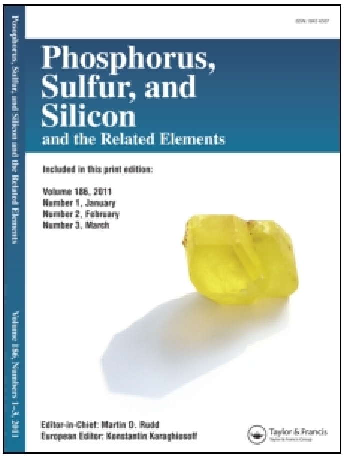

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S,N-Compounds via Amines and Sulphur Halides

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S,N-COMPOUNDS VIA AMINES AND SULPHUR HALIDES

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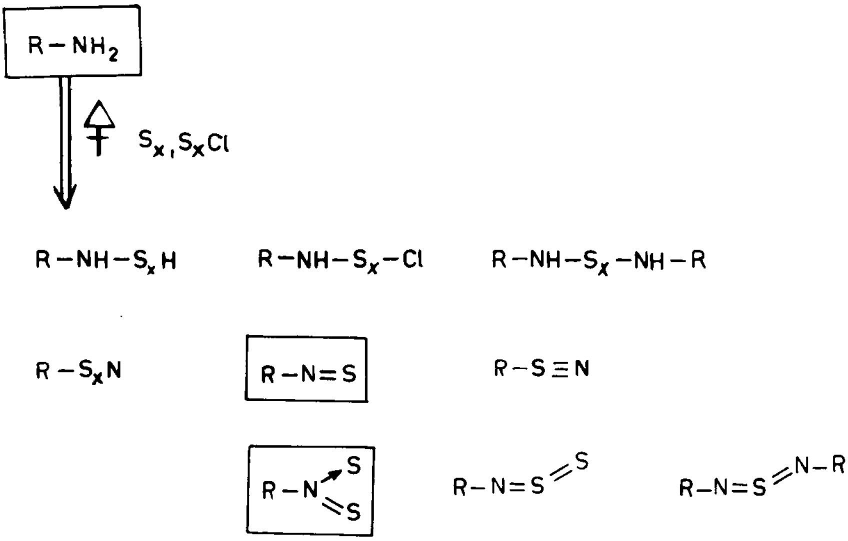
Abstract The many products got by reactions of amines with sulfur halides are discussed. Special attention is given to the intermediate thionitroso compounds, the N-thiosulfinylamines and the persistent radicals 1,2,3-dithiazolyles. New results about the course of the HERZ reaction are described.

First of all I wish to express my cordial thanks to the organizing committee, especially to professor Kresze, for the invitation to read a paper at this Sulphur Symposium.

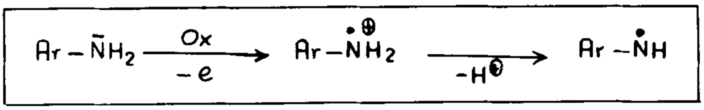
For about 4 years we have intensively studied the field of organic S,N-bonds mainly with respect to new compounds containing S,N-double bonds.



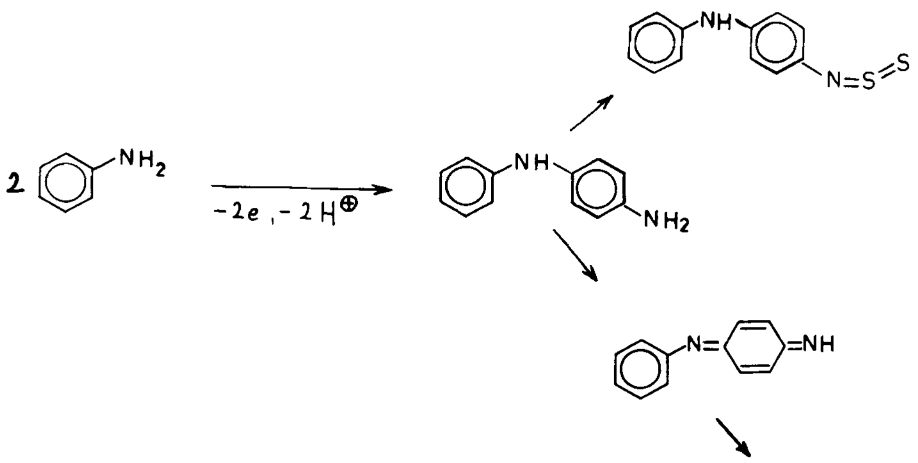
Reactions of industrially easily accessible aliphatic, aromatic and heterocyclic amines, enamines, and hydrazines with industrially available sulphur halides lead to a great variety of S,N-compounds. Due to their unusual structure, in this connection thionitroso and dithionitro groups as well as thiazyles are of special interest. Up till now, compounds with these functional groups are unknown in substance.

We have been interested in the question whether amines and hydrazines can be transformed by sulphur or sulphur halides to give these unknown series of groups with sulphur-nitrogen double bonds. On the other hand, the formation of azo compounds from these S,N-intermediates by desulphurization was to be proved.

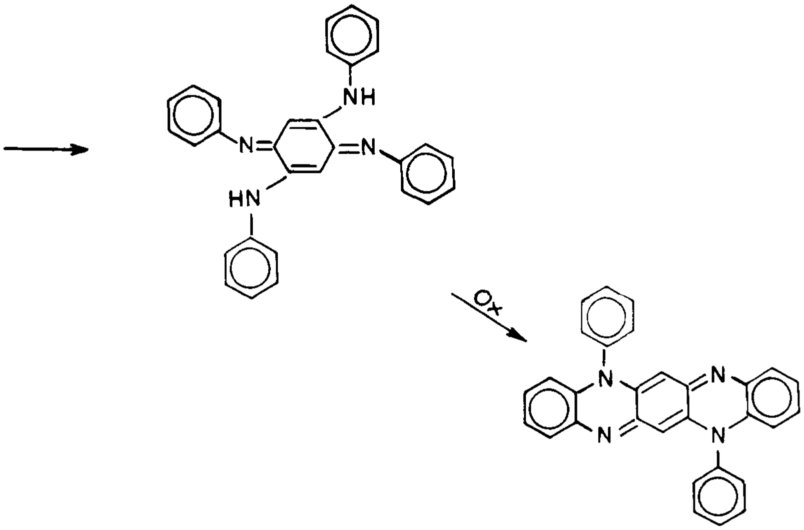
Depending on the reaction conditions used, a great number of sulphur-containing and also sulphur-free compounds have been isolated. For instance, starting from aniline more than 3o S-compounds can be detected.



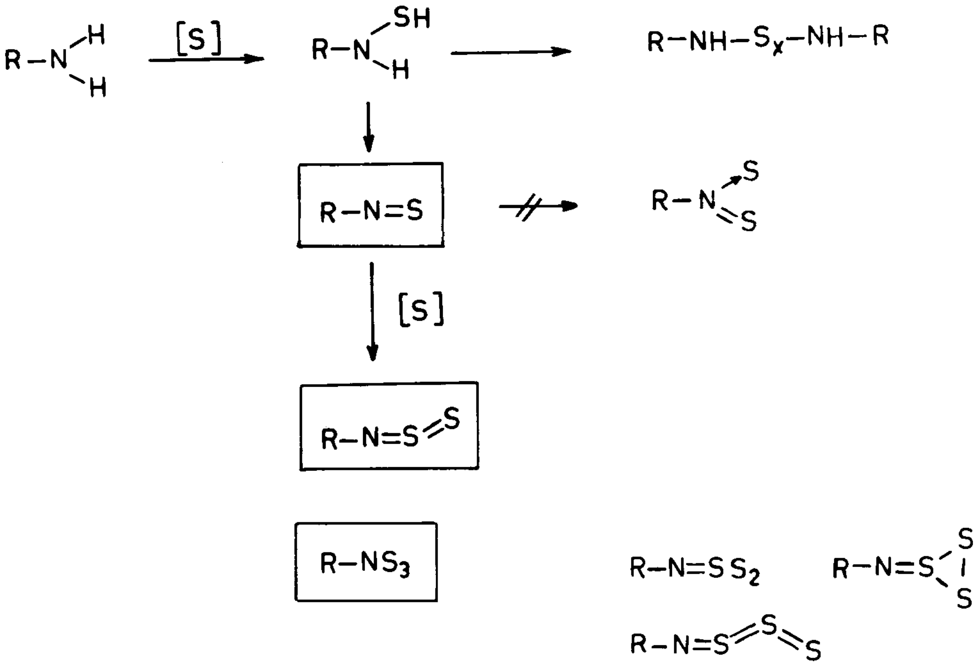
$$\boxed{Ar-\bar{N}H_2 \xrightarrow[-e]{Ox} Ar-\overset{\bullet\oplus}{N}H_2 \xrightarrow[-H^{\oplus}]{} Ar-\overset{\bullet}{N}H}$$



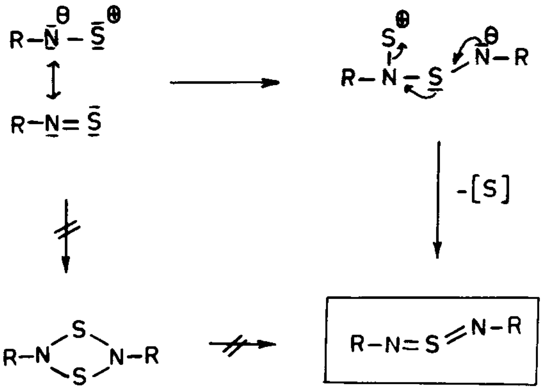
The explanation of this variety of products can be derived from the special character of sulphur halides acting as alkylating as well a oxidizing agents.
For example, with aniline deeply coloured products derived from amino diphenylamine have been isolated and characterized. They show the principle structures of



such oxidation products. We will not discuss this type of reaction in details.
As a rule an insertion of sulphur occurs.
Via the thionitroso group an oxidation reaction leads to N-thiosulfinylamines. In addition to this thiooxide of the thionitroso group a deeply red nitrogen-sulphur compound with three sulphur atoms attached to one nitrogen atom is formed.

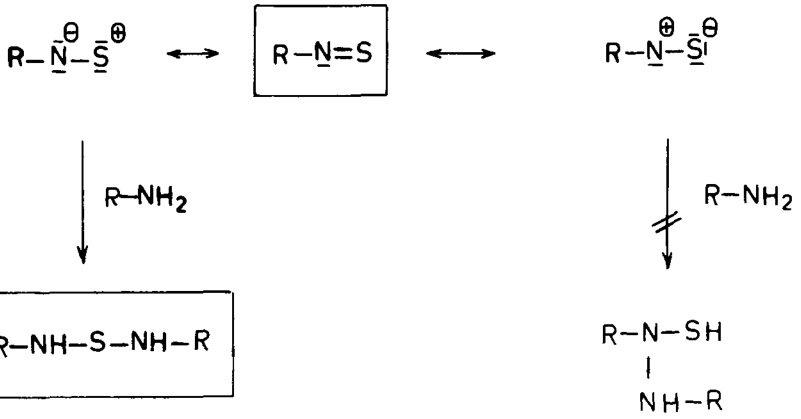


In spite of intensive efforts thionitroso compounds have not been isolated in substance.

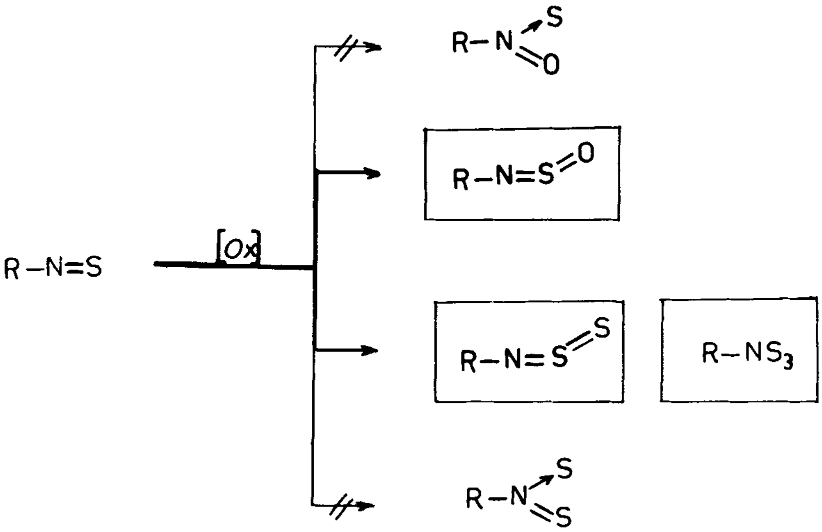


But without any doubt in a large number of sulphurization reactions of amines thionitroso compounds are real intermediates. They can be trapped, for instance, by cycloaddition reactions.

Which are other characteristic properties of thionitroso compounds? In the thionitroso group the direction of polarization is reverse to that of the nitroso group ("Umpolung"). Due to the positive charged sulphur atom the thionitroso group tends to desulphurize forming the corresponding sulphur diimide. We proved in detail that this desulphurization does not occur via a 4-membered ring. Of special interest is the reaction of amines with thionitroso intermediates to give diamino sulfides.

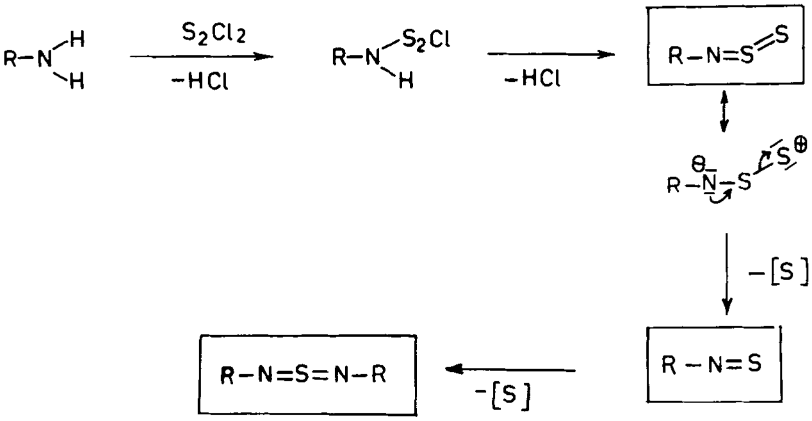


Also other nucleophiles react with thionitroso compounds in this thiophilic way. Finally it is remarkable that only the sulphur atom is attacked by further oxidation to give N-sulfinyl or N-thiosulfinyl amines.

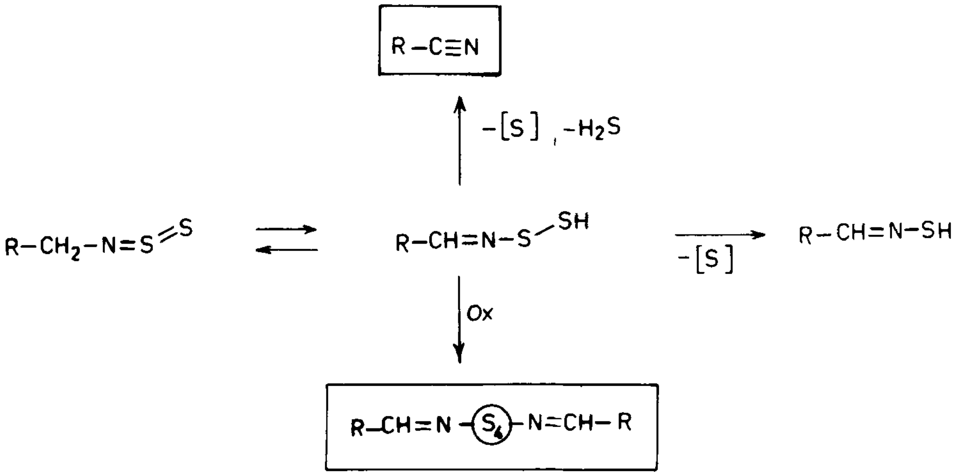


In all cases investigated until now, the nitrogen has not been oxidized.

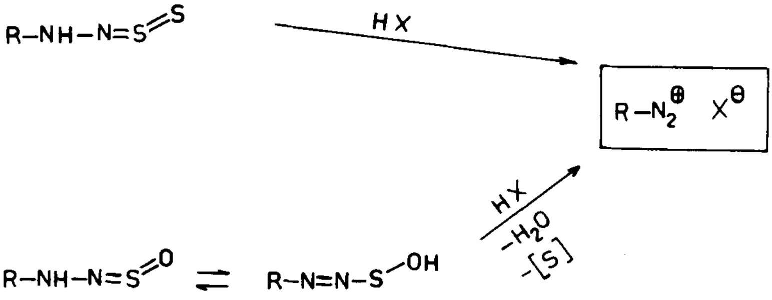
Evidently most reactions of primary amines with disulphur dichloride pass through N-thiosulfinyl amines as intermediates.



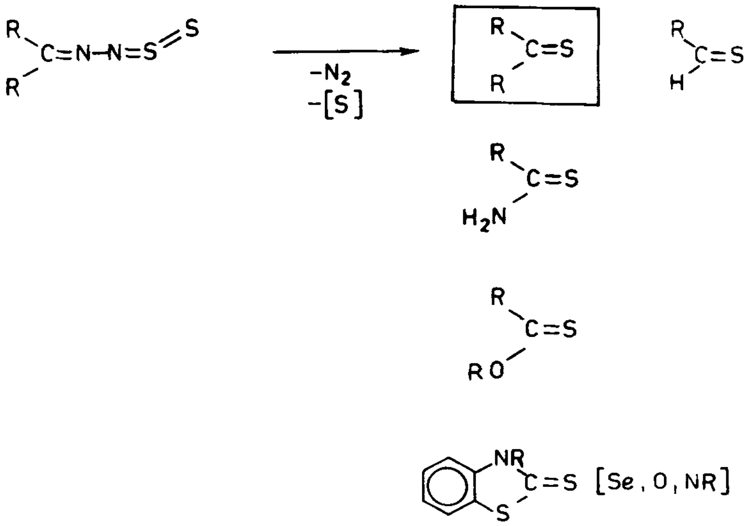
Exactly 1o years ago BARTON and coworkers described this exotic class of compounds for the first time [1]. The chemistry of these compounds has rapidly developed[2]. From our point of view the relatively favoured tendency of formation and, on the other hand, the high reactivity should only be mentioned. The N-thiosulfinyl amines, too, tend to desulphurize to give predominantly sulphur diimides. In principle this desulphurization is analogous to the formation of sulphur diimides starting from the thionitroso group. The reaction of aliphatic primary amines with disulphur dichloride also leads to N-thiosulfinyl amines.



Due to their tendency to tautomerize, relatively stable dimeric tetrasulfides can be isolated. They are products of an oxidative stabilization. Under somewhat more drastic conditions nitriles are formed. N-Thiosulfinyl hydrazines are produced by reacting hydrazines with disulphur dichloride.



These compounds are potential diazonium salts, suitable for storage. Such potential diazonium salts can also be prepared by reaction of hydrazines with thionyl chloride. In quantitative yield, the corresponding diazinium salt is formed from the relatively stable N-sulfinyl hydrazine by acidification. 2 years ago an efficient thioketone synthesis as well as a synthesis of sterically hindered thioaldehydes have been reported by OKAZAKI and



R. Okazaki
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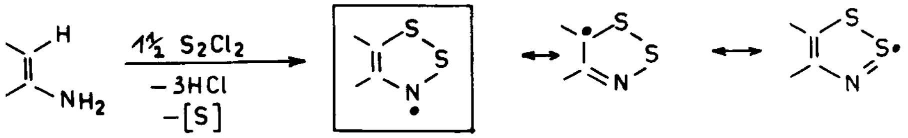
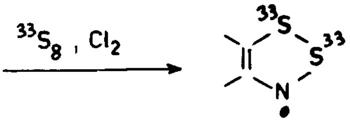
coworkers [3], starting with these compounds.
We found that this reaction can be generalized. For example using thionyl chloride instead of disulphur dichloride hydrazones of heterocyclic compounds can be transformed to the corresponded carbonyl compounds. This conversion occurs without water.
Thio o-esters also are accessible this way.
Now let us discuss further points of the reaction of sulphur halides with amines.





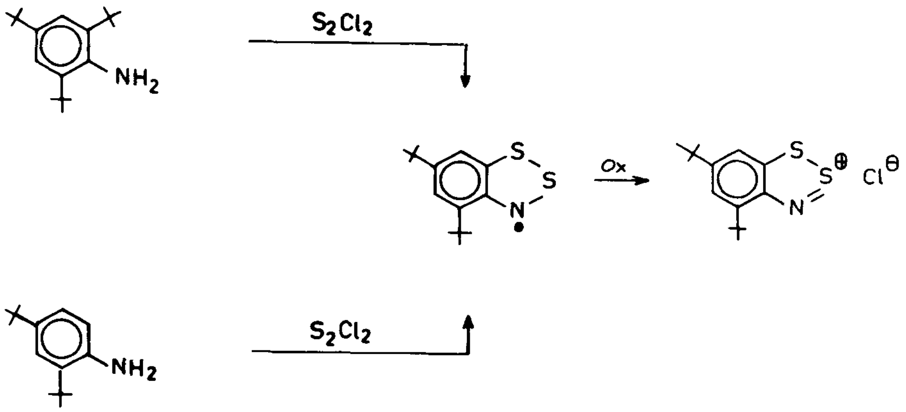
Relatively early during our attempts to synthesize thionitroso compounds we have observed by means of ESR spectroscopy amazingly stable organic sulphur- and nitrogen containing radicals.

Using the most modern methods available - the sulphur-33 technique included - we characterized the structure of these radicals to be 1,2,3-dithiazolyles [4].
These investigations were done in cooperation with Dr. BARTL from our Academy of Sciences and with Dr. STASKO from Bratislava, Czechoslovakia.
1,2,3-Dithiazolyles are a new class of persistent radicals, isomeric with the 1,3,2-compounds. They belong to the series of cyclic thioaminyls containing nitrogen as a formal centre of the radical electron.

They are stable in solution or in a solid matrix. We have just published details of syntheses and behavior of these new type of radicals. Therefore let's only discuss some selected results.

First, the tendency of formation of these radicals is extremely high. Many different starting materials are appropriate for generation and synthesis of 1,2,3-dithiazolyles. I will only deal, here, with the formation of the radicals by reaction of sulphur halides with aromatic and heterocyclic amines or enamines, respectively.

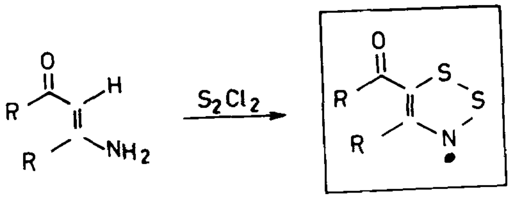
The best way for the preparation of 1,2,3-dithiazolyles is to solve the amine in carbon tetrachloride and to add a solution of disulphur dichloride in carbon tetrachloride. It is also possible to synthesize disulphur dichloride in the solvent used immediately before the synthesis of the radicals. So we have developed an efficient ultramicro synthesis of sulphur-33-labelled 1,2,3-dithiazolyles using sulphur-33. Substitution of disulphur dichloride by disulphur dibromide or chlorine by bromine, respectively, leads to less side reactions.

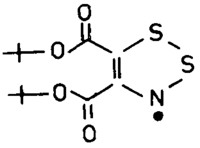


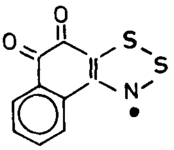
Both 2,4-di-tert.-butyl-aniline and 2,4,6-tri-tert.-butylaniline react with disulphur dichloride to give the same radical 4,6-di-tert.-butyl-benzo[d]-1,2,3-dithiazolyle. Starting from 2,4,6-tri-tert.-butylaniline the radical formation occurs with elimination of one tert.-butyl group as isobutene.

The corresponding 1,2,3-dithiazolium salt is formed by further oxidation of the radical. Under special conditions the formation of this salt can be the main reaction (see below).

An important extension of the direct synthesis of 1,2,3-dithiazolyles is based on the observation that enamines derived from β-dicarbonyl compounds react with sulphur dichloride to give very stable dithiazolyles with carbonyl groups adjacent to the heterocyclic ring.







For example, two extremely stable radicals are derived from amino fumaric acid di-tert.-butylester and amino naphthoquinone, respectively.

Especially the insertion of a carbonyl group into the position 5 of the 1,2,3-dithiazolyle system brings additional possibilities to delocalize the free unpaired electron in the radical. The result is a noticeable modification of the spin density distribution and consequently of the hyperfine splitting constants and g-factors in comparisation to the areno condensed 1,2,3-dithiazolyles.

These and also the other 1,2,3-dithiazolyles synthesized act as inhibitors in various radical reactions. We are engaged in studying the problem of the inhibitor activity of the radicals in correlation to their constitution. Solutions of areno-1,2,3-dithiazolyles are red or green.

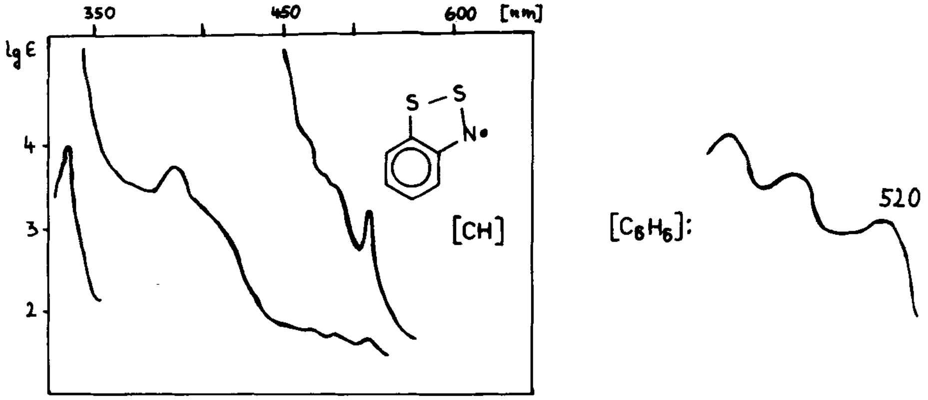
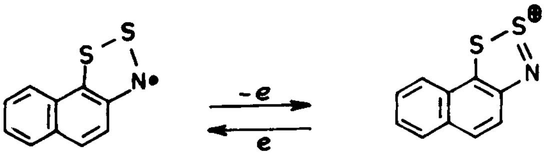


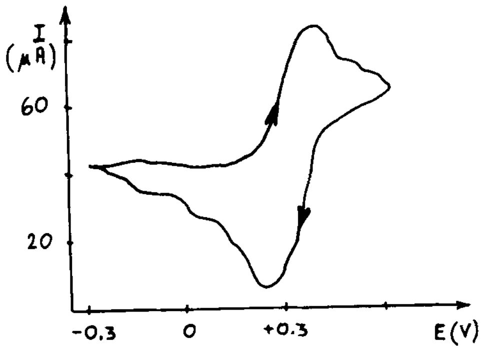
Figure 1: UV/VIS-Spectra of benzo-1,2,3-dithiazolyle, dissolved in cyclohexane [CH] and benzene.

(cf. Fig. 1 for the benzo derivative). The corresponding cation is insoluble in these solvents.

The uv-vis-spectra of the radicals and the corresponding cations are different, both in the fine structure and in the position of the absorption maxima, which are more hypsochromic in the case of the radicals.

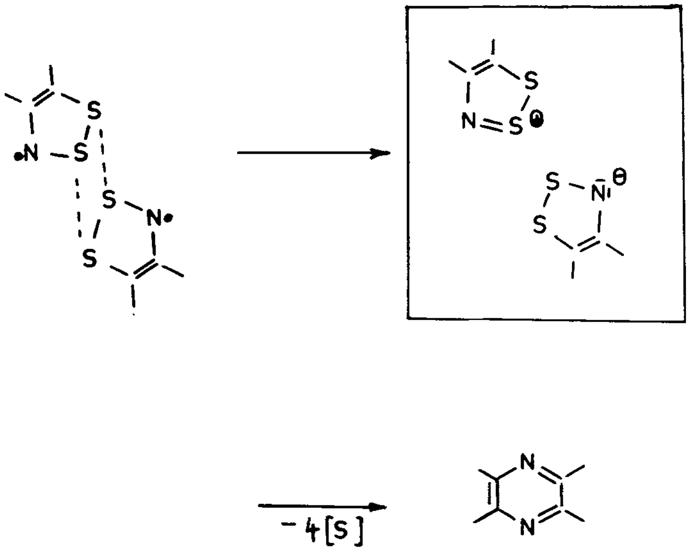
Molecular chlorine oxidizes the radicals to dithiazolium salts.





This reaction can be used to determine the radical concentration indirectly, because the resulting 1,2,3-dithiazolium salts precipitate quantitatively in appropriate solvents. The radical yields are about 25 per cent.

This reaction is reversible, that means that 1,2,3-dithiazolium salts, easily formed from the reaction of aromatic amines with disulphur dichloride, can be reduced to free radicals. The cyclic voltametry of the naphtho [2,1-d]-1,2,3-dithiazolium salts shows clearly that the electrochemical generation of 1,2,3-dithiazolyle radicals is also reversible.

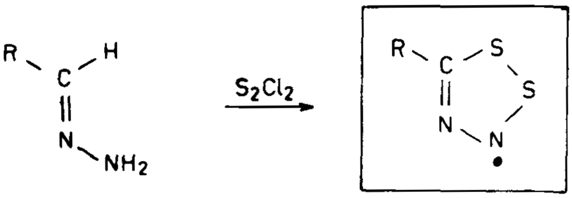


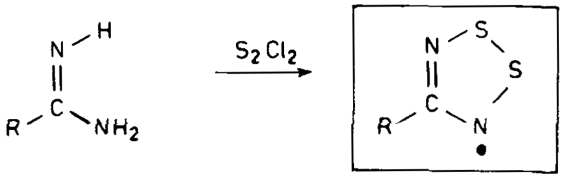
The areno 1,2,3-dithiazolyles are stable up to temperatures of about 12o°C. Above 15o° phenazines are formed. Naphtho [2,1-d]-1,2,3-dithiazol-2-oxide produces in this way 1,2,5,6-dibenzophenazine in a yield of 8o per cent.

A dimerization of the radicals to hydrazine derivatives has not been observed. The 1,2,3-dithiazolyles are not stable in protic solvents: in trichloromethane, already, the color of the radicals disappears and within a few minutes a salt-like precipitate is formed. The stabilization process is initiated by disproportion.

In the analogous reaction of hydrazones and amidines with sulphur dichloride, new radicals with two sulphur atoms and two nitrogen atoms in the heterocyclic ring are formed. These dithiadiazolyles are also available from the corresponding dithia-diazolium salts by reduction.

To summarize: Thionitrosocompounds and N-thiosulfinyl amines are primary products of the reaction of amines

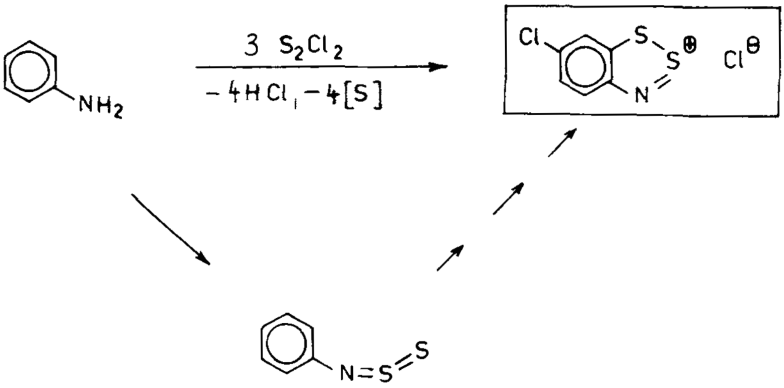




with sulfur halides. Their stabilization leads to sulfur diimides or to dithiazolyle radicals, predominantly under mild conditions.

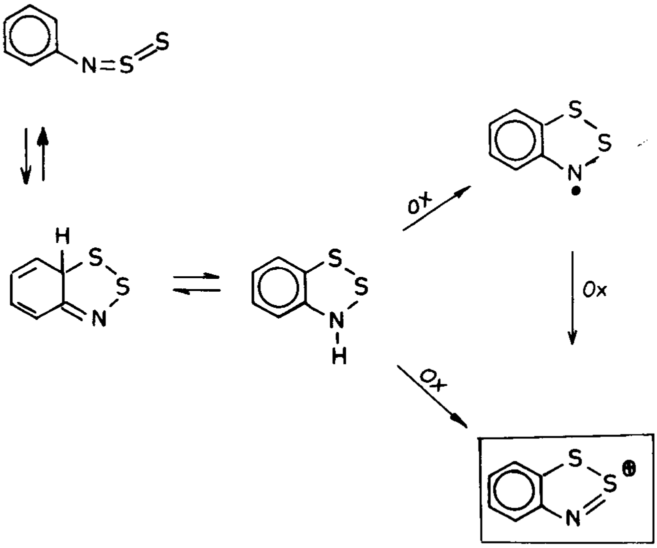
Moreover - as we found - the reaction is very sensitive to alterations in the reaction conditions.

Already 7o years ago R. HERZ described the formation of 1,2,3-dithiazolium salts by reaction of aromatic amines with disulphur dichloride. Relatively drastic reaction



conditions favoured the formation of the dithiazolium salt [5].

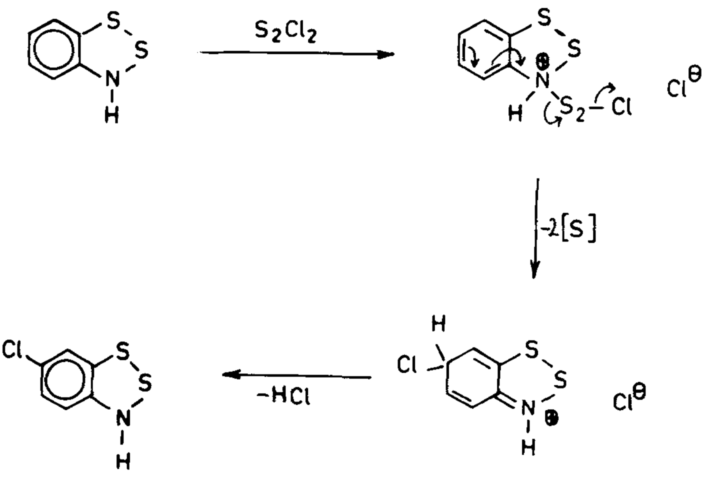
As we found, in this HERZ-reaction the formation of sulphur diimides is not favoured, but they are always detectable in traces.



Instead of desulfurization forming a sulphur diimide the intermediate N-thiosulfinylamine undergoes an intramolecular cycloaddition to give an areno 3- or -5-H-1,2,3-dithiazole. It should be mentioned that the heterocyclic ring system is formed <u>before</u> the benzene ring is chlorinated. This fact has already been discussed by GOMPPER in 1964 [6], but he could not prove this by experiments. Now we are able to do this:

ESR-spectroscopic investigations showed clearly that unchlorinated benzo[d]-1,2,3-dithiazolyle is the product from the reaction of aniline with disulphur dichloride under HERZ-reaction conditions.

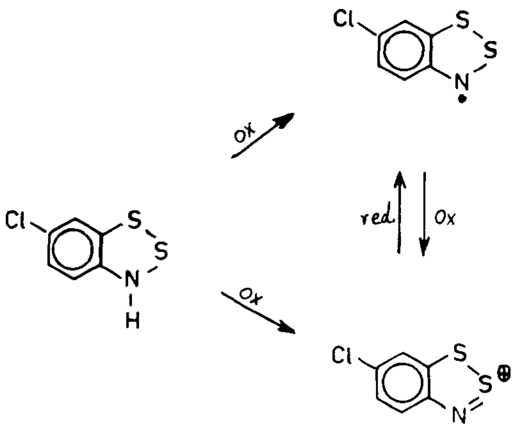
Also benzo[d]-1,2,3-dithiazolium chloride is formed as a side product. Here, disulphur dichloride acts as an oxidizing agent. Both unchlorinated products are stable against further chlorination.



The proper chlorination of the benzene ring is initiated by the attack of disulphur dichloride at the basic nitrogen atom of the benzo-3H-1,2,3-dithiazole.

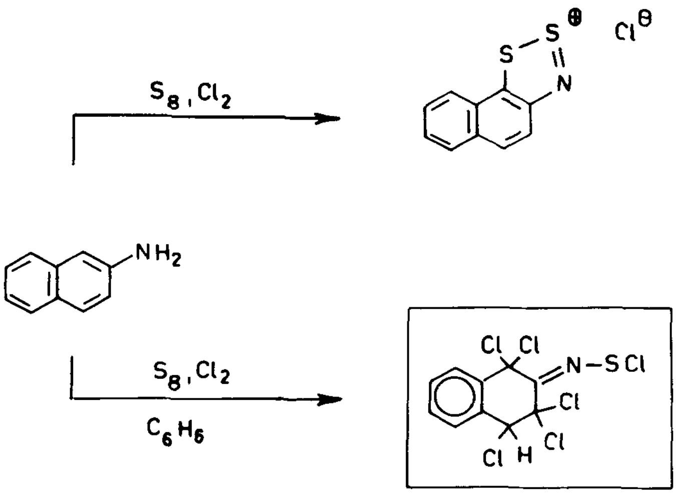
The nitrogen atom, now positively charged, causes a nucleophilic attack of the chloride anion in position 6. By elimination of hydrogen chloride and sulphur the aromatic 6π-system is reformed and 6-chloro benzo-3H-1,2,3-dithiazole is obtained. The hydrogen atom in position 6 is split off as a proton forming HCl. Finally, the 6-chlorobenzo-3H-1,2,3-dithiazole is oxidized by the excess of disulphur dichloride to form 6-chloro benzo-1,2,3-dithiazolium chloride.

We found that during this oxidation the radical 6-chlorobenzo-1,2,3-dithiazolyle is formed which under these conditions produces the dithiazolium salt.

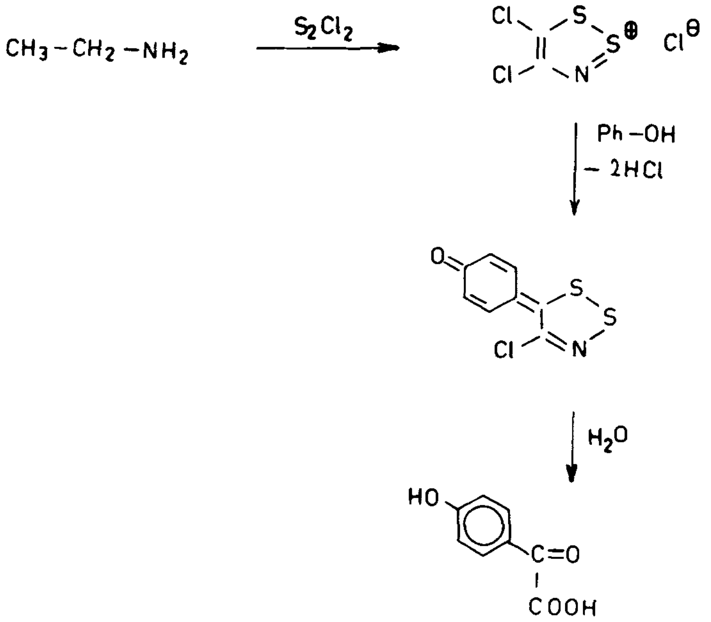


The relatively stable persistent radical can also be generated by reduction of the dithiazolium salt using metal powders for example.

Finally, for synthetic purposes, it is remarkable that the HERZ-reaction can be carried out as a one-pot-synthesis. It is only necessary to chlorinate a mixture of the amine hydrochloride and elemental sulphur. But this method, too, is sensitive to the reaction conditions



used: in benzene as solvent chlorothioiminopentachloro tetrahydronaphthalene is formed in high yields starting with β-naphthylamine.



The reaction of ethylamine hydrochloride with disulphur dichloride gives among other products 4,5-dichloro-1,2,3-dithiazolium chloride. This salt is also available in a high yield from chloroacetonitrile and S_2Cl_2.
We used this salt as a C_2-building block in organic syntheses. Thus, for instance, phenol reacts in 5-position forming the chinomethine system. Hydrolysis leads to α-oxocarboxylic acids: the dichloro-dithiazolium chloride acts as a potential oxalic acid dichloride.

It was my intention to demonstrate that primary amines undergo with sulphur halides a lot of special acylation and oxidation reactions leading to thionitroso compounds and N-thiosulfinyl amines. From N-thiosulfinyl amines the way is open to persistent dithiazolyle radicals and to dithiazolium salts.

Drawing your attention to the HERZ-reaction, I wanted to acquaint you with the complicated mechanism of this reaction and with the central position of N-thiosulfinyl amines. I tried to show you the close relationship between all compounds mentioned above and discussed in my report. Finally, I wish to thank my coworkers and colleagues who achieved together with some students of our department the above-reported results by enthusiastic work, especially Doz. Dr. Domschke and Dr. Bleisch.

If I should have succeeded in giving you some new impulses for your own work, my report has fullfilled its purpose.

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