The Chemistry of *o*-Phenylene Di-isothiocyanate. Part 1. Some Reactions with *N*-Nucleophiles

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Reactions of *o*-phenylene di-isothiocyanate are described with a variety of nitrogen nucleophiles. Primary and secondary amines and also substituted hydrazines give 1 : 1 reaction products, 1-substituted thiocarbamoyl benzimidazoline-2-thiones. Hydrazine gives a 2 : 1 reaction product, to be regarded as a hydrazine salt. The products from primary amines are relatively unstable, yielding isothiocyanates and benzimidazoline-2-thione. Some Schiff bases and derivatives of isoquinoline give rise to thiadiazinobenzimidazoles.

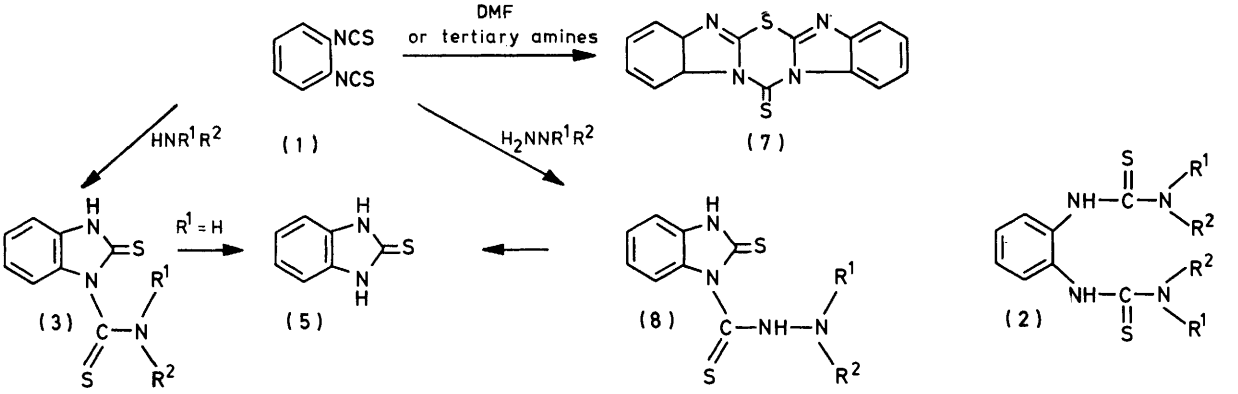
o-PHENYLENE DI-ISOTHIOCYANATE (1) was first obtained by Billeter and Steiner [1] in very low yield from the reaction of thiophosgene upon *o*-phenylene diamine, the main product being benzimidazoline-2-thione. These authors described a few properties of the di-isothiocyanate but no further work appears to have been published upon this reactive intermediate.

The di-isothiocyanate (1) may now be obtained in reasonable yield (50%) from benzimidazole.[2] The present work describes the behaviour of this di-isothiocyanate towards various nitrogen nucleophiles.

RESULTS AND DISCUSSION

Probably the most documented reactions of isothiocyanates are those with compounds containing a nitrogen–hydrogen bond.[3] Thus it would be expected that the di-isothiocyanate (1) would react with amines to form bis-substituted thioureas (2). Actually, (1) reacts with various primary and secondary amines on a 1 : 1 basis to give compounds of type (3a—r).

The di-isothiocyanate (1) reacts with morpholine to give (3m), the ^{13}C n.m.r. spectrum of which shows two thiocarbonyl signals at δ 175.1 and 165.9. Primary



a ; R^1 = H, R^2 = Ph
b ; R^1 = H, R^2 = 4-$NH_2C_6H_4$
c ; R^1 = H, R^2 = 4-ClC_6H_4
d ; R^1 = H, R^2 = 4-OHC_6H_4
e ; R^1 = H, R^2 = 2-NHC_6H_4
f ; R^1 = H, R^2 = 2-$CO_2HC_6H_4$
g ; R^1 = H, R^2 = 2-$CO_2MeC_6H_4$
h ; R^1 = H, R^2 = 2-OHC_6H_4
i ; R^1 = H, R^2 = 3-pyridyl
j ; R^1 = H, R^2 = 3-(2-CO_2Me)thiophenyl
k ; R^1 = H, R^2 = C_6H_{11}
l ; R^1 = H, R^2 = -C(Me)=CO_2Me
m ; R^1,R^2 = morpholinyl
n ; R^1 = Me, R^2 = 4-ClC_6H_4
o ; R^1 = Me, R^2 = 3-$NO_2C_6H_4$
p ; R^1 = Me, R^2 = 4-$NO_2C_6H_4$
q ; R^1 = Me, R^2 = CH_2Ph
r ; R^1 = R^2 = CH_2Ph

a ; R^1 = H, R^2 = CO_2Me
b ; R^1 = H, R^2 = Ph
c ; R^1 = R^2 = Me

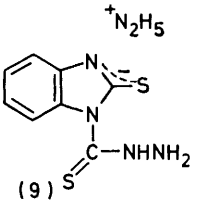
TABLE 1

1-(Substituted aminothiocarbonyl)benzimidazoline-2-thiones (3)

Compound	Starting amine	M.p.[a] (°C)	Solvent [t/h]	Cryst. from	Yield[b] (%)	Found (%) [Calc (%)]	100-MHz ^{1}H N.m.r. (except where stated) (δ from $SiMe_4$)
(3a)	$PhNH_2$	303—305	MeCN [0.5]	MeCN	59	C, 58.8; H, 3.9; N, 14.8 [C, 58.9; H, 3.9; N, 14.7]	7.15—7.6 (7 H, m, aromatics), 7.95—8.05 (2 H, m, 2 H and 6 H-Ph), 12.3 (1 H, NH, exch.), 13.0 (1 H, NH, exch.)
(3b)[c]	$4\text{-}NH_2C_6H_4NH_2$		MeCN [0.5]		70	C, 56.0; H, 4.0; N, 18.4 [C, 56.0; H, 4.0; N, 18.7]	decomposes in solution
(3c)	$4\text{-}ClC_6H_4NH_2$		MeCN [0.5]		95	C, 53.1; H, 3.1; N, 13.0 [C, 52.6; H, 3.2; N, 13.2]	7.17 (4 H, s, fused aromatics), 7.52 (4 H, s, benzenoid aromatics)
(3d)	$4\text{-}OHC_6H_4NH_2$	177—178	MeCN [0.5]		81	C, 55.5; H, 3.6; N, 13.7 [C, 55.8; H, 3.7; N, 14.0]	(60 MHz) 7.1—7.3 (4 H, m, fused aromatics), 7.2 (4 H, q, benzenoid aromatics), 9.7, 12.2, 13.0 (1 H, each, exch.)
(3e)	$2\text{-}NH_2C_6H_4NH_2$		Cyclohexane [2]		83	C, 56.2; H, 4.1; N, 18.5 [C, 56.0; H, 4.0; N, 18.7]	decomposes in solution
(3f)	$2\text{-}CO_2HC_6H_4NH_2$		Et_2O [18]	MeCN	34	C, 54.5; H, 3.2; N, 12.5 [C, 54.7; H, 3.3; N, 12.8]	(60 MHz) 7.2 (4 H, s, fused aromatics), 7.5—8.0 (4 H, m, benzenoid aromatics), 12.8 (1 H, exch.)
(3g)	$2\text{-}CO_2MeC_6H_4NH_2$		Et_2O [4]		33	C, 55.9; H, 3.8; N, 12.0 [C, 56.0; H, 3.8; N, 12.2]	4.0 (3 H, s, CO_2Me), 7.25 (4 H, s, fused aromatics), 7.5—8.2 (4 H, m, benzenoid aromatics), 12.0 (2 H, exch.)
(3h)	$2\text{-}OHC_6H_4NH_2$	263—265	MeCN [0.5]		90	C, 55.4; H, 3.6; N, 14.2 [C, 55.8; H, 3.7; N, 14.0]	7.15—7.65 (11 H, m, aromatics + exch.)
(3i)	3-NH_2-pyridine		MeCN [0.5]		79	C, 54.5; H, 3.5; N, 19.8 [C, 54.6; H, 3.5; N, 19.6]	7.15 (4 H, s, fused aromatics), 7.5 (1 H, m, β-pyridyl), 7.85 (1 H, m, γ-pyridyl), 8.6 (1 H, m, α-pyridyl)
(3j)	3-NH_2-thiophen-2-CO_2Me		Et_2O [18]	MeOH	52	C, 47.9; H, 3.0; N, 11.8 [C, 48.1; H, 3.2; N, 12.0]	3.7 (3 H, s, CO_2Me), 7.2 (1 H, d, thiophen-2H), 7.9 (1 H, d, thiophen-3H), 12.0 (2 H, exch.)
(3k)	$C_6H_{11}NH_2$		Et_2O [12]		80	C, 58.0; H, 5.6; N, 14.4 [C, 57.7; H, 5.8; N, 14.4]	1.4 (11 H, m, cyclohexyl), 7.2 (4 H, m, aromatics)
(3l)	$MeO_2CCH{=}C(Me)NH_2$	202 decomp.)	Et_2O [18]	Me_2CO–light petrol (40—60 °C)	36	C, 50.7; H, 4.3; N, 13.2 [C, 50.8; H, 4.2; N, 13.6]	2.3 (3 H, s, Me), 3.2 (3 H, s, CO_2Me), 7.1 (4 H, t, aromatics), 11.5 (3 H, exch.)
(3m)	Morpholine	250—251	MeCN [0.5]	EtOH–H_2O	69	C, 51.7; H, 4.8; N, 15.0 [C, 51.6; H, 4.7; N, 15.1]	3.65 (6 H, m, CH_2), 4.25 (2 H, degenerate t, CH_2 *cis* to C=S), 7.2 (4 H, s, aromatics)
(3n)	$4\text{-}ClC_6H_4NHMe$	176—178	Et_2O [2]	toluene	90	C, 54.2; H, 3.6; N, 12.3 [C, 53.95; H, 3.6; N, 12.6]	3.87 (3 H, s, NMe), 7.05—7.4 (8 H, m, aromatic)
(3o)	$3\text{-}NO_2C_6H_4NHMe$	230	Et_2O 2 days	toluene	23	C, 52.8; H, 3.5; N, 16.2 [C, 52.3; H, 3.5; N, 16.3]	3.9 (3 H,s, NMe), 7—8.5 (8 H, m, aromatic)
(3p)	$4\text{-}NO_2C_6H_4NHMe$	195—205	Et_2O 2 days	toluene	14	C, 52.4; H, 3.4; N, 16.1 [C, 52.3; H, 3.5; N, 16.3]	(60 MHz) 3.87 (3 H, s, NMe), 6.5—8.4 (8 H, m, aromatic)
(3q)	$PhCH_2NHMe$	145—146	Et_2O [18]	toluene	80	C, 61.8; H, 4.9; N, 13.5 [C, 61.35; H, 4.9; N, 13.4]	3.0 (3 H, s, NMe), 5.4 (2 H, d, CH_2), 7.0—7.7 (9 H, m, aromatic)
(3r)	$(PhCH_2)_2NH$	199—200	Et_2O [3]	toluene	55	C, 67.6; H, 4.9; N, 10.8 [C, 67.85; H, 4.9; N, 10.8]	4.8 (2 H, d, CH_2), 5.5 (2 H, d, CH_2), 7.0—7.7 (14 H, m, aromatic)
(5)[d]	Pr^iNH_2	305—310	MeCN [0.2]		68	C, 55.6; H, 4.0; N, 18.4 [C, 56.0; H, 4.0; N, 18.7]	
(5)[d]	Bu^tNH_2	300—304	Et_2O [4]		60		
(7)[e]	$2\text{-}NO_2C_6H_4NH_2$	190—192	MeCN [18]	MeCN	30	C, 58.4; H, 2.6; N, 18.2 [C, 58.5; H, 2.5; N, 18.1]	

[a] If no melting point is quoted, compound was unstable to heat. Compounds melted at *ca.* 150 °C, resolidified, then melted again at >290 °C. [b] Crude yield, not optimised. [c] If a three-fold excess of (1) used, then (6) was obtained in 40% yield. [d] See refs. 1 and 5; lit. m.p. 303—304 °C. [e] See ref. 2.

amines could give products with a structure of type (3; R^1 = H) (non-symmetrical) or (4) (symmetrical). Reaction of the di-isothiocyanate (1) with *p*-chloroaniline *gave* a product, the ^{13}C n.m.r. spectrum of which showed three signals at low field, two major signals at δ 173.8 and 167.1, and a minor signal at δ 168.3. After heating at 60 °C in [$^2H_6$]dimethyl sulphoxide for several hours the major peak had disappeared leaving the minor signal at low field. From chemical evidence we have shown that the amine–isothiocyanate reaction product undergoes thermal decomposition into benzimidazoline-2-thione [4] (5) and *p*-chlorophenyl isothiocyanate. The



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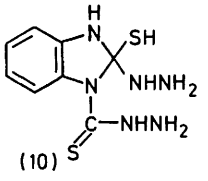

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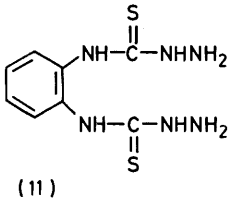

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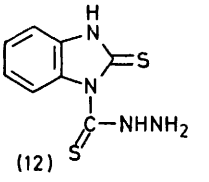

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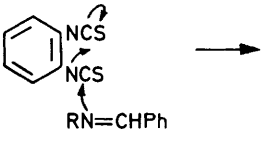

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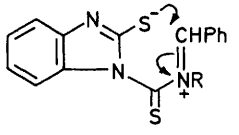

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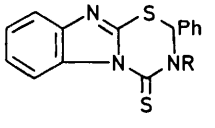
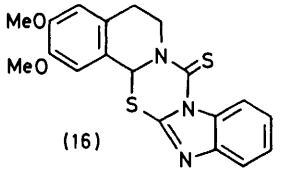


(14) a ; R = Me
b ; R = CH_2Ph



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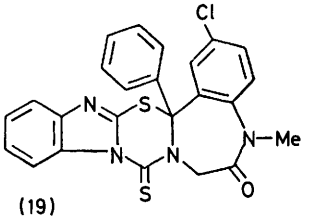

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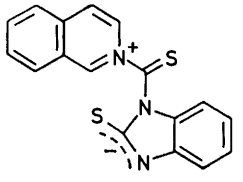

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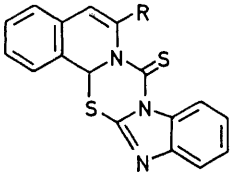

(17) a ; R = H
b ; R = Br

signal at low field (δ 168.3) can therefore be attributed to the thiocarbonyl signal of benzimidazoline-2-thione. These observations may be rationalised by structure (3c) for the pure product.

The thermal fragmentation of certain thioureas into amines and isothiocyanates has been reported previously by Gebhardt [5] and other workers.[6]

The properties of compounds (3) obtained from amines and the di-isothiocyanate (1) are shown in Table 1. Those from *o*- and *p*-phenylenediamines gave the mono-products (3e) and (3b), respectively. Using a three-fold excess of (1) we were able to isolate from *p*-phenylene-*diamine* the bis-product (6).

Products from aliphatic primary amines proved to be very unstable and benzimidazoline-2-thione was the main product isolated in the reactions with isopropylamine and t-butylamine (Table 1). Cyclohexylamine, however, gave the expected thione (3k).

Attention was next directed to the preparation of thiones from secondary bases. *N*-Methylaniline reacted normally to yield a crude thione (3; R^1 = Me, R^2 = Ph), which crystallised from methanol as pale yellow needles, m.p. 180—181 °C. We found that other solvents, *e.g.* toluene and chloroform, formed complexes with the thione. The complexes lost their solvent of crystallisation at *ca.* 105 °C. The effect of groups in the aromatic nucleus of the attacking nucleophile appears to be critical for complex formation. We found that *p*-Cl and *m*- or *p*-NO_2 groups prevented the formation of solvent complexes in the thiones formed from these secondary amines. In like manner the thiones (3q) and (3r) formed from methylbenzylamine and dibenzylamine respectively also failed to form solvent complexes.

Reaction of tertiary amines, dimethylformamide, and certain other nucleophiles (*e.g.* nitroaniline) with the di-isothiocyanate (1) gave the pentacyclic compound [2] (7) previously prepared by Haugwitz and Narayan [7] from 2-thiocyanatobenzimidazole and carbon disulphide in basic medium.

Treatment of the di-isothiocyanate (1) with *NN*-dimethylhydrazine gave one product, the ^{13}C n.m.r. spectrum of which showed two thiocarbonyl signals at δ 176.0 and 166.8. The product has therefore structure (8c). Structure (4; R = NMe_2), which is symmetrical, may be discounted.

Other substituted hydrazines, *e.g.* methoxycarbonylhydrazine and phenylhydrazine, reacted with the di-isothiocyanate (1) in the now expected manner and products (8a) and (8b), respectively, were obtained.

Treatment of the di-isothiocyanate (1) with hydrazine

gave a 1 : 2 product $C_8H_{12}N_6S_2$. The mass spectrum showed a parent ion at *m/e* 224 (accurate mass 224.0192, *i.e.* $C_8H_8N_4S_2$), with fragments at *m/e* 150 (benzimidazoline-2-thione) and 74 (NH_2NCS). Examination of the i.r. spectra showed the presence of an amine salt (centred at 2 700 cm^{-1}) which was absent in the product, $C_8H_8N_4S_2$, obtained by careful treatment of the $C_8H_{12}N_6S_2$ compound with sodium hydroxide followed by neutralisation with mineral acid. This evidence suggested the salt structure (9) for the product $C_8H_{12}N_6S_2$, and eliminated the covalent addition product (10) or the symmetrical thiosemicarbazide (11). Further evidence for the salt structure (9) followed from its re-formation from the $C_8H_8N_4S_2$ product (12) and hydrazine.

Finally, we found that treatment of the di-isothiocyanate with Diazepam, a benzodiazepine tranquilliser, gave the expected addition over the C=N bond to yield the thiadiazine (19).

EXPERIMENTAL

N.m.r. spectra were obtained with a Varian HA 100 or HA 100D or a Perkin-Elmer R12 spectrometer using $(CD_3)_2SO$ as solvent unless otherwise stated ($SiMe_4$ internal standard). Mass spectra were measured with a Hitachi RMU 6E or A.E.I. MS9 spectrometer. M.p.s were determined with a Büchi oil-bath apparatus or Kofler block hot-stage apparatus (KB).

Reactions of Amines, Hydrazines, and Schiff Bases with the Di-isothiocyanate (1) (*Tables* 1, 2, *and* 3). *General Procedure.*—A solution (10 ml) of the appropriate base (3.3 mmol) was added to a filtered solution of *o*-phenylene di-isothiocyanate (1) (3 mmol) in solvent (20 ml). After stirring at ambient temperature for the stated time the precipitated product was filtered off and washed with solvent and was normally pure enough for analytical purposes without further crystallisation. [No parents ions were detected for compounds (3a—3m)].

Stability of 1-(p-*chloroanilinothiocarbonyl*)*benzimidazoline-2-thione* (3c). 1-(*p*-Chloroanilinothiocarbonyl)benzimidazoline-2-thione (2 g) was refluxed for 16 h in 1,2-dimethoxyethane (50 ml) (solution was complete after 1 h) and the solvent was then removed. The residue was extracted with light petroleum (b.p. 60—80 °C). The product (0.9 g) remaining was identical (m.p., i.r. spectrum) with benzimidazoline-2-thione. Evaporation of the light-petroleum extract gave *p*-chlorophenylene isothiocyanate (1.0 g), identical (m.p., i.r. spectrum) with an authentic specimen.

1-(*Methylanilinothiocarbonyl*)*benzimidazoline-2-thione* (3; R^1 = Me, R^2 = Ph). *N*-Methylaniline (0.96 g, 0.009 mol) in ether (5 ml) was added with stirring to a filtered solution of *o*-phenylene di-isothiocyanate (1.65 g, 0.0086 mol) in

TABLE 2

1-(Substituted hydrazinothiocarbonyl)benzimidazoline-2-thiones (8)

Compound	Starting hydrazine	M.p.[a] (°C)	Solvent [*t*/h]	Yield[b] (%)	Found (%) [Calc. (%)]	100-MHz ^{1}H N.m.r. (δ)
(8a)	NH_2NHCO_2Me		MeCN [0.5]	60	C, 43.0; H, 3.6; N, 20.3 [C, 42.6; H, 3.5; N, 19.9]	3.8 (3 H, s, Me), 7.5 (4 H, m, aromatics), 10.2 (1 H, exch.), 13.0 (1 H, exch.)
(8b)	NH_2NHPh		Et_2O [4]	37	C, 56.3; H, 4.0; N, 18.9 [C, 56.0; H, 4.0; N, 18.7]	7.0 (2 H, br, exch.), 7.25 (4 H, m, fused aromatics), 7.35 (5 H, s, Ph), 13.0 (1 H, exch.)
(8c)	NH_2NMe_2		Et_2O [4]	59	C, 47.5; H, 4.9; N, 22.2 [C, 47.6; H, 4.8; N, 22.2]	3.1 (6 H, brs, 2Me), 7.2 (4 H, s, aromatics), 12.6 (1 H, exch.)

[a] See footnote of Table 1. [b] Crude yield; not optimised.

Attention was then directed to the reactions of (1) with Schiff bases (13). Thus *N*-benzylidenemethylamine and *N*-benzylidenebenzylamine with the di-isothiocyanate (1) gave the thiadiazines (14a) and (14b), respectively, presumably by way of the ionic intermediate (15). However, Schiff bases from aromatic primary amines [*e.g.* (13; R = Ph or C_6H_4OH-*p*) and (1)] gave the substituted benzimidazoline-2-thiones (3a) and (3d), in which benzaldehyde had been lost during the course of the reaction. 6,7-Dimethoxy-3,4-dihydroisoquinoline, acting as a cyclic Schiff base, and (1) gave the pentacyclic compound (16). Isoquinoline and its 3-bromo-derivative both reacted readily with the di-isothiocyanate (1) to give the thiadiazines (17a) and (17b), respectively. A chloroform solution of the pentacyclic (17a) on standing for 2 d showed some decomposition back to the starting materials.

The alternative ionic structure (18) must also be considered for the reaction product from isoquinoline. No further work has been done to support this hypothesis.

TABLE 3

Reactions of (1) with Schiff bases (13)

Compound	Starting base	M.p. (°C)	Solvent (*t*/h)	Cryst. from	Yield (%)	Found (%) [Calc. (%)]	^{1}H N.m.r. (δ)
(3a)	PhCH=NPh	303—305	MeCN [0 5]	MeCN	59	see table 1	
(3b)	PhCH=NC$_6$H$_4$-4 OH	177—178	MeCN [4]	Me_2CO–petrol (40—60 °C)	81	see table 1	
(14a)	PhCH=NMe	174	MeCN [4]	EtOH	48	C, 61.9; H, 4.1; N, 13.2 [C, 61.7; H, 4.2; N, 13.5]	(60 MHz), 3.8 (3 H, s, Me), 6.9 (1 H, s, H-2), 7.3 (8 H, m, aromatics), 8.7 (1 H, m, H-5)
(14b)	PhCH=NCH$_2$Ph	173	MeCN [4]	EtOH	47	C, 67.8; H, 4.4; N, 10.6 [C, 68.2; H, 4.4; N, 10.9]	(100 MHz) 5.5 (2 H, q, CH_2, *J* 16 Hz), 6.8 (1 H, s, H-2), 7.3 (13 H, m, aromatics), 8.6 (1 H, m, H-5)

ether (45 ml). After 1 h the reaction was complete (t.l.c.). After removal of the solvent and trituration with toluene the yellow oil (2.9 g) gave needles. Recrystallisation from toluene gave a *toluene complex* of the *thione* (2.65 g, 79%) as pale yellow needles, m.p. 106—107 °C, remelting at 180—181 °C (KB) (Found: C, 67.4; H, 5.4; N, 10.5. $C_{22}H_{21}N_3S_2$ requires C, 67.5; H, 5.4; N, 10.7%); δ[$CDCl_3$ + $(CD_3)_2SO$] 2.3 (3 H, s, Ar-*Me*), 3.87 (3 H, s, PhN*Me*), and 7.0—7.25 (*14 H*, m, aromatic).

In a repeat experiment, after removal of the solvent a sample of the product (1.5 g) purified from chloroform gave a *chloroform complex* of the *thione* (0.82 g, 44%) as pale yellow needles, m.p. 105 °C, remelting at 185 °C (KB) (Found: C, 46.2; H, 3.4; N, 10.2. $C_{16}H_{14}Cl_3N_3S_2$ requires C, 45.9; H, 3.35; N, 10.05%); δ[$CDCl_3$ + $(CD_3)_2SO$] 3.95 (3 H, s, NMe), 7.05—7.3 (9 H, m, aromatic), 7.5 (1 H, s, $CHCl_3$).

In a like manner a sample of the product (1.5 g) crystallised from methanol to give the *thione* (0.85 g, 64%) as pale yellow needles, m.p. 180—181 °C (Found: C, 60.0; H, 4.3; N, 14.0. $C_{15}H_{13}N_3S_2$ requires C, 60.2; H, 4.35; N, 14.05%); δ[$(CD_3)_2SO$] 4.0 (3 H, s, NMe) and 7.2—7.7 (9 H, m, aromatic).

Reaction of o-*Phenylenedi-isothiocyanate with Hydrazine.*—A filtered solution of *o*-phenylene di-isothiocyanate (0.8 g, 0.004 mol) in acetonitrile (25 ml) was added with stirring to hydrazine hydrate (0.425 ml, 0.0085 mol) in acetonitrile (25 ml) with ice-cooling over 5 min. After stirring for 30 min the product (0.8 g) was collected and washed with acetonitrile. Recrystallisation from water–ethanol (1 : 4) gave the *hydrazine salt* of (N-*hydrazinothiocarbonyl*)-*benzimidazoline*-2-*thione* (8; $R^1 = R^2 = H$) as pale cream needles, m.p. (KB) sintered at 170 °C, crystals converted into plates, finally, melting at 270 °C (Found: C, 37.6; H, 4.6; N, 32.9; S, 25.1. $C_8H_{12}N_6S_2$ requires C, 37.5; H, 4.7; N, 32.8; S, 25.0%); δ[$(CD_3)_2SO$] 6.2—6.8 (10 H, 6 s, NH + H_2O) and 7.1 (4 H, s, aromatic). The salt could be decomposed as follows. The hydrazine salt (0.3 g) was dissolved in 2N sodium hydroxide (10 ml), the solution was acidified with ice-cold 2N hydrochloric acid (11 ml) and the *product* (0.27 g) collected and washed with water. Recrystallisation from water–ethanol (1 : 4) gave (N-*hydrazinothiocarbonyl*)*benzimidazoline*-2-*thione* (8; $R^1 = R^2 = H$) as pale cream prismatic needles, m.p. (KB) gradual change at 185 °C from needles to prisms, which finally melted at 295 °C (Found: C, 42.9; H, 3.4; N, 24.5; S, 28.2. $C_8H_8N_4S_2$ requires C, 42.85; H, 3.6; N, 25.0; S, 28.55%).

7,13b-*Dihydroisoquino*[2,1′:5,6][1,3,5]*thiadiazino*[3,2-a]-*benzimidazole*-6-*thione* (17a).—A solution of isoquinoline (0.56 ml, 4.8 mmol) in ether (10 ml) was added to a solution of the di-isothiocyanate (1) (0.9 g, 4.6 mmol) in ether (10 ml). After 10 min the *product* was collected and washed with cyclohexane (1.3 g, 90%), m.p. 116—117 °C (from cyclohexane–ethyl acetate) (Found: C, 63.5; H, 3.4; N, 13.0. $C_{17}H_{11}N_3S_2$ requires C, 63.5; H, 3.4; N, 13.1%); δ($CDCl_3$); unstable in solution.

Similarly (17b) was obtained in 58% yield using 3-bromoisoquinoline, m.p. 96—98 °C (from ether–acetonitrile) (Found: C, 50.9; H, 2.5; N, 10.3. $C_{17}H_{10}BrN_3S_2$ requires C, 51.0; H, 2.5; N, 10.5%); δ($CDCl_3$) 7.6—7.8 (4 H, m, aromatics), 8.1—8.5 (4 H, m, aromatics), 8.95 (1 H, s, H-12), and 9.55 (1 H, s, H-6a).

In a similar manner (16) was obtained in 82% yield using 3,4-dihydro-6,7-dimethoxyisoquinoline and acetonitrile as solvent, m.p. 211 °C (from ethyl acetate) (Found: C, 59.7; H, 4.3; N, 11.0. $C_{19}H_{12}N_3O_2S_2$ requires C, 59.6; H, 4.5; N, 11.0%); δ($CDCl_3$) 3.0—4.0 (3 H, m, H_a), 3.82 (3 H, s, OMe), 3.9 (3 H, s, OMe), 5.0—5.3 (1 H, m, H_c), 6.3 (1 H, s, H_c), 6.75 and 6.8 (2 H, 2 s, aromatics adjacent to OMe), 7.2—7.7 (3 H, m, benzimidazole aromatics), and 8.9 (1 H, m, benzimidazole-H adjacent to C=S); *m/e* 383 (M^+) and 325 (M^+ − NCS).

2-*Chloro*-5-*methyl*-6-*oxo*-16a-*phenyl*-6,7-*dihydrobenzimidazo*[1′,2′:5,6][1,3,5]*thiadiazino*[3,2-d][1,5]*benzodiazepine*-5H-9-*thione* (19).—A solution of Diazepam [8] (568 mg, 2 mmol) in acetonitrile (10 ml) was added to a filtered solution of *o*-phenylene di-isothiocyanate (384 mg, 2 mmol) in acetonitrile (10 ml). After 24 h the *product* (360 mg) was collected and washed with acetonitrile, m.p. 180 °C (Found: C, 60.5; H, 3.6; N, 11.6; S, 13.4. $C_{24}H_{17}ClN_4OS_2$ requires C, 60.45; H, 3.6; N, 11.75; S, 13.4%); *m/e* 476 (M^+).

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