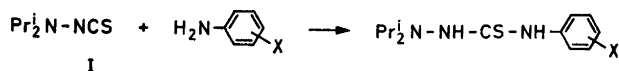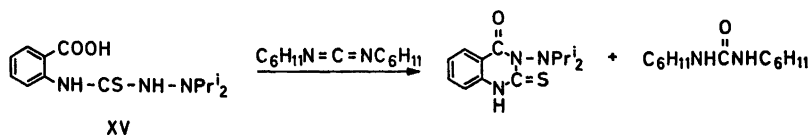# N-Isothiocyanatoamines

VII. Structural Influence on the Reaction between N-Isothiocyanato-diisopropylamine and Amines and Hydrazides

UFFE ANTHONI, CHARLES LARSEN and
PER HALFDAN NIELSEN

*Chemical Laboratory II (General and Organic Chemistry), University of Copenhagen,
The H. C. Ørsted Institute, Copenhagen, Denmark*

In the reaction between N-isothiocyanatodiisopropylamine (I) and differently substituted anilines, it was found that the formation of 1,1-diisopropyl-4-arylthiosemicarbazides was not influenced by the presence of OH, CH_2OH, COOH, $COOCH_3$, or $CONH_2$ groups. By contrast, aminothiophenols were attacked by I at the thiol function and this proved to be the case also for their reaction with methyl and phenyl isothiocyanate. When (I) was allowed to react with the phenylenediamines, the monothiosemicarbazide was obtained from the o- and the p-isomers but the bisthiosemicarbazide from the m-isomer. Aminopyridines and -quinolines showed little or no reactivity with the amino group in the 2- or the 4-position but gave the normal reaction if the amino group was in the 3- or the 8-position. Of the carbazic acid derivatives investigated, only those with a free amino group gave the expected thiocarbonohydrazides. The first member of a new class of compound, 1,1-diisopropyl-4-methoxythio-semicarbazide, has been prepared.

In an earlier study of this series[1] it was observed that N-isothiocyanatodiisopropylamine (I) reacted readily with amines and hydrazines to give thiosemicarbazides and thiocarbonohydrazides. These results prompted the study of reactions of I with a wider range of amines and hydrazines. The results are summarized in Table 1. The general utility of the reaction was confirmed by the synthesis of substituted 1,1-diisopropyl-4-phenylthiosemi-carbazides from variously substituted anilines.

$$Pr_2^i N-NCS \quad + \quad H_2N-\langle\!\!\langle\rangle\!\!\rangle_X \quad \longrightarrow \quad Pr_2^i N-NH-CS-NH-\langle\!\!\langle\rangle\!\!\rangle_X$$

I

Yields ranging from 52 to 86 % were encountered in this reaction with X=OH (IX—XI), CH$_2$OH (XIV), COOH (XV), COOCH$_3$ (XVI), and CONH$_2$ (XVII). Several of these compounds were considered to be of interest as precursors for condensed heterocyclic systems. However, attempts to cyclize XV with acids, bases, or by the methods described by Werbel [2] for condensation of allyl isothiocyanate with anthranilic acid were unsuccessful. The inability of XV to cyclize under these conditions might be due to the fact that XV in basic medium exists preferentially as the corresponding base and in acid medium as the corresponding acid. To test this hypothesis, XV was treated with dicyclohexylcarbodiimide in an inert solvent. By this procedure we succeeded in isolating 3-diisopropylamino-2-thioxo-1,2,3,4-tetrahydro-4-quinazolone in 20 % yield together with a somewhat higher yield of 1,3-dicyclohexylurea:

Isothiocyanates are well known to be relatively unreactive towards aliphatic hydroxyl groups; for example, they give hydroxyethylthioureas when allowed to react with 2-aminoethanol.[3,4] In the same way, (I) gave a 65 % yield of the hydroxyethylthiosemicarbazide (XIX).
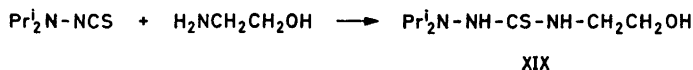

In contrast, the experiments now described demonstrate that in the case of aromatic compounds carrying both a thiol and an amino group, a preferential attack occurs on the thiol group. Thus, by mixing ethanolic solutions of I and o- (or p-)aminothiophenol in equimolar proportions, a rapid exothermic reaction took place, and solid o- (or p-)aminophenyl N,N-diisopropyldithiocarbazate (XII or XIII) crystallized.
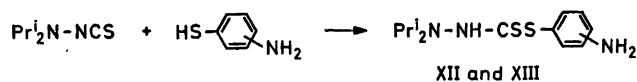
The only reaction between compounds of this type so far described is that between o-aminothiophenol and phenyl isothiocyanate.[5] When these were heated together in equimolar proportions hydrogen sulfide was evolved and 2-anilinobenzothiazole was formed. No attempts have been made to establish whether the initial attack is on the thiol or on the amine group. A related reaction is that between o-aminothiophenol and aromatic carbodiimides,[6] which has been shown to proceed by successive formation of the S- and S,N-derivatives. To obtain additional information on the problem of

S- versus N-attack, the reaction between *o*-aminothiophenol and phenyl isothiocyanate was reinvestigated. Ethanolic solutions, allowed to react 15 min at room temperature, gave the expected *S*-(*o*-aminophenyl)phenyldithio-carbamate, which, when heated just above the melting point, cyclized with evolution of hydrogen sulfide.
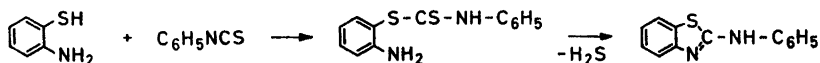
The reaction between methyl isothiocyanate and *o*-aminothiophenol at room temperature gave in the same way *S*-(*o*-aminophenyl)methyldithio-carbamate. This compound was quite stable to heat, but on treatment with 4 N hydrochloric acid, methylamine was eliminated immediately with cycliza-tion to benzothiazole-2-thione.
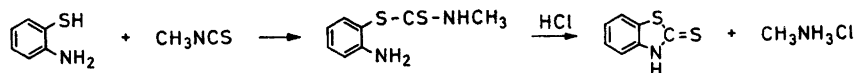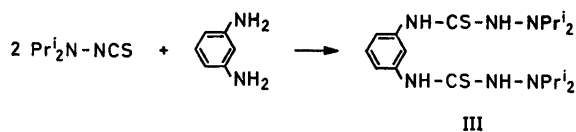
The possibility of these initial *S*-attacks being in some way connected with the *ortho* relationship between the amine and the thiol groups was ruled out by the finding that methyl isothiocyanate reacts with *p*-aminothiophenol to give *S*-(*p*-aminophenyl)methyldithiocarbamate. To summarize, the reac-tivity of the aromatic groups concerned towards the isothiocyanate function appears to decrease in the order $SH > NH_2 > OH$, which corresponds to the sequence found for carbodiimides.[6] On the other hand, experiments showed that XII was resistant to acidic and basic cyclization (*cf.* XV above). This contrasts with the results obtained with carbodiimides [6] and with *S*-(*o*-amino-phenyl)dithiocarbamates and must in some way be connected with the presence of the basic diisopropylamino group in XII and XV.

In the aliphatic series it has been shown [7] that phenyl isothiocyanate reacts with 2-aminoethanethiol to give in turn the *N*- and the *N,S*-substituted product, whilst aliphatic isothiocyanates give *N,S*-disubstituted products regardless of the relative amounts of isothiocyanate and aminothiol. Experi-ments showed that (I) invariably reacted with both the NH_2 and the SH group of 2-aminoethanethiol even when present in deficient amount, and the product was *N,S*-bis(3,3-diisopropylthiocarbazoyl)aminoethanethiol (XXII).
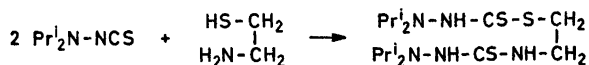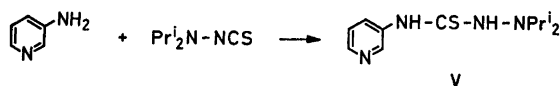
XXII

In the case of the three isomeric phenylenediamines, the reaction with (I) was expected to give mixtures of mono- and disubstituted products. This is probably true only for 1,3-phenylenediamine, which gave a 20 % yield of 1,1,1′,1′-tetraisopropyl-4,4′-*m*-phenylenebisthiosemicarbazide (III).

2 Pr$^i_2$N−NCS + [structure: benzene ring with two NH$_2$ groups] ⟶ [structure: benzene ring with two NH−CS−NH−NPr$^i_2$ groups]

III

The expected monosubstituted product could not be obtained from the reaction mixture by recrystallization or column or thin layer chromatography. In all cases only a red gum was isolated in *ca.* 30 % yield, showing, however, some of the characteristics in the infrared spectrum expected for the mono-substituted product. A quite different result was obtained by allowing (I) to react with 1,2- or 1,4-phenylenediamine. Even when a considerable excess of (I) was present, only the monosubstituted derivatives (II and IV) were obtained. The explanation is probably that II and IV separate from the reaction mixture within a few minutes, which hinders further attack of (I) on the free amino group.

As expected, the reaction between (I) and *N*-phenyl-1,2-phenylenediamine resulted in attack exclusively on the primary amino group to give the *N*-phenyl derivative of II, (XXV). We further found the reactivity of the amino group to be unchanged when it is situated in the 3-position of pyridine and quinoline as well as in the 8-position in quinoline. From these amines 4-heteroarylthiosemicarbazides were formed, *e.g.* with 3-aminopyridine, 1,1-diisopropyl-4-(3-pyridyl)thiosemicarbazide (V):

[structure: pyridine ring with NH$_2$] + Pr$^i_2$N−NCS ⟶ [structure: pyridine ring with NH−CS−NH−NPr$^i_2$]

V

On the contrary, amino groups in the 2- and 4-positions in pyridine and quinoline were very unreactive towards (I). In benzene as solvent, no reaction occurred even on boiling for 10 min, and with ethanol we only succeeded in isolating a thiosemicarbazide (VI) from 4-aminopyridine. In 2- and 4-amino-pyridine, which do not tautomerize,[8] resonance stabilization causes an electron deficiency on the amino group. The low reactivity is then understandable on the basis of a nucleophilic attack of the amino group on the isothiocyanate carbon as the primary step in these reactions.

We have previously shown[1] that (I) reacts readily with hydrazines and compounds containing either the −CONHNH$_2$, the −CSNHNH$_2$, or the −SO$_2$NHNH$_2$ group to give substituted thiocarbonohydrazides. With the −CSNH$_2$ group (and the −CSeNH$_2$ group) nitriles are formed,[9] but no reaction was encountered with the −CONH$_2$ group. To supplement these results we tried the reactions between (I) and some derivatives of dithiocarbazic acid. Addition of (I) to ethanolic solutions of methyl 3,3-dimethyldithio-carbazate or ethyl 2-methyldithiocarbazate showed that only the latter reacted, giving the thiocarbonohydrazide XX.
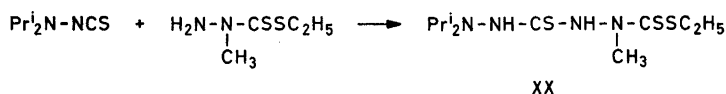
Pr$^i_2$N−NCS + H$_2$N−N−CSSC$_2$H$_5$ ⟶ Pr$^i_2$N−NH−CS−NH−N−CSSC$_2$H$_5$
                        | |
                       CH$_3$ CH$_3$

XX

Table 1. Products of the reactions of *N*-isothiocyanatodiisopropylamine (I) with compounds containing amino or hydrazino groups.
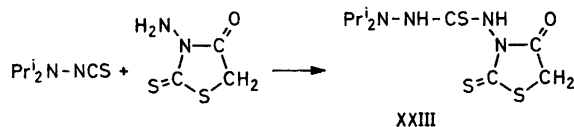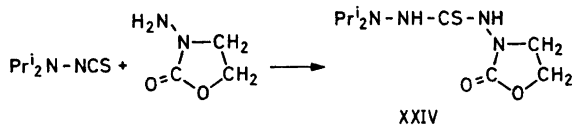
Reagent	Prepared	Meth-od	Yield, %	M.p. °C.	Formula	Analyses (C, H, N, S)
1,2-Phenylenediamine	1,1-Diisopropyl-4-(o-aminophenyl)thio-semicarbazide (II)	D	55 [a]	194–195	$C_{13}H_{22}N_4S$	Found: 58.25; 8.41; 20.66; 12.16 Calc.: 58.62; 8.33; 21.04; 12.03
1,3-Phenylenediamine	1,1,1',1'-Tetraisopropyl-4,4'-m-phenylenebisthiosemicarbazide (III)	G	20 [b]	175–176	$C_{20}H_{36}N_6S_2$	Found: 56.40; 8.48; 19.90; — Calc.: 56.56; 8.55; 19.79; —
1,4-Phenylenediamine	1,1-Diisopropyl-4-(p-aminophenyl)thio-semicarbazide (IV)	D	69 [a]	201–203	$C_{13}H_{22}N_4S$	Found: 58.70; 8.27; 20.97; — Calc.: 58.62; 8.33; 21.04; —
3-Aminopyridine	1,1-Diisopropyl-4-(3-pyridyl)-thiosemicarbazide (V)	G	40 [b]	168–169	$C_{12}H_{20}N_4S$	Found: 57.08; 7.88; 22.18; 12.65 Calc.: 57.10; 7.99; 22.20; 12.70
4-Aminopyridine	1,1-Diisopropyl-4-(4-pyridyl)-thiosemicarbazide (VI)	G	46 [b]	127–128	$C_{12}H_{20}N_4S \cdot \frac{1}{4}H_2O$	Found: 56.10; 7.77; 21.84; 12.44 Calc.: 56.10; 8.04; 21.82; 12.48
3-Aminoquinoline	1,1-Diisopropyl-4-(3-quinolyl)-thiosemicarbazide (VII)	F	73 [a]	177–178	$C_{16}H_{22}N_4S$	Found: 63.70; 7.29; 18.70; 10.70 Calc.: 63.54; 7.33; 18.53; 10.60
8-Aminoquinoline	1,1-Diisopropyl-4-(8-quinolyl)-thiosemicarbazide (VIII)	D	52 [a]	159–160	$C_{16}H_{22}N_4S$	Found: 63.30; 7.37; 18.38; 10.49 Calc.: 63.54; 7.33; 18.53; 10.60
2-Aminophenol	1,1-Diisopropyl-4-(o-hydroxyphenyl)-thiosemicarbazide (IX)	G	61 [b]	152–153	$C_{13}H_{21}N_3OS$	Found: 58.20; 8.12; 15.69; 12.16 Calc.: 58.39; 7.92; 15.72; 11.99
3-Aminophenol	1,1-Diisopropyl-4-(m-hydroxyphenyl)-thiosemicarbazide (X)	G	60 [b]	119–120	$C_{13}H_{21}N_3OS$	Found: 58.30; 7.91; 15.69; 11.98 Calc.: 58.39; 7.92; 15.72; 11.99
4-Aminophenol	1,1-Diisopropyl-4-(p-hydroxyphenyl)-thiosemicarbazide (XI)	E	55 [b]	161–162	$C_{13}H_{21}N_3OS$	Found: 58.25; 7.82; 15.60; 11.85 Calc.: 58.39; 7.92; 15.72; 11.99
2-Aminothiophenol	2-Aminophenyl N,N-diisopropyl-dithiocarbazate (XII)	D	39 [a]	134–135	$C_{13}H_{21}N_3S_2$	Found: 54.75; 7.50; 14.74; 22.50 Calc.: 55.08; 7.47; 14.83; 22.62

Table 1. Continued.

Starting amine	Product	Solvent	Yield (%)	M.p. (°C)	Formula	Analysis (C; H; N; S)
4-Aminothiophenol	4-Aminophenyl N,N-diisopropyl-dithiocarbazate (XIII)	D	90[a]	169–170	$C_{13}H_{21}N_3S_2$	Found: 54.90; 7.47; 14.86; 22.52 Calc.: 55.08; 7.47; 14.83; 22.62
2-Aminobenzyl alcohol	1,1-Diisopropyl-4-(o-hydroxymethyl-phenyl)thiosemicarbazide (XIV)	C	72	160–161	$C_{14}H_{23}N_3OS$	Found: 59.75; 8.30; 14.86; 11.38 Calc.: 59.75; 8.24; 14.94; 11.39
2-Aminobenzoic acid	1,1-Diisopropyl-4-(o-carboxyphenyl)-thiosemicarbazide (XV)	F	86	207–208	$C_{14}H_{21}N_3O_2S$	Found: 56.70; 7.26; 14.08; 11.04 Calc.: 56.73; 7.48; 14.18; 10.82
Methyl 2-amino-benzoate	1,1-Diisopropyl-4-(o-methoxycarbonyl-phenyl)thiosemicarbazide (XVI)	F	82	154–155	$C_{15}H_{23}N_3O_2S$	Found: 58.20; 7.52; 13.46; 10.55 Calc.: 58.22; 7.49; 13.58; 10.36
2-Aminobenzamide	1,1-Diisopropyl-4-(o-carbamoylphenyl)-thiosemicarbazide (XVII)	F	52[a]	197–198	$C_{14}H_{22}N_4OS$	Found: 57.10; 7.56; —; 10.93 Calc.: 57.11; 7.53; —; 10.89
4-Nitrobenzhydrazide	1,1-Diisopropyl-5-(p-nitrobenzoyl)-thiocarbonohydrazide (XVIII)	F	65	198–199	$C_{14}H_{21}N_5O_3S$	Found: 49.72; 6.24; 20.57; 9.10 Calc.: 49.54; 6.24; 20.64; 9.45
2-Aminoethanol	1,1-Diisopropyl-4-(β-hydroxyethyl)-thiosemicarbazide (XIX)	B	65	80–81	$C_9H_{21}N_3OS$	Found: 49.58; 9.79; 19.40; — Calc.: 49.28; 9.65; 19.16; —
Ethyl 2-methyldithio-carbazate	Ethyl 2-methyl-3-(N,N-diisopropylthio-carbazoyl)dithiocarbazate (XX)	F	66	182–183	$C_{11}H_{24}N_4S_3$	Found: 43.08; 7.91; 31.10; — Calc.: 42.82; 7.84; 31.17; —
Methoxyamine	1,1-Diisopropyl-4-methoxythiosemi-carbazide (XXI)	A	70[c]	95–96	$C_8H_{19}N_3OS$	Found: 47.28; 9.49; 20.51; — Calc.: 46.80; 9.33; 20.47; —
2-Aminoethanethiol	N,S-Bis(3,3-diisopropylthiocarbazoyl)-aminoethanethiol (XXII)	D	70[a]	185–186	$C_{16}H_{35}N_5S_3$	Found: 48.72; 8.94; 18.33; — Calc.: 48.81; 8.96; 18.29; —
3-Aminorhodanine	2-Thioxo-3-(N,N-diisopropylthiocar-bazoyl)amino-4-thiazolidone (XXIII)	F	40[a]	164–165	$C_{10}H_{18}N_4OS_3$	Found: 38.92; 5.69; 18.33; — Calc.: 39.19; 5.92; 18.29; —
3-Amino-2-oxazolidone	3-(N,N-Diisopropylthiocarbazoyl)-amino-2-oxazolidone (XXIV)	F	48[a]	163–164	$C_{10}H_{20}N_4O_2S$	Found: 46.17; 7.77; 21.79; — Calc.: 46.13; 7.74; 21.52; —
N-Phenyl-1,2-phenyl-enediamine	1,1-Diisopropyl-4-(2-anilinophenyl)-thiosemicarbazide (XXV)	F	56[a]	134–135	$C_{19}H_{26}N_4S$	Found: 66.60; 7.75; 16.43; — Calc.: 66.62; 7.65; 16.36; —

Solvents used for recrystallization: [a] Ethanol. [b] Ethanol-water. [c] Cyclohexane.

The reactions between (I) and 3-amino-2-oxazolidone, a cyclic carbazate, or 3-aminorhodanine, a cyclic acyl dithiocarbazate, both resulted in introduction of the N,N-diisopropylthiocarbazoyl group on the amino groups to give XXIV and XXIII, respectively.

$$
\text{Pr}^i_2\text{N-NCS} + \underset{\displaystyle \substack{\text{O=C} \diagdown_\text{O} \diagup \text{CH}_2}}{\overset{\displaystyle \substack{\text{H}_2\text{N} \diagdown \\ \text{N—CH}_2}}{}} \longrightarrow \underset{\displaystyle \substack{\text{O=C} \diagdown_\text{O} \diagup \text{CH}_2}}{\overset{\displaystyle \substack{\text{Pr}^i_2\text{N-NH-CS-NH} \\ \text{N—CH}_2}}{}}
$$

XXIV

$$
\text{Pr}^i_2\text{N-NCS} + \underset{\displaystyle \substack{\text{S=C} \diagdown_\text{S} \diagup \text{CH}_2}}{\overset{\displaystyle \substack{\text{H}_2\text{N} \diagdown \quad \text{O} \\ \text{N—C}}}{}} \longrightarrow \underset{\displaystyle \substack{\text{S=C} \diagdown_\text{S} \diagup \text{CH}_2}}{\overset{\displaystyle \substack{\text{Pr}^i_2\text{N-NH-CS-NH} \quad \text{O} \\ \text{N—C}}}{}}
$$

XXIII

As an example of a hitherto uninvestigated class of compound, 4-alkoxy-thiosemicarbazides, 1,1-diisopropyl-4-methoxythiosemicarbazide (XXI) was prepared from (I) and methoxyamine. These compounds will be discussed in some detail in a forthcoming publication from this laboratory.

$$\text{Pr}^i_2\text{N-NCS} + \text{H}_2\text{N-OCH}_3 \longrightarrow \text{Pr}^i_2\text{N-NH-CS-NH-OCH}_3$$

XXI
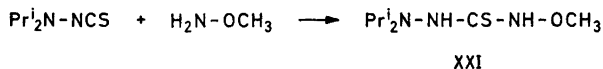
EXPERIMENTAL

Conditions and equipment used for the physical measurements were those described in part II of this series.[10]

N-*Isothiocyanatodiisopropylamine (I)*. *Improved method.* We have previously reported on the generation of (I) from N,N-diisopropylhydrazine *via* 1-(N,N-diisopropylthio-carbazoyl)imidazole.[1] The modified procedure given here is superior not only in giving a product in higher yield and of higher purity, but also in being convenient for the preparation of (I) on a larger scale, *i.e.* 1 g portions instead of 100—200 mg protions. Crude thiocarbonyldiimidazole (8.9 g) [11] was dissolved in thoroughly dried chloroform (80 ml) and benzene (20 ml). To the stirred solution, a solution of N,N-diisopropylhydrazine (5.8 g) in dry benzene (20 ml) was added dropwise during 1/2 h. Stirring was continued for another 1/2 h at room temperature, and the reaction mixture was extracted *rapidly* with three 50 ml portions of water and dried *immediately* with sodium sulphate or magnesium sulphate by shaking. The solvents were removed *in vacuo* to give 80—85 % of product, suitable for thermolysis. To ensure a good yield (70—90 %), in this latter reaction, the intermediate was heated to a temperature just below the m.p. before the vacuum system was connected. This modification circumvents the troubles arising from insufficient heat transfer during the thermolysis and thus allows greater portions to be thermolyzed at one time. We have found that if freshly prepared (I) is at once dissolved in ethanol to make a 10 % solution it may be stored in the cold for several weeks before the content of (I) diminishes. Decomposition is readily seen by the separation of a colourless crystalline product from the ethanolic solution, the structure of which is at present being investigated.

Reaction of (I) with the amines and hydrazine derivatives in Table 1. The directions given below refer to entry "Method", Table 1. Supplementary remarks are given for a few compounds deviating from the general methods in the preparation. *Method A.* The reagents were combined directly, and if an exothermic reaction started, cooling in ice was sufficient to moderate the reaction. The crystalline product obtained after scratching

for some time with a spatula was washed with pentane to remove unreacted (I). *Method B.* The reactants were dissolved in chloroform, and the solutions mixed. The reaction mixture was heated briefly to the boiling point once or twice and allowed to stand, and a crystalline product was obtained by cooling and adding pentane. *Method C.* As method B, but dry benzene was used instead as the medium and addition of pentane was not necessary to obtain the product. *Method D.* An ethanolic solution of (I) (10 %) was added in small portions to the other reagent. After the exothermic reaction had subsided, the reaction mixture was allowed to stand for 10 min. The crystalline product was filtered off and washed with ethanol. *Method E.* As method D, but it was necessary to add water to the reaction mixture to effect precipitation of the product, which was washed with aqueous ethanol. *Method F.* As method D, but since no exothermic reaction was observed, the reaction mixture was heated to the boiling point once or twice to be sure that the reaction had gone to completion. *Method G.* As method F, but with addition of water to the reaction mixture to induce precipitation and washing of the crude product with aqueous ethanol. All compounds were colourless except VIII (yellow) and XXIII (pale red). In the case of VI, IX, XV, and XVIII, boiling of the reaction mixture was continued for 10 min. Evaporation of the solvents was only necessary to obtain VI. It was isolated as an oil which crystallized on prolonged scratching.

Identification of II—XXV. Analysis and infrared spectroscopy were in most cases sufficient for unambiguous identification of the reaction products. The introduction of the *N,N*-diisopropylthiocarbazoyl group on nitrogen was invariably followed by the appearance of a very strong band in the region between 1500 and 1600 cm^{-1}, which is characteristic of the thioureide grouping and is obviously the counterpart to the "B band" previously reported for thioamides.[12] In the case of VI the identity of this band was checked by deuteration. Since the only band notably influenced was the strongest in this region, being observed at 1536 cm^{-1}, we may conclude that a coupling has occurred with the NH vibration, as would be expected by analogy to the results obtained with secondary aliphatic thioamides.[12] The location of the NH stretching vibration of the *N,N*-diisopropylthiocarbazoyl group was at the same time determined to be 3160 cm^{-1}. Since a corresponding, strong and broad band was found at the same position in all our products, it can be used as an additional criterion for this structure. The presence or absence of primary amino groups, which was of interest in connection with the reactivity of the bifunctional reagents, was easily determined by a combined investigation of the NH stretching region and the NH_2 deformation region at 3200—3500 cm^{-1} and 1600—1650 cm^{-1}. In this way the identities of the compounds II—VIII, XIV—XVI, and XIX—XXV were established. In addition it was ascertained that the compounds IX—XI were soluble and the compounds XII—XIII insoluble in aqueous sodium hydroxide, in accordance with the assigned structures. In the case of XVII it was necessary to establish the position of the NH stretching vibrations originating from the amino group relative to the bands from the amide NH_2. Comparison of the infrared spectrum of 2-aminobenzamide with that of benzamide showed that at least the band at 3440 cm^{-1} in the former compound must be due to the amino group. Two bands at *ca.* 3200 cm^{-1} and 3340—3380 cm^{-1} were observed in both compounds and are taken as indicative of the amide NH_2. In XVII only the two latter bands were present, which showed that (I) had attacked the aromatic amino group.

S-(*o-Aminophenyl*) *methyldithiocarbamate.* This compound was prepared by the action of methyl isothiocyanate (145 mg) on 2-aminothiophenol (250 mg). The components were dissolved together in ethanol and the solution allowed to stand at room temperature for 24 h. By careful addition of small portions of water and scratching, a yellowish crystalline product could be obtained. This was recrystallized from cyclohexane to give a 81 % yield of colourless crystals, m.p. 81—82°C. The compound was identified by the infrared spectrum (bands at 1610 cm^{-1} and 3330+3425 cm^{-1} but no bands from SH stretching vibrations) and by insolubility in base. (Found: C 48.40; H 5.07; N 13.97; S 32.20. Calc. for $C_8H_{10}N_2S_2$: C 48.45; H 5.08; N 14.13; S 32.33).

2-Benzothiazolethione. *S*-(*o*-Aminophenyl) methyldithiocarbamate (500 mg) was dissolved in glacial acetic acid (5 ml) and the solution refluxed for 1 h. While still hot it was poured on ice (50 g), and the colourless precipitate was filtered off. Recrystallization from benzene afforded the pure material with m.p. 170—172°C. (Found: C 50.35; H 2.96; N 8.28. Calc. for $C_7H_5NS_2$: C 50.27; H 3.01; N 8.38). If 4 N HCl was used as solvent instead, precipitation was observed 1/2 min after heat was applied. The material was

identified as a mixture of methylammonium chloride and 2-benzothiazolethione. The compound has been prepared previously in several different ways; m.p. 174°C.[13]

S-(p-Aminophenyl) methyldithiocarbamate. This compound was prepared like the *o*-isomer, in 77 % yield. Recrystallization from a benzene-pentane mixture gave a colourless material, m.p. 103−104°C. It was identified in the same way as the *o*-isomer. (Found: C 48.05; H 5.05; N 13.94; S 32.18. Calc. for $C_8H_{10}N_2S_2$: C 48.45; H 5.08; N 14.13; S 32.33).

S-(o-Aminophenyl) phenyldithiocarbamate. To an ethanolic solution of 2-aminothiophenol (250 mg) was added phenyl isothiocyanate (270 mg). The solution was allowed to stand for 15 min; a weakly exothermic reaction was observed. A crystalline product was obtained in 60 % yield by dropwise addition of water and cooling. This was recrystallized from cyclohexane (25 ml) to give a colourless, crystalline material, m.p. 79−80°C. (Found: C 60.25; H 4.73; N 10.73; S 24.68. Calc. for $C_{13}H_{12}N_2S_2$: C 59.96; H 4.65; N 10.76; S 24.63). It was identified by its infrared spectrum and by being insoluble in sodium hydroxide. If kept over the m.p. for a time, it resolidified to give colourless crystals, m.p. 157−159°C. This compound has also been obtained directly from 2-aminothiophenol and phenyl isothiocyanate under forcing conditions and has been shown to be 2-anilinobenzothiazole.[5]

Condensation of anthranilic acid with methyl isothiocyanate. This experiment was considered of interest in view of the unexpected resistance to cyclization observed for XV and XII, discussed in the text. Equimolar amounts of the reactants were dissolved in ethanol and allowed to stand for 24 h at room temperature. A colourless crystalline material, m.p. 247−250°C, was obtained in good yield and could be recrystallized from ethanol without changing its m.p. It was concluded from analysis and by analogy to the corresponding reaction with allyl isothiocyanate[2] to be 3-methyl-2-thioxo-1,2,3,4-tetrahydro-4-quinazolone. This result shows that, in contrast to XV, the initially formed 1-methyl-3-(o-carboxyphenyl)thiourea cyclizes with loss of water even on standing in solution at room temperature. (Found: C 56.35; H 4.35; N 14.39. Calc. for $C_9H_8N_2OS$: C 56.23; H 4.19; N 14.58).

Cyclization of XV. A mixture of XV (150 mg) and dicyclohexylcarbodiimide (200 mg) was melted together for a short time and the melt allowed to cool. The fusion was repeated twice. After addition of benzene (5 ml), the solution was refluxed for 3 days. The precipitated dicyclohexylurea was filtered off and the solvents evaporated to give an oil, which deposited crystals on standing for a month. The crystals were separated and recrystallized from ethanol to give a 20 % yield of colourless material, m.p. 117−118°C. Infrared spectrum and analysis were consistent with the formulation of this compound as 3-diisopropylamino-2-thioxo-1,2,3,4-tetrahydro-4-quinazolone, by analogy to the reaction described above. (Found: C 60.88; H 6.97; N 15.17. Calc. for $C_{14}H_{20}N_3OS$: C 60.40; H 7.24; N 15.10).

REFERENCES

1. Anthoni, U., Larsen, Ch. and Nielsen, P. H. *Acta Chem. Scand.* **21** (1967) 2061.
2. Werbel, L. M. *J. Org. Chem.* **32** (1967) 462.
3. Knorr, L. and Rössler, P. *Ber.* **36** (1903) 1278.
4. Cherbuliez, E., Baehler, Br., Jindra, H., Weber, G., Wyss, G. and Rabinowitz, J. *Helv. Chim. Acta* **48** (1965) 1069.
5. Hofmann, A. W. *Ber.* **20** (1887) 1788, 1796.
6. Kurzer, F. and Sanderson, P. M. *J Chem. Soc.* **1962** 230.
7. Ferris, A. F. and Schutz, B. A. *J. Org. Chem.* **28** (1963) 3140.
8. Ramiah, K. V. and Puraeik, P. G. *J. Mol. Spectry.* **7** (1961) 89.
9. Anthoni, U., Larsen, Ch. and Nielsen, P. H. *Acta Chem. Scand.* **21** (1967) 2580.
10. Anthoni, U., Larsen, Ch. and Nielsen, P. H. *Acta Chem. Scand.* **21** (1967) 1201.
11. Staab, H. A. and Walther, G. *Ann.* **657** (1962) 98.
12. Jensen, K. A. and Nielsen, P. H. *Acta Chem. Scand.* **20** (1966) 597.
13. Jacobson, P. and Frankenbacher, A. *Ber.* **24** (1891) 1400.