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Forty Years of Heterocyclic Sulfur Chemistry

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FORTY YEARS OF HETEROCYCLIC SULFUR CHEMISTRY

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Beginning in 1947, our studies were initially mainly devoted to 1,2-dithiole-3-thiones and their derivatives but were rapidly extended to other types of heterocyclic sulfur compounds: thiopyrans, thiocoumarins, thiochromones, thioisocoumarins, 3,1-benzothiazine-4-thiones and 1,2-dihydro-3,1-benzothiazine-4-thiones. In the course of these researches, some other heterocycles were also obtained such as thiophenes and 2,1-benzisothiazoles.

Starting in 1958, considerable attention was given to compounds in which partial bonding exists between sulfur and oxygen or between several sulfur atoms. At first our work mainly concerned α-(1,2-dithiol-3-ylidene) ketones and 1,6,6aλ^4-trithiapentalenes but later dealt also with other heterocyclic compounds, containing for instance thiopyran rings, and with extended structures in which the partial bonding affects four or five sulfur atoms in line.

Last, in the course of our studies on heterocycles containing nitrogen and sulfur, we discovered new phosphorus-containing heterocyclic compounds, the 1,2-dihydro-3,1,2λ^5-benzothiazaphosphinine-2,4-dithiones.

Key words: 3,1-Benzothiazines, 1,2-dithiole-3-thiones, N. Lozac'h, Quinazolines, thiopyrans, 1,6,6aλ^4-trithiapentalenes.

CONTENTS

FOREWORD

Our interest for organic sulfur chemistry began with a study of 5-(4-methoxyphenyl)-1,2-dithiole-3-thione which was interesting for its action on bile secretion. Furthermore, synthesis of this compound by heating sulfur with anethole gave acceptable yields, showing that reaction of sulfur with organic compounds could be a good tool for some syntheses. As this type of reaction, at that time, was far from being well known, it looked promising to explore this field. These studies began at Ecole Normale Supérieure in Paris and, after 1949, were continued in Caen University.

These reactions of sulfur led to a variety of compounds for which we have been led to study other preparative methods among which the use of tetraphosphorus decasulfide proved to be of peculiar importance.

In the year 1958, while studying the reaction of sulfur with cinnamylidene-acetophenones, α-(1,2-dithiol-3-ylidene)ketones were obtained which gave 1,6,6aλ^4-trithiapentalenes by reaction with tetraphosphorus decasulfide. These first results soon developed into a general study of partial bonding in sulfur compounds, a subject which arose the interest of several teams of theoretical and physical chemists, especially those working on X-ray structural analysis.

This line of study occupied our laboratory for many years and culminated in the synthesis of partial-bond systems involving five sulfur atoms in line. Owing to its novelty, this topic has attracted the attention of many other laboratories and more complete information on these and related subjects can be gathered from the following reviews:

- The Chemistry of the 1,2-Dithiole Ring, by N. Lozac'h and J. Vialle, in "The Chemistry of Organic Sulfur Compounds" Vol. 2, Chapter 10, pp. 257–285 (Pergamon, 1966).
- The 1,2- and 1,3-Dithiolium Ions, by H. Prinzbach and E. Futterer, in "Advances in Heterocyclic Chemistry", Vol. 7, pp. 39–102 (Academic Press, 1966).
- 1,6,6aS^{IV}-Trithiapentalenes and Related Structures, by N. Lozac'h, in "Advances in Heterocyclic Chemistry", Vol. 13, pp. 161–234 (Academic Press, 1971).
- The 1,2- and 1,3-Dithiolium Ions by N. Lozac'h and M. Stavaux, in "Advances in Heterocyclic Chemistry", Vol. 27 pp. 151–239 (Academic Press, 1980).
- The Physical Chemistry of 1,2-Dithiole Compounds - The Question of Aromaticity, by C. Th. Pedersen, *Sulfur Rep.*, **1**, 1 (1980).
- 1,2-Dithiole-3-thiones and 1,2-Dithiol-3-ones, by C. Th. Pedersen, in "Advances in Heterocyclic Chemistry", Vol. 31, pp. 63–113 (Academic Press, 1982).
- 1,6,6aλ^4-Trithiapentalenes and Related Systems, in "Comprehensive Heterocyclic Chemistry", Chapter 4. 38, pp. 1049–1070 (Pergamon, 1984).

In 1960, studies in a different field were also undertaken. Until then, our laboratory had been mainly interested in sulfur and oxygen heterocycles, among which were the benzothiopyrans. Dr. L. Legrand then suggested that aza derivatives of these systems were of interest and this led to a rather extensive study of 3,1-benzothiazine-4-thiones and of 1,2-dihydro-3,1-benzothiazine-4-thiones. These compounds proved to be useful synthetic intermediates for obtaining diverse quinazoline derivatives, some of them of pharmacological interest. Last, during these studies, new phosphorus-containing

heterocycles, the 1,2-dihydro-3,1,2λ^5-benzothiazaphosphinine-2,4-dithiones, were obtained and proved to be useful synthesis intermediates.

On the chemistry of the above sulfur, nitrogen and phosphorus heterocycles, two reviews have been published:

— Hydrazone Formation with Thioisocoumarins and Related Reactions, by N. Lozac'h and L. Legrand, *Int. J. Sulfur Chem.*, **C-6**, 65 (1971).

— Recent Progress in the Chemistry of Thiocarbonyl Derivatives of Sulfur, Nitrogen and Phosphorus Heterocycles, by N. Lozac'h, *Int. J. Sulfur Chem.*, **B-6**, 131 (1971).

This paper deals essentially with work done in our own laboratory but many related studies have been conducted by other teams with whom we have had, along the years, fruitful exchanges. Among the colleagues with whom we have particularly collaborated, I should cite A. Hordvik (Bergen and Tromsø), Y. Mollier (Caen and Rouen), C. Th. Pedersen (Odense), H. Quiniou (Caen and Nantes), A. Thuillier (Caen) and J. Vialle (Caen).

1. PREPARATION OF 1,2-DITHIOLE-3-THIONES

1.1. Reaction of Sulfur with Hydrocarbon Chains

Our first studies concerned reaction of sulfur with 1(or 3)-arylpropenes and resulted in the formation of 5-aryl-1,2-dithiole-3-thiones (Fig. 1) in which the aryl substituent was 4-methoxyphenyl[1,2,3,4], 4-hydroxy-3-methoxyphenyl[3], 3,4-dimethoxyphenyl[5], 3,4-methylenedioxyphenyl[5] or 3-methoxy-4-(methoxycarbonyl-methylenoxy)phenyl[6].

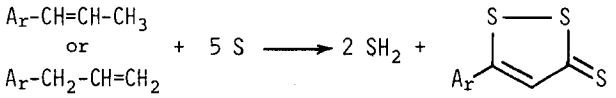


Figure 1.

At the beginning, few things were known about syntheses and properties of 1,2-dithiole-3-thiones and this led us to develop a systematic study of these compounds, the more so as 5-(4-methoxyphenyl)-1,2-dithiole-3-thione proved to have interesting pharmacological properties (as a choleretic). With 3-carbon chains included in cyclic systems, reaction of sulfur can lead to condensed-ring 1,2-dithiole-3-thiones. This happens for instance with 1-methylacenaphthylene which yields acenaphtho[1,2-*c*][1,2]dithiole-9-thione (**A**, Fig. 2)[6]. Formation of the 1,2-dithiole ring can be accompanied by dehydrogenation of other parts of the molecule. For instance, 1-methylcyclohexene led to 1,2-benzodithiole-3-thione[7,8], 4-methyl-1,2-dihydronaphthalene gave naphtho[2,1-

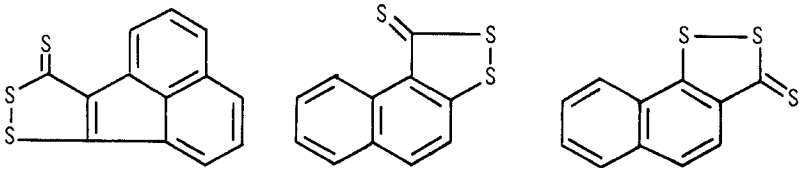


Figure 2.

c][1,2]dithiole-1-thione (**B**, Fig. 2)[8] and 3-methyl-1,2-dihydronaphthalene gave naphtho[1,2-*c*]-1,2-dithiole-3-thione (**C**, Fig. 2)[8]. Sulfuration of substituted propynes appeared to be unsatisfactory[9].

Initially, these reactions were carried out without solvent but later we found that a solvent such as biphenyl[9], ethyl benzoate[9] or 1,2,3,4-tetrahydronaphthalene[10] could be useful and a number of diversely substituted 1,2-dithiole-3-thiones have been prepared by reaction of sulfur either in the presence or absence of a solvent. In this way we obtained diverse 1,2-dithiole-3-thiones with various substituents such as substituted phenyls[9], alkyl and phenyl[10], 2-thienyl[11,12,13].

Sulfuration of hydrocarbon chains is affected by steric factors. For instance, 2-isopropyl-1,3,5-trimethylbenzene leads to small quantities of 4-(2,4,6-trimethylphenyl)-1,2-dithiole-3-thione but the main product is 3,3,4,6-tetramethyldithiophthalide (Fig. 3)[14].

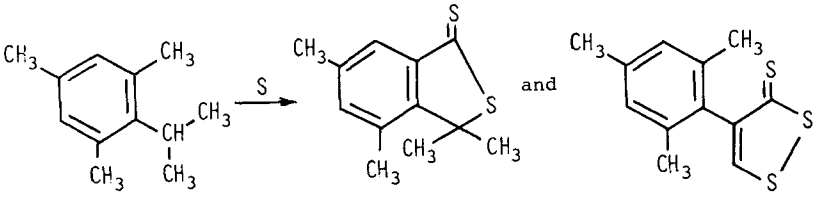


Figure 3.

With *o*-allylphenols, reaction of sulfur seldom gave 5-aryl-1,2-dithiole-3-thiones but 2-thiocoumarins and sometimes dithiocoumarins were generally obtained. With 1-allyl-2-methoxybenzene and some of its derivatives, 1,2-dithiole-3-thiones have been obtained, together with dithiocoumarins (Fig. 4)[5,15].

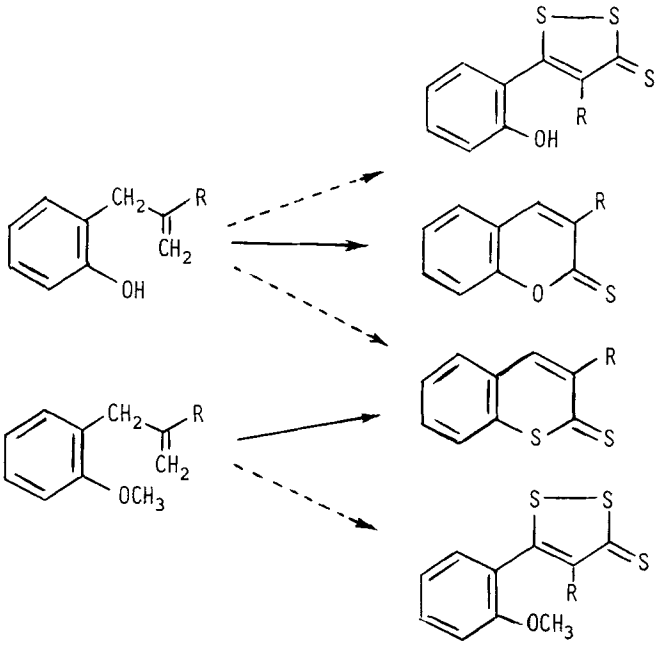


Figure 4.

Owing to possible dehydration to alkenic hydrocarbons, alcohols were likely starting materials for obtaining 1,2-dithiole-3-thiones and some experiments have been made in order to test this possibility. Three alkanols have been used: 2-methylpropan-2-ol, 2-methylbutan-2-ol and 3-methylbutan-1-ol[16]. With elemental sulfur alone, no appreciable result was obtained but with a mixture of sulfur and tetraphosphorus decasulfide the expected 1,2-dithiole-3-thiones were obtained, in yields ranging from 2 to 13%. These results being moderately encouraging, this study was not further developed.

Linalool (3,7-dimethylocta-1,6-dien-3-ol) with sulfur in ethyl benzoate gave, in 10% yield, 5-(4,5-dimethyl-2-thienyl)-4-methyl-1,2-dithiole-3-thione (Fig. 5)[17].

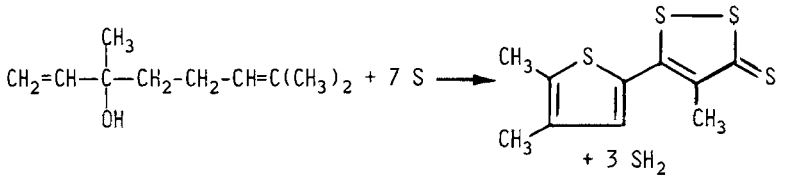


Figure 5.

With alkynols, the results were still less encouraging[16]. With alkynediols, reaction with sulfur led to derivatives of thieno[3,2-*b*]thiophen described in Section 5.

Reaction of sulfur on halogenated carbon chains can be accompanied by dehalogenation. For instance, 2-bromo-1-(4-methoxyphenyl)propene, heated with sulfur, gives 5-(4-methoxyphenyl)-1,2-dithiole-3-thione[9].

At the temperatures (180–220 °C) used for obtaining 1,2-dithiole-3-thiones, sulfur alone generally does not attack keto groups. This has been shown with isophorone[18] which gave, around 200 °C, two different ketodithiolethiones (**A** and **B**, Fig. 6), together with a derivative of [1]benzothiono[3,2-*b*][1]benzothiophene whose formation is discussed in Section 5.

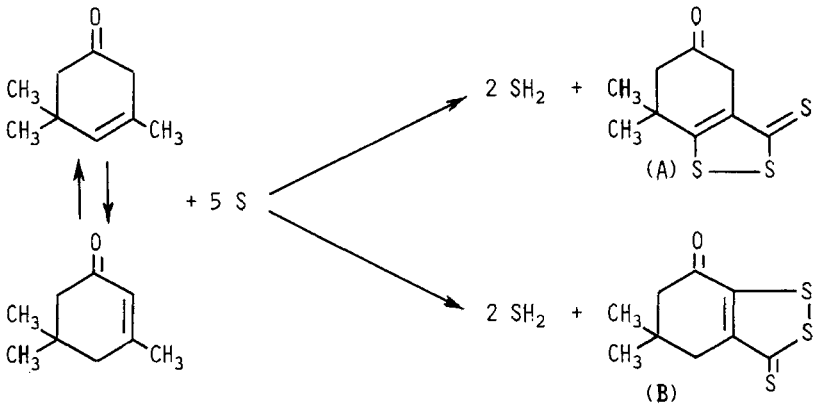


Figure 6.

1.2. Reaction of β-Keto Esters with Tetraphosphorus Decasulfide

Another route to 1,2-dithiole-3-thiones was explored later: reaction of tetraphosphorus decasulfide with β-keto esters[19]. Contrary to what happens with sulfur, this method does

not affect generally the rest of the molecule. For instance, ethyl 2-oxocyclohexanecarboxylate leads to 4,5,6,7-tetrahydro-1,2-benzodithiole-3-thione[8,19] while reaction of sulfur with 1-methylcyclohexene, as said above, leads to 1,2-benzodithiole-3-thione[7]. Similarly, ethyl 2-oxocyclopentane-carboxylate gives 5,6-dihydro-4*H*-cyclopenta-1,2-dithiole-3-thione[8,19].

While reaction of sulfur with hydrocarbon chains often leads to poor yields, reaction of tetraphosphorus decasulfide on β-keto esters gives in most cases satisfactory yields and therefore, since 1952, has been largely used in our laboratory for the preparation of 1,2-dithiole-3-thiones, as shown in Fig. 7, with various substituents such as:

alkyl and dialkyl[8,10,19];
phenyl and methyl, phenyl[8,19];
styryl[21];
thienyl and alkyl, thienyl[11,12,13];
pyridyl and alkyl, pyridyl[10].

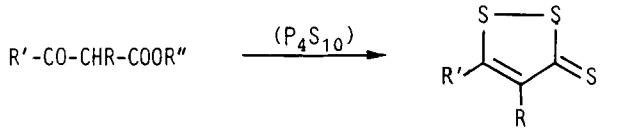


Figure 7.

Analogous results were independently obtained by A. Lüttringhaus and W. Cleve[20] who used a mixture of sulfur and tetraphosphorus decasulfide.

1.3. Reaction of Ketones with Sulfur and Tetraphosphorus Decasulfide

1,2-Dithiole-3-thiones have been obtained from ketonic starting materials by reaction with a mixture of sulfur and tetraphosphorus decasulfide[9], namely:

5-phenyl-1,2-dithiole-3-thione from propiophenone or phenylacetone;
5-(4-methoxyphenyl)-1,2-dithiole-3-thione from *p*-methoxypropiophenone or (4-methoxyphenyl)acetone.

A further study concerned preparation of eighteen 1,2-dithiole-3-thiones[22] by heating diverse ketones in biphenyl with a mixture of sulfur and tetraphosphorus decasulfide. For instance, 4,5-diphenyl-1,2-dithiole-3-thione was obtained, in 25% yield, from 1,2-diphenylpropan-1-one as shown in Fig. 8.

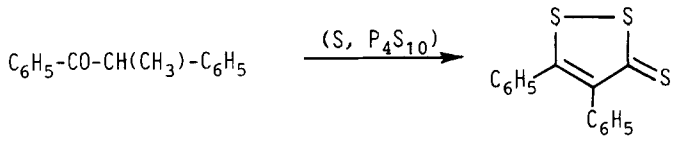


Figure 8.

Satisfactory yields (29 to 34%) were also obtained with isobutyrophenone and four of its derivatives with methyl substituents on the benzene ring[22] as indicated in Fig. 9.

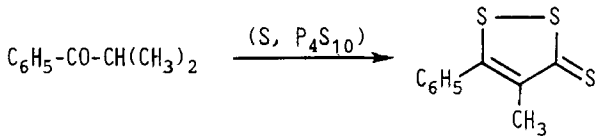


Figure 9.

However, with isobutyrophenones possessing methoxy substituents on the benzene ring, yields were poor[22,23]. In the case of *o*-methoxyisobutyrophenones, together with small amounts of 1,2-dithiole-3-thiones, small quantities of dithiocoumarins were obtained[23].

If a ketonic chain is halogenated, formation of a 1,2-dithiole-3-thione by reaction of a mixture of sulfur and tetraphosphorus decasulfide is accompanied by dehalogenation. For instance 3,4-dichloro(or dibromo)-3-methyl-2-butanone gave, in very low yields, 4,5-dimethyl-1,2-dithiole-3-thione[24].

In the case of halogenated acylbenzenes, during the formation of a 1,2-dithiole-3-thione, halogen atoms on the acyl chain are eliminated while halogen atoms on the benzene ring remain[24].

1.4. Sulfuration of β-Keto Aldehydes

1,2-Dithiole-3-thiones have been obtained by reaction of tetraphosphorus decasulfide with sodium salts of keto-enols[12], as shown by the example given in Fig. 10.

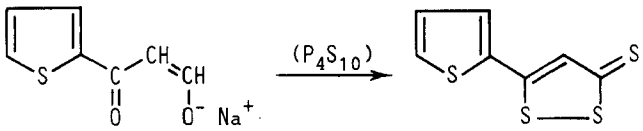


Figure 10.

Simultaneous reaction of sulfur and tetraphosphorus decasulfide upon β-keto aldehydes led to seventeen 1,2-dithiole-3-thiones[25].

With derivatives of 3-(2-methoxyphenyl)-3-oxopropanal yields of 1,2-dithiole-3-thiones are generally low and other heterocycles can be obtained, such as thiocoumarins and thiochromones[25] (see Section 7.2).

1.5. Miscellaneous Preparations of 1,2-Dithiole-3-thiones

Apart from the preceding methods, few other reactions have been used occasionally in our laboratory.

Reaction of tetraphosphorus decasulfide with 1-sulfobenzoic acid imide (saccharin) gives 1,2-benzodithiole-3-thione. This method, described in 1916 by A. Mannessier[26], appears to be the first having led to a 1,2-dithiole-3-thione correctly described. The same procedure, applied to 1-sulfo-2-naphthoic acid imide gave us naphtho[1,2-*c*]-1,2-dithiole-3-thione, also obtained by reaction of sulfur with 3-methyl-1,2-dihydronaphthalene[8]. This reaction is shown in Fig. 11.

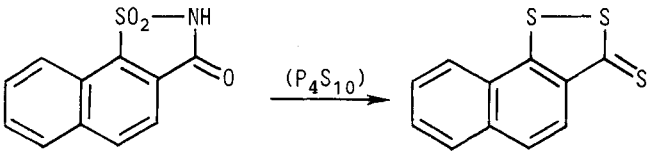


Figure 11.

Reaction of tetraphosphorus decasulfide with 2,2′-dithiodibenzoic acid was known to give 1,2-benzodithiole-3-thione[27]. As shown in Fig. 12, the same method, applied to 3,3′-dithiodi(2-naphthoic) acid, gave us naphtho[2,3-*c*]-1,2-dithiole-3-thione[8].

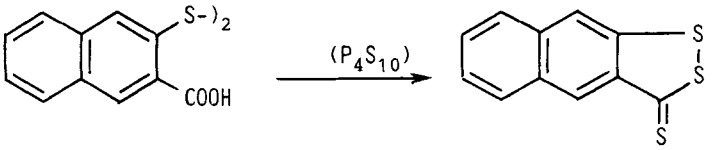


Figure 12.

2. CHEMICAL PROPERTIES OF 1,2-DITHIOLE-3-THIONES AND OF THEIR FUNCTIONAL DERIVATIVES

2.1. Reactions of the Thione Group

During our earlier studies we had been particularly interested in the formation of sparsely soluble addition compounds from which the 1,2-dithiole-3-thiones could be regenerated. This was specially useful for isolating dithiolethiones from the tarry mixtures obtained by reaction of sulfur with organic compounds.

It was found that various 1,2-dithiole-3-thiones give addition compounds with halogens[4], mercury dichloride[4], antimony tri- and pentachloride[4,28], tin tetrachloride[4,28], bismuth trichloride[28], thionyl chloride[28], and sulfuryl chloride[28]. In the light of present knowledge, addition compounds formed with halogens are probably 1,2-dithiolylium derivatives (Fig. 13).

X = Cl, Br or I

Figure 13.

Addition compounds formed with mercury dichloride may have a similar structure but no definitive structural proof seems to exist. The situation is the same with antimony and tin derivatives but the fact that antimony pentachloride gives an addition compound of the type $LSbCl_5$ while tin tetrachloride leads to a formula L_2SnCl_4 suggests that these are coordination compounds whose central atom has the coordination number 6. However, no definitive conclusion can be drawn owing to the lack of evidence from X-ray structural analysis.

Particularly important derivatives are those obtained by reaction of methyl iodide or dimethyl sulfate with 1,2-dithiole-3-thiones[12,13]. These derivatives are 3-methylthio-1,2-dithiolylium iodides or methylsulfates and are very useful for introducing a 1,2-dithiole ring in a structure.

Other reactions of the thione group involve replacement of the sulfur atom by another atom or group.

Potassium permanganate dissolved in acetone proved to be a good selective oxidation agent, giving in a first step a 1,2-dithiol-3-one, further action leading to the oxidation of the dithiole ring to a carboxyl group[5].

Hydroxylamine, reacting with diverse 1,2-dithiole-3-thiones, gave the corresponding oximes[8,10,12,13].

1,2-Dithiole-3-thiones were also shown to react with active methylene compounds. For instance, 5-aryl-1,2-dithiole-5-thiones react with acenaphthenone to give a 2-(5-aryl-1,2-dithiol-3-ylidene)acenaphthen-1-one while with a 1,2-dithiole-3-thione without an aryl substituent in position 5, the dithiole ring is opened and a 7-thiafluoranthene-10-thione is obtained[29].

2.2. *Reactions of Side Chains*

A 5-methyl substituent of a 1,2-dithiole-3-thione can undergo a crotonic condensation with benzaldehydes or furfural, in the presence of small amounts of piperidine[21], as shown in Fig. 14.

This method is particularly useful for obtaining 5-[2-(2-furyl)vinyl]-1,2-dithiole-3-thiones because these compounds cannot be obtained by reaction of tetraphosphorus decasulfide with ethyl 5-(2-furyl)-3-oxopent-4-enoate[21].

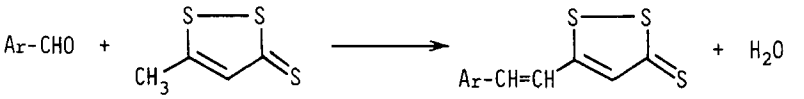


Figure 14.

Reaction of 4-nitroso-*N*,*N*-dimethylaniline with the 5-methyl substituent of a 1,2-dithiole-3-thione gave two products: a 5-[(4-dimethylaminophenyl)-iminomethyl]-1,2-dithiole-3-thione and the corresponding imine *N*-oxide (nitrone)[30].

2.3. *Substitution of the Dithiole Ring*

Owing to its positive charge, the dithiole ring undergoes with difficulty electrophilic substitution. Halogenation by chlorine or bromine has been observed in boiling acetic acid in the case of some 5-aryl-1,2-dithiole-3-thiones[31]. However, there is simultaneous attack of the thione group and the resulting product was a 5-aryl-4-halogeno-1,2-dithiol-3-one.

2.4. *Modification of the Dithiole Ring*

1-(*N*,*N*-Diethylamino)propyne and 1-(*N*,*N*-diethylamino)-2-phenylacetylene reacting with diverse 1,2-dithiole-3-thiones, 1,2-dithiol-3-ones or *N*-phenyl-1,2-dithiol-3-imines

gave [2 + 3] cycloaddition. In some cases, formation of thiopyran derivatives was observed[32]. With a 5-substituted 1,2-dithiole-3-thione the main product was an α-(1,3-dithiol-2-ylidene)thioketone (**A**, Fig. 15), sometimes accompanied by a 1,6,6aλ^4-trithiapentalene (**B**, Fig. 15) if the 1,2-dithiole-3-thione used was not substituted at position 4. In this case, the thioketone **A** isomerized to the trithiapentalene **B** upon heating with sulfur or thioacetamide[32].

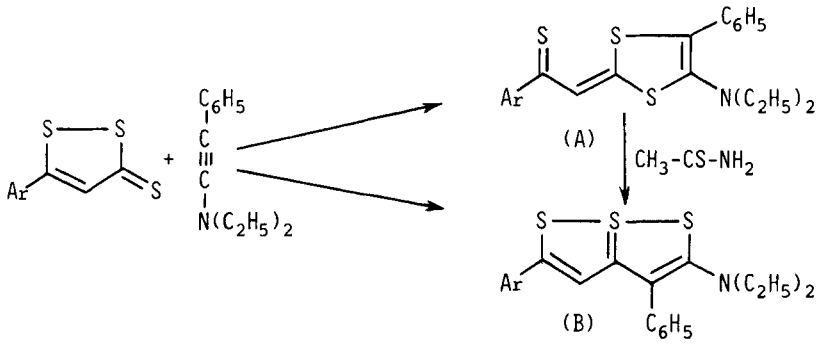


Figure 15.

With a 1,2-dithiole-3-thione unsubstituted at position 5, ynamines opened the dithiole ring and thiopyran-2-thiones, as well as thiopyran-4-thiones, were obtained[32], as shown in Fig. 16.

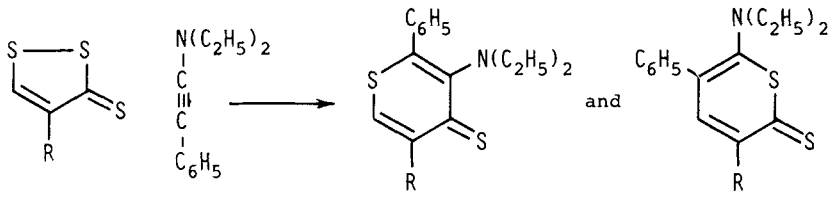


Figure 16.

4(or 5)-Aryl-1,2-dithiol-3-ones reacting with 1-(*N*,*N*-diethylamino)-2-phenylacetylene led to α-[5-(*N*,*N*-diethylamino)-4-phenyl-1,3,-oxathiol-2-ylidene]-thioaldehydes or thioketones (**A**, Fig. 17). Similarly, 5-aryl-*N*-phenyl-1,2-dithiol-3-imines gave α-[4-(*N*,*N*-diethylamino)-5-methyl (or phenyl)-3-phenyl-3*H*-1,3-thiazol-2-ylidene]thioacetophenones (**B**, Fig. 17)[32].

(A) R = H; R′ = Ar
or R = Ar; R′ = H

(B) R = CH_3 or C_6H_5

Figure 17.

3. REACTIONS OF CATIONS CONTAINING A 1,2-DITHIOLE RING

3.1. 3-Alkylthio-1,2-dithiolylium Cations

5-Aryl-3-methylthio-1,2-dithiolylium cations, reacting with active methylene compounds, gave 5-aryl-1,2-dithiol-3-ylidene derivatives[33,34,35]. More details are given in Section 9.

3-Methylthio-5-(4-methoxyphenyl)-1,2-dithiolylium iodide, reacting with 1-naphthol in the presence of pyridine, gave 2-[5-(4-methoxyphenyl)-1,2-dithiol-3-ylidene]-2*H*-naphthalen-1-one[36].

3-Methylthio-1,2-dithiolylium cations reacting with aromatic primary amines led to *N*-aryl-1,2-dithiol-3-imines[33,37], as shown also by other authors[38]. However, we found that 3-methylthio-1,2-dithiolylium cations not substituted at position 5 react with aromatic primary amines giving methyl 3-(arylamino)propene dithioates. Similarly, as shown in Fig. 18, the 5-methyl-1,2-dithiolylium cation led to methyl 3-(arylamino)but-2-enedithioates[37].

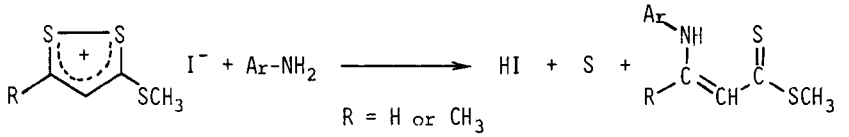


Figure 18.

As shown in Fig. 19, 1-(*N*,*N*-diethylamino)propyne reacted, in acetonitrile, with diverse 3-methylthio-1,2-dithiolylium cations and the reaction mixture, when treated with aqueous sodium hydrogen sulfide, led to thiopyran-2-thiones[39].

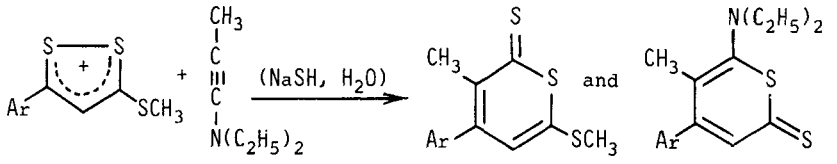


Figure 19.

3.2. 3-Chloro(or bromo)-1,2-dithiolylium Cations

These cations are readily obtained by reaction of phosphorus oxychloride or oxybromide, respectively, with 1,2-dithiol-3-ones.

5-Aryl-3-halo-1,2-dithiolylium cations were made to react with phenols, naphthols and their methyl ethers. It was found that this condensation can occur in the ortho or para position relative to a hydroxy or methoxy group. In the case of a phenol or naphthol, the resulting cation can be deprotonated to a compound which may be considered either as a (1,2-dithiol-3-ylidene) ketone or as a (1,2-dithiol-3-ylio)phenolate or -naphtholate[36].

Fig. 20 shows the reaction of 1-naphthol for which condensation takes place at position 4 (para).

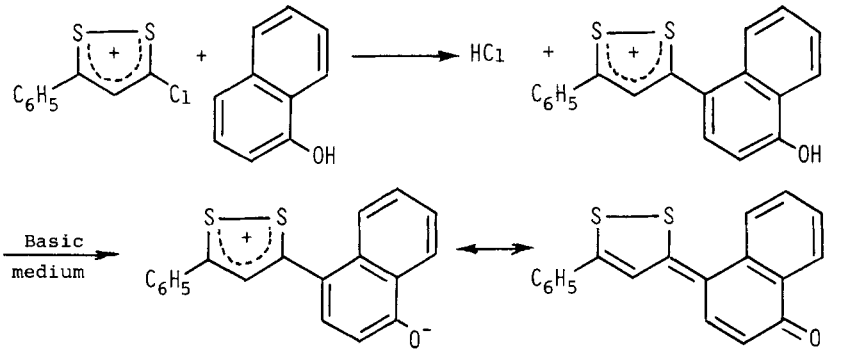


Figure 20.

For other diverse phenols, naphthols and their methyl ethers, reaction occurred at the following positions[36]:
Resorcinol, at 4; 3-methoxyphenol, at 4 and 6; 1,3-dimethoxybenzene, at 4; 3,5-dimethoxyphenol, at 2 and 4; 3-methoxycatechol, at 6; 2-naphthol, at 1; naphthalene-2,6-diol, at 1; 1-methoxynaphthalene, at 2; 2-methoxynaphthalene, at 1.

3.3. Other Cations Derived from 1,2-Dithiole

As shown in Fig. 21, 3-aryl-1,2-dithiolylium cations, obtained by peracetic acid oxidation of 5-aryl-1,2-dithiole-3-thiones, reacting with aliphatic secondary amines, formed (*N*,*N*-dialkylamino)-1-arylprop-2-ene-1-thiones[40].

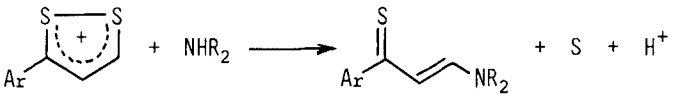


Figure 21.

The reaction of 1,2-dithiolylium cations without functional substituents such as methylthio or chloro, with carbonyl compounds, is described in Section 9.4.

The reaction product of 1,2-dithiol-3-iminium cations with 1-(*N*,*N*-diethylamino)-propyne, treated with hydrogen sulfide, 1-(*N*,*N*-diethylamino)-1,6,6aλ^4-trithiapentalene whereas, after treatment with aqueous sodium hydrogen sulfide, not only this trithiapentalene, but also a 2-(*N*,*N*-diethylamino)thiopyran-4-thione was obtained[39]. This is shown in Fig. 22.

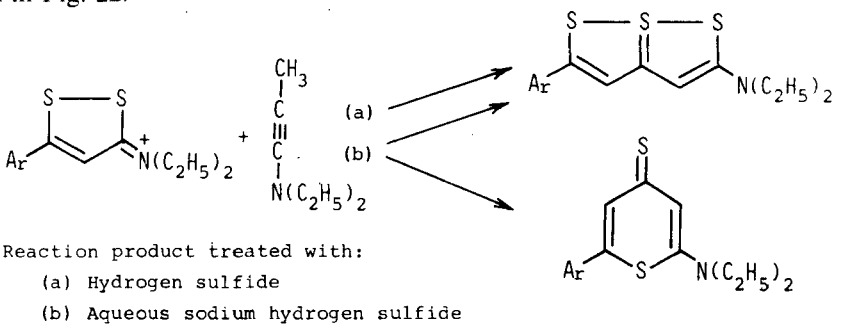
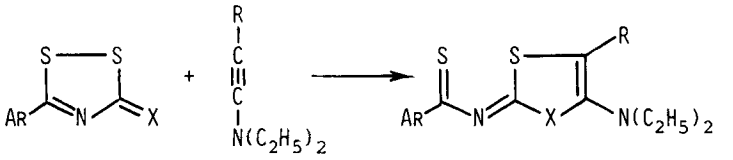


Figure 22.

4. CYCLOADDITIONS OF 1,2,4-DITHIAZOLE AND 1,3-DITHIOLE DERIVATIVES

The complex results obtained in the reaction of ynamines with 1,2-dithiole derivatives prompted us to study the reaction of closely related structures containing 1,2,4-dithiazole or 1,3-dithiole rings.

In the reaction of 1-(*N*,*N*-diethylamino)propyne or of 1-(*N*,*N*-diethylamino)-2-phenylacetylene with 1,2,4-dithiazol-3-ones and with the corresponding thiones, a [2+3] cycloaddition was observed. *N*-(1,3-Oxathiol-2-ylidene)-thiobenzamides and *N*-(1,3-dithiol-2-ylidene)thiobenzamides, respectively, were obtained (Fig. 23). The structures of these compounds were established by mass spectrometry, ^{1}H NMR spectrometry and an X-ray structural analysis of *N*-[4-(*N*,*N*-diethylamino)-5-methyl-1,3-dithiol-2-ylidene]-4-methoxythiobenzamide[41].

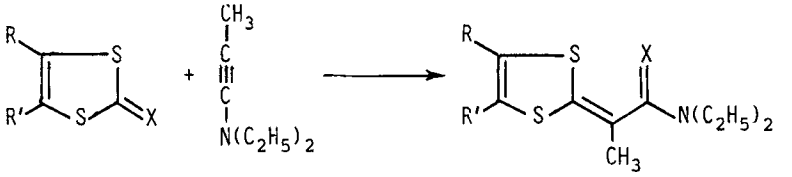


R = C_6H_5, X = S

R = CH_3, X = O or S

Figure 23.

Contrary to the preceding results, 1,3-dithiol-2-ones and the corresponding thiones reacted with the same ynamines according to a [2+2] cycloaddition mechanims[42]. As shown in Fig. 24, *N*,*N*-diethyl-α-(1,3-dithiol-2-ylidene)amides and thioamides, respectively, were obtained.



X = O or S

Figure 24.

The structure of the preceding thioamides was confirmed by an independent synthesis: reaction of an alkyne with a 5-(*N*,*N*-diethylamino)-1,2-dithiole-3-thione[42] (Fig. 25).

The above thioamides have also been obtained by reaction of ynamines with a 2-methylthio-1,3-dithiolylium cation and subsequent treatment of the ionic intermediate with sodium hydrogen sulfide or pyridine[42].

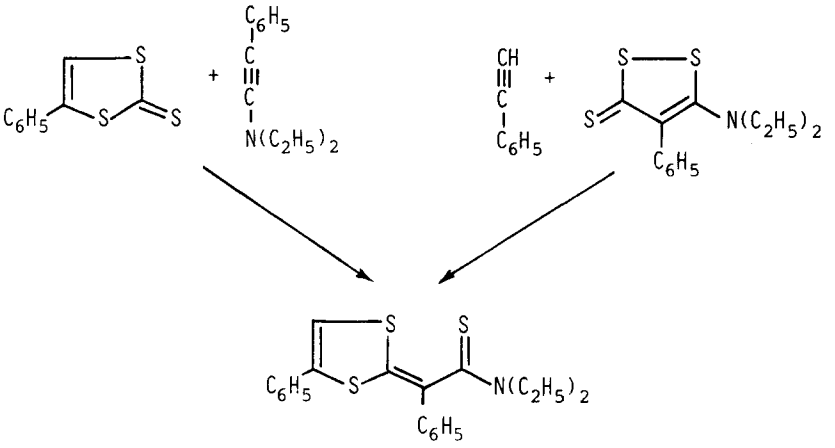


Figure 25.

5. THIOPHENES AND THIENO[3,2-*b*]THIOPHENES

In reactions of sulfur with organic compounds, apart from the formation of 1,2-dithiole-3-thiones, we have occasionally obtained thiophene derivatives as in the example given in Fig. 26, which was the first preparation of 2,3′-bithienyl[12].

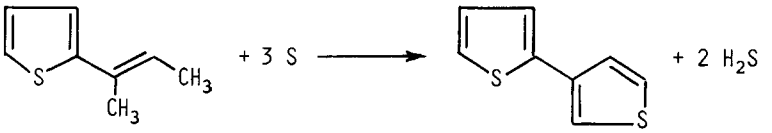


Figure 26.

Thiophene and 1,2-dithiole rings can also be formed simultaneously, as we found in the case of 2,6-dimethylocta-2,4,6-triene which gave 5-(4,5-dimethyl-2-thienyl)-4-methyl-1,2-dithiole-3-thione[17].

As already said in Section 1.1, 3,3,4,6-tetramethyldithiophthalide, that is to say 3,3,4,6-tetramethyl-3*H*-2-benzothiophene-1-thione, has been obtained by heating sulfur with 2-isopropyl-1,3,5-trimethylbenzene[14].

Thieno[3.2-*b*]thiophenes have been obtained by reaction of sulfur with derivatives of but-2-yne-1,4-diol[16], as indicated in Fig. 27.

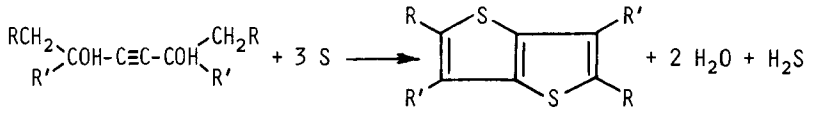


Figure 27.

As said in Section 1.1, a diketo derivative of [1]benzothieno[3,2-*b*][1]-benzothiophene was obtained, among other products, during the reaction of sulfur, at 200 °C, with isophorone[18]. The same compound has been obtained by heating, at 250 °C, 5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-1,2-benzodithiole-3-thione[18], as shown in Fig. 28.

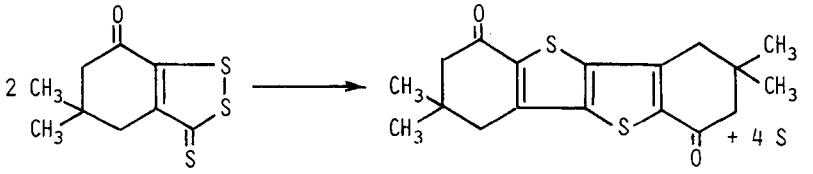


Figure 28.

5,6-Dihydrocyclopenta[*b*]thiophen-4-ones have been obtained by reaction of sulfur at 200 °C with diverse 2-isopropylidenecyclopentanones[43,44]. Similarly, 2-isopropylideneindan-1-one led to 2-methylindeno[1,2-*b*]thiophen-4-one while 2-arylmethylene-3-methylindan-1-ones gave 1-arylindeno[1,2-*c*]thiophen-8-ones[45].

It was already known that 2,5-dimethyl-1,6,6aλ^4-trithiapentalene could undergo, in strongly basic medium, a rearrangement leading to a thiophene derivative[46,47]. We have studied other reactions of this type which are described in Section 10.4.

6. THIOBENZOPHENONES AND ARYL THIENYL THIOKETONES

After having obtained a number of 1,2-dithiole-3-thiones it appeared useful to compare their infrared absorption spectra to those of other thiocarbonyl compounds. For this purpose, we have selected thiobenzophenones because many other simple thiocarbonyl compounds are too readily enolized or polymerized. Ten thiobenzophenones diversely substituted by methyl or methoxy groups have been obtained by reaction of tetraphosphorus decasulfide with the corresponding benzophenones and their infrared spectra have been measured[48].

Aryl thienyl thioketones have been prepared in the same way, also in order to study the stretching vibration of the thiocarbonyl group[49,50].

7. COMPOUNDS CONTAINING THE THIOPYRAN RING

7.1. Thiopyrans

Dienamines derived from aliphatic methyl ketones react with carbon disulfide giving compounds which have been shown to be derivatives of 4-morpholino-5,6-dihydrothiopyran-2-thione[51].

Thiopyran-2-thiones have been prepared in good yields by reaction of 1,2-dithiole-3-thiones not substituted at position 5 with enamines derived from pyrrolidine[52,53].

1,2-Dithiole-3-thiones not substituted at position 5, reacting with ynamines, gave 2-(*N*,*N*-diethylamino)thiopyran-4-thiones and 6-(*N*,*N*-diethylamino)-thiopyran-2-thiones[32]. On the other hand, formation of thiopyran-2-thiones from ynamines and 3-methylthio-1,2-dithiolylium cations[39] is described in Section 3.1.

Last, α-(thiopyran-2-ylidene) thioketones have been particularly studied because of their structural relationship with 1,6,6aλ^4-trithiapentalenes (see Section 12).

7.2. Thiocoumarins and Thiochromones

Various 2-thiocoumarins have been obtained by heating sulfur with diversely substituted 2-allylphenols and 2-(2-methylallyl)phenols[5,15]. In some cases, the corresponding dithiocoumarins were also obtained[15]. Under the same conditions 1-allyl-2-naphthol and 2-allyl-1-naphthol led, respectively, to naphtho[2,1-*b*]pyran-3-thione and to naphtho[1,2-*b*]pyran-2-thione. With the methyl ethers of the preceding phenols, dithiocoumarins were generally obtained, often with 1,2-dithiole-3-thiones[15]. These reactions are summarized in Fig. 4, Section 1.1 As shown in Fig. 29, 1-allyl-2-methoxynaphthalene and 2-allyl-1-methoxynaphthalene, heated with sulfur, gave, respectively, naphtho[2,1-*b*]thiopyran-3-thione and naphtho[1,2-*b*]thiopyran-2-thione[15].

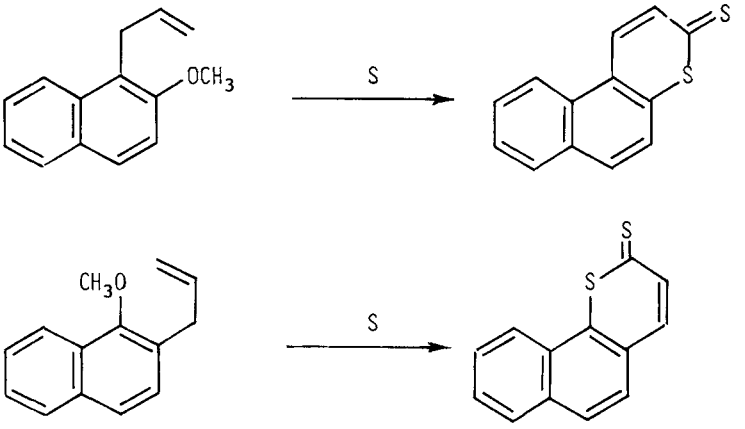


Figure 29.

As already said in Section 1.3, small yields of dithiocoumarins were obtained by heating a mixture of sulfur and tetraphosphorus decasulfide with *o*-hydroxy-, *o*-methoxy- and *o*-(methylthio)isobutyrophenones[23].

Nine 2-arylnaphtho[1,2-*b*]pyran-4-thiones have been obtained, in yields ranging from 8 to 55%, by heating with sulfur, at 200–210 °C, various 2-(3-arylprop-2-enylidene)-3,4-dihydro-2*H*-naphthalen-1-ones. Smaller quantities of 2-(5-aryl-1,2-dithiol-3-ylio)-1-naphtholates were also obtained[54]. On this subject, consult also Section 9.1.

The above pyran-4-thiones have been oxidized to the corresponding pyran-4-ones with potassium permanganate in acetone. Conversely, the pyran-4-ones gave the corresponding pyran-4-thiones by reaction with tetraphosphorus decasulfide[54].

Reaction of tetraphosphorus decasulfide, sometimes mixed with sulfur, with 3-(2-methoxyphenyl)-2-methyl-3-oxopropanal and with its derivatives substituted on the phenyl group gave complicated results. According to the starting material and to the presence or absence of elemental sulfur, the following compounds were obtained: 1,2-dithiole-3-thiones, 4-thiochromones, 2-thiocoumarins. As shown in Fig. 30, it seems

that tetraphosphorus decasulfide alone leads to a 4-thiochromone which can be isomerized to a 2-thiocoumarin by sulfur[25].

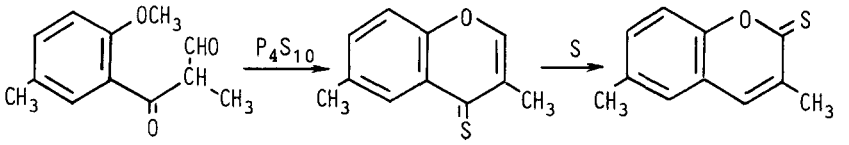


Figure 30.

1-Aryl-3-(2-hydroxyphenyl)propane-1,3-diones, treated with tetraphosphorus decasulfide in pyridine, gave, in good yields (22 to 65%), 2-aryl-4-thiochromones, with smaller quantities of 2-(5-aryl-1,2-dithiol-3-ylio)-phenolates. In a similar way, 1-aryl-3-(2-hydroxy-1-naphthyl)propane-1,3-diones gave predominantly 3-arylnaphtho[2,1-*b*]pyran-4-thiones with smaller amounts of 1-(5-aryl-1,2-dithiol-3-ylio)-2-naphtholates[55].

As shown in Fig. 31, by reaction with tetraphosphorus decasulfide, 2-methyl-3-(5-methyl-2-methylthio-phenyl)-3-oxopropanal led to a mixture of 3,6-dimethyldithiochromone, 3,6-dimethyldithiocoumarin and 4-methyl-5-(5-methyl-2-methylthiophenyl)-1,2-dithiole-3-thione[25].

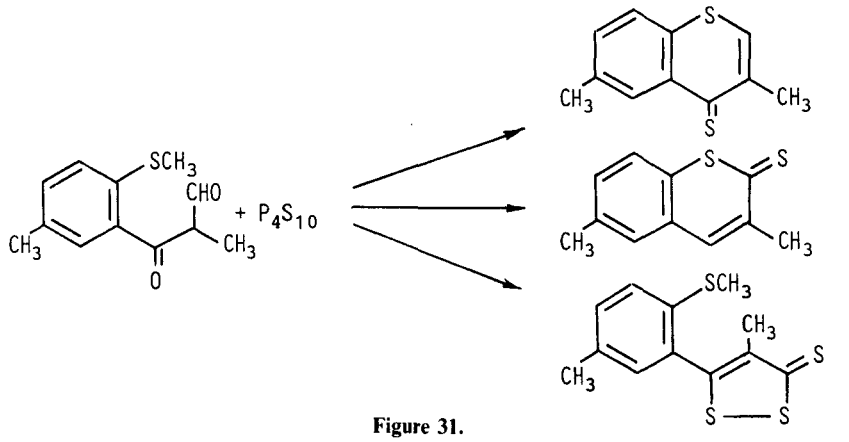


Figure 31.

The fact that isomeric thiochromones and thiocoumarins could be obtained simultaneously in various reactions led us to study their identification by infrared spectroscopy and to compare the vibrations due to the carbonyl to those due to the thiocarbonyl in compounds having otherwise identical structures[56]. This led us also to study other syntheses of thiocoumarins and thiochromones by Friedel-Crafts cyclization of 3-(arylthio)-acryloyl chlorides. In the presence of polyphosphoric acid or tin tetrachloride, 1-thiochromones are obtained but, if the catalyst is aluminium trichloride, a mixture of 1-thiochromone and 1-thiocoumarin is often obtained (Fig. 32)[57].

1-Thiochromones and 1-thiocoumarins reacting with tetraphosphorus decasulfide in boiling xylene gave, respectively, dithiochromones and dithiocoumarins. However, at higher temperatures, dithiochromones were isomerized to dithiocoumarins[57].

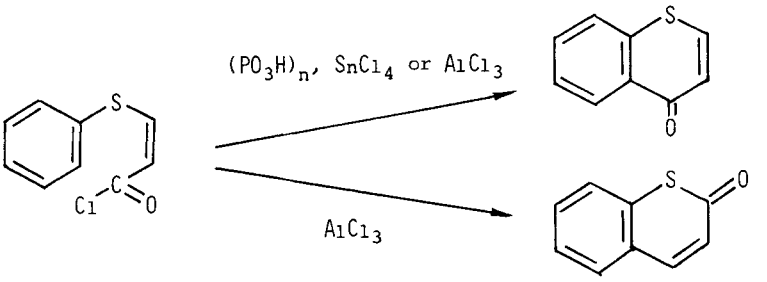


Figure 32.

7.3. *Thio- and Dithioisocoumarins*

After having studied syntheses and some properties of 3,1-benzothiazine-4-thiones (Section 13), we wished to compare with them compounds differing only by replacement of nitrogen by carbon, namely, dithioisocoumarins. Our work concerned initially derivatives of 3-arylisocoumarins which are readily accessible from homophthalic acid anhydride. The most convenient syntheses of 3-aryl-thio(and dithio)isocoumarins are shown in Fig. 33. 3-Arylisocoumarins or 2-(aroylmethyl)benzoic acids were transformed into 3-aryl-1-thioisocoumarins by reaction with tetraphosphorus decasulfide, while, under the same conditions, methyl 2-(aroylmethyl)benzoates gave generally a mixture of 3-aryl-1-thioisocoumarin and 3-aryl-dithioisocoumarin[58]. Secondary aliphatic amines, such as dimethylamine, attack 3-aryl-1-thioisocoumarins: the 3-aroylmethyl-*N*,*N*-dialkyl-thiobenzamides thus obtained, reacting with tetraphosphorus decasulfide, gave, with very good yields, 3-aryl-dithioisocoumarins[59]. The latter were oxidized with good yields (70 to 80%) by potassium permanganate dissolved in acetone to 3-aryl-2-thioisocoumarins[58].

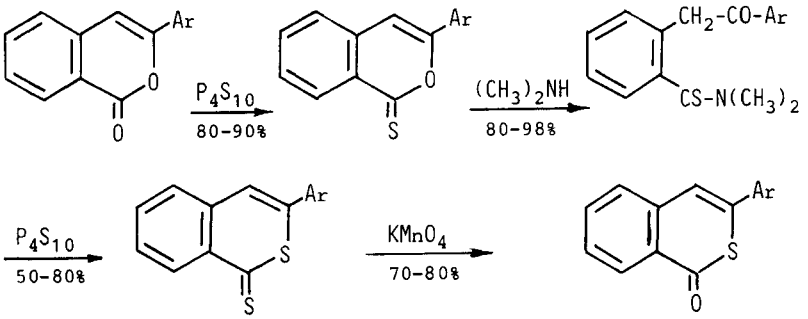


Figure 33.

Tetraphosphorus decasulfide reacting with alkyl hydrogen homophthalates or with dialkyl homophthalates gave a mixture of 3-alkoxy-dithioisocoumarins and of 3-alkylthio-dithioisocoumarins. Some of these compounds resulted from a migration of an alkoxy or of an alkylthio group. These results have shed some light on the mechanism of sulfuration by tetraphosphorus decasulfide and are summarized in Fig. 34 showing the various compounds obtained[60].

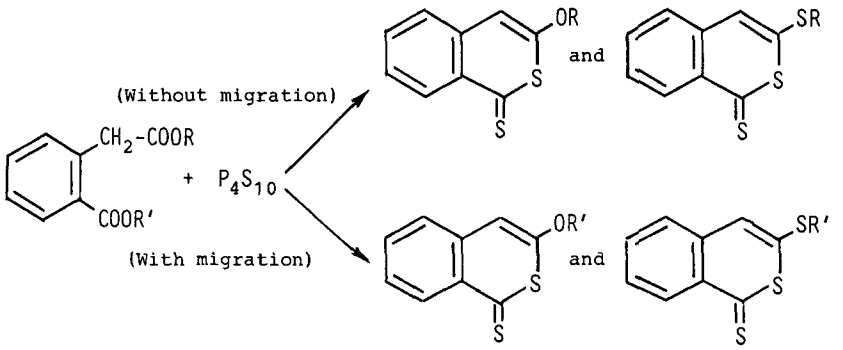


Figure 34.

3-Alkoxy- or 3-(alkylthio)-dithioisocoumarins were readily oxidized to the corresponding 2-thioisocoumarins by potassium permanganate or benzonitrile *N*-oxide[60].

3-Aryl-1-thioisocoumarins underwent a variety of reactions with amines and hydrazines, leading to interesting syntheses of isoquinoline derivatives. Fig. 35 shows how 3-aryl-1-thioisocoumarins reacted with aliphatic primary amines giving 2-(acylmethyl)-thiobenzamides which, in the presence of a strong acid, cyclized to give 2-alkyl-3-aryl-2*H*-isoquinoline-1-thiones[61].

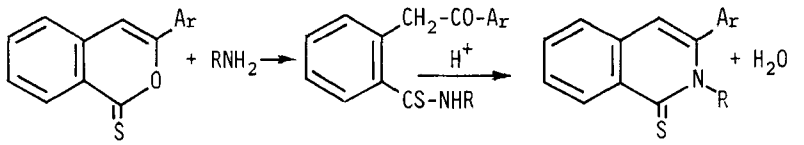


Figure 35.

In the absence of strong acids, 3-aryl-1-thioisocoumarins reacted with arylamines as shown in Fig. 36, giving mainly 3-aryl-1-arylimino-1*H*-isochromenes[61].

Figure 36.

As shown in Fig. 37, in the presence of a strong acid, arylamines reacting with 3-aryl-1-thioisocoumarins gave, in various proportions, derivatives of 2*H*-isoquinolin-1-one (**A**), of 2*H*-isoquinoline-1-thione (**B**) and of 1-imino-1,2-dihydroisoquinoline (**C**)[61].

As already said, dialkylamines reacting with 3-aryl-1-thioisocoumarins gave 2-aroylmethyl-*N*,*N*-dialkyl-thiobenzamides[59], but with pyrrolidine or piperidine the above-mentioned thiobenzamide reacted with another mole of amine and an enamine-thioamide was obtained[62].

NMR having shown that hindered rotation exists for 2-aroylmethyl-*N*,*N*-dialkyl-thiobenzamides[59], we wished to see what happens with the more hindered structures obtained from 3,4-diaryl-1-thioisocoumarins and secondary amines. With dimethyla-

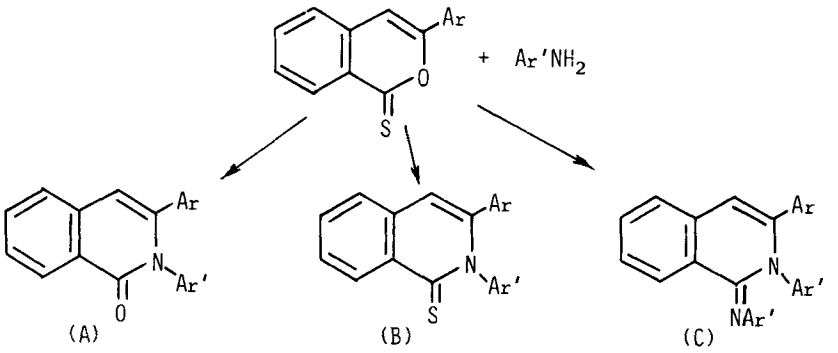


Figure 37.

mine, pyrrolidine or piperidine, 2-(aroyl-aryl-methyl)-*N*,*N*-dialkyl-thiobenzamides were obtained for which the existence of two conformers was established by NMR[63]. These thiobenzamides, reacting with tetraphosphorus decasulfide, gave 3,4-dithioisocoumarins in good yields[63].

As indicated in Fig. 38, 3-aryl-1-thioisocoumarins gave, with an equimolar quantity of hydrazine, 1-hydrazono-1*H*-isochromenes (**A**). Phenylhydrazine reacted in the same way[64]. With excess hydrazine, an isoquinoline (**B**) and an azine derived from 2-amino-3-aryl-2*H*-isoquinolin-1-one (**C**) were also obtained[64].

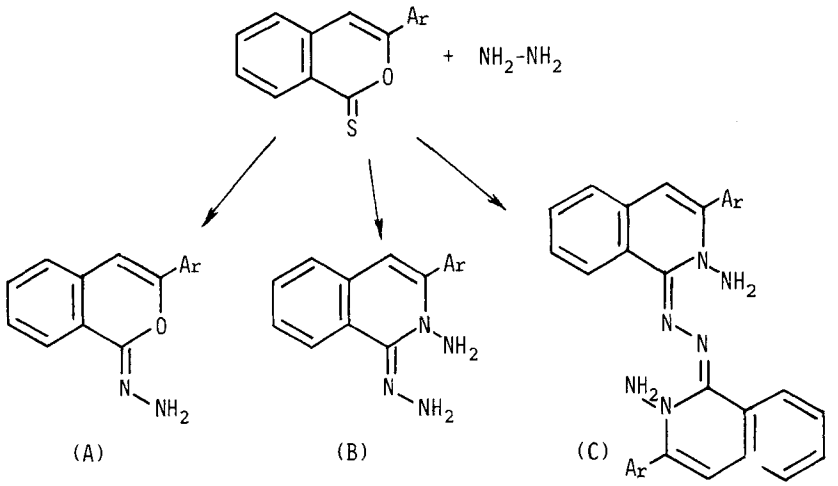


Figure 38.

Some 1-thioisocoumarins reacting with diazomethane gave derivatives of dispiro[isochromene-1:4′-(1,3-dithiolane)-5′:1″-isochromene][65].

As shown in Fig. 39, 3-aryl-2-thioisocoumarins reacting with pyrrolidine or piperidine led to enamine-benzamides[62].

Reaction of 3-aryl-2-thioisocoumarins with hydrazine was of peculiar interest because it was known that hydrazine and 3-phenylisocoumarin gave 4-phenyl-2,5-dihydro-2,3-

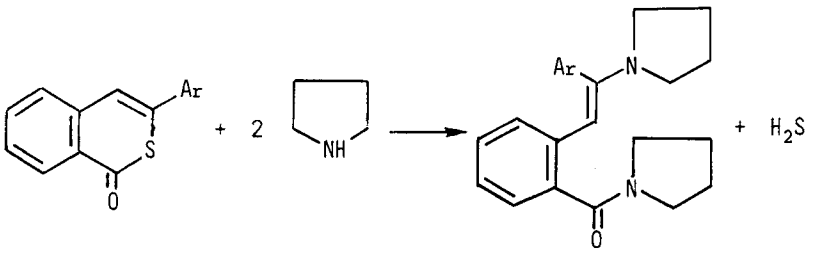


Figure 39.

benzodiazepin-1-one[66]. Therefore, the question arose whether a dihydro-2,3-benzodiazepin-1-one or a 2-amino-2*H*-isoquinolin-1-one could be obtained by reaction of hydrazine with a 3-aryl-2-thioisocoumarin. We found that this reaction gave 4-aryl-2,5-dihydro-2,3-benzodiazepin-1-ones as shown in Fig. 40. These compounds gave the corresponding thiones by reaction with tetraphosphorus decasulfide and isomerized to 2-amino-3-aryl-2*H*-isoquinolin-1-ones upon heating with hydrogen chloride in aqueous ethanol[67].

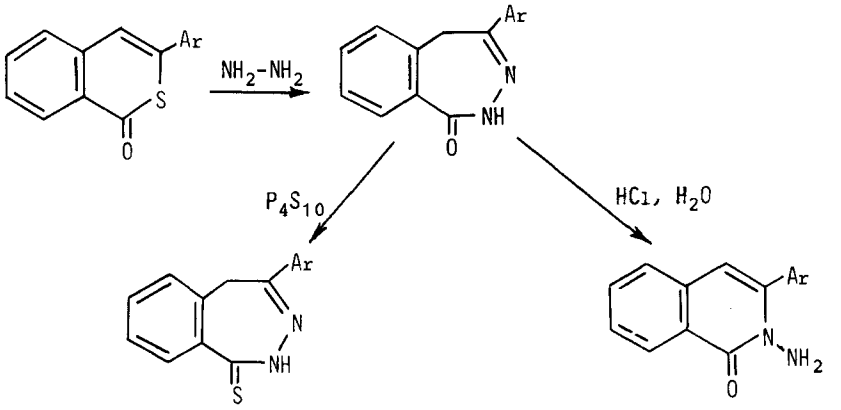


Figure 40.

Dithioisocoumarins reacting with aliphatic or aromatic primary amines gave 1-alkyl(or aryl)imino-1*H*-thioisochromenes which could be isomerized in acidic medium, leading mainly to 2*H*-isoquinoline-1-thiones[61]. With pyrrolidine or piperidine, enamine-thiobenzamides were obtained[62].

Dithioisocoumarins and hydrazine, in equimolar quantities, gave 1-hydrazono-1*H*-thioisochromenes. Phenylhydrazine reacted similarly. With excess hydrazine, dithioisocoumarins gave 2-amino-1-hydrazono-1,2-dihydroisoquinolines[68].

Diazomethane with 3,4-dihydro-dithioisocoumarin gave the *cis* (achiral) and the *trans* (racemic) isomers of dispiro[1,3-dithiolanebis-4:1′,5:1″-(3,4-dihydro-2-thioisochromene)][65].

In order to establish structural relationships by ESCA spectra, the following compounds have been compared: 1-thio, 2-thio, dithio, 1-phenylimido, 2-thio-1-phenylimi-

do derivatives of 3-(4-methylphenyl)isocoumarin, 3-(4-methylphenyl)-2*H*-isoquinolin-1-one, the corresponding thione and phenylimide[69].

8. PARTIAL BONDING IN SULFUR COMPOUNDS

In our laboratory, on the basis of infrared spectra, G. Guillouzo[70] suggested that compounds obtained by G. Traverso and M. Sanesi[71] by reaction of potassium hydrogen sulfide with pyran-4-thiones were in fact α-(1,2-dithiol-3-ylidene)ketones (**A**, Fig. 41) and that some interaction exists between the carbonyl oxygen and a sulfur atom of the dithiole ring. At the same time, S. Bezzi, M. Mammi and C. Garbuglio[72] showed, by X-ray structural analysis, that in one corresponding α-(1,2-dithiol-3-ylidene) thioketone (**B**, Fig. 41) the three sulfur atoms are practically on a straight line and that the distances between the central sulfur atom and the other sulfur atoms are equal. In the following years, this symmetry led to a preference, for such structures, of 1,6,6aλ^4-trithiapentalene names corresponding to formulae such as **C** (Fig. 41).

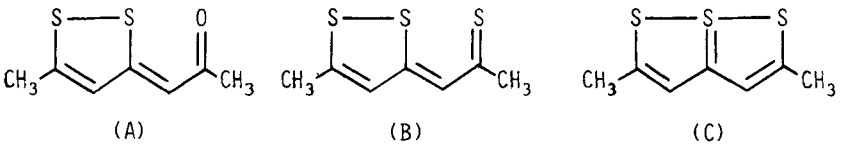


Figure 41.

These first results led to further studies of the bonding existing in related compounds between the 1,2-dithiole ring and the neighbouring carbonyl or thiocarbonyl. For instance, we showed that, in α-(1,2-dithiol-3-ylidene) ketones, the O-S interaction can be measured by the lowering of the carbonyl stretching frequency[73]. Infrared spectra of α-(1,2-dithiol-3-ylidene)ketones and of the corresponding 1,6,6aλ^4-trithiapentalenes were also compared in order to define the value of the stretching frequency of C-S bonds[73,74].

These observations arose rapidly the interest of theoretical chemists and various concepts were put forward such as "single bond–no-bond resonance", describing, more or less precisely, the redistribution of bonding electrons.

In these circumstances, our laboratory developed syntheses of new compounds for which numerous structural analyses were often made by the group of A. Hordvik (Bergen) and showed the effect of partial bonding on bond lengths.

Among other physical studies related to our work, one should cite ESCA determinations made in the laboratory of K. Siegbahn (Uppsala)[75] and photoelectron spectra studied by R. Gleiter and V. Hornung (Basle)[76].

The contribution of our laboratory to the study of α-(1,2-dithiol-3-ylidene) carbonyl compounds and of 1,6,6aλ^4-trithiapentalenes is described in Sections 9 and 10, respectively.

In the course of this work, it appeared to us that the relationships between 1,2-dithiolylium cations, 1,2-dithiole-3-thiones and 1,6,6aλ^4-trithiapentalenes could probably be extended to compounds containing more than three sulfur atoms involved in partial bonding phenomena. These extended relationships appear in Fig. 42 which compares

1,2-dithiolylium cations (**A**), 1,2-dithiole-3-thiones (**B**), α-(1,2-dithiol-3-ylidene) thioketones (i.e. 1,6,6aλ^4-trithiapentalenes) (**C**), 3-(1,2-dithiol-3-ylidenemethyl)-1,2-dithiolylium cations (**D**), 5-(1,2-dithiol-3-ylidenemethyl)-1,2-dithiole-3-thiones (**E**) and α,α′-bis(1,2-dithiol-3-ylidene) thioketones (**F**). Our studies of structures **D**, **E** and **F** are described in Section 11.

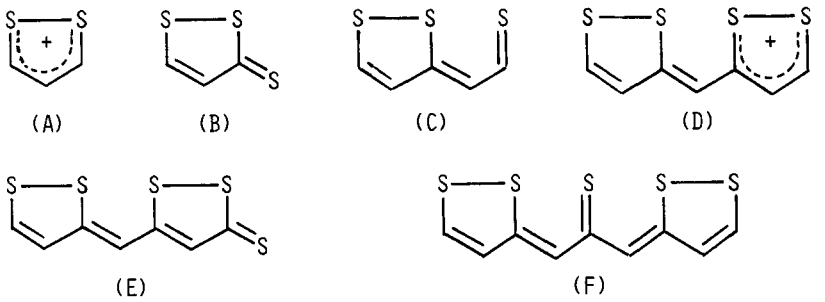


Figure 42.

Another development of our studies of partial bonding concerns derivatives of thiopyran similar to those of 1,2-dithiole. The analogy between 1,2-dithiolylium cations and thiopyrylium cations can be further extended as shown by the structures given in Fig. 43: thiopyrylium cations (**A**), thiopyran-2-thiones (**B**), α-(thiopyran-2-ylidene) thioketones (**C**), 2-(thiopyran-2-ylidenemethyl)thiopyrylium cations (**D**). Our work on this type of partial bonding is described in Section 12.

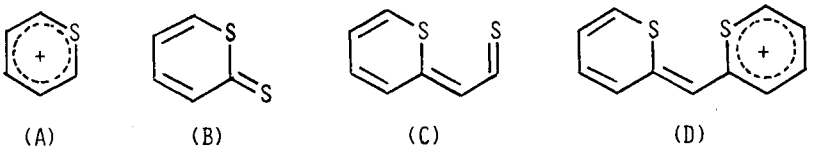


Figure 43.

9. α-(1,2-DITHIOL-3-YLIDENE) CARBONYL COMPOUNDS

As there is no existing terminology for partial bonding, the corresponding structures have been given various types of names based on usual bonding concepts. For instance, α-(1,2-dithiol-3-ylidene) ketones (**A**, Fig. 44) can also be considered as 1-oxa-6,6aλ^4-dithiapentalenes, the latter names having the advantage of stressing the O-S interaction. Moreover, in the case of 6-(1,2-dithiol-3-ylidene)cyclohexa-2,4-dien-1-ones, 2-(1,2-dithiol-3-ylio)-phenolate names, corresponding to the ionic structure **C** (Fig. 44), are often preferred because they express the aromatic nature of the benzene ring.

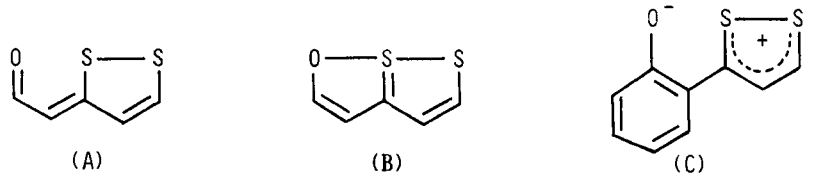


Figure 44.

9.1. *Reaction of Sulfur with α,γ-Diethylenic Carbonyl Compounds*

As indicated in Section 2.2, H. Quiniou had obtained 5-styryl-1,2-dithiole-3-thiones by reaction of benzaldehydes with 5-methyl-1,2-dithiole-3-thione[21]. On the other hand, E. Baumann and E. Fromm[77] had shown, as early as 1897, that ethyl cinnamate reacts with sulfur to form 5-phenyl-1,2-dithiol-3-one. This fact made us think that sulfuration of cinnamylidenemalonic esters could lead to 4-alkoxycarbonyl-5-styryl-1,2-dithiol-3-ones. This did not happen but, as shown in Fig. 45, (1,2-dithiol-3-ylidene)malonic esters were obtained instead[78,79].

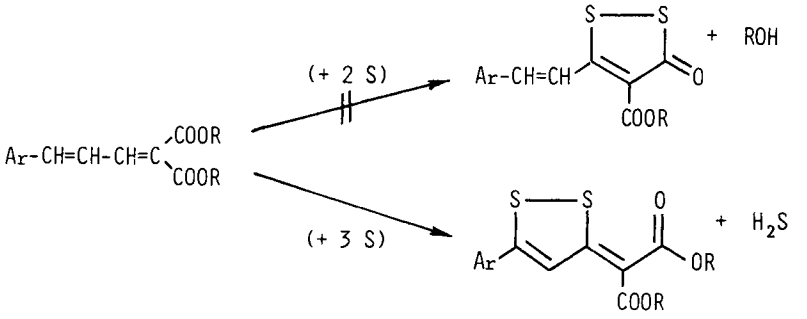


Figure 45.

Partial saponification of (5-aryl-1,2-dithiol-3-ylidene)malonic esters, followed by decarboxylation, gave (5-aryl-1,2-dithiol-3-ylidene)acetic esters for which infrared spectra showed an interaction between the carbonyl and the dithiole ring[80].

By reaction of sulfur, at 220 °C, with α,γ-diethylenic ketones, two types of compounds were obtained[81], as shown in Fig. 46: α-(1,2-dithiol-3-ylidene) ketones (**A**) and 2-acylthiophenes (**B**).

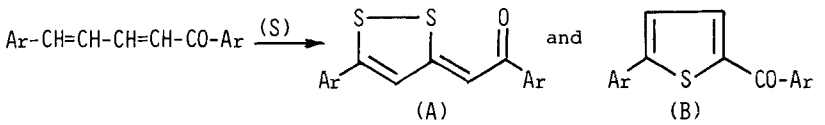


Figure 46.

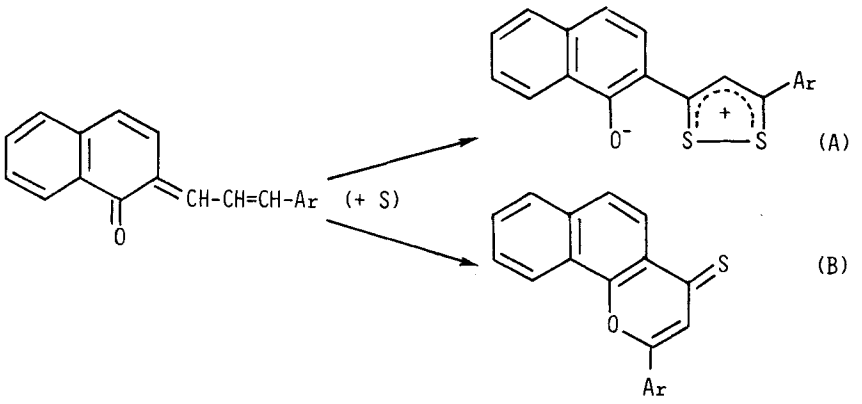


Figure 47.

In a similar way, ethyl cinnamylideneacylacetates led to ethyl (5-phenyl-1,2-dithiol-3-ylidene)acylacetates together with 2-acyl-5-phenyl-thiophenes[82].

When sulfur was heated at 200 °C with 2- cinnamylidenecyclohexanone, formation of the dithiole ring was accompanied by dehydrogenation of the cyclohexane ring and a 2-(1,2-dithiol-3-ylio)phenolate was obtained[83,84]. In a similar way, as shown in Fig. 47, diverse 2-cinnamylidene-3,4-dihydro-2*H*-naphthalen-1-ones led to 2-(5-aryl-1,2-dithiol-3-ylio)-1-naphtholates (**A**), the main products being, as said in Section 7.2, 2-aryl-naphtho[1,2-*b*]-pyran-4-thiones (**B**)[54].

9.2. *Reaction of Tetraphosphorus Decasulfide with β,δ-Triketones or β,δ-Diketo Phenols*

Although tetraphosphorus decasulfide reacting with β,δ-triketones mainly gave 1,6,6aλ^4-trithiapentalenes, in some cases α-(1-2-dithiol-3-ylidene) ketones have also been obtained[55]. When this reaction is applied to an asymmetric triketone, two different α-(1,2-dithiol-3-ylidene) ketones can be obtained and we showed that NMR in the presence of tris(dipivaloylmethanato)europium can establish the structure of the compound thus obtained[85].

When tetraphosphorus decasulfide reacts with β,δ-diketo phenols, only carbonyl oxygens are replaced by sulfur and the phenolic oxygen remains. As shown in Fig. 48, 2-(5-aryl-1,2-dithiol-3-ylio)phenolates have been obtained in this way, accompanied by 2-aryl-4-thiochromones[55], as already said in Section 7.2.

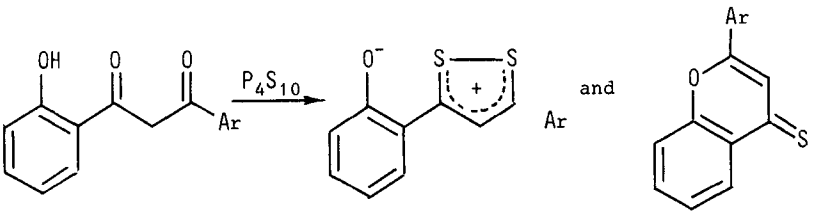


Figure 48.

Similarly, 1-aryl-3-(2-hydroxy-1-naphthyl)propane-1,3-diones gave 1-(5-aryl-1,2-dithiol-3-ylio)-2-naphtholates together with 3-arylnaphtho[2,1-*b*]-pyran-1-thiones[55].

9.3. *Reaction of Potassium Hydrogen Sulfide with Pyran-4-thiones*

As already said in Section 8, this reaction, initially described by G. Traverso et al.[71,86,87], has been at the origin of our interest for α-(1,2-dithiol-3-ylidene) ketones. We have studied it also later in order to establish the structure of products obtained from pyran-4-thiones which were not symmetrically substituted[88].

9.4. *Reaction of 1,2-Dithiole Derivatives with Carbonyl Compounds*

Y. Mollier and other co-workers have obtained a wide variety of α-(1,2-dithiol-3-ylidene) carbonyl compounds by reaction of 1,2-dithiole-3-thiones[29,54], or rather of 3-methylthio-1,2-dithiolylium cations, with diverse compounds such as: cyclohexane-

1,3-dione[73], 5,5-dimethylcyclohexane-1,3-dione[34], acenaphthenone[29,33], indane-1,3-dione[34], phenalane-1,3-dione[34,73], benzoylacetonitrile[35], ethyl cyanoacetate[34,35], cyanoacetamide[35], barbituric acid[34], rhodanine[34].

2-(5-Aryl-1,2-dithiol-3-ylio)phenolates have also been obtained by reaction of 5-aryl-3-methylthio-1,2-dithiolylium cations with phenolate anions[83,84]. Analogous results were obtained with 1-naphthol in the presence of pyridine[36] (see Section 3.1).

Reaction of 5-aryl-3-chloro(or bromo)-1,2-dithiolylium cations with phenols or phenol ethers[36] has been described in Section 3.1.

1,2-Dithiolylium cations without leaving groups at position 3 reacted also with CH_2 groups adjoining a carbonyl, leading to α-(1,2-dithiol-3-ylidene) carbonyl compounds. This reaction has been applied to cyclohexanone[83], 1*H*-3,4-dihydronaphthalen-2-one[89], 1,3-diphenylpropane-1,3-dione[35,74], ethyl benzoylacetate[74], diethyl malonate[35], malonanilide[35].

9.5. Reaction of 1,2-Dithiole-3-thiones with Diazo Esters or Diazo Ketones

At 150 °C, ethyl diazoacetate reacted with 5-aryl-4-methyl-1,2-dithiole-3-thiones, giving mainly ethyl (5-aryl-4-methyl-1,2-dithiol-3-ylidene)acetates. If there was no substituent on the carbon 4 of the dithiole ring, diethyl 2-(5-aryl-1,2-dithiol-3-ylidene)succinates were obtained. Under the same conditions, as shown in Fig. 49, diazo ketones reacting with 5-aryl-1,2-dithiole-3-thiones gave α-(5-aryl-1,2-dithiol-3-ylidene) ketones[89]. This reaction has been valuable for the synthesis of extended structures (see Section 11.3).

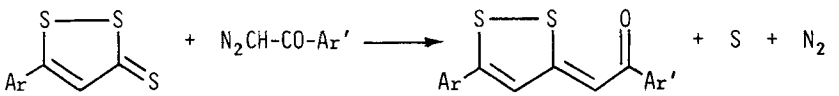


Figure 49.

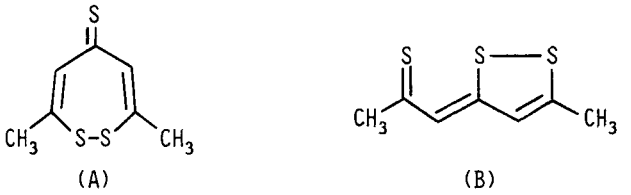
9.6. Partial Oxidation of 1,6,6aλ⁴-Trithiapentalenes

This reaction has been performed with benzonitrile *N*-oxide. If the starting material is not symmetrically substituted, two different products could be expected. We have shown that their structure could be established by NMR in the presence of tris(dipivaloylmethanato)europium[85].

10. 1,6,6aλ⁴-TRITHIAPENTALENES

10.1. Reaction of Tetraphosphorus Decasulfide with β,δ-Triketones

In the year 1925, F. Arndt, P. Nachtwey and J. Pusch[90], by reaction of heptane-2,4,6-trione with tetraphosphorus decasulfide, obtained a compound to which they attributed formula **A** (Fig. 50). As indicated in Section 8, in our laboratory, G. Guillouzo[70] suggested that this compound should rather be represented by formula **B** (Fig. 50) and this work initiated our interest for 1,6,6aλ⁴-trithiapentalenes and related structures.



(A) (B)

Figure 50.

The development of this synthesis was delayed until practical methods for obtaining β,δ-triketones became available. One of these methods is acylation of ketones by esters in the presence of sodium hydride and it has been used for preparing a number of 1,6,6aλ⁴-trithiapentalenes[55,91].

10.2. Reaction of Tetraphosphorus Decasulfide with α-(1,2-Dithiol-3-ylidene) Ketones

This method has been widely used for the preparation of 1,6,6aλ⁴-trithiapentalenes. As shown in Fig. 51, it led to the important observation that the same 1,6,6aλ⁴-trithiapentalene is obtained from two different α-(1,2-dithiol-3-ylidene) ketones[81,92], a strong argument supporting the symmetry of the 1,6,6aλ⁴-trithiapentalene structure.

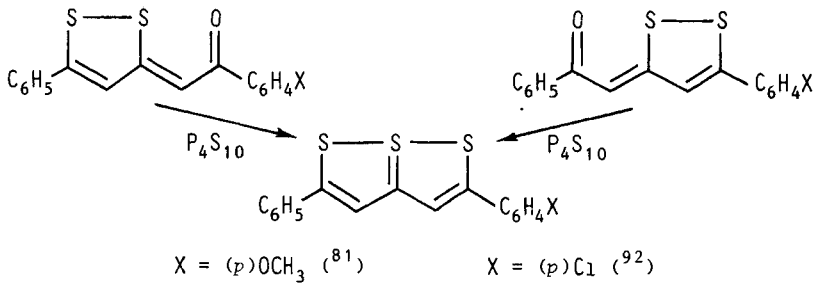


Figure 51.

10.3. Reaction of 1,2-Dithiole Derivatives with Thiocarbonyl Compounds

Owing to the relative instability of many thiocarbonyl compounds, this reaction has been much less used than the corresponding one with carbonyl compounds. Nevertheless, we obtained 2-amino-5-aryl-3-cyano-1,6,6aλ⁴-trithiapentalene by treating 5-aryl-3-methylthio-1,2-dithiolylium cations with cyanothioacetamide[35].

10.4. Modification of 1,6,6aλ⁴-Trithiapentalenes

In moderately basic medium, a methyl or methylene group substituted at position 5 in a 2-aryl-1,6,6aλ⁴-trithiapentalene reacted with aromatic aldehydes giving diversely substituted 2-aryl-5-styryl-1,6,6aλ⁴-trithiapentalenes. The same reaction, applied to 2,5-dimethyl-1,6,6aλ⁴-trithiapentalene led to 2,5-distyryl-1,6,6aλ⁴-trithiapentalene[93].

On the other hand it was known that, in strongly basic medium, 2-methyl-1,6,6aλ⁴-trithiapentalenes rearrange to dianions which can be methylated[46,47]. For this reaction we have suggested[94] the mechanism given in Fig. 52.

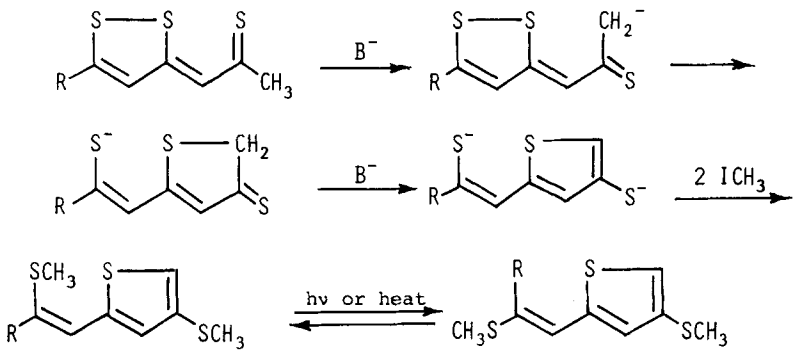


Figure 52.

In the compound obtained after methylation, the 2-(methylthio)vinyl group has the Z configuration and can be partially isomerized to the E configuration by UV irradiation. Thermal isomerization has also been observed[95].

The same mechanism applies if the CH_3 group is replaced by a CH_2R, provided that the free rotation of the CH_2R exists. This is not the case if the CH_2 is part of a ring such as a cyclohexane ring. This limitation has been put to account for the synthesis of extended structures (Section 11.2).

Now, if the methyl on position 2 were replaced by an isopropyl, we thought that the rearrangement indicated in Fig. 52 had to stop half-way. In fact, as shown in Fig. 53 we found that, after methylation, an α-(5,5-dimethyl-4-methylthio-5*H*-thiophen-2-ylidene) thioketone was obtained[96,97].

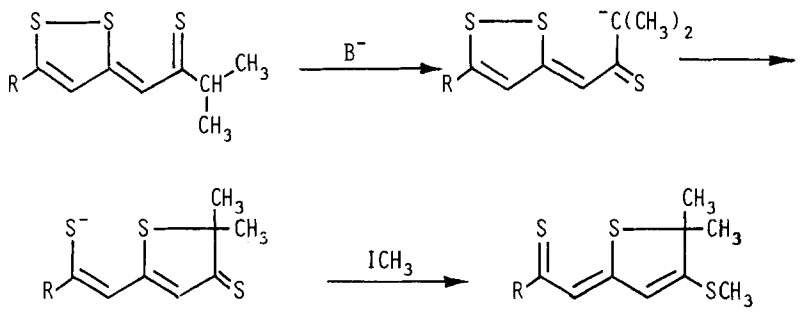


Figure 53.

11. EXTENDED STRUCTURES CONTAINING 1,2-DITHIOLE RINGS

1,6,6aλ^4-Trithiapentalenes can also be considered as α-(1,2-dithiol-3-ylidene) thioketones for which an interaction exists between the thioketo sulfur and the dithiole ring, leading to a structure containing three sulfur atoms in a straight line.

The question arose naturally whether such an interaction could exist between two neighbouring 1,2-dithiole rings or even between a thioketo sulfur and two 1,2-dithiole rings.

A first answer was given by E. Klingsberg[98] who, by reaction of the 5-phenyl-3-methylthio-1,2-dithiolylium cation with the 3-methyl-5-phenyl-1,2-dithiolylium cation, obtained the 3-phenyl-5-(5-phenyl-1,2-dithiol-3-ylidenemethyl)-1,2-dithiolylium cation. For the latter, an X-ray structure analysis by A. Hordvik[99] showed that the four sulfur atoms are nearly aligned, the two central sulfur atoms being about 3.05 Å apart. These facts indicate clearly the existence of an interaction between the two 1,2-dithiole rings.

We have also studied these 4-sulfur cations, but from another point of view: their rearrangement by deprotonation (Section 11.1).

The above results led M. Stavaux to undertake the synthesis of compounds having five sulfur atoms in line. The first step of this synthesis consisted in the preparation of 7-(1,2-dithiol-3-ylidene)-4,5,6,7-tetrahydro-1,2-benzodithiole-3-thiones which have four sulfur atoms in line (Section 11.2).

Last, some 2,6-bis(1,2-dithiol-3-ylidene)-cyclohexanethiones were obtained which proved to have five sulfur atoms in line (Section 11.3).

11.1. 3-(1,2-Dithiol-3-ylidenemethyl)-1,2-dithiolylium Cations

Diversely substituted cations of this type, heated under reflux in pyridine, rearranged with loss of a proton to a 2-(1,2-dithiol-3-ylidene)-2*H*-thiophene-3-thione (**A**, Fig. 54) which contains a 1,6,6aλ^4-trithiapentalene system[100,101]. These trithiapentalenes are red. In two cases, a blue isomer of the trithiapentalene has been obtained, for which formula **B** (Fig. 54) has been proposed[101].

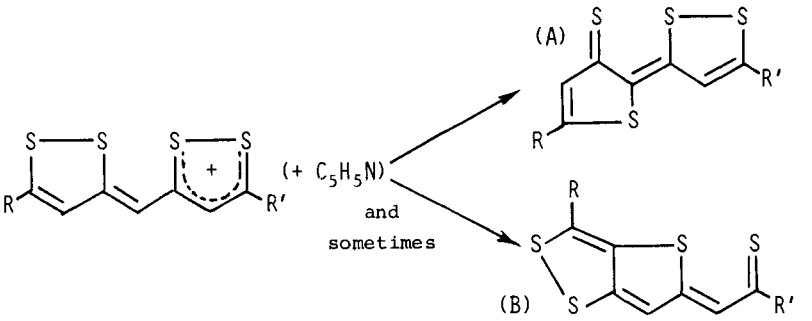


Figure 54.

11.2. 7-(1,2-Dithiol-3-ylidene)-4,5,6,7-tetrahydro-1,2-benzodithiole-3-thiones

In the presence of sodium hydride, methyl benzoate or pivalate reacted with the methyl group of 2-acetylcyclohexanone. The resulting β,δ-triketones were transformed by tetraphosphorus decasulfide into 4,5,6,7-tetrahydro-1,8,8aλ^4-trithiacyclopent[*a*]indenes (**A**, Fig. 55)[91]. In strongly basic medium, these compounds do not undergo the usual rearrangement of 2-alkyl-1,6,6aλ^4-trithiapentalenes, the six-carbon ring preventing the rotation necessary for this rearrangement (Section 10.4). For this reason it was possible, by reaction with carbon disulfide in strongly basic medium, to obtain a dianion for which structure **B** (Fig. 55) is one possible form[94,102,103].

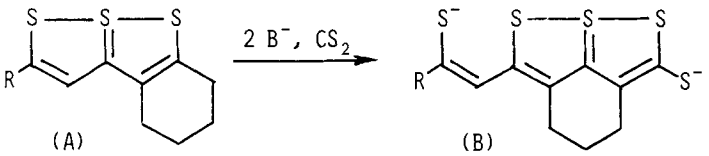
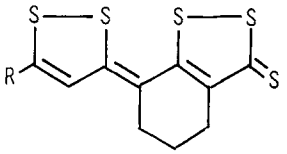


Figure 55.

By acidification of the above dianion, an unstable dimercaptan was formed which led, by air oxidation, to a 7-(1,2-dithiol-3-ylidene)-4,5,6,7-tetrahydro-1,2-benzodithiole-3-thione (Fig. 56)[94,103].



The structure given in Fig. 56 has been confirmed by an X-ray structure analysis carried out by J. Sletten in Bergen[104].

By preventing oxidation of the above dianion it has been possible to alkylate it and diverse (alkylthio)-trithiapentalenes were obtained. With methyl iodide, we obtained the bis-(methylthio) compound **A** (Fig. 57) while 1,2-dibromoethane gave a 1,3-dithiole derivative **B** (Fig. 57)[94,102,103].

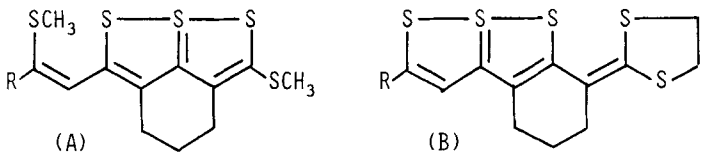


Figure 57.

Structure **A** and **B** (Fig. 57) have been confirmed by X-ray structure analysis[105].

11.3. 2,6-Bis(1,2-dithiol-3-ylidene)cyclohexanethiones

The objective of M. Stavaux was the preparation of such compounds using 7-(1,2-dithiol-3-ylidene)-4,5,6,7-tetrahydro-1,2-benzodithiole-3-thiones (**A**, Fig. 58) as starting material.

The first idea has been to condense these compounds with acetylenes because it was known that, in some cases, 1,2-dithiole-3-thiones, reacting with acetylenes, give 1,6,6aλ^4-trithiapentalenes. However, the expected result was not obtained, as only 7-(1,3-dithiol-2-ylidene)-1,8,8aλ^4-trithiacyclopent[*a*]indenes (**B**, Fig. 58) were formed[106,107,108].

Therefore, another trithiapentalene synthesis had to be used. It was the reaction of a diazoketone with compound **A** (Fig. 58). This gave an α-[7-(1,2-dithiol-3-ylidene)-4,5,6,7-tetrahydro-1,2-benzodithiol-3-ylidene] ketone (**C**, Fig. 58). The latter was finally

treated with tetraphosphorus decasulfide, leading to the expected 2,6-bis(1,2-dithiol-3-ylidene)cyclohexanethione (**D**, Fig. 58)[106,107,109]

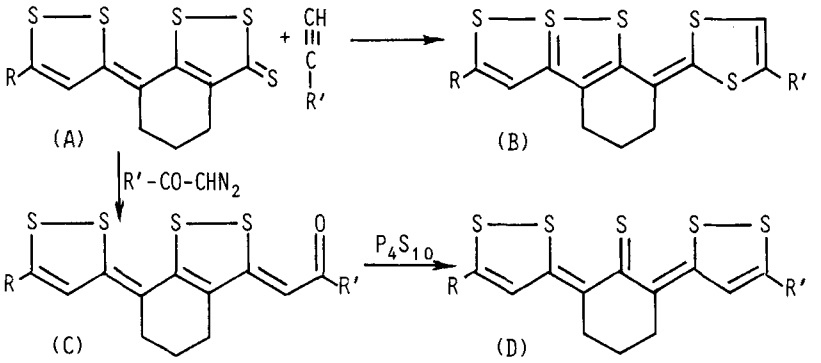


Figure 58.

X-Ray structure analysis has confirmed the formulae attributed in Fig. 58 to compounds **C**[110] and **D**[111,112].

12. PARTIAL BONDING IN THIOPYRAN DERIVATIVES

Following our studies on partial bonding in α-(1,2-dithiol-3-ylidene) ketones (**A**, Fig. 59) and in 1,6,6aλ^4-trithiapentalenes (**B**, Fig. 59), we expected to observe similar phenomena with α-(thiopyran-2-ylidene) ketones (**C**, Fig. 59) and with 1,7aλ^4-dithiaindenes (**D**, Fig. 59).

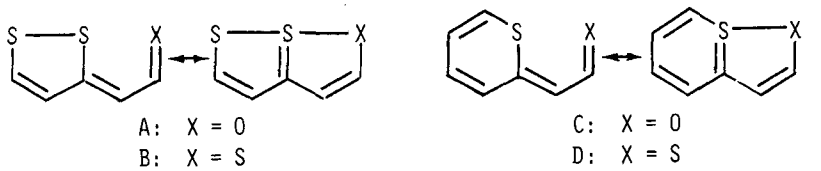


Figure 59.

The existence of an O-S interaction in compounds **C** has been established by comparing the infrared spectrum of a "normal" compound **C** with the spectrum of its ^{18}O isotopically modified analogue[113]; furthermore, chemical analogies were found between **A** and **C** and between **B** and **D** (Fig. 59).

12.1. α-(Thiopyran-2-ylidene) Carbonyl Compounds

Such compounds have been obtained by reaction of 2-(methylthio)-thiopyrylium cations with various ketones or esters: pentane-2,4-dione[113], indane-1,3-dione[113], cyanoacetophenone[113], ethyl cyanoacetate[113], ethyl acetylacetate[114], ethyl benzoylacetate[114], diethyl malonate[114]. This reaction failed with acetophenone but, as shown in Fig. 60, (4,6-diph-

enyl-thiopyran-2-ylidene)acetophenone has been obtained according to two other methods: reaction of 4,6-diphenylthiopyran-2-thione with diazoacetophenone or with phenacyl bromide[113].

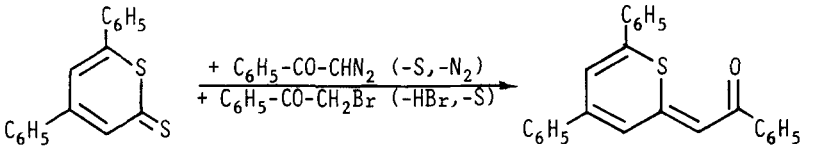


Figure 60.

Further study of these reactions showed that diverse by-products could be obtained, depending upon the substituents of the thiopyran-2-thione and upon the solvent used.

α-Bromo ketones yielded first 2-(acylmethylthio)-thiopyrylium cations (**A**, Fig. 61) which, in the presence of polar solvents (e.g. ethanol, *N*,*N*-dimethylformamide, pyridine, acetic acid), gave diverse compounds[115]. The major products, shown in Fig. 61, were: α-(thiopyran-2-ylidene) ketones (**B**), α,α′-dithiobis[α-(thiopyran-2-ylidene)] ketones (**C**), 2-(thiopyran-2-ylidenemethyl)thiopyrylium cations (**D**) and bis-(thiopyran-2-ylidenes) (**E**).

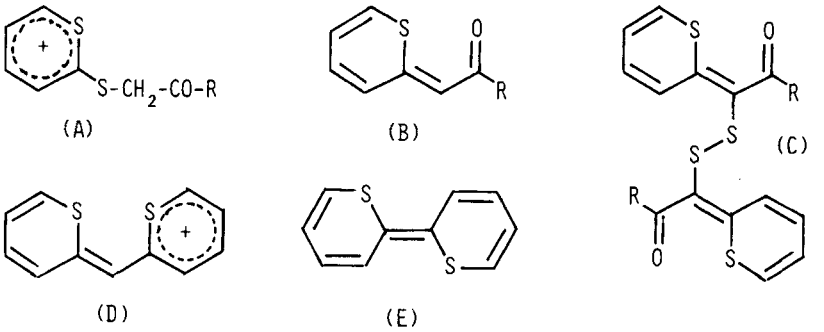


Figure 61.

Ethyl diazoacetate, reacting with 4,6-diarylthiopyran-2-thiones, gave mainly the diester disulfides shown in Fig. 62. This reaction involves a partial oxidation[116].

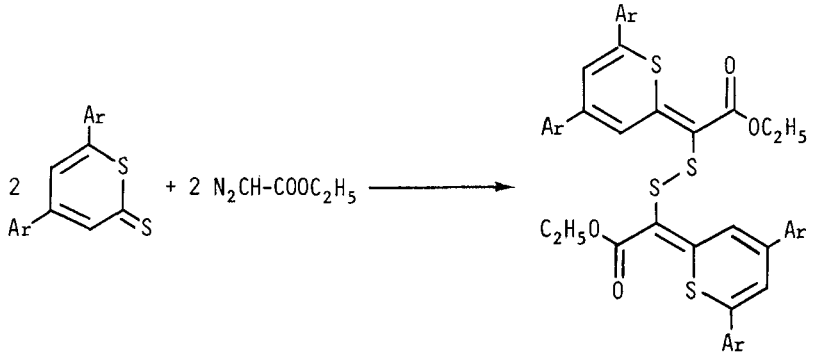


Figure 62.

With diverse thiopyran-2-thiones, diazoacetone gave various types of compounds[116]. The major products are indicated in Fig. 63.

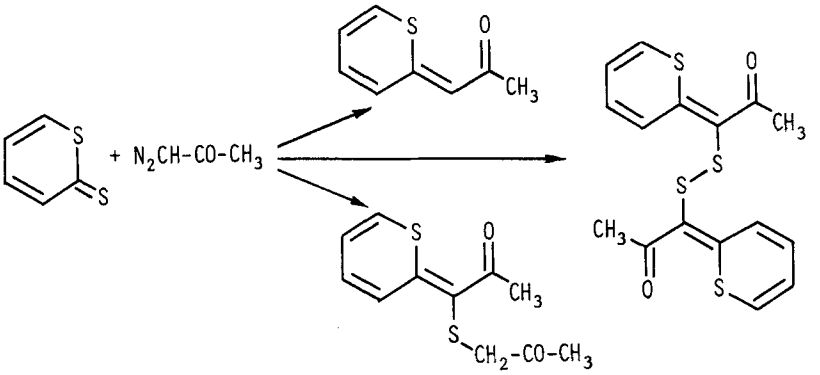


Figure 63.

Our first results[113] obtained with diazoacetophenones were confirmed: the reaction gave essentially α-(thiopyran-2-ylidene)acetophenones[116].

In α-(thiopyran-2-ylidene) ketones, the stable form has a Z configuration of the ylidene bond, as a result of the O-S partial bonding. By irradiation, this Z form is isomerized to the E configuration and the latter reverts to the initial Z form by a dark process[117].

For ethyl (4,6-diphenylthiopyran-2-ylidene)acylacetates, IR spectra indicate that the O-S interaction affects the keto carbonyl and not the ester carbonyl. In the case of ethyl (4,6-diphenylthiopyran-2-ylidene)-cyanoacetate, the interaction with sulfur affects, as expected, the ester carbonyl[114].

1,7aλ^4-Dithiaindenes, that is to say, α-(thiopyran-2-ylidene)thioketones, could be obtained by heating the corresponding carbonyl compound with tetraphosphorus decasulfide[113].

12.2. 2-(Thiopyran-2-ylidenemethyl)thiopyrylium Cations

We have undertaken the study of these cations in order to compare them with 3-(1,2-dithiol-3-ylidenemethyl)-1,2-dithiolylium cations (Section 11.1). We found that cations having the thiopyran structures are much stabler than those containing 1,2-dithiole rings. For instance, we did not observe rearrangement of 2-(thiopyran-2-ylidenemethyl)thiopyrylium cations by deprotonation in pyridine[118].

2-(Thiopyran-2-ylidenemethyl)thiopyrylium cations have been prepared by heating 2-(acylmethylthio)-thiopyrylium bromides in acetic acid or ethanol[115,118]. As indicated in Fig. 64, they have also been obtained by reaction of 2-(methylthio)-thiopyrylium iodides with malonic acid, in acetic acid with small quantities of pyridine[118].

In strong acids, cations **A** (Fig. 64) are protonated. The resulting dications exist in two conformations if, at position 3, the thiopyran rings are substituted[118].

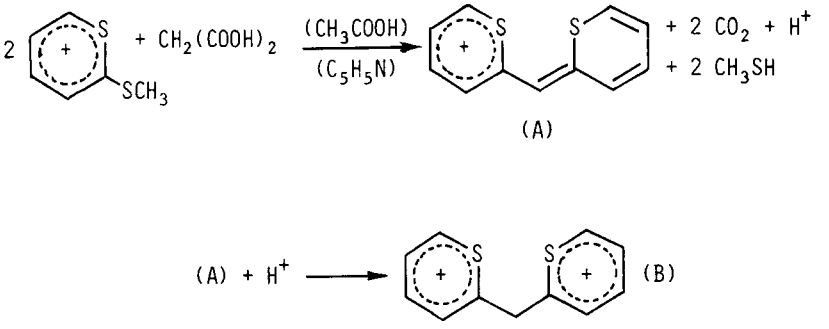


Figure 64.

12.3. 3-(Thiopyran-2-ylidenemethyl)-1,2-dithiolylium Cations

Having studied 3-(1,2-dithiol-3-ylidenemethyl)-1,2-dithiolylium cations and 2-(thiopyran-2-ylidenemethyl)thiopyrylium cations, it seemed interesting to examine similar cations containing both 1,2-dithiole and thiopyran rings.

2-(Methylthio)-thiopyrylium cations reacting, in boiling butan-1-ol, with 3-aryl-5-methyl-1,2-dithiolylium cations gave 3-aryl-5-(thiopyran-2-ylidenemethyl)-1,2-dithiolylium cations (**A**, Fig. 65) which can as well be considered as 2-(5-aryl-1,2-dithiol-3-ylidenemethyl)thiopyrylium cations (**B**, Fig. 65)[119].

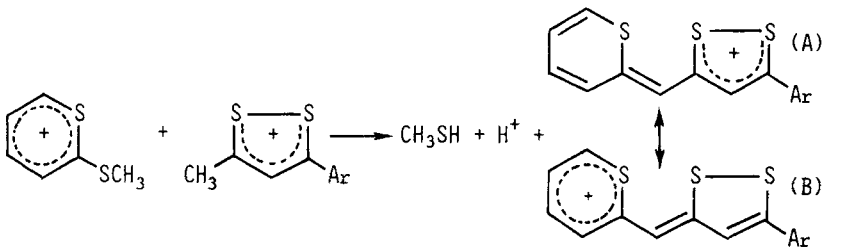


Figure 65.

The preceding cations, treated with triethylamine, gave products which could not be isolated. The reaction mixture was therefore directly treated with benzonitrile *N*-oxide and then we could isolate compounds **B** (Fig. 66). We deduced from this fact that the initial reaction product had structure **A** (Fig. 66)[119].

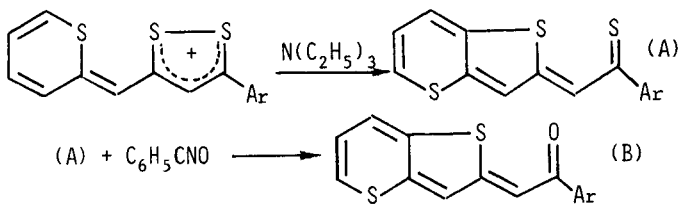


Figure 66.

The above rearrangement is analogous to the one we observed in a few cases with 3-(1,2-dithiol-3-ylidenemethyl)-1,2-dithiolylium cations and which led to the compounds **B** of Fig. 54 (Section 11.1).

13. 4*H*-3,1-BENZOTHIAZINE DERIVATIVES

13.1. 3,1-Benzothiazine-4-thiones

These compounds were obtained by heating tetraphosphorus decasulfide with 2-(acylamino)benzoic acids or esters[120]. They were found to be rather stable in acidic media but were attacked by bases such as aqueous sodium hydroxide. This led, after acidification, to 2-(acylamino)thiobenzoic acids. The latter, by heating, gave 3,1-benzoxazin-4-ones which, by reaction with tetraphosphorus decasulfide, gave back the initial 3,1-benzothiazine-4-thiones, as indicated in Fig. 67.

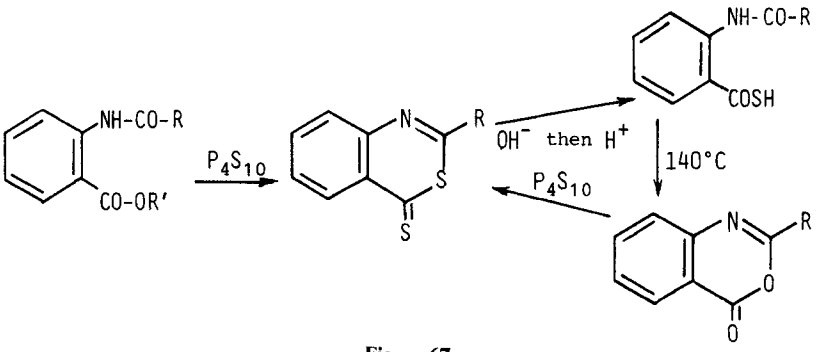


Figure 67.

Ammonia, reacting with 3,1-benzothiazine-4-thiones gave quinazoline-4-thiols, tautomers of 3*H*-quinazoline-4-thiones[121]. Similarly, aliphatic or aromatic primary amines gave us 3-alkyl(or aryl)-3*H*-quinazoline-4-thiones[122]. The likely intermediates, 2-(thioacylamino)-thiobenzamides, have not been found then but were later isolated, in particular cases, by W. Walter and J. Voss[123]. A further study showed us that, depending upon the steric characteristics of the amine reagent and of the 2-substituent of the benzothiazine, 4-imino-4*H*-3,1-benzothiazines could also be obtained (Fig. 68). The latter, treated with ethanol in acidic medium led to the corresponding 3*H*-quinazoline-4-thiones or to 2-(thioacylamino)-benzoates[124].

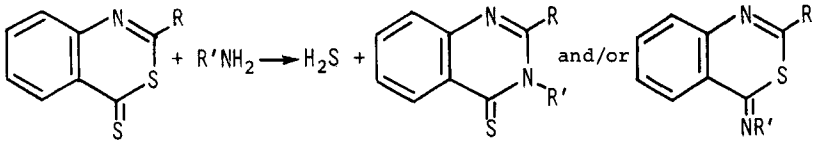
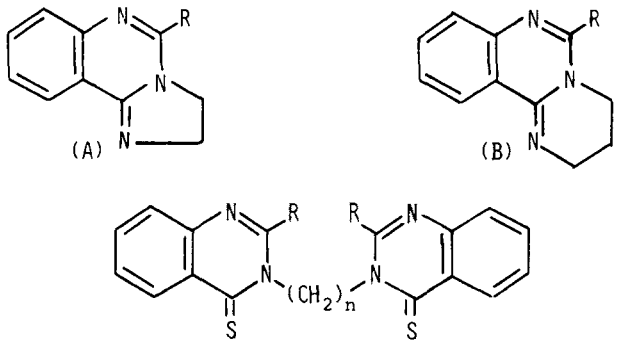


Figure 68.

The observation that both the endocyclic and exocyclic sulfur atoms of 1,3-benzothiazine-4-thiones could be replaced by an amine nitrogen suggested that diamines could lead to ortho-fused (at atoms 3–4) quinazoline systems. In fact, this was found in

the case of ethane-1,2-diamine and of propane-1,3-diamine which gave, respectively, 2,3-dihydroimidazo[1,2-*c*]quinazolines (**A**, Fig. 69) and 3,4-dihydro-2*H*-pyrimido[1,2-*c*]quinazolines (**B**, Fig. 69). 3,3′-Oligomethylenebis-(3*H*-quinazoline-4-thiones) were also obtained with ethane-1,2-diamine and propane-1,3-diamine. This type of compound (**C**, Fig. 69) was generally the only one obtained with α,ω-oligomethylenediamines with more than three methylene groups[125].



(C) n = 2,3,4 or 5

Figure 69.

In benzene, secondary aliphatic amines reacted with 3,1-benzothiazine-4-thiones, giving 2-thioacylamino-thiobenzamides[126,127] which gave back the initial benzothiazinethiones upon heating with acetic acid[127]. In ethanol, however, secondary aliphatic amines reacting with a 3,1-benzothiazine-4-thione, underwent partial dealkylation and 3-alkyl-3*H*-quinazoline-4-thiones were obtained[126].

Primary-secondary diamines NH_2-$(CH_2)_n$-NHR reacted with 3,1-benzothiazine-4-thiones, leading to 3-alkyl(or aryl)aminoalkyl-3*H*-quinazoline-4-thiones. A similar result was obtained with primary-tertiary diamines NH_2-$(CH_2)_n$-NR_2[128].

In the presence of triethylamine, amino acids such as glycine or alanine reacted with 3,1-benzothiazine-4-thiones giving (4-thioxo-4*H*-quinazolin-3-yl) carboxylic acids, as shown in Fig. 70. A similar reaction was observed with the corresponding amino esters[129].

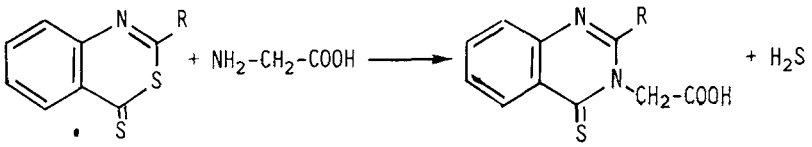


Figure 70.

3,1-Benzothiazine-4-thiones reacting with hydroxylamine gave 3-hydroxy-3*H*-quinazoline-4-thiones[121]. Hydrazine, phenylhydrazine and semicarbazide, by reaction with 3,1-benzothiazine-4-thiones, gave, respectively, 3-amino-, 3-phenylamino- and 3-ureido-3*H*-quinazoline-4-thiones[130] as shown in Fig. 71.

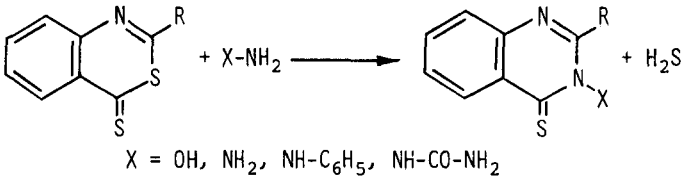


Figure 71.

Methyl or ethyl hydrazinecarboxylates, reacting with 3,1-benzothiazine-4-thiones gave variable amounts of alkyl (4-thioxo-4*H*-quinazolin-3-yl)- carbamates **A** and of alkyl 2-(3,1-benzothiazin-4-ylidene)hydrazinecarboxylates **B**, as shown in Fig. 72. It was found that the proportion of **A** and **B** depended upon th experimental conditions and upon the structure of the starting material, steric factors appearing important[131]. In the presence of triethylamine, triethylammonium 4-(2-alkoxycarbonylhydrazino)-4*H*-3,1-benzothiazine-4-thiolates (**C**, Fig. 72) could be isolated which, upon heating, gave the corresponding carbamates **A** in most cases and rarely **B**[131].

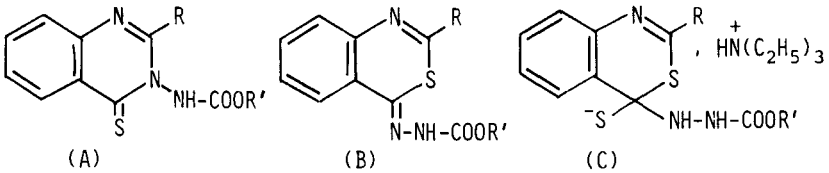


Figure 72.

Reaction of diazomethane with two moles of 2-aryl-3,1-benzothiazine-4-thione brought to light some interesting stereochemistry. As shown in Fig. 73, this reaction led to stereochemical isomers of 2,2″-diaryldispiro[3,1-benzothiazine-4:4′-(1,3-dithiolane)-5′:4″-(3,1-benzothiazine)]: the *cis* (achiral) isomer **A** and the *trans* (racemic) isomer **B** which were separated by chromatography on alumina[132,133]. As also shown in Fig. 73, both isomers could be stereospecifically desulfurized on Raney nickel, the *cis*-dispirane **A** leading to a *cis*-bis(3,1-benzothiazin-4-ylidene) **C**, while the *trans*-dispirane **B** led to the corresponding *trans* compound **D**[132,134].

One mole of a 2-aryl-3,1-benzothiazine-4-thione reacting with one mole of diazoacetophenone gave a (2-aryl-3,1-benzothiazin-4-ylidene)acetophenone in which some O-S partial bonding was shown to exist[135].

As already said in Section 2.2, we had shown that, in mildly basic medium, aromatic aldehydes reacted with 5-methyl-1,2-dithiole-3-thiones, giving 5-styryl-1,2-dithiole-3-thiones[21]. We expected a similar reaction for 2-methyl-3,1-benzothiazine-4-thiones and found that aromatic aldehydes could transform the 2-methyl substituent into a 2-styryl which had the E configuration[136].

13.2. 3,1-Benzothiazin-4-ones

These compounds have been obtained in various ways, such as by cyclization of 2-(acylamino)-thiobenzoic acids (see Section 13.1) or by oxidation of 3,1-benzothiazine-

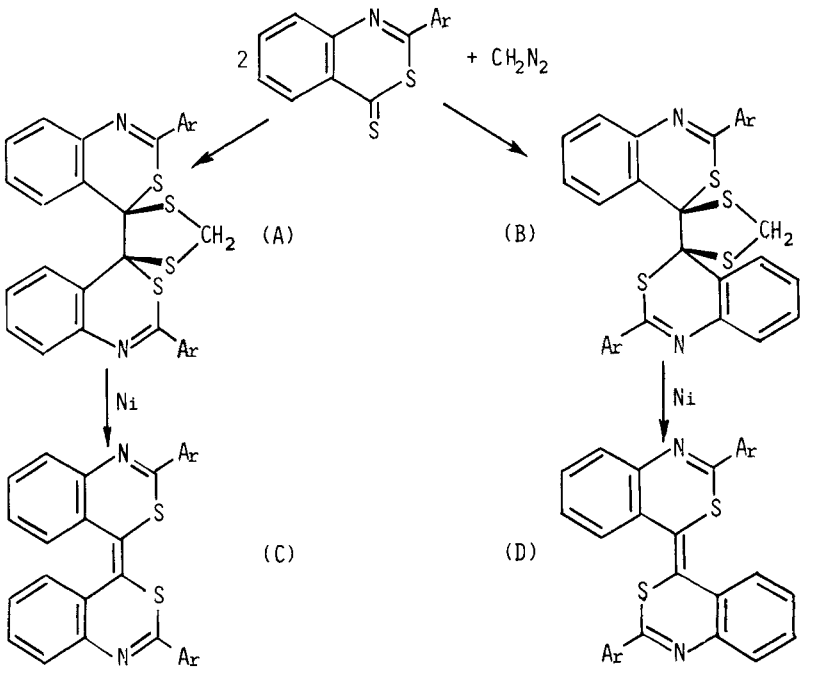


Figure 73.

4-thiones, either with potassium permanganate in acetone or with mercuric acetate in acetic acid[120].

With primary amines, 3,1-benzothiazin-4-ones often gave directly a 3*H*-quinazolin-4-one but sometimes the intermediate 2-(thioacylamino)-benzamide could be obtained and, as shown in Fig. 74, was cyclized into a 3*H*-quinazolin-4-one by heating[122].

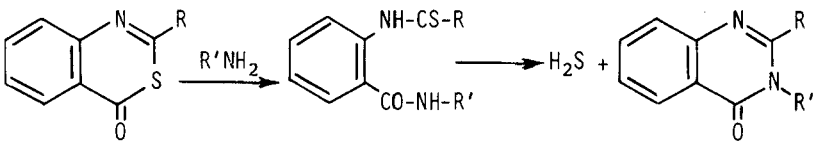


Figure 74.

Ammonia reacted differently. An addition product was formed which, upon heating, regenerated the initial 3,1-benzothiazin-4-one by loss of ammonia[121].

Ethane-1,2-diamine reacting with a 3,1-benzothiazin-4-one gave a 3,3′-ethylenebis-(3*H*-quinazolin-4-one) and/or a 3-(2-aminoethyl)-3*H*-quinazolin-4-one[128].

In benzene, secondary aliphatic amines reacted with 3,1-benzothiazin-4-ones yielding 2-(thioacylamino)-benzamides. If this reaction was effected in methanol or ethanol, a methyl(or ethyl) 2-(thioacylamino)-benzoate was also obtained[127]. With diverse amino acids (glycine, alanine, methionine, tryptophan), in the presence of triethylamine, 3,1-benzothiazin-4-ones gave (4-oxo-4*H*-quinazolin-3-yl) carboxylic acids whose anti-inflammatory activity has been tested[129].

Hydroxylamine[121], hydrazine[130], phenylhydrazine[130] and semicarbazide[130] reacting with 3,1-benzothiazin-4-ones gave, respectively, 3-hydroxy-, 3-amino-, 3-phenylamino- and 3-ureido-3*H*-quinazolin-4-ones. Alkyl hydrazinecarboxylates with 2-alkyl(or aryl)-3,1-benzothiazin-4-ones yielded (4-oxo-4*H*-quinazolin-3-yl)carbamates which could also be obtained by oxidation of the corresponding thiocarbamates with potassium permanganate or benzonitrile N-oxide[131].

13.3. 3H-Quinazoline-4-thiones and 3H-Quinazolin-4-ones

A number of these compounds have been obtained as indicated in Sections 13.1 and 13.2, so the present section mainly concerns their chemical properties.

3*H*-Quinazolin-4-ones reacting with tetraphosphorus decasulfide gave the corresponding thiones[121]. 3-Hydroxy-3*H*-quinazoline-4-thiones were reduced by red phosphorus and iodine, giving the corresponding 3*H*-quinazoline-4-thiones. In the same way, 3-hydroxy-3*H*-quinazolin-4-ones were reduced to 3*H*-quinazolin-4-ones[121].

We observed that 3-[2-(*N*-alkylamino)ethyl]-3*H*-quinazoline-4-thiones were readily hydrolysed to the corresponding quinazolinones in neutral medium while 3-[2-(*N*-arylamino)ethyl]-3*H*-quinazoline-4-thiones, under the same conditions, were stable. As shown in Fig. 75, we have explained this different behaviour by the formation of an intermediary cyclic isomer of the quinazolinethione which is formed only if the amino group is basic enough for attack on the thione group[128].

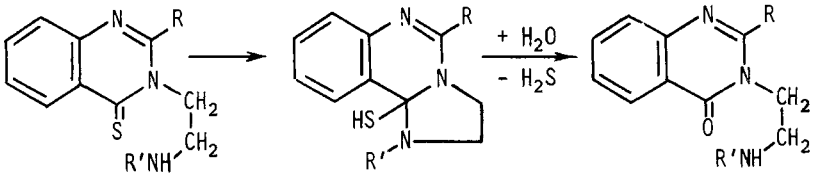


Figure 75.

Quinazoline-4-thiols, tautomers of 3*H*-quinazoline-4-thiones, which were obtained by reaction of ammonia with 3,1-benzothiazine-4-thiones, have been *S*-alkylated in basic medium with methyl iodide or ethyl bromide.

The 4-(alklthio)-quinazolines thus obtained, when treated with a sodium alkoxide, led to 4-(alkoxy)-quinazolines[137].

Reacting with hydrazine, alkyl (2-aryl-4-thioxo-4*H*-quinazolin-3-yl)-acetates yielded 6-aryl-2*H*,4*H*-[1,2,4-triazino][4-3-*c*]quinazolin-3-ones[138]. This ring formation is shown in Fig. 76.

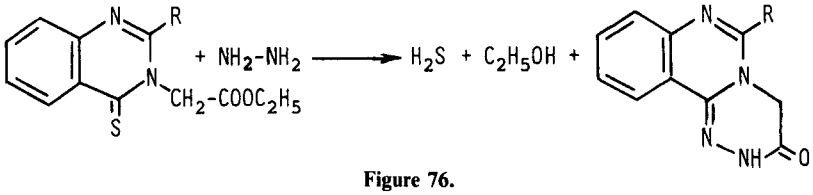


Figure 76.

Apart from the above-mentioned derivatives of 3*H*-quinazoline-4-thione, we have also obtained some derivatives of 1*H*-quinazoline-4-thione by thermolysis of 1-aryl-4-hydroxyimino-1,4-dihydro-2*H*-3,1-benzothiazines[139]. These compounds are considered in Section 14.5.

14. 1,4-DIHYDRO-2*H*-3,1-BENZOTHIAZINE DERIVATIVES

14.1. 1,2-Dihydro-3,1-benzothiazine-4-thiones

Tetraphosphorus decasulfide reacting with 1,2-dihydro-3,1-benzoxazin-4-ones gave us mainly 1,2-dihydro-3,1-benzothiazine-4-thiones, sometimes with smaller amounts of 1,2-dihydro-3,1-benzoxazine-4-thiones[140].

As shown in Fig. 77, we found that a primary aliphatic amine reacts with a 1-alkyl(or aryl)-1,2-dihydro-3,1-benzothiazine-4-thione giving, in variable proportions, a 1-alkyl(or aryl)-4-alkylimino-1,4-dihydro-2*H*-3,1-benzothiazine (**A**) and a 2-[*N*-alkyl(or aryl)amino]-*N*-alkyl-thiobenzamide (**B**). 2-(*N*-Arylamino)-*N*-alkyl-thiobenzamides and methanal gave variable amounts of **A** and of 3-alkyl-1-aryl-2,3-dihydro-1*H*-quinazoline-4-thione (**C**). Under similar conditions, 2-(*N*-alkylamino)-*N*-alkyl-thiobenzamides gave only compounds of type **C**[141].

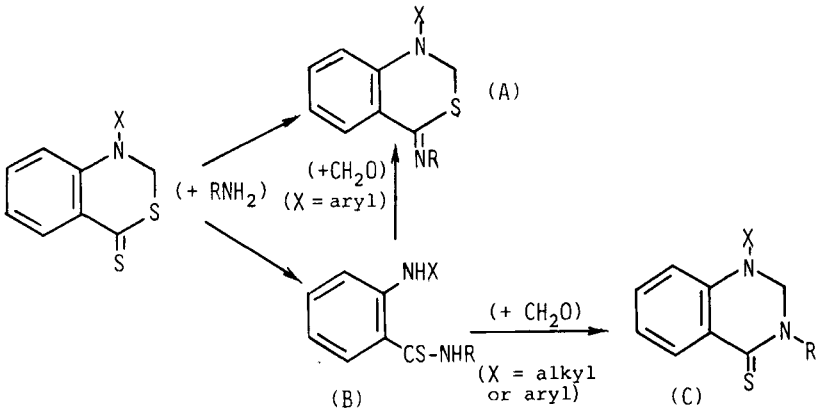


Figure 77.

Secondary aliphatic amines, reacting with 1-alkyl(or aryl)-1,2-dihydro-3,1-benzothiazine-4-thiones gave 2-[*N*-alkyl(or aryl)amino]-*N*,*N*-dialkyl-thiobenzamides which could be transformed into 2-[*N*-alkyl(or aryl)amino]-*N*,*N*-dialkyl-*S*-methyl-thiobenzamidinium iodides by reaction with methyl iodide[141].

As indicated in Fig. 78, primary aromatic amines, heated at 200 °C with 1-alkyl-1,2-dihydro-3,1-benzothiazine-4-thiones, gave 1-alkyl-3-aryl-2,3-dihydro-1*H*-quinazoline-4-thiones, sometimes with some 1-alkyl-3-aryl-1*H*,3*H*-quinazoline-2,4-dithiones. Under the same conditions, 1-aryl-1,2-dihydro-3,1-benzothiazine-4-thiones led to 2-(*N*-arylamino)-thiobenzanilides, in rare cases accompanied by 1,3-diaryl-1*H*,3*H*-quinazoline-2,4-dithiones[142].

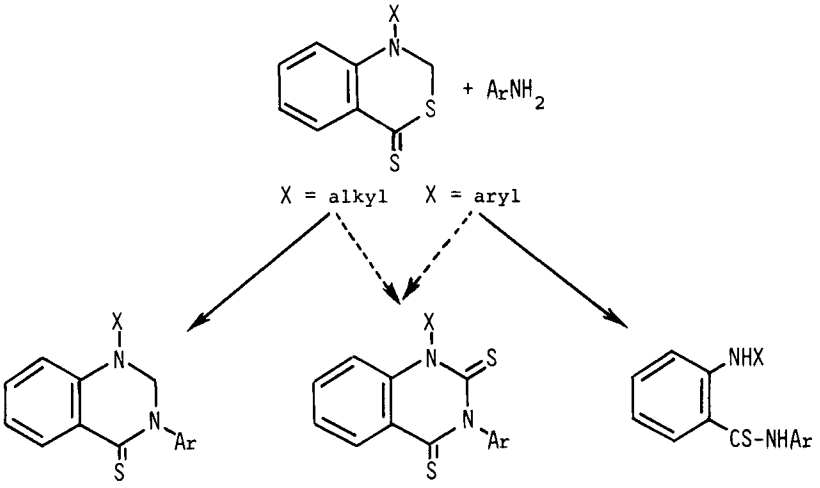


Figure 78.

In the above reactions, the formation of 1*H*,3*H*-quinazoline-2,4-dithiones is somewhat surprising and the sulfuration agent has not been identified. The only thing which could be said was that it acts like elemental sulfur which is able to transform into a thiocarbonyl the methylene group in 2,3-dihydro-1*H*-quinazoline-4-thiones[141].

Ethane-1,2-diamine with 1-alkyl(or aryl)-1,2-dihydro-3,1-benzothiazine-4-thiones in all cases gave 2-[2-(*N*-alkyl(or aryl)amino)-phenyl]-4,5-dihydro-1*H*-imidazoles (**A**, Fig. 79), sometimes accompanied by other products. If the substituent at position 1 in the starting material was alkyl, a 2,2′-bis(*N*-alkylamino)-*N*,*N*′-ethylemebis(thiobenzamide) (**B**, Fig. 79) could sometimes be obtained. On the other hand, if the substituent at position 1 in the starting material was aryl, 1,1′-diaryl-1,1′,2,2′-tetrahydro-4,4′-ethylenedinitrilobis(4*H*-3,1-benzothiazines) (**C**, Fig. 79) or 6-aryl-2,3,5,6-tetrahydroimidazo[1,2-*c*]quinazolines (**D**, Fig. 79) were in some cases obtained[143].

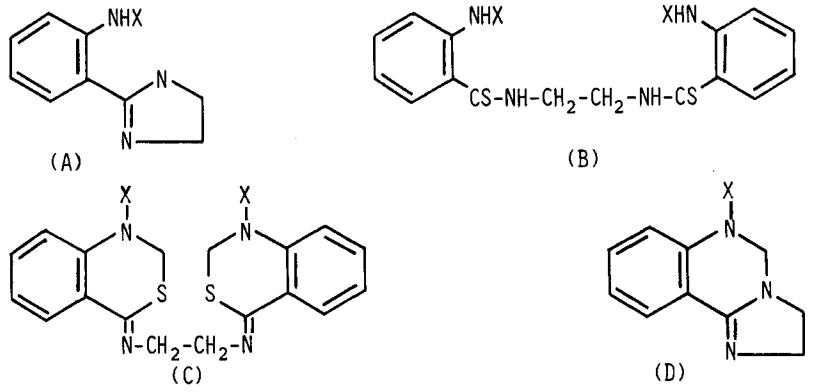
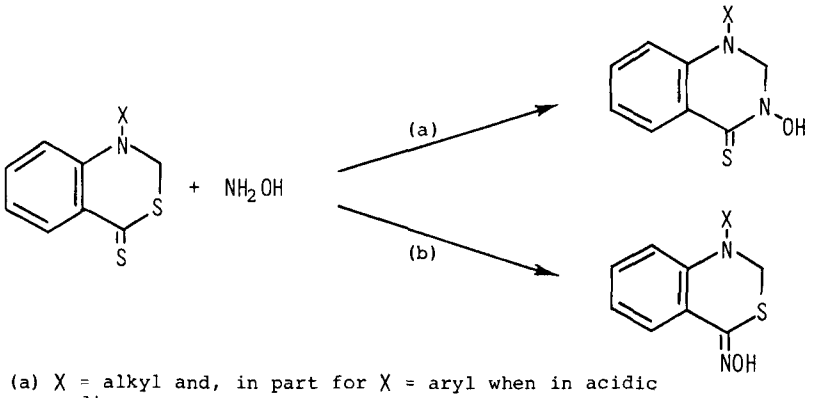


Figure 79.

Propane-1,3-diamine and 1,2-dihydro-3,1-benzothiazine-4-thiones generally gave 2-(2-aminophenyl)-1,4,5,6-tetrahydropyrimidines. If the dihydrobenzothiazinethione had an alkyl substituent at position 1, a 2,2′-bis(*N*-alkylamino)-*N*,*N*′-trimethylenebis(thiobenzamide) was also obtained[144]. Diamines NH_2-$(CH_2)_n$-NHH_2, with n > 3, reacted with 1-aryl-1,2-dihydro-3,1-benzothiazine-4-thiones leading to 1,1′-diaryl-1,1′,2,2′-tetrahydro-4,4′-oligomethylenedinitrilobis(4*H*-3,1-benzothiazines)[144].

As indicated in Fig. 80, hydroxylamine and 1-alkyl-1,2-dihydro3,1-benzothiazine-4-thiones gave 1-alkyl-3-hydroxy-2,-3-dihydro-1*H*-quinazoline-4-thiones. If the starting material had a 1-aryl substituent, hydroxylamine, in neutral medium, gave 1-aryl-4-hydroxyimino-1,4-dihydro-2*H*-3,1-benzothiazines, but, in acidic medium, while the preceding compounds were also obtained, they were generally accompanied by 1-aryl-3-hydroxy-2,3-dihydro-1*H*-quinazoline-4-thiones[139].



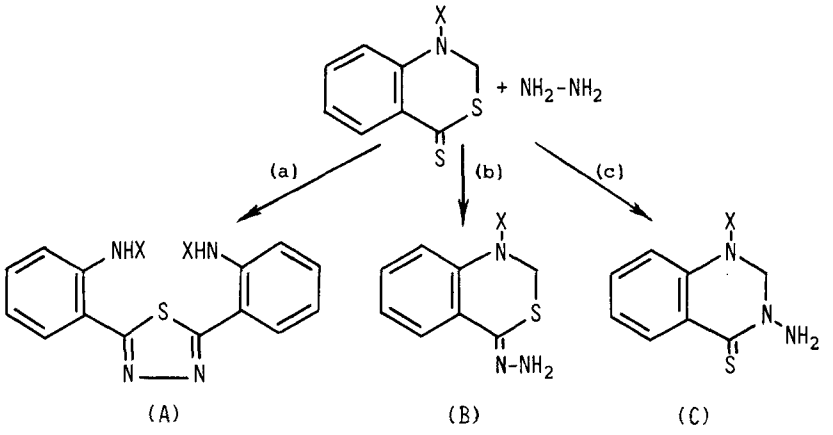
(a) X = alkyl and, in part for X = aryl when in acidic medium.
(b) X = aryl in neutral medium or, in part, in acidic medium.

Figure 80.

As shown in Fig. 81, reaction with hydrazine also depends upon the substituent at position 1 in the 1,2-dihydro-3,1-benzothiazine-4-thiones. With 1-alkyl or 1-aryl substituents, small quantities of a 1,3,4-thiadiazole derivative (**A**) were often found. However, with a 1-alkyl substituent, a good yield of 1-alkyl-3-amino-2,3-dihydro-1*H*-quinazoline-4-thione (**C**) was obtained while, with a 1-aryl substituent, the main product was a 1-aryl-4-hydrazono-1,4-dihydro-2*H*-3,1-benzothiazine (**B**). Thermal isomerization of the latter gave mainly a 1-aryl-3-amino-2,3-dihydro-1*H*-quinazoline-4-thione (**C**)[145].

Methylhydrazine and 1,1-dimethylhydrazine gave similar results. With 1-alkyl-1,2-dihydro-3,1-benzothiazine-4-thiones, 1-alkyl-3-(*N*-methyl(or *N*,*N*-dimethyl)-amino)-2,3-dihydro-1*H*-quinazoline-4-thiones were obtained while 1-aryl-1,2-dihydro-3,1-benzothiazine-4-thiones led to the corresponding hydrazones. The latter, by thermal isomerization, yielded 1-aryl-3-(*N*-methyl(or *N*,*N*-dimethyl)amino)-2,3-dihydro-1*H*-quinazoline-4-thiones[146]. However, heating of the above dimethylhydrazones, and in some cases of the methylhydrazones, led also to a cleavage of the N-N bond, leading to 1-aryl-2,3-dihydro-1*H*-quinazoline-4-thiones unsubstituted in position 3 (Fig. 82)[146].

Phenylhydrazine and 1-alkyl-1,2-dihydro-3,1-benzothiazine-4-thiones gave 1-alkyl-3-phenylamino-2,3-dihydro-1*H*-quinazoline-4-thiones but when there was an aryl instead



(a) X = alkyl or aryl; (b) X = aryl; (c) X = alkyl

Figure 81.

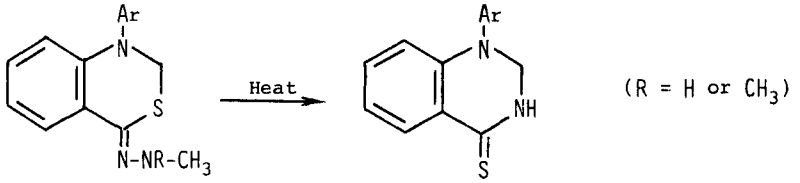


Figure 82.

of an alkyl at position 1, 1-aryl-4-phenylhydrazono-1,4-dihydro-2*H*-3,1-benzothiazines (**A**, Fig. 83) were obtained. The latter, as shown in Fig. 83, heated at 200 °C, gave, in variable proportions, 1-aryl-3-phenylamino-2,3-dihydro-1*H*-quinazoline-4-thiones (**B**, Fig. 83) and 1-aryl-2-phenylimino-1,3-dihydrobenzo[*c*]isothiazoles (**C**, Fig. 83)[147].

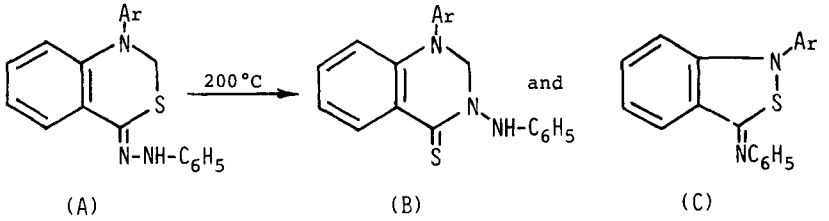


Figure 83.

As indicated in Fig. 84, alkyl hydrazinecarboxylates reacted with 1-alkyl(or aryl)-1,2-dihydro-3,1-benzothiazine-4-thiones giving alkyl (1-alkyl(or aryl)-4-thioxo-2,3-dihydro-1*H*-quinazolin-3-yl)carbamates (**A**).

Compounds **A** having a 1-aryl substituent, reacting with hydrazine, gave 7-aryl-6,7-dihydro-2*H*,4*H*-[1,2,4,5-tetrazino][2,3-*c*]quinazolin-3-ones (**B**)[138].

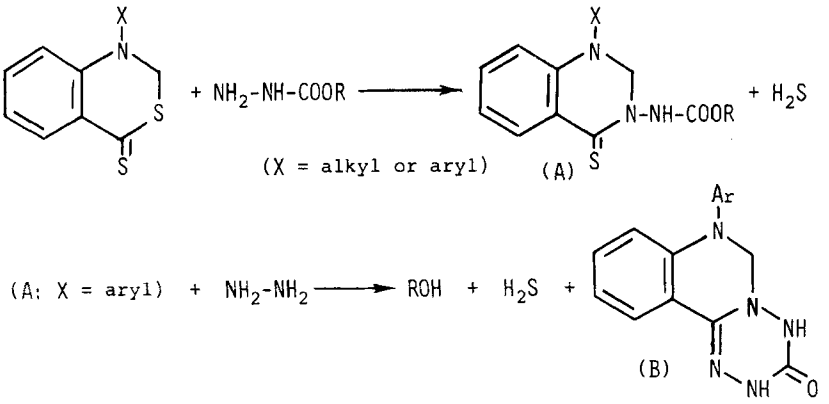


Figure 84.

In their reaction with 1-aryl-1,2-dihydro-3,1-benzothiazine-4-thiones, alkyl hydrazinecarboxylates differed from many nucleophiles X-NH_2 which generally led to derivatives of 1-aryl-1,2-dihydro-3,1-benzothiazin-4-imines. We thought that this difference came from a participation of the ester carbonyl in the condensation and we tested this hypothesis with diverse hydrazides. These reactions confirmed our surmise, as 3-acylamino-2,3-dihydro-1*H*-quinazoline-4-thiones were obtained, together with 2-(2-amino-phenyl)-1,3,4-thiadiazoles[148].

In Section 13.1, the results obtained in the reaction of diazomethane with 3,1-benzothiazine-4-thiones have been described. They led us to study the analogous reaction of 1,2-dihydro-3,1-benzothiazine-4-thiones. Two moles of 1-aryl-1,2-dihydro-3,1-benzothiazine-4-thione, reacting with one mole of diazomethane gave a mixture of *cis* (achiral) and *trans* (racemic) isomers of 1,1″-diaryl-1,1″,2,2″-tetrahydrodispiro[3,1-benzothiazine-4:4′-(1,3-dithiolane)-5′:4″-(3,1-benzothiazine)]. These isomers have been separated by chromatography and identified by NMR[149].

14.2. 1,2-Dihydro-3,1-benzothiazin-4-ones

These compounds have been obtained by potassium permanganate oxidation, in acetone, of the corresponding thiones[140].

Reaction of nucleophiles X-NH_2 with 1,2-dihydro-3,1-benzothiazin-4-ones proved to be quite different from what the same reagents gave with the corresponding thiones. No quinazoline derivative was found in appreciable amounts and generally opening of the heterocycle was observed, with formation of substituted benzamides. Thus, as indicated in Fig. 85, aliphatic or aromatic primary amines gave 2-arylamino-*N*-alkyl(or aryl)-benzamides[150].

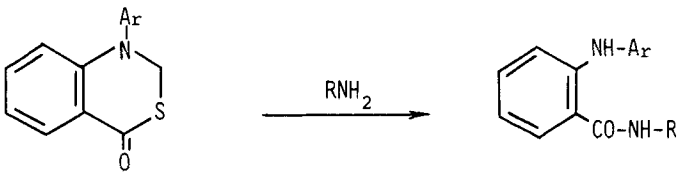


Figure 85.

1-Aryl-1,2-dihydro-3,1-benzothiazin-4-ones, reacting in ethanol with dimethylamine, pyrrolidine or piperidine led, respectively, to: (a) ethyl 2-(*N*-arylamino)-benzoate; (b) 2-(*N*-arylamino-*N*,*N*-tetramethylenebenzamide; (c) ethyl 2-(*N*-arylamino)benzoate with 2-(*N*-arylamino)-*N*,*N*-pentamethylenebenzamide[150]. Formation of an ester in the presence of a secondary aliphatic amine had also been observed with 3,1-benzothiazin-4-ones, as indicated in Section 13.2.

1-Alkyl(or aryl)-1,2-dihydro-3,1-benzothiazin-4-ones with hydrazine gave 2-[*N*-alkyl(or aryl)amino]-benzohydrazides[145].

14.3 2,3-Dihydro-1H-quinzaoline-4-thiones

In Section 14.1, various preparations of 2,3-dihydro-1*H*-quinazoline-4-thiones from 1,2-dihydro-3,1-benzothiazin-4-thiones have been described, but other methods have also been explored. For instance, as shown in Fig. 86, these compounds have been obtained by reaction of methanal with 2-(*N*-alkyl(or aryl)amino)-thiobenzamides or by heating, at 200 °C, with traces of hydrogen chloride, a 2-(alkylimino)-1,4-dihydro-2*H*-3,1-benzothiazine[141].

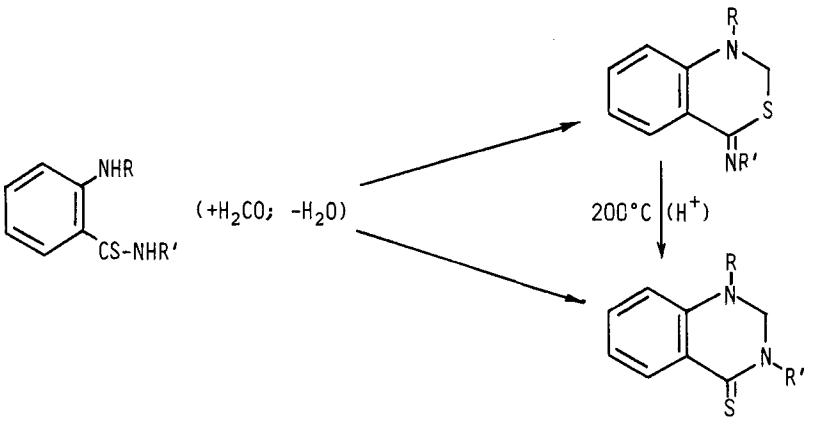


Figure 86.

Generally, in boiling xylene, tetraphosphorus decasulfide reacted with 1,3-diaryl-2,3-dihydro-1*H*-quinazolin-4-ones giving the corresponding thiones. In some cases, a thioamide was obtained by opening of the heterocycle or else a 1-aryl-4-(arylimino)-1,4-dihydro-2*H*-3,1-benzothiazine is formed[151].

By reaction of sulfur, the methylene group of 2,3-dihydro-1*H*-quinazoline-4-thiones is transformed into a thiocarbonyl[141,148] and the same reaction was observed with 1,3-diaryl-2,3-dihydro-1*H*-quinazoline-4-ones[151].

A surprising fact has been observed with two 1,3-dialkyl-2,3-dihydro-1*H*-quinazoline-4-thiones: potassium permanganate in acetone could oxidize the methylene group in position 2 without touching the thione group[141].

For diverse 2,3-dihydro-1*H*-quinazoline-4-thiones, oxidation of the thiocarbonyl to a carbonyl has been carried out with benzonitrile *N*-oxide[138,146,148].

2,3-Dihydro-1*H*-quinazoline-4-thiones, as well as their 3-(*N*-methylamino)-and 3-

(*N*,*N*-dimethylamino) derivatives have been attacked by methyl iodide. When unsubstituted in position 3, the resulting methylthio compound could be deprotonated, giving a 4-(methylthio)-1,2-dihydroquinazoline[146]. On the other hand, as indicated in Fig. 87, 3-(*N*,*N*-dimethylamino)-4-(methylthio)-1,2-dihydroquinazolin-3-ium cations reacted with methylamine, giving the corresponding 4-(methylimino) derivative[146].

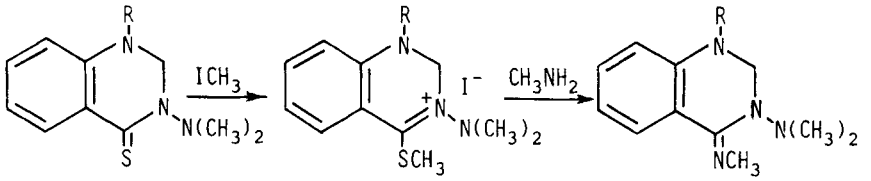


Figure 87.

As shown in Fig. 88, 6,7-dihydro-2*H*,4*H*-[1,2,4,5-tetrazino][2,3-*c*]-quinazolin-3-ones have been obtained by reaction of hydrazine with alkyl (4-thioxo-1,4-dihydro-2*H*-quinazolin-3-yl)carbamates[138].

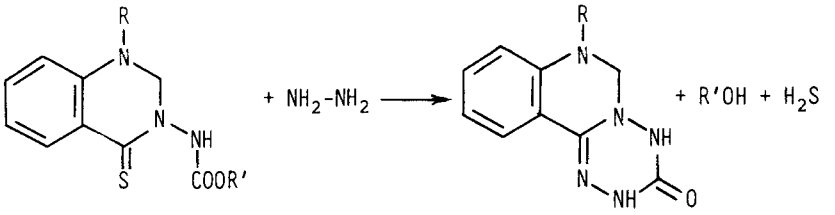


Figure 88.

14.4 Derivatives of 3,4-Dihydro-1H-quinazoline-2-thiones

The compounds concerned here are derived from 3,4-dihydro-1*H*-quinazoline-2-thiones by joining a fused five- or six-membered ring to atoms 3 and 4 of the quinazolinethione.

As shown in Fig. 89, 2,6-dihydro-3*H*-imidazo[1,2-*c*]quinazoline-5-thiones have been obtained either by reaction of carbon disulfide, in basic medium, with a 2-[2-(*N*-arylamino)phenyl]-4,5-dihydro-1*H*-imidazole (**A**) or by reaction of sulfur with a 6-aryl-2,3,5,6-tetrahydro-imidazo[1,2-*c*]quinazoline (**B**)[143].

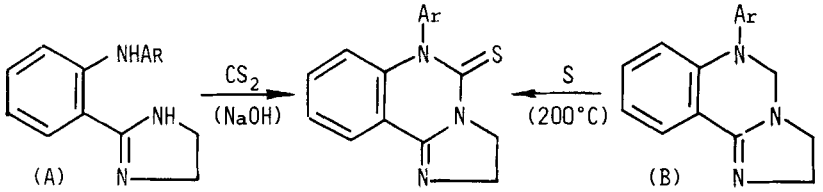


Figure 89.

Carbon disulfide condensation has also been applied to 2-[(*N*-alkyl(or aryl)amino)phenyl]-1,4,5,6-tetrahydropyrimidines, leading to 7-alkyl(or aryl)-2,3,4,7-tetrahydropyrimido[1,2-*c*]quinazoline-6-thiones[144].

14.5. 1H-Quinazoline-4-thiones

While 2,3-dihydro-1*H*-quinazoline-4-thiones were usually obtained by reaction of nitrogen nucleophiles with 1,2-dihydro-3,1-benzothiazine-4-thiones, we have obtained 1*H*-quinazoline-4-thiones by thermolysis of the compounds formed in the reaction of hydroxylamine with 1,2-dihydro-3,1-benzothiazine-4-thiones. For instance, by heating, 3-hydroxy-1-methyl-2,3-dihydro-1*H*-quinazoline-4-thione has been dehydrated to 1-methyl-1*H*-quinazoline-4-thione[139]. As indicated in Fig. 90, thermolysis of 1-aryl-3-hydroxy-2,3-dihydro-1*H*-quinazoline-4-thiones gave more complicated results. These compounds, as well as their isomers, the 1-aryl-4-(hydroxyimino)-1,4-dihydro-2*H*-3,1-benzothiazines, gave not only 1-aryl-1*H*-quinazoline-4-thiones (**A**), but also 1-aryl-1*H*-quinazolin-1-ones (**B**) and 1-aryl-2,3-dihydro-1*H*-quinazoline-4-thiones (**C**)[139].

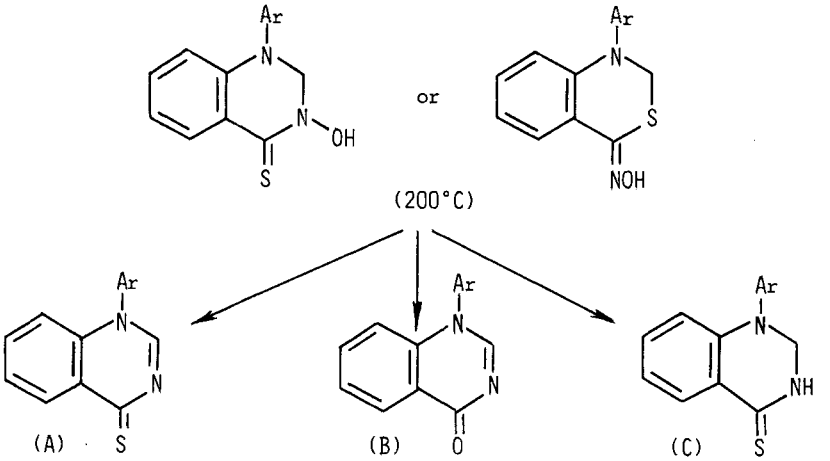


Figure 90.

1-Aryl-1*H*-quinazoline-4-thiones and methyl iodide gave 4-(methylthio)-quinazolin-1-ium iodides which were hydrolyzed in moderately basic medium to 1-aryl-1*H*-quinazolin-4-ones. The latter have been also obtained by reaction of benzonitrile *N*-oxide with the corresponding thiones[139].

1-Aryl-1*H*-quinazoline-4-thiones reacted easily with alkylamines, hydroxylamine or hydrazine giving imines, oximes or hydrazones, respectively[139].

15. 1,2-DIHYDRO-3,1,2λ^5-BENZOTHIAZAPHOSPHININE-2,4-DITHIONES

Various patents having described lubricating additives obtained by reaction of tetraphosphorus decasulfide with diverse secondary amines, we wished to know what this reaction would give with 2-[*N*-alkyl(or aryl)amino]-benzoic acids or esters.

In the case of the acids we obtained 2,1-benzisothiazole-3-thiones and 3,3′-bi(1*H*-2,1-benzisothiazol-3-ylidenes)[152]. More interesting results were obtained with alkyl 2-(*N*-arylamino)-benzoates[153]. As shown in Fig. 91, 1-aryl-2,1-benzisothiazole-3-thiones (**A**) were again obtained, but they were accompanied by a novel type of compound, 1-aryl-2-alkoxy-1,2-dihydro-3,1,2λ^5-benzothiazaphosphinine-2,4-dithiones (**B**).

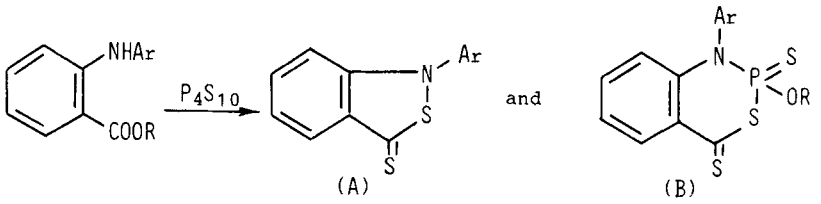


Figure 91.

We found that these compounds **B** are stable in acid or neutral medium, but fragile in basic medium. Their oxidation with potassium permanganate removed only the thiocarbonyl sulfur and 1-aryl-2-(alkoxy)-2-thioxo-1,2-dihydro-3,1,2λ^5-benzothiazaphosphinin-4-ones were obtained[153].

Dithiones (**B**) are easily handled and proved to be practical intermediates for the preparation of 2-(*N*-arylamino)-thiobenzamides and related compounds. They reacted with primary and secondary aliphatic amines in alcoholic medium, yielding 2-(*N*-arylamino)-thiobenzamides and alkylammonium *O*,*O*-dialkyl dithiophosphates[154].

With ethane-1,2-diamine, dithiones **B** gave 2,2′-bis(*N*-arylamino)-*N*,*N*′-ethylenebis (thiobenzamides) and 2-[2-(*N*-arylamino)phenyl]-4,5-dihydro-1*H*-imidazoles. Similarly, propane-1,3-diamine gave 2,2′-bis(*N*-arylamino)-*N*,*N*′-trimethylenebis-(thiobenzamides) and 2-[(*N*-arylamino)phenyl]-1,2,4,6-tetrahydropyrimidines[154]. In the same way, 2-aminoethanol led to thiobenzamides, often with 2-[2-(*N*-arylamino)-pheny]-4,5-dihydrooxazoles. As shown in Fig. 92, 2-aminoethanethiol gave, with good yields, 2-[2-(*N*-arylamino)phenyl]-4,5-dihydrothiazoles[154].

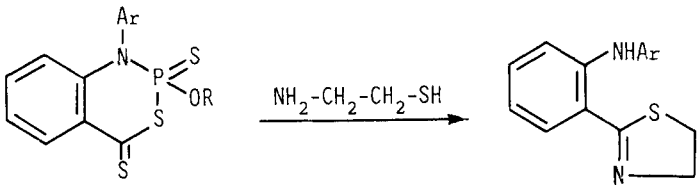


Figure 92.

16. OTHER SUBJECTS

16.1. Alkynols and Alkynediols

The chemistry of these compounds was the subject of my doctoral thesis presented before the University of Paris in 1945. Symmetrically substituted but-2-yne-1,4-diols were obtained according to known methods, but another procedure was devised for the synthesis of unsymmetrically substituted alkynediols, such as 2,6-dimethyloct-4-yne-3,6-diol.

Partial catalytic hydrogenation of alkynediols gave the corresponding alkenediols whose dehydration led to conjugated trienes. In this way, dehydration of 2,6-dimethyloct-4-ene-3,6-diol gave the acyclic terpene alloocimene, i.e. 2,6-dimethylocta-2,4,6-triene[155]. As said in Section 5, reaction of the latter with sulfur led to the simultaneous formation of a thiophene ring and of a 1,2-dithiole ring[17].

Heating alkynediols with acetic anhydride and mercuric acetate gave acetates of α-hydroxy ketones. For instance, hex-3-yne-2,5-diol led to 2-acetoxyhex-4-en-3-one[156] This reaction has been also applied to but-2-yne-1,4-diol[157].

Reaction of alkynediols with sulfur[16] has been described in Section 5.

16.2. Nomenclature

The problems inherent to the nomenclature of sulfur and nitrogen heterocycles arose my interest for this topic. I joined IUPAC in 1953. Titular Member of the Commission on Nomenclature of Organic Chemistry (CNOC) from 1953 to 1979, I have been Chairman from 1971 to 1977. From 1977 to 1987, I continued my participation as Associate Member.

The work of CNOC being essentially collective, I shall consider here my personal contributions only.

A survey of French Organic Nomenclature was first published[158], later followed by a book[159] issued in 1967. This book aimed at showing the advantages of a greater consistency of nomenclature rules. This can be attained only if new problems are tackled early enough to avoid appearance of contradictory procedures which are later difficult to eradicate.

A particular example is given by the numerical terms which were defined only up to 199 in the IUPAC Rules existing in 1967. The development of polymer chemistry led to think that this limit was too low and, in my book[160], I offered a method providing numerical terms up to 1999. This proposal was later taken into consideration by CNOC, further developed, provisionally published in 1963 and, in 1986, finally adopted[161].

Difficulties encountered in various domains, and particularly for assemblies of rings and chains, led me to imagine a more systematic nomenclature method including a sequential numbering of structures. Research along similar lines being then pursued by some Members of the Chemical Abstracts Service, a collaboration was established for developing what was henceforward known as Nodal Nomenclature. A first paper dealt with the numbering and naming of graphs[162]. A second paper described the application of the Nodal System to organic nomenclature[163] and a third paper showed the advantages of Nodal Numbering for uniquely identifying atoms in chemical structures[164].

What is particularly useful in Nodal Nomenclature is the construction of any name in successive well-defined steps, beginning with the definition of a graph showing the connections between the main constituents of the molecule. The choice of the "main" constituents remains arbitrary and depends largely upon chemical concepts in current use. For instance nothing (except commodity) forbids to consider every atom of a hydrocarbon as a "main" constituent which has to be included in the graph. However, almost everybody will be happy to take only carbon atoms as nodes of the graph, hydrogen atoms being implicitly added afterwards in order to satisfy the valencies of the other elements.

At any rate, when the chemical nature of the nodes has been decided, the description, and in the first place the numbering, of the graph are made according to strictly mathematical procedures leading to a unique description for any given graph. When this has been done, one has to come back to chemical considerations in order to include in

the name the necessary information about the chemical nature of the nodes and of the bonds.

Along the years, two nomenclature methods have progressively gained foremost importance: substitution nomenclature for organic chemistry and coordination nomenclature for inorganic chemistry. Both methods can use the Nodal Method for the description of graphs, their differences appearing only in the expression of the chemical nature of atoms and bonds.

The concepts which directed the creation of Nodal Nomenclature were not new. For instance, von Baeyer names for polycycles are somewhat akin to nodal names. The nodal system resulted in fact from a general reflection on the principles involved in the historical development of organic nomenclature which, for the layman, has become excessively complicated. Therefore, the principal objective of Nodal Nomenclature was to provide simpler, shorter and unambiguous rules.

As any language, chemical nomenclature has changed in the course of time but, owing to its relative youth and its scientific background, the chemical language is less irrational than common languages such as English or French, although the same defects resulting in useless complications, ambiguities and redundancies tend also to develop. IUPAC, by its action on nomenclature evolution, has played a very useful rôle, restricting, as much as possible, exceptions, alternatives and ambiguities. Nevertheless, a lot remains to be done and any significant general improvement presupposes the adoption of clear principles concerning nomenclature operations, that is to say, how a chemical feature is expressed in the name of a compound. These questions have been considered in two papers[165,166] in which the value of existing methods and their adaptability to the progress of chemistry have been discussed.

BIOGRAPHY OF N. LOZAC'H (by C. Th. Pedersen)

Professor Noël Lozac'h was born in Nantes, France, in 1915 and started his studies at l'Ecole Normale Supérieure in 1935. He obtained his doctoral degree from the Faculté de Sciences de Paris in 1945 and after a few years in Paris and Lille he came to Caen in 1949, where he became a full professor of chemistry in 1952, a position he held until his retirement in 1982 at which point he was made professor emeritus. Along with his scientific career professor Lozac'h found time to commit himself to administration, too. He was Head of the Chemistry Department 1952–1967 and Dean of the Faculty of Sciences 1956–1969, when he became director of l'Ecole Nationale Supérieure de Chimie de Caen, a position he held until the foundation of Institut des Sciences de la Matiére et du Rayonnement, where he was nominated director until he retired.

Professor Lozac'h is the father of the Caen group in Sulfur Chemistry. He is the author of nearly 150 publications in sulfur chemistry. His main research field has been heterocyclic sulfur compounds and thiones, especially related to the 1,2-dithiole series. By introducing the concept of no-bond—single-bond resonance he has explained the special bonding properties in trithiapentalene and given the background for the understanding of the chemistry of such linear multisulfur compounds.

During the past 30 years he has had a great influence on the development of sulfur chemistry in France as a great inspirator.

One other topic of interest to Professor Lozac'h is nomenclature. For many years he has been a member of The IUPAC Commission on Nomenclature and has published several papers on nomenclature, which are also mentioned in this account.

Professor Lozac'h is Chevalier de la Légion d'Honneur.

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