide from related molecules; thiolcarboxylic acids undergo nucleophilic addition to isothiocyanates to form *N*-alkyl-*S*-acyldithiocarbamates which then undergo 1,3-rearrangement concomitant with expulsion of carbon disulphide to form an amide.[22]

Treatment of 1-iodo-2-isothiocyanatocyclohexane (1) with thiourea in ethanol, or sulpholan (*cf.* ref. 23), followed by the addition of aqueous sodium hydroxide gave mixtures which contained mainly starting material and only low yields (≤7%) of the thiazolidine-2-thione (10). Reaction with *N*-acetylthiourea in refluxing ethanol, conditions which have been used successfully [24] for the synthesis of thiols which are sensitive to aqueous base, gave none of the thione (10) but afforded the thiazolidin-2-one (11) [1] (62%) and starting material (28%). Monitoring the reaction by t.l.c. provided no evidence for the transient intervention of thione (10). Thus, notwithstanding the greater nucleophilicity of sulphur towards carbon, the thiazolidin-2-one (11) is formed by attack of the alcohol solvent at the isothiocyanate carbon atom. In an independent reaction, treatment of (1) with boiling ethanol alone gave a quantitative yield of the cyclic imino-ether (7) which was converted gradually at room temperature into the thiazolidine-2-thione (10). To avoid the possibility of competitive reaction of the iodoisothiocyanate with a nucleophilic solvent, 1-methylpyrrolidin-2-one was used, but neither (10) nor (11) was detected (t.l.c.) after heating under reflux for 5 h; in benzene no reaction occurred after heating under reflux for 24 h. A possible explanation for the successful carbophilic additions of hydrosulphide anion and of alkane- and arene-thiolate anion, as opposed to the unsuccessful reactions with thiourea or *N*-acetylurea lies in HSAB theory.[25] Thus, the very soft thiocarbonyl sulphur atom of the urea derivatives may act preferentially as a thiophile, attacking the isothiocyanate sulphur atom to form a disulphide linkage which reverts to starting material during work-up. Treatment of the compound (1) with *O*-ethyl dithiocarbonate anion under a variety of conditions (Experimental) also gave starting material and a low yield of a mixture of products. Attempts to convert compound (11) into the thiazolidine-2-thione (10) with phosphorus pentasulphide [26] in either pyridine or acetonitrile were unsuccessful.

The thiazolidine-2-thione (10) was found to be an effective thiation agent for the conversion of oxirans into thiirans.[7] The oxiran (27) was treated with the thiazolidine-2-thione in deuteriodichloromethane and trifluoroacetic acid, and ^{1}H n.m.r. analysis of the product showed the immediate quantitative formation of 7-thiabicyclo[4.1.0]heptane (28). Likewise, 2α,3α-epoxy-5α-androstane (29) afforded a quantitative yield of 2β,3β-epithio-5α-androstane (30).[1]

EXPERIMENTAL

General experimental details are given in ref. 27.

Reaction of (E)-*Oct-4-ene with Iodine–Potassium Thiocyanate.*—A mixture of (*E*)-oct-4-ene (3.5 ml, 0.02 mol), iodine (14.6 g, 0.06 mol), and potassium thiocyanate (6.95 g, 0.07 mol) was stirred in chloroform at room temperature in the dark for 24 h. Work-up gave an oil (6.5 g) which contained isomeric iodothiocyanate and iodoisothiocyanate in the ratio *ca.* 2 : 1. A portion of the product was chromatographed on silica gel. Elution with hexane–chloroform (2 : 1) gave (i) erythro-4-*iodo*-5-*thiocyanato-octane* (60%) as an oil, b.p. 85—86° at 0.5 mmHg (Found: C, 36.4; H, 5.4; N, 4.9; I, 43.1. $C_9H_{16}INS$ requires C, 36.4; H, 5.4;

N, 4.7; I, 42.7%), $\nu_{max.}$ 2 160 cm^{-1} (SCN), $\delta(CDCl_3)$ 0.97, 1.00 (2t, CH_3), 1.78 (m, CH_2), 3.21 (m, $W_{\frac{1}{2}}$ 16 Hz, CHSCN), and 4.38 (d × d × d, J_{obs} 8, 5 Hz, CHI), *m/z* 297 ($M^{+\cdot}$), 239 ($M^{+\cdot}$ − SCN·), 170 ($M^{+\cdot}$ − I·), and 112 [$M^{+\cdot}$ − (I· + SCN·)], δ_C ($CDCl_3$) 13.0 (Me), 13.5 (Me), 20.2 (C-7), 22.8 (C-2), 36.5 (C-6), 39.5 (C-3), 40.9 (C-5), 57.5 (C-4), and 110.7 (SCN); and (ii) erythro-4-*iodo*-5-*isothiocyanato*-*octane* (13) (28%) as an oil, b.p. 102—103° at 0.5 mmHg (Found: C, 36.8; H, 5.4; N, 4.9; I, 43.1%), $\nu_{max.}$ 2 060 cm^{-1} (NCS), $\delta(CDCl_3)$ 0.98, 1.00 (2 t, CH_3), 1.67 (m, CH_2), 3.76 (m, $W_{\frac{1}{2}}$ 18 Hz, CHNCS), and 4.18 (m, $W_{\frac{1}{2}}$ 16 Hz, CHI), *m/z* 297 ($M^{+\cdot}$), 239 ($M^{+\cdot}$ − ·NCS), and 170 ($M^{+\cdot}$ − I·), δ_C ($CDCl_3$) 13.1 (Me), 13.5 (Me), 19.4 (C-7), 22.8 (C-2), 36.8 (C-6), 37.6 (C-3), 38.0 (C-5), 64.4 (C-4), and 133.0 (NCS).

The iodothiocyanate (3.33 g, 11.2 mmol) was treated with boron trifluoride–ether (3.52 ml, 28.0 mmol) at room temperature for 5 h. Work-up and chromatography on silica gel (hexane–chloroform, 2 : 1) gave the iodoisothiocyanate (13) (2.17 g, 65%).

Reactions of trans-1-*Iodo*-2-*isothiocyanatocyclohexane with Butane*-1-*thiol*.—(a) *Without solvent*. A solution of the *vic*-iodoisothiocyanate (1) (0.10 g, 0.38 mmol) in the minimal volume of butanethiol (0.10 ml, 0.93 mmol) was stood at room temperature for 92 h. Extraction with ether and work-up followed by p.l.c. (hexane–chloroform, 2 : 1) gave starting material (41%) and 2-*butylthio*-cis-3a,4,5,6,7,7a-*hexahydrobenzothiazole* (3) (6 mg, 7%) as a yellow oil, b.p. 150° at 1.2 mmHg (Found: C, 57.4; H, 8.5; N, 6.4; S, 28.0. $C_{11}H_{19}NS_2$ requires C, 57.6; H, 8.4; N, 6.1; S, 27.95%), $\nu_{max.}$ 1 540 (C=N),[12, 28] 1 300, and 978 cm^{-1} (2-thiazoline),[3b] δ 0.97 (t, *J* 7 Hz, CH_3), 1.55 (m, CH_2), 3.07 (t, *J* 7 Hz, SCH_2), 3.62 (m, J_{cis} 7, $W_{\frac{1}{2}}$ 15 Hz, CHS), and 3.95 (m, J_{cis} 7, $W_{\frac{1}{2}}$ 14 Hz, CHN), *m/z* 229 ($M^{+\cdot}$), and 173 ($M^{+\cdot}$ − C_4H_8), δ_C ($CDCl_3$) 42.4 (CH_3), 50.3 (C-6), 50.7 (butyl-CH_2), 51.8 (C-5), 57.3 (C-7), 58.1 (butyl-CH_2), 60.3 (C-4), 61.0 (SCH_2), 81.5 (C-7a), 102.9 (C-3a), and 194.4 (C-2).

(b) *With triethylamine in diethyl ether*. A mixture of the *vic*-iodoisothiocyanate (0.10 g, 0.38 mmol), triethylamine (104 µl, 0.76 mmol), and butanethiol (81 µl, 0.76 mmol) in ether (10 ml) was stirred at room temperature for 70 h. Work-up and p.l.c. gave the 2-thiazoline (3) (43 mg, 50%) and starting material (29%).

Reaction using a 1 : 1 : 1 mol. ratio of reactants gave an 18% yield of (3).

(c) *With triethylamine in tetrahydrofuran*. A mixture of the *vic*-iodoisothiocyanate (50 mg, 0.19 mmol), triethylamine (52 µl, 0.38 mmol), and butanethiol (40 µl, 0.38 mmol) in tetrahydrofuran (3 ml) was heated under reflux for 23 h. Work-up and p.l.c. gave the 2-thiazoline (3) (31 mg, 72%).

(d) *With Adogen* 464. A mixture of the *vic*-iodoisothiocyanate (0.10 g, 0.38 mmol), butanethiol (41 µl, 0.38 mmol), sodium hydroxide (30 mg, 0.76 mmol), and Adogen 464 (*ca.* 10 mg) in benzene (0.5 ml) and water (0.5 ml) was shaken vigorously at room temperature for 20 min. Work-up and p.l.c. gave the 2-thiazoline (3) (35 mg, 41%) and a mixture of minor products.

Repetition of the reaction using butanethiol (205 µl, 1.90 mmol) gave (i) the 2-thiazoline (3) (20 mg, 19%); (ii) 2,2-bis(butylthio)-*cis*-3a,4,5,6,7,7a-hexahydrobenzothiazolidine (9) (20 mg, 16%), $\nu_{max.}$ 3 365 cm^{-1} (NH), δ 1.26 (m, $W_{\frac{1}{2}}$ 27 Hz, CH_2 and CH_3), 3.18 (t, *J* 7 Hz, SCH_2), 4.14 (m, $W_{\frac{1}{2}}$ 36 Hz, CHS), and 6.90br (s, $W_{\frac{1}{2}}$ 24 Hz, NH), *m/z* no $M^{+\cdot}$, 229 ($M^{+\cdot}$ − BuSH); and (iii) a mixture of minor products.

Repetition of the reaction without the Adogen 464 gave starting material (20%), the 2-thiazoline (3) (39%), and two minor products. After 63 h the yields of starting material and the 2-thiazoline were 7 and 56%, respectively.

Reaction of trans-1-*Iodo*-2-*isothiocyanatocyclohexane with Benzenethiol*.—A solution of benzenethiol (345 µl, 3.37 mmol) and triethylamine (468 µl, 3.37 mmol) in tetrahydrofuran (18 ml) was added dropwise to a solution of the *vic*-iodoisothiocyanate (1) (0.45 g, 1.68 mmol) in oxygen-free tetrahydrofuran (9 ml). The stirred mixture was refluxed under argon for 1 h. Work-up gave an oil (0.4 g) which was separated by p.l.c. (hexane–chloroform, 1 : 1) into diphenyl disulphide (8) (40 mg, 5%) (correct i.r., ^1H n.m.r., and mass spectra) and 2-*phenylthio*-cis-3a,4,5,6,7,7a-*hexahydrobenzothiazole* (4) (0.33 g, 79%), a yellow oil, b.p. 190° at 1.2 mmHg (Found: C, 62.9; H, 6.4; N, 5.6; S, 25.3. $C_{13}H_{15}NS_2$ requires C, 62.6; H, 6.1; N, 5.6; S, 25.7%), $\nu_{max.}$ 1 545 (C=N), 1 300, and 982 cm^{-1} (2-thiazoline), δ 1.48 (m, CH_2), 3.55 (m, J_{cis} 5.5, $W_{\frac{1}{2}}$ 19 Hz, CHS), 3.95 (m, J_{cis} 5.5, $W_{\frac{1}{2}}$ 14 Hz, CHN), and 7.29 (m, Ph), *m/z* 249 ($M^{+\cdot}$), δ_C ($CDCl_3$) 50.4 (C-6), 51.7 (C-5), 57.3 (C-7), 58.2 (C-4), 81.3 (C-7a), 104.2 (C-3a), 157.9 (*ipso*-C), 157.9 (*m*-C), 158.4 (*p*-C), 163.9 (*o*-C), and 196.6 (C-2).

Reaction in the absence of argon gave diphenyl disulphide (19%) and the 2-thiazoline (4) (43%).

General Procedure for the Reaction of vic-*Iodoisothiocyanates with Sodium Sulphide*.—A solution of the *vic*-iodoisothiocyanate (1 mol. equiv.) and Adogen 464 (1 mg per 10 mg) in chloroform (0.5 ml per 0.10 g) was shaken vigorously with a solution of sodium sulphide nonahydrate (5 mol. equiv.) in water (1 ml per 0.4 g) at room temperature for the recorded time (Table 2). The mixture was extracted with chloroform and the extract was worked up to give a product which was purified by p.l.c. (chloroform).

cis-3a,4,5,6,7,7a-Hexahydrobenzothiazolidine-2-thione (10) crystallized from aqueous ethanol as needles, m.p. 111—113° (lit.,[15] 102—103°), $\nu_{max.}$ 3 380, 3 125 (NH), 1 450 (CSHNH), and 1 015 cm^{-1} (C=S), $\delta(CDCl_3)$ 1.60 (m, 5,6-H), 1.90 (m, 4,7-H), 3.88 (m, $W_{\frac{1}{2}}$ 19 Hz, 7a-H), 4.31 (m, $W_{\frac{1}{2}}$ 12 Hz, 3a-H), and 8.78 (m, 3-H), *m/z* 173 ($M^{+\cdot}$), δ_C ($CDCl_3$) 20.5 (C-5), 22.5 (C-6), 27.1 (C-7), 29.1 (C-4), 50.1 (C-7a), 63.1 (C-3a), and 201.4 (C-2).

trans-4,5-Diethylthiazolidine-2-thione (15) [12, 13] was obtained as a pale yellow oil, $\nu_{max.}$ 3 385, 3 140 (NH), 1 460 (CSNH), and 1 020 cm^{-1} (C=S), $\delta(CDCl_3)$ 1.00, 1.02 (2 t, *J* 7 Hz, CH_3), 1.80 (m, CH_2), 3.53 (q × d, *J* 4.2, 6.3, 7.2 Hz, CHS), 3.82 (d × t, *J* 6.0, 4.2 Hz, CHN), and 8.47br (m, NH), *m/z* 175 ($M^{+\cdot}$), and 146 ($M^{+\cdot}$ − Et·), δ_C ($CDCl_3$) 10.0 (5-CH_2CH_3), 11.6 (4-CH_2CH_3), 27.0 (5-CH_2CH_3), 29.0 (4-CH_2CH_3), 56.8 (C-5), 70.4 (C-4), and 199.1 (C-2).

trans-4,5-*Dipropylthiazolidine*-2-*thione* (16) was obtained as a yellow oil, b.p. 169° at 1.0 mmHg (Found: C, 53.5; H, 8.4; N, 7.1. $C_9H_{17}NS_2$ requires C, 53.2; H, 8.4; N, 6.9%), $\nu_{max.}$ 3 400, 3 130 (NH), 1 460 (CSNH), and 1 015, cm^{-1} (C=S), $\delta(CDCl_3)$ 0.93, 0.97 (2 t, *J* 6 Hz, CH_3), 1.57 (m, CH_2), 3.60 (d × t, *J* 4, 6.5 Hz, CHS), 3.90 (d × t, *J* 4.5, 6 Hz, CHN), and 9.14 (m, 3-H), *m/z* 203 ($M^{+\cdot}$), and 160 ($M^{+\cdot}$ − C_3H_7·), δ_C ($CDCl_3$) 13.6 (5-$CH_2CH_2CH_3$), 13.9 (4-$CH_2CH_2CH_3$), 19.1 (5-$CH_2CH_2CH_3$), 20.6 (4-$CH_2CH_2CH_3$), 36.0 (5-CH_2), 37.8 (4-CH_2), 55.6 (C-5), 69.2 (C-4), and 199.3 (C-2).

(E)-4-*Isothiocyanato*-*oct*-4-*ene* (18) was obtained as an oil, b.p. 67° at 2.0 mmHg (Found: C, 64.2; H, 8.95; N,

8.6; S, 18.5. $C_9H_{15}NS$ requires C, 63.8; H, 8.95; N, 8.3; S, 18.9%), $\nu_{max.}$ (film) 2 065br (NCS) and 1 642 cm^{-1} (C=C), $\delta(CDCl_3)$ 0.90, 0.93 (2 t, *J* 6 Hz, CH_3), 1.50 (m, 2,7-H), 2.10 (m, 3,6-H), and 5.55 (t, *J* 8 Hz, 5-H), *m/z* 169 ($M^{+\cdot}$), and 140 ($M^{+\cdot}$ − Et$^{\cdot}$).

r-5-*t-Butyl*-t-3a,4,5,6,7,7a-*hexahydrobenzothiazolidine*-2-*thione* (22) crystallized from dichloromethane–pentane as square prisms, m.p. 207—207.5° (Found: C, 57.6; H, 8.2; N, 6.2; S, 27.6. $C_{11}H_{19}NS_2$ requires C, 57.6; H, 8.4; N, 6.1; S, 28.0%), $\nu_{max.}$ 3 400, 3 140 (NH), 1 460 (CSNH), and 1 020 cm^{-1} (C=S), $\delta(CDCl_3)$ 0.88 (s, CMe_3), 1.66 (m, CH_2), 3.46 (d × d × d, *J* 8.8, 8.3, 6.5 Hz, 7a-H), 4.47 (m, $W_{\frac{1}{2}}$ 12 Hz, 3a-H), and 8.80 (m, $W_{\frac{1}{2}}$ 30 Hz, 3-H), *m/z* 229 ($M^{+\cdot}$).

r-6-*t-Butyl*-c-3a,4,5,6,7,7a-*hexahydrobenzothiazolidine*-2-*thione* (23) crystallized from dichloromethane–pentane as needles, m.p. 213—215° (Found: C, 57.8; H, 8.7; N, 5.8. $C_{11}H_{19}NS_2$ requires C, 57.6; H, 8.4; N, 6.1%), $\nu_{max.}$ 3 400, 3 140 (NH), 1 462 (CSNH), and 1 032 cm^{-1} (C=S), $\delta(CDCl_3)$ 0.86 (s, CMe_3), 1.67 (m, CH_2), 3.53 (d × d × d, *J* 9, 8.5, 5 Hz, 7a-H), 4.31 (m, $W_{\frac{1}{2}}$ 12 Hz, 3a-H), and 8.17 (m, 3-H), *m/z* 229 ($M^{+\cdot}$).

Reaction of trans-1-*Iodo*-2-*isocyanatocyclohexane with Sodium Sulphide*.—A solution of the *vic*-iodoisocyanate (2) [29] (0.73 g, 2.92 mmol) and Adogen 464 (90 mg) in chloroform (3.5 ml) was shaken vigorously with a solution of sodium sulphide nonahydrate (3.52 g, 14.6 mmol) in water (7.5 ml) at room temperature for 50 min. The mixture was worked up and the product was separated by multiple p.l.c. (hexane–chloroform, 2 : 1, 1 : 1, and 1 : 2) into (i) *cis*-3a,4,5,6,7,7a-hexahydrobenzothiazolidin-2-one (11) (39 mg, 9%) (correct i.r., ^1H n.m.r., and mass spectra [1]); (ii) *cis*-3a,4,5,6,7,7a-hexahydrobenzoxazolidine-2-thione (12) (12 mg, 3%), $\nu_{max.}$ ($CHCl_3$) 3 400, 3 200 (NH), and 1 472 cm^{-1} (NHCS), $\delta(CDCl_3)$ 1.56 (m, CH_2), 3.92 (d × d × d, *J* 9, 6, 2 Hz, 3a-H), 4.88 (d × t, *J* 7.2, 4.8 Hz, 7a-H), and 8.12 (m, $W_{\frac{1}{2}}$ 20 Hz, 3-H), *m/z* 157 ($M^{+\cdot}$), 114 ($M^{+\cdot}$ − $^{\cdot}$NHCS), and 81 [$M^{+\cdot}$ − (NHCS + OH$^{\cdot}$)]; (iii) *O-cis*-3a,4,5,6,7,7a-hexahydrobenzoxazol-2-yl *N*-(*trans*-2-iodocyclohexyl)thiocarbamate (24) (41 mg, 4%); and (iv) *S-cis*-3a,4,5,6,7,7a-hexahydrobenzoxazol-2-yl *N*-(*trans*-2-iodocyclohexyl)thiocarbamate (25) (41 mg, 4%). Compounds (24) and (25) gave identical i.r., ^1H n.m.r., and mass spectra, $\nu_{max.}$ ($CHCl_3$) 3 300 (NH), 1 685—1 710 (CO and NHCO), 1 520 (NHCS), and 1 175 cm^{-1} (C=S), $\delta(CDCl_3)$ 1.45 (m, CH_2), 4.26 (m, CH), 8.20 (s, NH), and 8.33 (s, NH), *m/z* 409 ($M^{+\cdot}$).

Reaction of trans-1-*Iodo*-2-*isothiocyanatocyclohexane with Diethylcarbamoyldithioato*-SS′-*thallium*.—A solution of diethylcarbamoyldithioato-*SS*′-thallium (26) [20,30] (5.3 g, 15.0 mmol) in chloroform (20 ml) was added over 3 h to a solution of the *vic*-iodoisothiocyanate (1) (2.0 g, 7.5 mmol) in chloroform (20 ml) and the mixture was heated under reflux for 44 h. The mixture was filtered and the filtrate was worked up to give an oil (3.70 g) which was chromatographed on silica gel. Elution with ether gave 2-*diethylamino*-cis-3a,4,5,6,7,7a-*hexahydrobenzothiazole* (6) (1.37 g, 86%) as a yellow oil, b.p. 80—81° at 2.5 mmHg (Found: C, 62.1; H, 9.4; N, 13.7. $C_{11}H_{20}N_2S$ requires C, 62.2; H, 9.5; N, 13.2%), $\nu_{max.}$ (film) 1 595 cm^{-1} (C=N), δ 1.13 (t, *J* 7 Hz, Me), 1.45 (m, 5,6-H), 1.67 (m, 4,7-H), 3.31 (q, *J* 7 Hz, CH_2Me), and 3.73 (m, $W_{\frac{1}{2}}$ 20 Hz, 3a,7a-H), *m/z* 212 ($M^{+\cdot}$), δ_C ($CDCl_3$) 13.6 (CH_2CH_3), 21.7 (C-6), 23.1 (C-5), 29.3 (C-7), 29.6 (C-4), 44.8 (CH_2CH_3), 52.3 (C-7a), 70.0 (C-3a), and 162.5 (C-2).

Repetition of the reaction in carbon tetrachloride gave the 2-thiazoline (6) (21%) and many minor products.

Treatment of the *vic*-iodoisothiocyanate (1) with diethylamine as for other amines,[1] followed by vigorous stirring with aqueous potassium hydroxide to decompose the hydroiodide salt, also gave the 2-thiazoline (6) (69%).

Reaction of trans-1-*Iodo*-2-*isothiocyanatocyclohexane with Thiourea*.—A solution of the *vic*-iodoisothiocyanate (1) (0.30 g, 1.12 mmol) and thiourea (94 mg, 1.23 mmol) in sulpholan (2.3 ml) was stirred at room temperature for 27 h, poured into 10% aqueous sodium hydroxide (7 ml), stirred for a further 30 min, and then neutralized with dilute aqueous hydrochloric acid. The mixture was extracted with ether and the extract was worked up to give an oil which was separated by p.l.c. (hexane–chloroform, 2 : 1) into (i) *cis*-3a,4,5,6,7,7a-hexahydrobenzothiazolidine-2-thione (10) (14 mg, 7%); (ii) *cis*-3a,4,5,6,7,7a-hexahydrobenzothiazolidin-2-one (11) (trace); and (iii) a mixture of minor products.

Repetition of the reaction in 50% aqueous ethanol gave starting material (55%) and a mixture of minor products containing the 2-thione (10) and the thiazolidin-2-one (11).

Repetition of the reaction using *N*-(aminothiocarbonyl)-acetamide [31] in place of the thiourea and heating under reflux for 24 h gave the thiazolidin-2-one (11) (63%), starting material (28%), and a minor product.

Reaction of trans-1-*Iodo*-2-*isothiocyanatocyclohexane with Ethanol*.—A solution of the *vic*-iodoisothiocyanate (1) (0.10 g, 0.38 mmol) in ethanol (3 ml) was heated under reflux for 24 h. T.l.c. analysis indicated the formation of the imino-ether (7), which was converted over 1.5 days at room temperature into the thiazolidin-2-one (11). Work-up gave compound (11) (58 mg, 97%).

Reaction of trans-1-*Iodo*-2-*isothiocyanatocyclohexane with O-Ethyldithiocarbonate Anion*.—The *vic*-iodoisothiocyanate (1) (1 mol. equiv.) was treated with *O*-ethylcarbonodithioato-*SS*′-potassium (or -thallium [20]) (1, 1.5, or 5 mol equiv.) in either acetone, chloroform, or sulpholan, with or without added phase-transfer reagent Adogen 464 or 18-crown-6 at room temperature or under reflux for periods ranging from 0.3 h to 14 days. All reactions gave starting material and mixtures of minor products.

Reactions of cis-3a,4,5,6,7,7a-*Hexahydrobenzothiazolidine*-2-*thione as a Sulphur-transfer Reagent*.—(a) *With* 7-*oxabicyclo*[4.1.0]*heptane*. A solution of the thiazolidine-2-thione (10) (30 mg, 0.17 mmol) and 7-oxabicyclo[4.1.0]-heptane (27) (18 μl, 0.17 mmol) in deuteriodichloromethane (0.3 ml) in a ^1H n.m.r. tube was treated with trifluoroacetic acid (13 μl, 0.17 mmol). In the ^1H n.m.r. spectrum, the epoxy-proton signal (δ 3.05) disappeared and a new signal appeared at δ 3.20 (thiiran); similarly, the signals due to the thiation reagent (10) at δ 3.60—4.40 and 8.12 were replaced by signals at δ 3.50—4.17 (*cis*-thiazolidinone) and 6.57. Work-up gave the thiazolidin-2-one (11) and 7-thiabicyclo-[4.1.0]heptane (28).[1]

(b) *With* 2α,3α-*Epoxy*-5α-*androstane*. A solution of the thiazolidine-2-thione (10) (50 mg, 0.29 mmol) and the 2α,3α-epoxide (29) (79 mg, 0.29 mmol) in deuteriodichloromethane (0.3 ml) was treated with trifluoroacetic acid (23 μl, 0.29 mmol) as in (a). The ^1H n.m.r. spectrum indicated a quantitative yield of the thiiran (30). Work-up and p.l.c. (hexane–chloroform, 1 : 1) gave 2β,3β-epithio-5α-androstane [1] and the thiazolidin-2-one (11).

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EXPERIMENTAL

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