#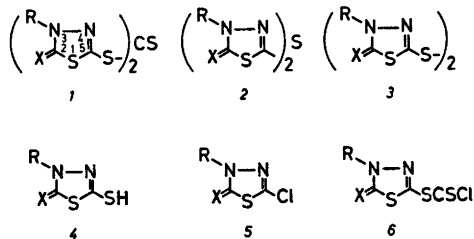 The Reaction between Thiophosgene and Hydrazines. Formation of Trithiocarbonates with N,S-Ambident 1,3,4-Thiadiazolines as Intermediates

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The reaction between substituted hydrazinium salts and thiophosgene in water has been reinvestigated. Previous suggestions that the products are N-isothiocyanatoamines have been disproved. If methyl- or phenylhydrazinium chloride are employed in the reactions 5,5-thiocarbonyldithiobis[3-methyl-1,3,4-thiadiazol-2(3H)-one] (1a) and 5,5-thiocarbonyldithiobis[3-phenyl-1,3,4-thiadiazol-2(3H)-one] (1c), respectively, are formed as the main products. Several by-products and one key intermediate were isolated. Each was characterized by comparison to samples prepared by alternative synthetic methods and by information obtained from ^{13}C NMR, and IR spectrometry. A mechanism involving 5-mercapto-1,3,4-thiadiazol-2(3H)-ones and thiones as intermediates is proposed and the literature relating to N,S ambident reagents reviewed.

In 1937 Beckett and Dyson[1] found that the reaction between thiophosgene and hydrazines


in general leads to the formation of thiocarbonohydrazides. Subsequent work has questioned this result only in few cases, cf., e.g., Hayes[2] and Sherman.[3]

When the reaction was performed in hydrochloric acid Beckett and Dyson obtained products which were formulated as N-isothiocyanatoamines. However, our previous investigations concerning N-isothiocyanatoalkylamines have disclosed methods of preparation,[4-6] properties,[7-12] and tendency to dimerization[13] characteristic of N-isothiocyanatoamines which appear to be quite different from those described by Beckett and Dyson. This initiated a study of the reaction between thiophosgene and various hydrazine derivatives which has led to an elucidation[14-16] of the structures of several products claimed to be N-isothiocyanatoamines. In the present paper a reinvestigation of the reaction between methyl- or phenylhydrazinium salts and thiophosgene is presented.

Ambiguous results were obtained by Beckett and Dyson[1] on reacting methylhydrazinium sulfate with thiophosgene. The proposed structure for the reaction product was based on its reaction with aniline, claimed to give 1-methyl-4-phenylthiosemicarbazide. However, the melting point given[1] for this compound is quite different from that of authentic 1-methyl-4-phenylthiosemicarbazide,[17] but agrees well with that of 2-methyl-4-phenylthiosemicarbazide.[17]
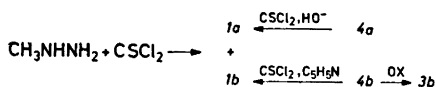
Scheme 1.

The above controversy has now been settled by a chromatographic separation of the main constituents of the product formed by the reaction between an aqueous solution of methylhydrazinium sulfate and thiophosgene. The compounds were identified as trithiocarbonates by independent syntheses as outlined in Scheme 1. The formulation of *1a* and *1b* as trithiocarbonates is based upon the assumption that thiophosgene attacks sulfur in preference to nitrogen (*cf.* discussion later).

Both *1a* and *1b* formed 1,3-diphenylthiourea and the anilinium salts of *4a* and *4b* on boiling with a solution of aniline in benzene. The formation of the methylphenylthiosemicarbazide found by Beckett and Dyson, must be explained by the presence of a small amount of unreacted thiophosgene and/or methylhydrazine in the crude mixture, since no trace of this compound was found when the reaction was performed with aniline and the purified reaction product *1a* or *1b*.

The formation of 1,3,4-thiadiazoline derivatives in the reaction between methylhydrazinium sulfate and thiophosgene led us to reinvestigate the reaction between phenylhydrazinium chloride and thiophosgene. According to Beckett and Dyson this reaction results in the formation of 1,2,4-triisothiocyanatobenzene and phenylisothiocyanate. We obtained a compound with the same melting point as given for the alleged triisothiocyanatobenzene but with a different elemental analysis. Physical and chemical evidence (discussed in connection with Scheme 2) identified this compound as the trithiocarbonate *1c*. Only very small amounts of phenylisothiocyanate were formed.

The product obtained by refluxing *1c* with aniline was identified as a mixture of two salts of 5-mercapto-3-phenyl-1,3,4-thiadiazol-2(3*H*)-one, *4c*. One of the salts is, as expected, the anilinium salt, the other is the 1,3-diphenylformamidinium salt (*cf.* the discussion given in connection with Scheme 3). Treatment of *1c* with ammonia similarly gave the ammonium

salt of *4c* in addition to ammonium thiocyanate. On boiling with ethanol *1c* formed the disulfide *3c*, the oxidation product of the initially formed thiol. The products obtained by Beckett and Dyson had approximately the same melting points as the above products but were formulated quite differently.

These results show that the reaction between hydrazinium salts and thiophosgene generally results in the formation of 1,3,4-thiadiazoline derivatives. To elucidate how this ring system is formed the crude product has been separated by column chromatography with the purpose of isolating and identifying its minor constituents. In addition to traces of phenylisothiocyanate and *ca.* 35 % unidentified, presumably high molecular weight substances, the following 5 fractions, given in the order of decreasing flow velocity, were isolated (*cf.* Scheme 2).

*6c*: 5-[(Chlorothiocarbonyl)thio]-3-phenyl-1,3,4-thiadiazol-2(3*H*)-one.

5c: 5-Chloro-3-phenyl-1,3,4-thiadiazol-2(3*H*)-one.

1d: 5,5-Thiocarbonyldithiobis[3-phenyl-1,3,4-thiadiazole-2-(3*H*)-thione].

1c: 5,5-Thiocarbonyldithiobis[3-phenyl-1,3,4-thiadiazol-2(3*H*)-one].

2c and *3c*: A mixture of 5,5-thio and 5,5-dithiobis[3-phenyl-1,3,4-thiadiazol-2(3*H*)-one].

The identity of *1c* was established by comparison to an authentic specimen prepared from 5-mercapto-3-phenyl-1,3,4-thiadiazol-2(3*H*)-one (*4c*) and thiophosgene. Substance *4c* was prepared according to Busch[18] and characterized by oxidation to the disulfide *3c*.
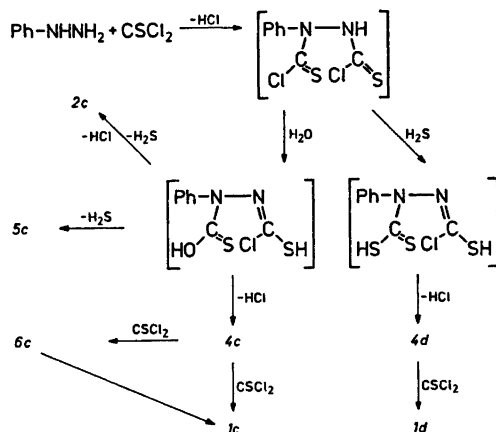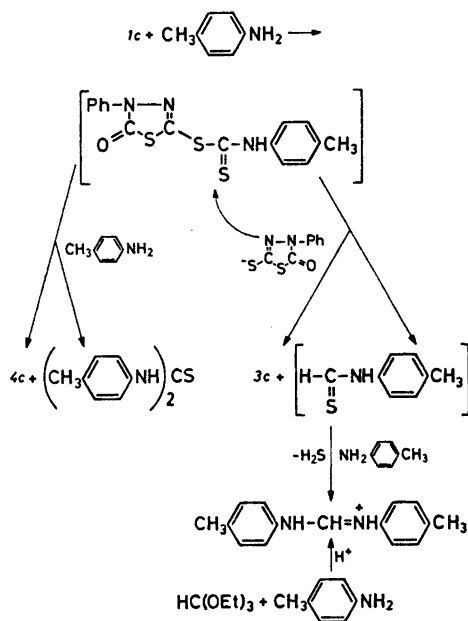

Scheme 2.

The identity of *1d* was also confirmed by comparison to authentic material prepared from the potassium salt of 5-mercapto-3-phenyl-1,3,4-thiadiazole-2(3H)-thione (*4d*) and thiophosgene according to the directions given by Runge *et al.*[19] The structure of *4d* was characterized by oxidation to the disulfide *3d*.

A logical scheme to encompass the formation of the products *5c, 6c, 2c, 1c* and *1d* is shown in Scheme 2. The reaction between methylhydrazinium sulfate and thiophosgene discussed above (Scheme 1) proceeds by a similar route. By analogy with the acylation of derivatives of hydrazine, which almost invariably[20] gives 1,2-diacylhydrazines, the initial steps probably involve attack of thiophosgene on both nitrogen atoms in phenylhydrazine. The bis(thioacid chloride) formed undergoes rapid hydrolysis in the aqueous medium and the resulting intermediate can either release hydrogen sulfide with formation of *5c* or eliminate hydrogen chloride to give the 1,3,4-thiadiazoline ring. Further attack by thiophosgene gives *6c* and *1c*. The latter is very probably formed *via 6c* as an intermediate. The formation of *1d* can be explained by a similar mechanism from the initially formed bis(thioacid chloride) and hydrogen sulfide. Hydrogen sulfide either originates from hydrolysis of thiophosgene or is a by-product in the formation of *5c*.

An unusual pattern was noted in the reaction between *1c* and aniline. In order to distinguish clearly between the phenyl group originating from *1c* and that from aniline we chose to investigate instead the reaction between *1c* and *p*-toluidine. The results are shown in Scheme 3. From *1c* four products were obtained in approximately equal yields. Two of the products, 1,3-di(*p*-tolyl)thiourea and the *p*-toluidinium salt of *4c*, arise from the straightforward reaction between *1c* and an excess of *p*-toluidine. The remaining products, the disulfide *3c* and the 1,3-di(*p*-tolyl)formamidinium salt of *4c*, can be explained by invoking the reaction sequence shown to the right in Scheme 3. Nucleophilic attack of *p*-toluidine on the trithiocarbonate group of *1c* initially gives a dithiocarbamate and, in addition, the thiolate of *4c*. The strongly nucleophilic character of the sulfur atom in this anion apparently results in its attack on the dithiocarbamate
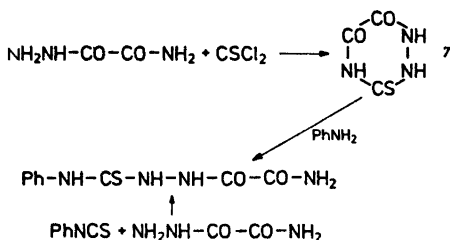
Scheme 3.

competitive to the expected attack of *p*-toluidine. The proposed attack on sulfur is analogous to the reaction of related selenium compounds.[21] Also a similar attack was recently reported for thiols and isothioureas at elevated temperatures.[22] In the present case, the attack leads to the formation of the disulfide *3c*, and in a well known type of reaction[23] the *N*-thioformyl-*p*-toluidine simultaneously formed is converted by excess *p*-toluidine into 1,3-di-(*p*-tolyl)formamidine, isolated as the salt of *4c*. This salt was identical to material prepared from the authentic formamidine (Backer and Wanmaker[24]) and 5-mercapto-3-phenyl-1,3,4-thiadiazol-2(3*H*)-one (*4c*).

The reaction between 1,2-dimethylhydrazinium chloride and thiophosgene gives a mixture of 3,4-dimethyl-5-thioxo-1,3,4-thiadiazolidin-2-one, *4e*, and 3,4-dimethyl-1,3,4-thiadiazolidine-2,5-dithione, *4f* in the ratio 2:1. This result parallels very closely that discussed above and supports the proposal (Scheme 2) that hydrolysis/thiolysis of the initially formed bis(thioacid chloride) takes place prior to the formation of the trithiocarbonate.

Finally we have studied two reactions which

Scheme 4.

according to Beckett and Dyson also should give rise to isothiocyanatoamines. In the reaction between thiophosgene and oxamohydrazide ("semioxamazide"), the reaction product was identified as 3-thioxohexahydro-1,2,4-triazine-5,6-dione (7) (Scheme 4). It undergoes ring-opening on treatment with aniline and forms 1-oxamoyl-4-phenylthiosemicarbazide

The other reaction is that between *p*-nitrophenylhydrazine and thiophosgene. The crude product was shown by column chromatography to consist of several compounds. The main fraction was identified as the 5,5-thiocarbonyldithiobis[3-(4-nitrophenyl)-1,3,4-thiadiazol-2(3*H*)-one] (*1e*).

SULFUR vs. NITROGEN ATTACK ON AMBIDENT HETEROAROMATIC COMPOUNDS

From the results described above it can be concluded that the reaction between hydrazines and thiophosgene in aqueous hydrochloric acid proceeds *via* mercaptothiadiazolines, *4* (Scheme 5) to give trithiocarbonates, *1*, rather than thioureides, *1'*.
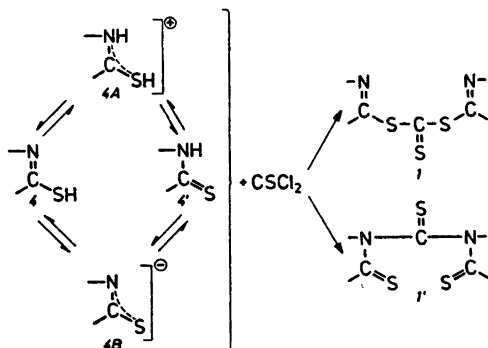

Scheme 5.

In order to clarify the factors responsible for the preferential attack of sulfur, the nature of the reacting species *4* must be considered. Tautomerisation gives the thione structure, *4'*, which could, however, only be established for *4a* in the solid state by infrared spectroscopy. Infrared spectra of the thiols *4b* − *4d* in KBr and *4a* − *4d* in chloroform solution did not show detectable amounts of the thione isomers *4a'* − *4d'*. Provided the reaction of *4* with thiophosgene occurs in aqueous solution, prototropic equilibria are set up leading to formation of thiolate ions, *4B*, and the protonated species, *4A*. Kjellin and Sandström [25] have recently investigated the thione-thiole protonation equilibria of a series of oxazoline-, thiazoline-, and imidazoline-2-thiones. Since the pK_{HA} of compounds containing structure *4A* was found to be < 0, and since thiophosgene is in general much less susceptible to electrophilic than to nucleophilic attack [26] it is expected, that the presence of *4A* in the reaction mixture is insignificant. The reaction accordingly proceeds by attack of one or more of the three ambident nucleophilic species *4B*, *4*, and *4'* on thiophosgene.

It is usually assumed [19,27−30] that alkylation or acylation of ambident nucleophiles containing competing *N* and *S* points of attack yields the *S*-derivatives. Cases are known in which *S*-attack is unambiguously proved by formation of a cyclic trithiocarbonate.[31] However, evidence has been presented [32−36] to show that *S*-attack is not necessarily the rule and should be confirmed in each case. Furthermore, cases have been reported in which S to N acyl migrations occur [37] as have compounds in which N to S migrations occur instead.[38]

The factors determining nitrogen *vs.* sulfur attack have been discussed by several authors.[39] In a recent study of glucosidation of 2,5-dimercapto-1,3,4-thiadiazole it was concluded that the rules derived by Kornblum *et al.*[40] were followed to give *S*-glycosides preferentially when the reaction proceeds *via* an S_N2 mechanism. By contrast *N*-glycosides are obtained if mercury salts, known to promote the S_N1 pathway, are present.[41] Halasa and Smith [32] were able to predict the conditions for *N*- *vs.* *S*-attack of the ambident anion of benzothiazoline-2-thione by using the oxibase scale. Since however the result is determined at least

Table 1. ^{13}C NMR chemical shifts (δ) in (3H)-thiadiazoles downfield from TMS.
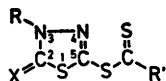
Compound	C(2)	C(5)	R'C=S	R(3)[a]
1a	170.3	138.8	211.1	34.9
1b	188.3	144.9	208.0	39.1
1c	168.8	140.3	209.9	137.1, 128.0, 129.2, 122.1
1d	188.1	146.1	207.2	137.8, 129.7, 129.2, 125.8
3b	187.2	152.6		39.1
3c	167.8	147.5		137.0, 127.2, 128.8, 121.3
3d	187.2	153.7		138.0, 129.5, 129.1, 125.6
4a	169.8	140.1		34.3
4b	186.6	148.4		38.8
4c	168.2	142.1		137.3, 127.1, 128.9, 121.5
4d	186.3	149.4		138.0, 129.1, 128.9, 125.5
4e	163.6	177.9		35.1,[b] 33.4[b]
4f	180.1	180.1		36.7[b]
5c	167.1	137.9		137.3, 127.5, 129.1, 121.7
6c	168.6	142.3	189.8	137.2, 128.0, 129.2, 122.1

[a] For R = Ph the numbers given are in order of increasing peak area (1:1:2:2). [b] Me(3) and Me(4).

by the pH[37] and the temperature [32,42] unambiguous criteria were needed in order to distinguish between the possible final products, *1* and *1'* (Scheme 5) arising from the reaction between thiophosgene and hydrazines.

^{13}C NMR spectroscopy was found to be a most convenient method for the distinguishing between *1* and *1'*. Also considerable IR spectroscopic evidence substantiating the suggested structure of the compounds *1 − 6* was collected during the investigations. The two categories of data are described separately in the following sections.

^{13}C NMR SPECTRA

The capability of ^{13}C NMR to differentiate between the trithiocarbonate and the thioureide structure (*1* and *1'* Scheme 5) becomes evident by comparison of ^{13}C NMR shieldings of the compounds examined in this study and appropriate model compounds. The chemical shift data and assignments are summarized in Table 1. For the thiols *4a − d* and the disulfides *3b − d* the assignments are straightforward. Thus, in addition to the resonances for R (CH$_3$ or Ph, see Table 1), which are readily identified, the spectra contain only two peaks.

The low field peak is assigned to C(2) because of the large downfield shift (~ 20 ppm) observed when oxygen is replaced by sulfur at this carbon atom (*e.g.* when going from *4a* to *4b* see Table 1). The high field peak is consequently assigned to C(5), and it is only slightly shifted by the substitution.

The ^{13}C shieldings of C(5) for *4a − d* show that the compounds in chloroform exist predominantly in the thiol form *4* (see Scheme 5). First the large chemical shift difference of more that 30 ppm between C(2) and C(5) in the spectra of *4b* and *4d* is not compatible with a thione structure, *4'*, in which these two carbon atoms would be expected to be nearly equivalent. Furthermore, the ^{13}C NMR spectra of the disulfides *3b − d* are very similar to those of compounds *4a − d*.

The spectra of the trithiocarbonates *1a − d* display in addition to the peaks for the R group three peaks with very different chemical shifts (see Table 1). The C(2) resonance may be identified in a manner similar to that used for compounds *3* and *4*. The shielding of C(2) is seen to be nearly the same in the corresponding compounds with structures *1*, *3*, and *4*. The two remaining peaks in the spectra of *1a − d* are found at approximately 210 and 140 ppm,

neither of which can correspond to the thio-ureide structure (*1'*). In the latter case both peaks should represent thiocarbonyl carbons where one [C(5)] should be very similar to C(5) in *4e* and *4f* ($\delta \sim 180$) and the other R'C = S would be expected to fall around δ 170 − 180; *cf.* thiocarbonyl shieldings in the model compounds thiocarbonohydrazide: δ 181.3; 1,1-' thiocarbonyldiimidazole: δ 172.8, 1,3-diphenyl-thiourea: δ 179.9. On the other hand, the presence of two peaks around 210 and 140 ppm is what would be expected for the trithio-carbonate structure, *1*. Here, a chemical shift value of ~ 140 ppm is expected for C(5) by comparison with compounds of types *3* and *4*. The peak at δ 210 is then ascribed to R'C = S, in good agreement with the value of δ 224

found for the thiocarbonyl carbon in diphenyl trithiocarbonate. The evidence is thus conclusive that the compounds *1a − d* possess the trithio-carbonate structure *1*.

The ^{13}C chemical shifts for the chlorine compounds *5c* and *6c* included in Table 1 fit the pattern shown by the other compounds examined. A small upfield shift is observed at C(5) in compound *5c* relative to the other oxygen-containing compounds. In contrast, the chlorine atom causes a large upfield (~ 20 ppm) shift for the adjacent carbon atom in compound *6c*. Similarly, a large difference in shielding of the thiocarbonyl carbon is found for diphenyl trithiocarbonate (δ 224) and phenyl chloro-dithioformate (δ 197).
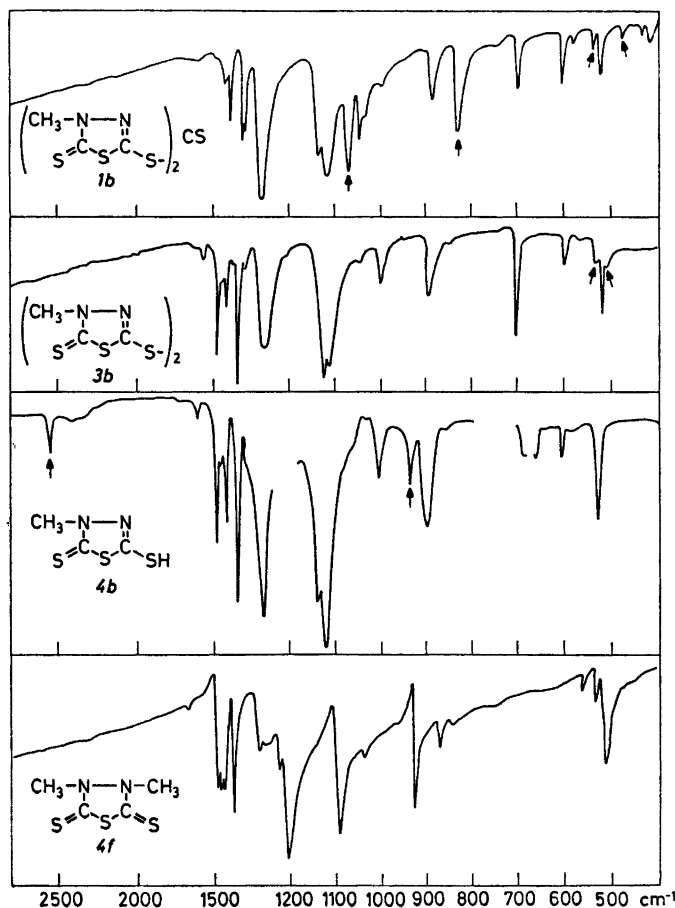

Fig. 1. Infrared spectra of *1b*, *3b*, *4f* (KBr) and *4b* (CHCl₃) in the range 400 − 2700 cm⁻¹. The bands discussed in the text are indicated by arrows.

INFRARED SPECTRA

Infrared spectroscopy provides evidence that the products of the reaction between thiophosgene and hydrazinium salts are trithiocarbonates, *1*, rather than thioureides, *1'*. The method can be exemplified by considering the infrared spectra shown in Fig. 1. The dithione *4f* (KBr) has necessarily the structure shown since the thione-thiol tautomerism is effectively prevented by the two methyl groups. Comparison with the infrared spectra of related compounds indicates that this compound displays features characteristic of a thione structure *4'*. On the other hand, the thiol *4b* (CHCl$_3$), the disulfide *3b* (KBr), and the trithiocarbonate *1b* (KBr) are derived from the tautomeric thiol structure *4*. Thus we might expect the infrared spectra of these compounds to exhibit a pattern typical of this structure. Of course, since electron delocalisation will tend to diminish the apparent differences expected from the formulas given in Fig. 1, only experiments can show whether the infrared spectra of compounds with a *4'* and *4* structure can in fact be used to distinguish between these structures.

From Fig. 1 it is seen that the spectra of all four compounds are similar in the range 1250 – 1500 cm^{-1}, while the spectrum of *4f* is different from the spectra of *1b*, *3b*, and *4b* in the region between 400 and 1250 cm^{-1}. The compounds with structure *4* are characterized by the following nine bands (approximate location, cm^{-1}): 1120 (doublet), 1050w, 1000w – m, 895m, 700m, 600m, 575vw, and 525m. Though some of these bands are also seen in the spectrum of *4f*, the general pattern is clearly different. The same is true when the changes originating in the presence of an extra methyl group are taken into account.

The nine bands characteristic of the 3-methyl-1,3,4-thiadiazole-2(3H)-thione moiety are essentially independent of the changes in the substituent in the series *4b*, *3b*, and *1b*. Accordingly structure *4* can be recognized by investigating the infrared region between 400 and 1250 cm^{-1}.

The interpretation of the differences in the spectra of *4b* and *3b* (indicated by arrows) is facilitated by the data available for benzenethiol [43] and for diaryldisulfides.[44] The band at

2560 cm^{-1} in *4b* is then satisfactorily established as the S – H stretching vibration and the band at 936 cm^{-1} as originating mainly in C – S – H bending. On oxidation of the thiol *4b* to the disulfide *3b* both these bands disappear and are replaced by two weak bands at 507 and 530 cm^{-1}. The latter absorption is ascribed to S – S stretching which is generally only observed as very weak absorption in the infrared, although it is usually prominent in the Raman spectrum.[44]

In a similar way we can explain the differences between the spectra of *3b* and *1b* (indicated by arrows) as a replacement of the S – S stretching absorption in *3b* by bands characteristic of the CS$_3$ group. The corresponding 6 bands have positions which can be readily estimated from the results obtained by a complete vibrational analysis of ethylene trithiocarbonate.[45] The three stretching vibrations of the trithiocarbonate group have been found near 1060 cm^{-1} (very strong), 830 – 880 cm^{-1} (strong), and 500 cm^{-1} (medium) and compare favourably with those observed in the spectrum of *1b* at 1075, 834, and 480/540 cm^{-1}. Of the remaining vibrations of the trithiocarbonate group only the out-of-plane deformation vibration is expected within the region investigated, probably between 400 and 500 cm^{-1} where three weak bands are observed in *1b*. The remaining bands are attributed to over- and combination tones of the lower fundamentals. In our opinion this analysis of the infrared spectrum of *1b* proves it to be a trithiocarbonate provided of course that the spectral data are incompatible with those of the thioureide structure *1b'*. Thus thioureides exhibit [46] a strong band in the range 1400 – 1600 cm^{-1} which is not found in the spectrum of *1b*. Since the region in question is devoid of other strong absorption the possibility that the latter band is masked by other absorption can be excluded.

The method works equally well within the aromatic series as evidenced by the spectra shown in Fig. 2 (CCl$_4$ solution). It is seen that the spectra of *4c* and *5c* are very similar apart from the two bands at 2560 cm^{-1} (S – H stretching) and 933 cm^{-1} (C – S – H deformation). Since the structure of *5c* was not confirmed by independent synthesis this serves to verify the presence of the 3-phenyl-
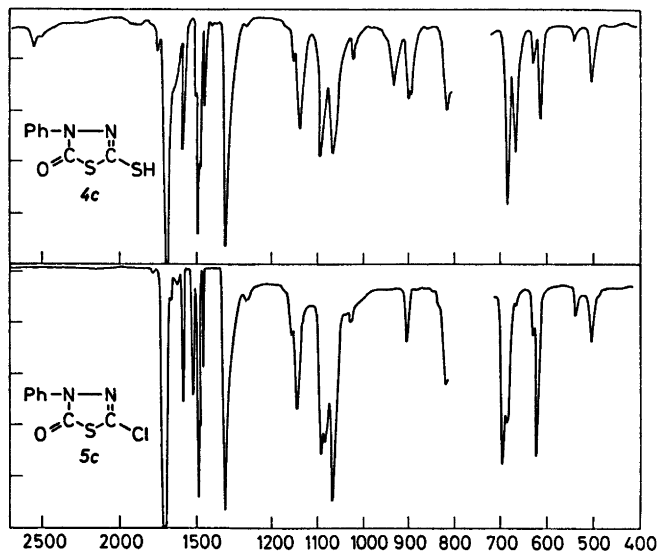
Fig. 2. Infrared spectra of *4c* and *5c* (CCl₄) in the range 400 – 2650 cm⁻¹.

1,3,4-thiadiazol-2(3*H*)-one group in *5c* and, in connection with results obtained from elemental analysis and mass spectrometry, establishes the formula given.

EXPERIMENTAL

General. Microanalyses were carried out in the Microanalysis department of this laboratory. Satisfactory elemental analyses were obtained for all new compounds and key intermediates. Melting points were determined on a Büchi melting point apparatus and are not corrected. The separations by preparative layer chromatography (PLC) were performed with portions of 0.5 – 1.0 g using 20 × 100 cm plates with silica gel (2.5 mm, Merck PF₂₅₄₊₃₆₆). The plates were developed 2 – 4 times with a mixture of benzene, chloroform, and hexane and the fractions isolated by continuous extraction with chloroform in a Soxhlet tube. For preparative-scale separations by column chromatography, columns were constructed from 30 cm lengths of 20 mm i.d. glass tubing slurry-packed with silica gel (Merck, 0.040 – 0.063 mm) or cationotropic aluminium oxide (Merck 90).

Spectra. Noise-decoupled ¹³C NMR spectra were determined with a Bruker WH 90 system (22.63 MHz) operating in the Fourier transform mode. All samples were examined as 5 – 15 % (w/v) solutions in CDCl₃ and shieldings were measured relative to internal TMS. For the compounds *1a – 1d* a trace of tris(2,4-pentanedionato)chromiumIII) was added to decrease the

relaxation time of the trithiocarbonate carbon atom.[47] This was found to be without influence (< 0.05 ppm) on the chemical shift values.

The infrared spectra in the range 400 – 4000 cm⁻¹ were recorded on a Perkin-Elmer model 337 grating infrared spectrophotometer.

Mass spectra were obtained using an AEI MS-902 mass spectrometer operating at 70 eV. The source temperature was kept between 120 and 180 °C. Exact mass measurements were performed at a resolution of 5 000 (10 % valley definition) using heptacosafluorotributyl-amine to provide reference masses.

The electronic spectra were recorded using 1 cm cells on a Unicam SP 1800 Ultraviolet Spectrophotometer in CHCl₃ solvent.

Identification of products. In general, the fractions obtained from the chromatographic separations were identified in the following way: A pure product was obtained from the center cut of a band or by recrystallization from an appropriate solvent. The formula was indicated by analysis (C, H, Cl, N, S) and the structure from the combined information obtained from infrared, NMR, and mass spectrometry. Comparison with authentic specimens included comparison of spectroscopic data and mixed melting point determination whenever practicable. In most instances (exluding, *e.g.*, some salts) the compounds were provisionally identified by their behaviour on thin layer chromatography (colour, R_F-value, colour on irradiation with ultraviolet light).

The reaction between methylhydrazinium sulfate and thiophosgene. Following the directions given by Beckett and Dyson,[1] a solution of methylhydrazinium sulfate (14 g) in water

(700 ml) was shaken vigorously with thiophosgene (15 g) added in one portion at room temperature. A slightly exothermic reaction took place and an orange solid separated. In order to ensure complete reaction the mixture was allowed to stand for an additional 2 h with occasional shaking and the solid was filtered off. Thin layer chromatography showed it to consist of several components of which the two major ones have been identified. The crude product was extracted with ethyl acetate and the extract chromatographed on a cationotropic aluminium oxide column. The column was eluted with a chloroform-carbon disulfide mixture (1:3), and the two major fractions were collected. The first was identified as 5,5-thiocarbonyldithiobis(3-methyl-1,3,4-thiadiazole-2(3*H*)-thione) (*1b*) by comparison with an authentic sample (see below) and constituted from 8 − 20 % of the total amount of these two fractions. The second (80 − 90 %) was identical to 5,5-thiocarbonyldithiobis[3-methyl-1,3,4-thiadiazol-2(3*H*)-one] (*1a*) prepared by a different route as described below.

*5-Mercapto-3-methyl-1,3,4-thiadiazole-2(3*H*)-thione (4b).* Methylhydrazine was treated with an excess of carbon disulfide in pyridine solution according to the method described for 1,3,4-thiadiazole-2,5-dithiol by Sandström.[48] An almost quantitative yield of the colourless crystalline pyridinium salt of *4b*, m.p. 134 − 135°C, was obtained. The pyridinium salt was dissolved in a minimum amount of water. The solution was filtered and poured into an excess of 6 N hydrochloric acid at 0 °C. Colourless crystals with a m.p. 68 − 69 °C [49] were obtained in 70 % yield.

*5,5-Dithiobis[3-methyl-1,3,4-thiadiazole-2(3*H*)-thione] (3b).* To an aqueous ethanolic (1:1) solution of the pyridinium salt of *4b* was added the equivalent amount of iodine. After addition of water, the precipitated ochre-yellow powder was filtered off and dried. Recrystallization from ethyl acetate gave the pure compound, m.p. 139 − 140 °C. The yield was almost quantitative.

*5,5-Thiocarbonyldithiobis(3-methyl-1,3,4-thiadiazole-2(3*H*)-thione) (1b).* Thiophosgene (0.02 mol) was added dropwise to a stirred solution of the pyridinium salt of *4b* (0.04 mol) in water (25 ml). The precipitate was collected and washed with water. Recrystallization four times from ethyl acetate gave orange coloured crystals of m.p. 139 − 140 °C. Yield 60 %.

*5-Mercapto-3-methyl-1,3,4-thiadiazol-2(3*H*)-one (4a).* Crude ethyl 2-methylcarbazate (0.1 mol, prepared according to Sasse) [50] was dissolved in ethanol (150 ml) and carbon disulfide (0.1 mol) was added followed by a solution of potassium hydroxide (0.1 mol) in ethanol (100 ml). After refluxing for 30 min the solution was allowed to stand overnight. The colourless, crystalline *potassium 3-ethoxycarbonyl-3-methyldithiocarbazate* was filtered off, washed with a little ethanol; 70 %

yield; m.p. 204 − 205 °C (dec.). The crude product was boiled in abs. ethanol for 10 h, and the solution taken to dryness *in vacuo*. Recrystallization from 50 % aqueous ethanol furnished the slightly impure *potassium salt of 4a* of m.p. 270 − 275 °C (dec.) in 50 % yield. Acidification as outlined for the preparation of *4b* afforded *4a* as colourless crystals, m.p. 82 − 83 °C; yield 70 %.

*5,5-Thiocarbonyldithiobis(3-methyl-1,3,4-thiadiazol-2(3*H*)-one (1a).* Thiophosgene (0.02 mol) was added dropwise with stirring to a solution of the potassium salt of *4a* (0.04 mol) in water (25 ml). The precipitate was filtered off and recrystallized from a chloroform-pentane mixture to give *1a*, an orange crystalline material, m.p. 186 − 187 °C, in 70 % yield.

Reaction between 1b and aniline. Aniline (0.004 mol) was added to *1b* (0.001 mol) dissolved in benzene (25 ml). The orange colour of the solution faded rapidly followed by formation of a colourless crystalline product. This was filtered off and recrystallized from benzene-chloroform (1:1) to a m.p. of 99 − 100°C. The product was identical to the *anilinium salt of* 4b prepared from *4b* and aniline in diethyl ether. The yield was almost quantitative. Evaporation of the mother liquor furnished almost the expected amount of 1,3-diphenylthiourea (m.p. 153 − 154 °C) identical to an authentic specimen prepared from aniline and phenyl isothiocyanate. When the reaction was carried out in ethanol instead of benzene the orange colour of the solution faded on boiling *1b* (0.001 mol) with aniline (0.004 mol) for a few minutes. The solution was evaporated to dryness. The residue consisted of 1,3-diphenylthiourea and starting material (recovery *ca.* 10 %), which were separated by fractional recrystallization.

Reaction between 1a *and aniline.* The procedure outlined above for the reaction of *1b* with aniline was followed. The *anilinium salt of* 4a, m.p. 111 − 112 °C, precipitated as a colourless crystalline compound. Again 1,3-diphenylthiourea was isolated in almost quantitative yield from the benzene solution by evaporation to dryness.

Reaction between phenylhydrazine and thiophosgene. Phenylhydrazine (10 g) and thiophosgene (15 g) were allowed to react in hydrochloric acid as described by Beckett and Dyson.[1] The resultant orange-coloured, sticky solid was extracted with benzene to give upon evaporation an orange-red oil (10.5 g). The residue from the benzene extraction was phenylhydrazinium chloride (*ca.* 2 g) and water.

Separation of the main components was accomplished by the following method. Triturating the oil with pentane (250 ml) in 25 ml portions gave, after evaporation of the pentane, an orange-coloured oil (4 g) consisting mainly of *5c* and *6c*, but some phenyl isothiocyanate and *1c* was also present. The residue from the pentane extraction was suspended in acetone

leaving *1c* (1 g). Evaporation of the acetone gave a residue (5.5 g) containing *1c* as the main product. It was found advantageous to separate the crude product into these pentane- and acetone-soluble fractions prior to the complete separation of each fraction by column chromatography. The elutions began with a 1:1 mixture of CCl₄/benzene, proceeded to pure benzene and concluded with pure chloroform.

We may summarize the information obtained from the chromatographic separations as follows: The first band to emerge was identified as *phenyl isothiocyanate* (100 mg). We did not establish whether this compound originated from an aniline impurity in the phenylhydrazine used for the reaction. The second band consisted of an unidentified mixture of at least three compounds (60 mg). Next the yellow crystalline *5-[(chlorothiocarbonyl)thio]-3-phenyl-1,3,4-thia-diazol-2(3H)-one, 6c*, was eluted (2.30 g); m.p. 42 – 43 °C from pentane. The fourth component consisted of a yellow oil (0.30 g) identified as *5-chloro-3-phenyl-1,3,4-thiadiazol-2(3H)-one, 5c*. The two compounds *5c* and *6c* were not compared to authentic materials, but the structures proposed above were consistent with recorded IR, MS, and ¹³C NMR spectra.

5,5-Thiocarbonyldithiobis[3-phenyl-1,3,4-thia-diazole-2(3H)-thione] (1d) was isolated next (100 mg) and identified by comparison with an authentic sample (*vide infra*).

Then we obtained 2 g of *5,5-thiocarbonyl-dithiobis-[3-phenyl-1,3,4-thiadiazol-2(3H)-one] (1c)* characterized by comparison with an authentic sample prepared as described below. The following fraction (150 mg) was identified by mass spectrometry to be a mixture of *5,5-thiobis[3-phenyl-1,3,4-thiazol-2(3H)-one], 2c, and 5,5-dithiobis[3-phenyl-1,3,4-thiadiazol-2(3H)-one], 3c*, the elemental composition of which was confirmed by high resolution MS. The ensuing fractions were eluted with pure chloroform and consisted of unidentified reddish, oily products.

5-Mercapto-3-phenyl-1,3,4-thiadiazol-2(3H)-one (4c). This compound was prepared according to the directions given by Busch[18] in 51 % yield. It was purified by dissolution in sodium hydroxide and reprecipitation with hydrochloric acid. Recrystallization from pentane gave colourless crystals. M.p. 84.5 – 85.5 °C (Busch:[18] 86 – 87 °C).

5,5-Dithiobis[3-phenyl-1,3,4-thiadiazol-2(3H)-one] (3c). Adding an equivalent amount of iodine in abs. ethanol to a solution of *4c* in benzene gave, after precipitation with pentane, a 75 % yield of yellow crystals, m.p. 77 – 77.5 °C (lit.[18] 78 – 79 °C).

5,5-Thiocarbonyldithiobis[3-phenyl-1,3,4-thia-diazol-2(3H)-one] (1c). Mixing *4c* with the calculated amount of thiophosgene in benzene solution gave *1c*, in good yield. It was recrystallized from benzene and CCl₄ to orange-yellow crystals; m.p. 156 °C. An identical compound could be obtained in poor yield by mixing

the reactants in aqueous hydrochloric acid, *i.e.* under the general conditions used by Beckett and Dyson[1] in their experiments. The electronic spectrum of this compound shows maxima at $\lambda = 249$ nm ($\varepsilon = 17$ 600), $\lambda = 275$ nm ($\varepsilon = 18$ 800), and $\lambda = 296$ nm ($\varepsilon = 19$ 000).

5-Mercapto-3-phenyl-1,3,4-thiadiazole-2(3H)-thione (4d). The potassium salt of *4d*[18] was dissolved in a minimum amount of water. The filtered solution was poured into 6 N hydrochloric acid at 0 °C. The yield of colourless crystals was 70 %. M.p. 76 – 77 °C.

5,5-Dithiobis[3-phenyl-1,3,4-thiadiazole-2(3H)-thione] (3d). The potassium salt of *4d*[18] was dissolved in aqueous ethanol (1:1). The equivalent amount of iodine in ethanol was added and *3d* separated immediately as yellow crystals in almost quantitative yield, m.p. 117 – 118 °C (from ethanol).

5,5-Thiocarbonyldithiobis(3-phenyl-1,3,4-thia-diazole-2(3H)-thione) (1d) was prepared according to Runge *et. al.*[19] After recrystallization from ethyl acetate the m.p was 150 – 151 °C and C, H, N, and S analysis confirmed the results of Runge *et. al.* The electronic spectrum of this compound shows maxima at $\lambda = 242$ nm ($\varepsilon = 20$ 000); $\lambda = 275$ nm ($\varepsilon = 18$ 500), $\lambda = 305$ nm($\varepsilon = 21$ 000) and $\lambda = 332$ nm ($\varepsilon = 19$ 000).

1,3-Di-p-tolylformamidine was prepared according to the directions given by Backer and Wanmaker;[24] m.p. 141.5 – 142.5 °C from pentane, (lit.[24] 143 – 144 °C).

Action of p-toluidine on 1c. By adding *p*-toluidine (1.33 g) dissolved in benzene (5 ml) to the orange-coloured solution of *1c* (1 g) in benzene (20 ml) at 50 °C the reaction mixture was immediately decolorized. The solution was refluxed for 3 h and allowed to cool for an additional 3 h. The colourless crystalline *p-toluidinium salt of 4c* (0.41 g) was collected, m.p. 167 – 167.5 °C. The compound was identified by comparison with an authentic specimen, prepared in nearly quantitative yield by mixing equimolar amounts of *p*-toluidine and *4c* in benzene; colourless needles, m.p. 164.5 – 165.5 °C from benzene. Furthermore, the salt liberated *p*-toluidine and *4c* on successive treatment with sodium hydroxide and hydrochloric acid.

From the mother liquor the colourless crystalline *1,3-di-p-tolylformamidinium salt of 4c* precipitated (0.36 g); m.p. 165.5 – 167 °C after recrystallization from benzene. The identity of this compound was established by comparison with authentic material precipitated in almost quantitative yield as colourless crystals by mixing equimolar amounts of the appropriate formamidine and *4c* in benzene; m.p. 165.5 – 167.5 °C. Furthermore, successive treatment of the salt with sodium hydroxide and hydrochloric acid liberated *1,3-di-p-tolyl-formamidine* and *4c*, respectively, both identified by comparison with authentic samples.

On concentrating the remaining mother liquor almost to dryness, 0.25 g *1,3-di-p-tolyl-*

thiourea, m.p. 178 – 179 °C, separated. This was identified by elemental analysis and by comparison with an authentic sample. The remaining material was separated by chromatography on a 2,3 × 20 cm column of silica gel eluting first with a chloroform-hexane mixture (1:3) and finally with pure chloroform. The major component was identified as *3c*, (0.2 g) with a m.p. (after recrystallization from pentane) of 76 – 76.5 °C.

Action of ammonia on 1c. Dry ammonia was passed through a solution of *1c* in benzene. After a few minutes the colour faded and a colourless product precipitated. This was identified as a mixture of ammonium thiocyanate and the *ammonium salt* of *4c*. The latter compound was identical to a sample prepared as follows. Dry ammonia was passed through a solution of *4c* in benzene. The reaction mixture was heated to the boiling point, and colourless crystals precipitated in almost quantitative yield. M.p. ca 191 °C.

Action of ethanol on 1c. A mixture of *1c* (0.001 mol) and ethanol (12 ml) was refluxed for 12 h. The precipitated yellow oil was dissolved by adding 5 ml of boiling ethanol to the mixture, which upon cooling and scratching afforded a 75 % yield of *3c*.

Action of thiophosgene on 1,2-dimethylhydrazine. An aqueous solution (20 ml) of 1,2-dimethylhydrazinium chloride (0.01 mol) was shaken for 1 h with thiophosgene (0.02 mol). 1 g of the isolated solid was separated by PLC into two fractions. *3,4-Dimethyl-1,3,4-thiadiazolidine-2,5-dithione (4f)* (300 mg) was obtained as colourless crystals, m.p. 164 – 165 °C from pentane. Previously m.p. of 163 – 164 °C [51] and 168 – 169 °C [53] were reported for the same compound. The other fraction was identified as *3,4-dimethyl-5-thioxo-1,3,4-thiadiazolidin-2-one (4e)*, 600 mg. Light yellow crystals of m.p. 112 – 113 °C after recrystallization from pentane.

3-Thioxo-hexahydro-1,2,4-triazine-5,6-dione (7). Semioxamazide hydrochloride and thiophosgene were allowed to react in aqueous suspension following the procedure described by Beckett and Dyson.[1] The product (65 % yield) was purified by recrystallization from nitrobenzene as recommended to give 27 % of yellowish crystals, m.p. 219 – 223 °C (dec.). (Found: C 24.63; H 2.04; N 28.90; S 21.74. Calc. for $C_3H_3N_3O_2S$: C 24.83; H 2.08; N 28.97; S 22.06). Beckett and Dyson obtained a compound with almost identical m.p. (223 °C) but with a sulfur content of 29.25 %.

The compound 7 was treated with aniline according to the directions given by Beckett and Dyson, and it was confirmed that *1-oxamoyl-4-phenylthiosemicarbazide* was formed. This was identical to a sample prepared from semioxamazide and phenyl isothiocyanate (Scheme 4).

5,5-Thiocarbonyldithiobis[3-(4-nitrophenyl)-1,3,4-thiadiazol-2(3H)-one] (1e). 4-Nitrophenylhydrazine was shaken with thiophosgene

following the directions given by Beckett and Dyson.[1] 1 g of the dark brown crude material was dissolved in chloroform and chromatographed on a column of neutral aluminium oxide. The main fraction (700 mg) was collected and *1e* precipitated with pentane. Orange crystals with m.p. 60 – 61 °C.

REFERENCES

1. Beckett, T. and Dyson, G. M. *J. Chem. Soc.* (1937) 1358.
2. Hayes, K. J. *U.S. Patent* 2,830,046 (1958).
3. Sherman, W. R. *U. S. Patent* 2,918,473 (1959).
4. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 20 (1966) 1714.
5. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 21 (1967) 2061.
6. Larsen, C., Anthoni, U. and Nielsen, P. H. *Acta Chem. Scand.* 23 (1969) 320.
7. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 21 (1967) 2571.
8. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 21 (1967) 2580.
9. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 22. (1968) 1898.
10. Anthoni, U., Dahl, O., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 23 (1969) 943.
11. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 23 (1969) 1439.
12. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 23 (1969) 3385.
13. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 22 (1968) 309.
14. Anthoni, U., Larsen, C. and Nielsen, P. H. *Acta Chem. Scand.* 21 (1967) 1201.
15. Anthoni, U., Dahl, B. M., Larsen, C. and Nielsen, P. H. *To be published.*
16. Anthoni, U. and Nielsen, P. H. *Acta Chem. Scand. B* 28 (1974) 489.
17. Jensen, K. A., Anthoni, U., Kägi, B., Larsen, C. and Pedersen, C. Th. *Acta Chem. Scand.* 22 (1968) 1.
18. Busch, M. *Ber. Deut. Chem. Ges.* 27 (1894) 2507.
19. Runge, F., El-Hewehi, Z. and Taeger, E. *J. Prakt. Chem. (4)* 7 (1958) 279.
20. Houben, J. and Weyl, T. *Methoden der Organischen Chemie*, 4th Ed. 1967, Vol. 10/2, 123 ff.
21. Henriksen, L. and Kristiansen, E. S. S. *Ann. N. Y. Acad. Sci.* 192 (1972) 101.
22. Vowinkel, E. and Claussen, G. *Chem. Ber.* 107 (1974) 898.
23. Bernthsen, A. *Justus Liebigs Ann. Chem.* 184 (1877) 321; 192 (1878) 1.
24. Backer, H. J. and Wanmaker, W. L. *Rec. Trav. Chim. Pays-Bas* 68 (1949) 247.
25. Kjellin, G. and Sandström, J. *Acta Chem. Scand.* 23 (1969) 2888.

26. Tilles, H. *Thiophosgene.* In Kharasch, N. and Meyers, C., Eds., *The Chemistry of Organic Sulfur Compounds*, Pergamon, Oxford 1966.
27. Ray, P. C. and Guha, B. C. *Quart. J. Indian Chem. Soc. 3* (1926) 23.
28. Zbirovsky, M. and Ettel, V. *Chem. Listy 51* (1957) 2094; *Collect. Czech. Chem. Commun. 23* (1958) 1896.
29. *Chem. Abstr. 62* (1965) P16259b; *69* (1968) P28466e; P112206c; *72* (1970) P12366p; P56297f; *71* (1969) P3399p; *74* (1971) P81774h.
30. Runge, F., El-Hewehi, Z. and Taeger, E. *J. Prakt. Chem. 18* (1962) 262.
31. Sasse, K., Wegler, R., Unterstenhöfer, G. and Grewe, F. *Angew. Chem. 72* (1960) 973.
32. Halasa, A. F. and Smith, Jr., G. E. P. *J. Org. Chem. 36* (1971) 636.
33. Dyer, E., Farris, Jr., R. E., Minnier, C. E. and Tokizawa, M. *J. Org. Chem. 34* (1969) 973.
34. Miller, B. and O'Leary, Jr., T. P. *J. Org. Chem. 27* (1962) 3382.
35. Kuhlow, G., Teichmann, H. and Hilgetag, G. *Z. Chem. 5* (1965) 179.
36. Barnikow, G. and Strickmann, G. *Chem. Ber. 100* (1967) 1428.
37. Pratt, R. F. and Bruice, T. C. *J. Amer. Chem. Soc. 94* (1972) 2823.
38. Chanon, M., Gallo, R., Surzur, J.-M. and Metzger, J. *Bull. Soc. Chim. Fr.* (1968) 2881, 2885.
39. Klopman, G. *Chemical Reactivity and Reaction Paths*, Wiley, New York 1974.
40. Kornblum, N., Smiley, R. A., Blackwood, R. K. and Iffland, D. C. *J. Amer. Chem. Soc. 77* (1955) 6269.
41. Wagner, G. and Dietzsch, B. *J. Prakt. Chem 315* (1973) 915.
42. Kolesova, M. B., Maksimova, L. I. and Elpov, A. V. *Zh. Org. Khim. 9* (1973) 2613.
43. Scott, D. W., McCullough, J. P., Hubbard, W. N., Messerly, J. F., Hossenlopp, I. A., Frow, F. R. and Waddington, G. *J. Amer. Chem. Soc. 78* (1956) 5463.
44. Allum, K. G., Creighton, J. A., Green, J. H. S., Minkoff, G. J. and Prince, L. J. S. *Spectrochim. Acta. A 24* (1968) 927.
45. Borch, G., Henriksen, L., Nielsen, P. H. and Klaboe, P. *Spectrochim. Acta A 29* (1973) 1109.
46. Jensen, K. A. and Nielsen, P. H. *Acta Chem. Scand. 20* (1966) 597.
47. Ganzow, O. A., Burke, A. R. and La Mar, G. N. *Chem. Commun.* (1972) 456.
48. Sandström, J. *Acta Chem. Scand. 15* (1961) 1295.
49. Ziegele, E. *J. Prakt. Chem. 60* (1899) 40, 41.
50. Sasse, K. *Justus Liebigs Ann. Chem. 735* (1970) 158, 188.
51. Grashey, R., Huisgen, R., Sun, K. K. and Moriarty, R. M. *J. Org. Chem. 30* (1965) 74.
52. Thorn, G. C. *Can. J. Chem. 38* (1960) 1439.