Russian Chemical Reviews **77** (6) 521 – 546 (2008) © 2008 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2008v077n06ABEH003784

Synthesis and properties of 1,2,3-dithiazoles

L S Konstantinova, O A Rakitin

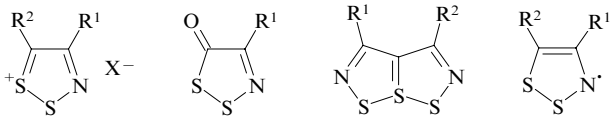
Contents

I.	Introduction	521
II.	Methods of synthesis	521
III.	Chemical properties	528
IV.	Spectral studies	540
V.	Quantum chemical calculations of 1,2,3-dithiazole molecules	544
VI.	Biological activity and applications of 1,2,3-dithiazoles	544

Abstract. Data on the methods for the synthesis and properties of 1,2,3-dithiazoles published over the last 15 years are reviewed and described systematically. The bibliography includes 103 references.

I. Introduction

Among the five-membered heterocycles containing nitrogen and sulfur atoms, 1,2,3-dithiazoles are important compounds due to their unusual physical properties, biological activity and various chemical transformations of their derivatives. This class also includes positively charged monocyclic and fused 1,2,3-dithiazoles **1**, neutral 1,2,3-dithiazol-5-ones **2** and bicyclic heteropentalenes **3**. Also of great interest are stable fused 1,2,3-dithiazolyl radicals **4**, which have recently been actively investigated as potential conductors and magnetic materials.



1 **2** **3** **4**

Monocyclic dithiazoles are mostly obtained from the key compound, 4,5-dichloro-1,2,3-dithiazolium chloride ($R^1 = R^2 = X = Cl$, **1a**), called the Appel salt.[1] 1,2,3-Dithiazoles fused with the benzene ring and known as the Hertz salts were first synthesised over 80 years ago. These compounds are being actively studied now, although methods for their synthesis differ from the classical ones.

L S Konstantinova, O A Rakitin N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 119991 Moscow, Russian Federation. Fax (7-499) 135 53 28, e-mail: dlt@ioc.ac.ru (L S Konstantinova), tel. (7-499) 135 53 27, e-mail: orakitin@ioc.ac.ru (O A Rakitin)

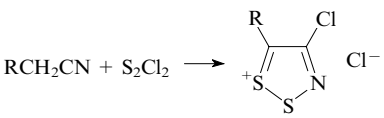
Received 7 February 2008
Uspekhi Khimii **77** (6) 551 – 577 (2008); translated by L G Smolina

The properties of 1,2,3-dithiazoles are most comprehensively considered in a special chapter of the monograph *Comprehensive Heterocyclic Chemistry II* published in 1996.[2] The review[3] by Kim (1998) was mainly devoted to the Appel salt chemistry. The present review presents data on the syntheses and reactions of 1,2,3-dithiazoles obtained over the recent 15 years (before December 2007).

II. Methods of synthesis

1. 1,2,3-Dithiazolium salts

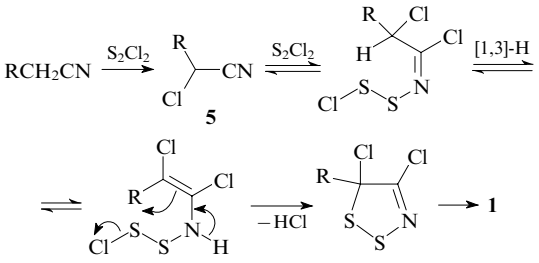
The Appel salt (**1a**) was first prepared[4] by a reaction of acetonitrile with sulfur monochloride and erroneously identified as unstable 2,3,4-trichloro-1,2,3-dithiazole. Later Appel *et al.*[1] synthesised compound **1a** from chloroacetonitrile and S_2Cl_2 in dichloromethane; today this is recognised as the most convenient procedure. The Appel salt was also obtained[5] by a reaction of sulfur monochloride with ethylamine, but the product yield and the reaction conditions were not reported. Recently, a number of 5-substituted 4-chloro-1,2,3-dithiazolium cation chlorides **1a**–**h** were synthesised from monosubstituted acetonitriles.[6,7]



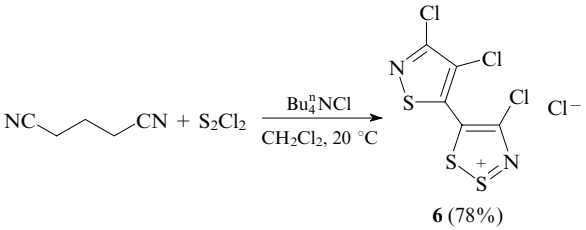
1a–**h** (20% – 85%)

R = Cl (**a**), Br (**b**), CN (**c**), SMe (**d**), C_6F_5 (**e**), Ph (**f**), 4-$MeOC_6H_4$ (**g**), 4-$O_2NC_6H_4$ (**h**).

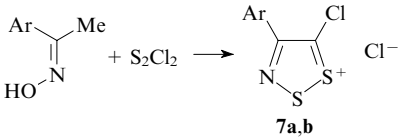
Various mechanisms were suggested for the transformation of substituted acetonitriles into 1,2,3-dithiazolium salts, but no strict evidence has been obtained so far in support of any of these mechanisms. It is assumed that the first stage of this reaction is chlorination of acetonitrile with sulfur monochloride to α-chloroacetonitrile **5**, as demonstrated in the case of acetonitrile[1] or phenylacetonitrile.[8] The next stages are obviously the addition of S_2Cl_2 to the cyano group, cyclisation, and ionisation of dithiazole.



The reaction product of glutaronitrile with sulfur monochloride was identified [9] as (isothiazolyl)dithiazolium chloride **6**, but the reaction mechanism was not discussed.

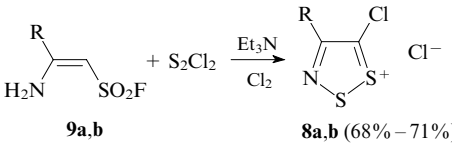


The possibility of synthesis of 4-substituted 5-chloro-1,2,3-dithiazolium chlorides **7a**,**b** was demonstrated in the case of the reactions of acetophenone oximes and *p*-nitroacetophenone with S_2Cl_2.[10, 11]



Ar = Ph (**a**), 4-$O_2NC_6H_4$ (**b**).

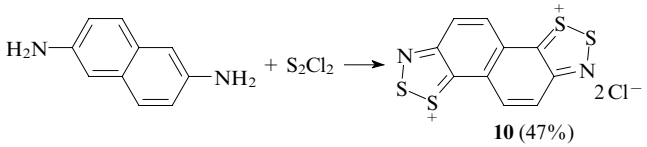
Similar polyfluoroalkyl derivatives of these salts, namely, compounds **8a**,**b**, were obtained in high yields by the reactions of fluorosulfonyl-substituted enamines **9a**,**b** with S_2Cl_2 and subsequent treatment with an excess of chlorine.[12]



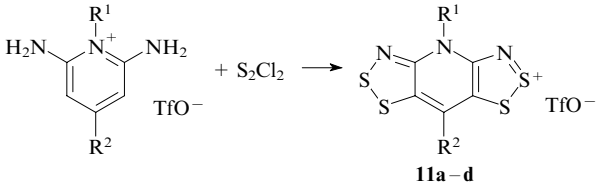
R = C_3F_7 (**a**), $H(CF_2)_5$ (**b**).

The most popular procedure for the synthesis of 1,2,3-dithiazoles fused with the benzene ring is the reaction of aromatic amines with sulfur monochloride. Previous data on this reaction are summarised in a review;[13] here we consider only methods for the preparation of 1,2,3-dithiazoles fused with other heterocycles and compounds with two dithiazole rings. In recent years, researchers paid great attention to the synthesis of these derivatives and investigation of their properties.

As a result of the so-called Hertz double condensation, naphthobis(1,2,3-dithiazolium) dichloride **10** was obtained from 2,6-diaminonaphthalene and sulfur monochloride.[14]

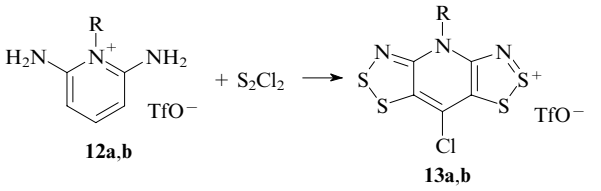


N-Alkyl-substituted 2,6-diaminopyridinium salts can also be readily transformed into bis(1,2,3-dithiazolo)pyridinium salts **11a**–**d**.[15]



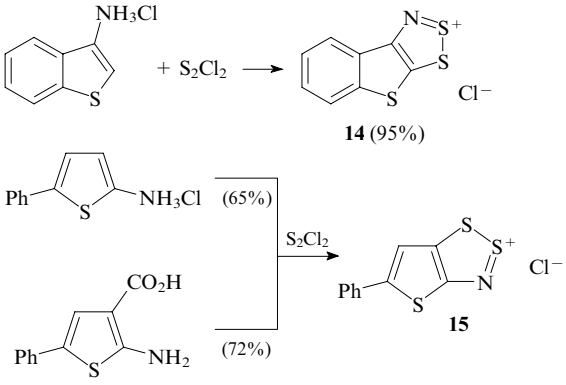
R^1 = Me: R^2 = Me (**a**), Ph (**b**); R^1 = Et: R^2 = Me (**c**), Ph (**d**).

If the reaction is performed with pyridinium salts **12a**,**b** bearing no substituents at position 4, the formation of bis(dithiazolo)pyridinium salts **13a**,**b** is accompanied by chlorination of the product.[16, 17]

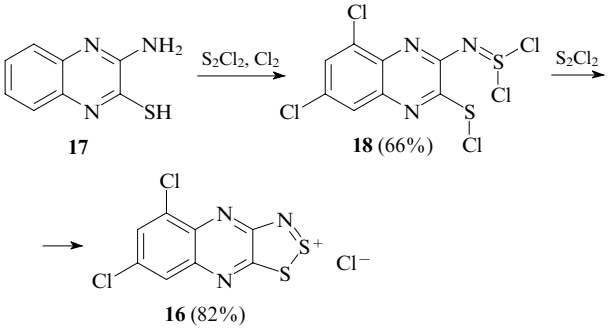


R = Me (**a**), Et (**b**).

Several examples of the transformation of aminothiophenes into dithiazolium salts have been reported.[18, 19] For example, thienodithiazolium salts **14** and **15** were obtained in good yields. The reaction occurred smoothly even where the *ortho*-position relative to the amino group in the heterocycle was occupied by a carboxyl group.

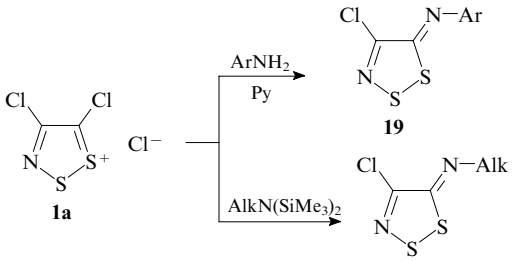


A two-stage procedure was suggested [20] for the synthesis of quinoxalino-1,2,3-dithiazolium chloride **16**, which involved a reaction of aminoquinoxalinethiol **17** with a mixture of S_2Cl_2 and molecular chlorine and subsequent treatment of the reaction product **18** with sulfur monochloride.

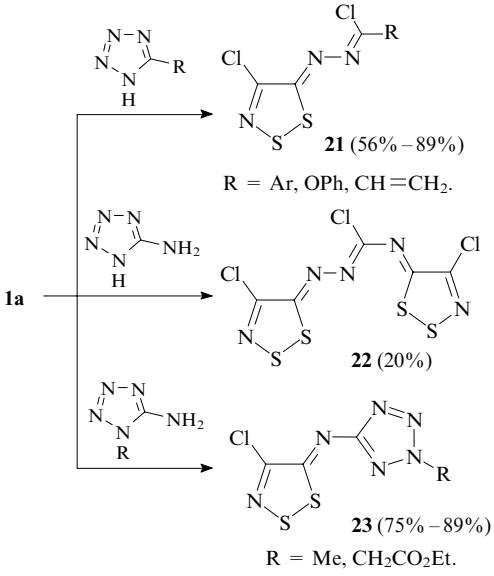


2. 5-Arylimino-4-chloro-5*H*-1,2,3-dithiazoles

As is known, the Appel salt (**1a**) readily undergoes a nucleophilic attack on the C(5) atom of the heterocycle. Thus, arylamines react with **1a** to form 5-arylimino-4-chloro-5*H*-1,2,3-dithiazoles **19**.[1] The liberated HCl is scavenged with an excess of the aromatic amine or pyridine (Py). This reaction occurs with almost all known aromatic and primary heteroaromatic amines; the yields of (het)arylimino-1,2,3-dithiazoles are generally high. Although aliphatic amines reacted vigorously with salt **1a**, the reaction products were not isolated. Less basic *N*,*N*-bis(trimethylsilyl)amines afforded alkylimino-1,2,3-dithiazoles **20**, but their yields were up to 48%.[1,21]

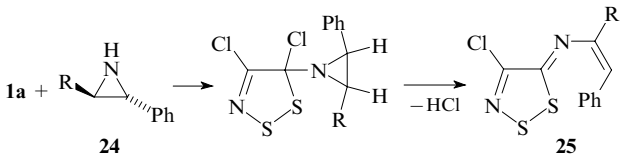


5-Substituted tetrazoles react with Appel salt **1a** at room temperature to form hydrazonoyl chlorides **21** in good yields.[22]



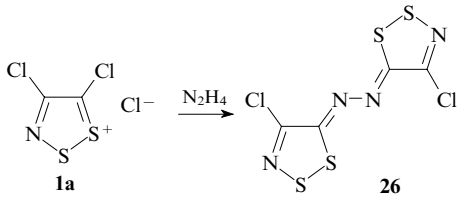
The reaction of 5-aminotetrazole with 2 equivalents of **1a** leads to bis(imino)dithiazole **22**. It is assumed that the attack of the nitrogen atom of the tetrazole ring on the carbon atom of the Appel salt is followed by cleavage of the tetrazole ring. Tetrazoles with a substituent at the N(1) atom of the tetrazole ring react with **1a** in the same way as other aromatic and heteroaromatic primary amines to form iminoadducts **23**.

An unusual synthesis of *N*-vinyl-1,2,3-dithiazolylideneimines from the Appel salt and aziridines was recently suggested by Krayushkin and co-workers.[23] It was shown that the reaction of the *trans*-isomer of ethyl 3-phenylaziridinecarboxylate or amide (**24**) with the Appel salt led to only one of the possible isomers, namely, to compound **25**. Evidently, cleavage of the aziridine ring occurred concurrently with the formation of a C=N double bond.

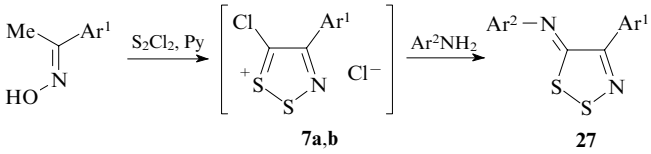


R = CO_2Et, $C(O)NH_2$.

Bis(1,2,3-dithiazolyl)azine **26** was synthesised from the Appel salt and hydrazine in order to evaluate the electronic and steric effects of the bridge on the interaction between the two dithiazole rings.[24]

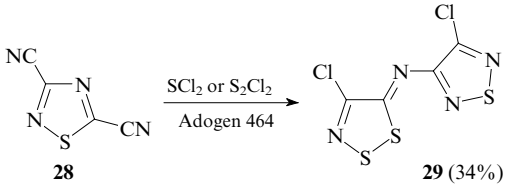


The analogues of the Appel salt (**7a**,**b**) obtained from acetophenone oxime and its 4-nitro derivative can be transformed, without being isolated, into 5-arylimino derivatives **27**.[11]



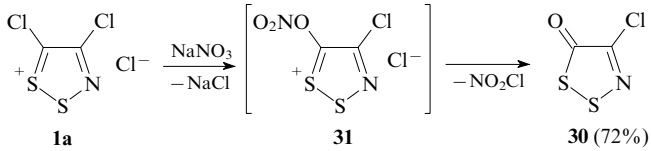
Ar[1] = Ph (**a**), 4-$O_2NC_6H_4$ (**b**).

The reaction of 3,5-dicyano-1,2,4-thiadiazole (**28**) with sulfur chloride (SCl_2 or S_2Cl_2) in the presence of the catalytic amounts of the quaternary ammonium salt Adogen 464 [$MeAlk_3NCl$, Alk = C_nH_{n+1} (n = 8 – 10)] afforded [25] hetarylimine **29**.

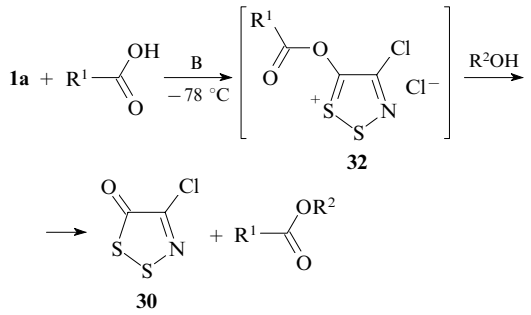


3. 1,2,3-Dithiazol-3-ones

In the presence of moisture, the Appel salt **1a** quickly decomposed with liberation of HCl and formation of a brown mass from which dithiazolone **30** could be isolated by sublimation.[1] Compound **30** was also obtained by reaction of salt **1a** with sodium nitrate in dichloromethane (yield 72%). The mechanism of this transformation involves a nucleophilic attack of the nitrate ion on the C(5) atom and elimination of nitroyl chloride from intermediate **31**.[1]

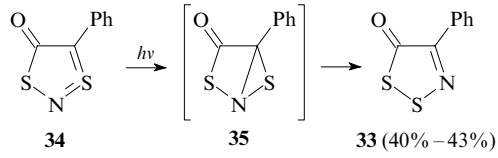


The reaction of **1a** with carboxylic acids in the presence of 2,6-dimethylpyridine at −78 °C and subsequent treatment with an alcohol also leads to dithiazolone **30**.[26] The authors assumed the formation compound **32** (analogue of intermediate **31**) as an intermediate, which reacted with the alcohol to form the ester of the starting carboxylic acid. Primary alcohols gave higher yields of esters (65% – 84%) than secondary and tertiary alcohols (39% – 59%). This is possibly explained by steric effects during the attack of the alcohol molecule on salt **32**. This reaction was suggested as a method for esterification of carboxylic acids under mild conditions.

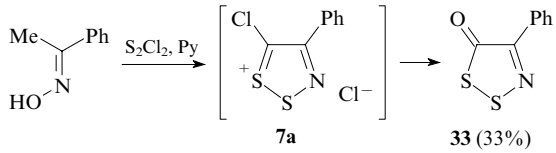


B is 2,6-dimethylpyridine.

4-Phenyl-1,2,3-dithiazol-5-one (**33**) was prepared by photoisomerisation of 5-phenyl-1,3,2-dithiazol-4-one (**34**) in various chlorinated solvents (CH_2Cl_2, CCl_4).[10,27] The product yields were low. Ketone **33** probably formed from bicyclic intermediate **35**.

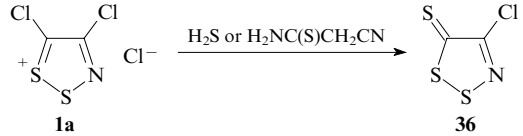


An alternative method for the synthesis of ketone **33** is *in situ* hydrolysis of 1,2,3-dithiazolium salt **7a** formed from acetophenone oxime and sulfur monochloride, but the yield again was low (33%).[10]

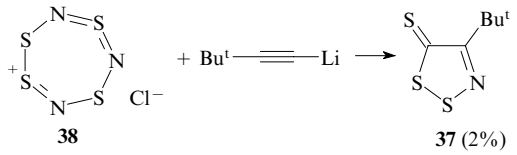


4. 1,2,3-Dithiazole-3-thiones

Treatment of the Appel salt **1a** with hydrogen sulfide in acetonitrile at room temperature leads to thione **36** (yield 69%).[1] The use of 2-cyanothioacetamide as a reagent in dichloromethane increased the yield of product **36** to 89%.[3]

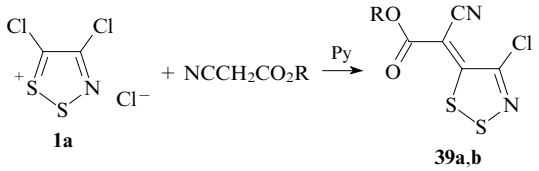


4-(*tert*-Butyl)-1,2,3-dithizole-5-thione (**37**) was isolated as one of the reaction products of tetrathiatriazepinium chloride **38** with lithium *tert*-butylacetylenide (the isomeric 1,3,2-dithiazole was the major product).[27]



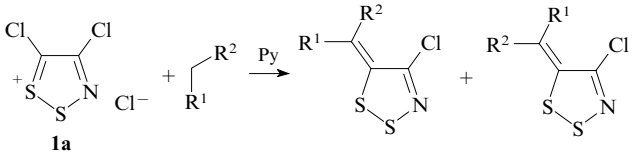
5. 5-Alkylidene-5*H*-1,2,3-dithiazoles

Appel established [1] that cyanoacetates reacted with salt **1a** in the presence of pyridine at room temperature to form dithiazol-5-ylidene derivatives **39a**,**b**.



R = Me (**a**, 68%), Et (**b**, 76%).

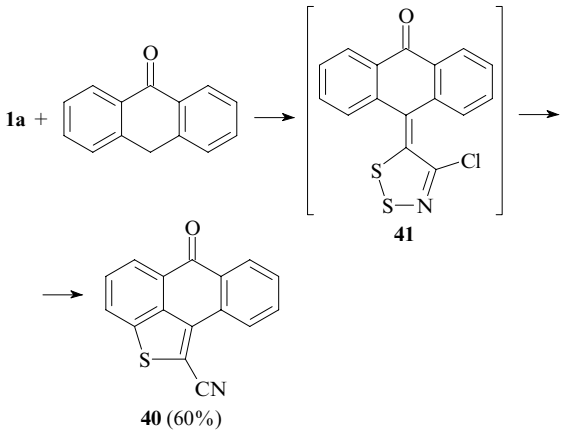
This reaction was later extended to a wide range of compounds with an activated methylene group. The reagents were both acyclic compounds with a nitro, trifluoroacetyl, benzoyl and ethoxycarbonyl groups and cyclic compounds (barbituric acid, Meldrum's acid and dimedone); the latter formed ylidenes in higher yields.[28,29] This process is not stereospecific; the asymmetric compounds mostly form inseparable mixtures of regio isomers; their ratio is determined by ^1H, ^{13}C, and ^{19}F NMR spectroscopy.



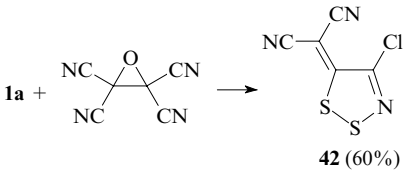
R^1, R^2 = NO_2, $C(O)CF_3$, C(O)Ph, CO_2Et, CN, *etc.*

At the same time, in similar reactions with compounds possessing lower CH-acidity (for example, diethyl malonate, pentane-2,4-dione, phenylacetonitrile, diphenylmethane, *etc.*), the corresponding ylidenes are not formed.[29]

The reaction of anthranone with the Appel salt leads to tetracyclic fused thiophene **40**.[29] Intermediate ylidene **41** obviously undergoes intramolecular cyclisation with liberation of sulfur and HCl.

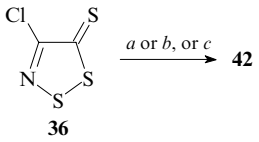


It was found [30] that in its reaction with tetracyanoethylene oxide (TCNEO), the Appel salt **1a** unexpectedly formed dicyanomethylene derivative **42**.



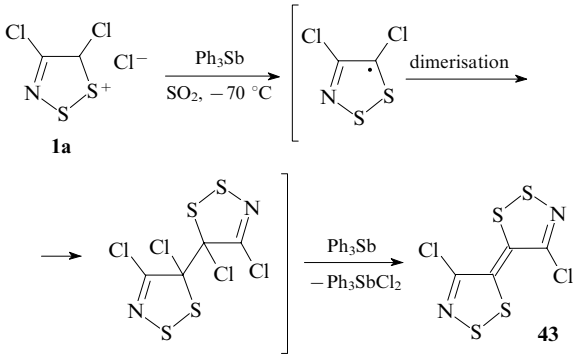
42 (60%)

4-Chloro-1,2,3-dithiazole-5-thione (**36**) proved a convenient starting compound for the synthesis of ylidene derivatives of this series. Thus dicyanomethylene adduct **42** was prepared by the reaction of compound **36** with tetracyanoethylene (TCNE) or its oxide [29] and also with the dihalo derivatives of malononitrile.[31]

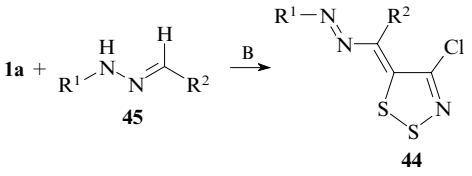


(*a*) TCNE (53% yield), (*b*) TCNEO (72%), (*c*) $X_2C(CN)_2$ (X = Cl, Br; 76%–85%).

Tetrathiadiazafulvalene **43**, formed in the reaction of the Appel salt with two equivalents of triphenylantimony, can be considered a formal ylidene derivative of 1,2,3-dithiazole.[32] The highest yield of product **43** (30%) was achieved when the reaction was conducted in liquid SO_2 at −70 °C. It is noteworthy that compound **43** is the first example of heterofulvalene systems; the reaction mechanism is presented below.

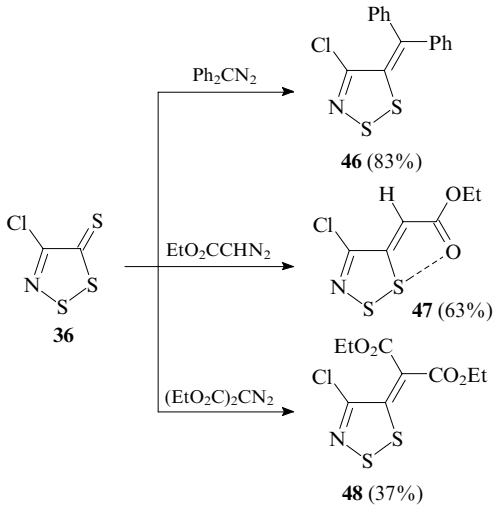


The azomethylene derivatives of 1,2,3-dithiazoles **44** were first obtained by the reaction of the Appel salt with *N*-monosubstituted hydrazones **45**.[33] These products can be formed through the generation of the carbonium anion from hydrazone **45** under the action of a base and its further addition to salt **1a**.

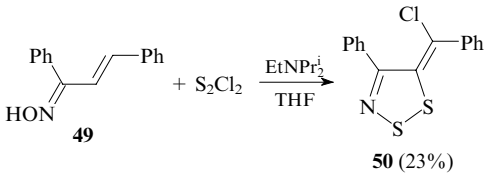


B is 2,4,6-trimethylpyridine; R^1 = Ar, C(O)Ar; R^2 = NO_2, 4-$O_2NC_6H_4$.

Diphenyldiazomethane reacted with thione **36** at room temperature to form alkylidene derivative **46**. A similar reaction of **36** with ethyl diazoacetate occurred on refluxing in benzene and with diethyl diazomalonate on refluxing in xylene, but the yields of ylidenes **47** and **48** were lower.[30] In the case of the unsymmetrically substituted ylidene compound **47**, only one stereoisomer formed due to the O···S interaction, detected by IR spectroscopy.



The reaction of benzylideneacetophenone oxime **49** with sulfur monochloride and ethyldiisopropylamine in tetrahydrofuran leads to dithiazole **50**.[34]

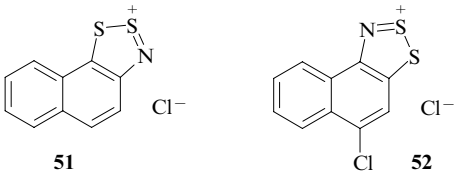


6. Fused 1,2,3-dithiazoles

Synthesis of the 1,2,3-dithiazolium cations fused with the benzene ring by reactions of aromatic amines with sulfur monochloride is one of the most popular methods (called the Hertz reaction) for the preparation of this class of compounds. As mentioned above, this reaction has been known for more than eight decades, but is often used nowadays as well. Below we give examples of syntheses of salts formed by 1,2,3-dithiazolium cation fused with heterocycles and data on the chemistry of the classical Hertz salts obtained in recent years.

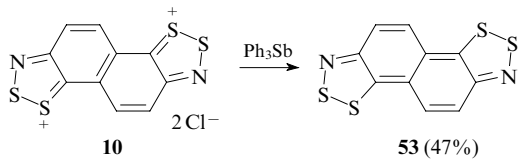
a. Syntheses from cyclic amines

Recently, the traditional approach to the synthesis of the Hertz salts was investigated for 1- and 2-aminonaphthalenes.[35] In the case of 2-aminonaphthalene, the reactions with sulfur halides occur with closure of the dithiazole ring at the position 1 of naphthalene, which is more reactive, and lead to product **51** with a good yield (54%). At the same time, similar reactions of 1-aminonaphthalene occur with chlorination of the position 4 in naphthalene to give compound **52**.



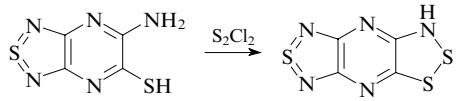
Bis(1,2,3-dithiazoles) is a relatively new class of heterocyclic compounds. One of the recent great achievements was the development of a procedure for the synthesis of these compounds by the reduction of the Hertz bissalts under the

action of triphenylantimony [for example, reduction of salt **10** to the neutral bis(dithiazole) **53**].[14]



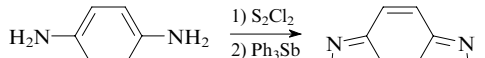
10 **53** (47%)

A series of fused 1,2,3-dithiazoles were synthesised by Oakley and co-workers[36] who performed reactions of aromatic and heteroaromatic *o*-aminothiols with sulfur monochloride. This approach is a substitute for the traditional route, namely, the Hertz reaction, which could not be accomplished for aromatic amines. Synthesis of tricyclic dithiazole **54** in a virtually quantitative yield is an example.

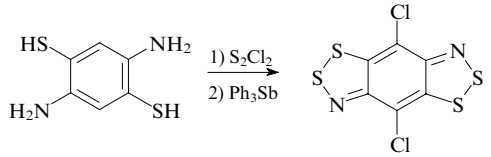


54 (97%)

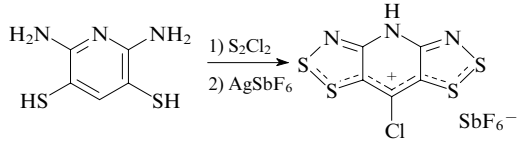
The greatest success was achieved when this procedure was used for the synthesis of bis(1,2,3-dithiazoles) from diaminoarenedithiols. In this way neutral bis(dithiazoles) **55** and **56** (after reduction with triphenylantimony) and salt **57**, which are stable against oxidation with atmospheric oxygen, were synthesised. The reaction was occasionally accompanied by chlorination of the benzene or pyridine ring.[37–39]



55 (60%)

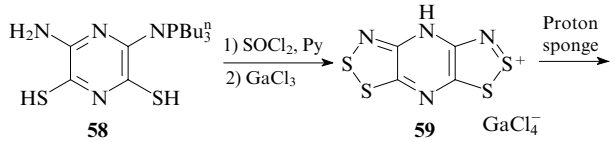


56 (49%)

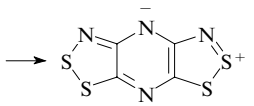


57 (75%)

5-Amino-3-phosphoranylideneaminopyrazine-2,6-dithiol **58** is currently the only known precursor for the synthesis of bis(1,2,3-dithiazolo)pyrazine **59**.[40,41] The reaction of azaphosphorane **58** with thionyl chloride in the presence of pyridine leads to dithiazolium chloride, and the latter is tranformed into dithiazolium tetrachlorogallate **59**, which is soluble in organic solvents. Treatment of **59** with 1,8-bis(dimethylamino)naphthalene ('Proton sponge') leads to bis(dithiazolium) zwitterion **60**, which is a rare type of heterocyclic structure.

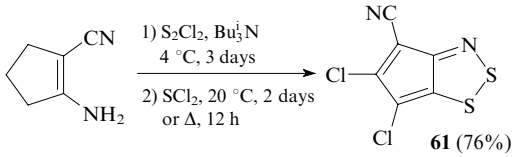


58 **59**

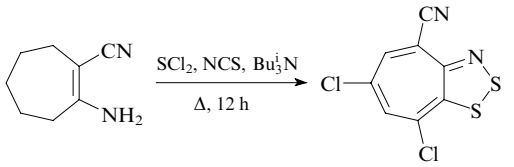


60

2-Aminocyclopent-1-enecarbonitrile successively reacts with S_2Cl_2 (in the presence of triisobutylamine) and SCl_2 to form chlorinated cyclopentadithiazole **61**.[42] In the case of 2-aminocyclohept-1-enecarbonitrile, *N*-chlorosuccinimide (NCS) is used instead of sulfur dichloride, but the yield of **62** is much lower.



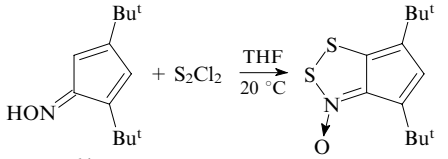
61 (76%)



62 (40%)

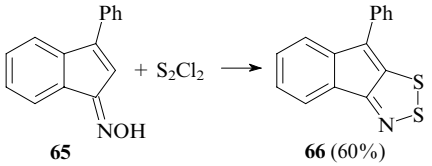
b. Synthesis from cyclic ketone oximes

The tranformations of cyclic ketone oximes into fused 1,2,3-dithiazoles were actively studied in recent years and possibly involve the formation of dithiazole *N*-oxides. However, the only known *N*-oxide **63** was isolated from the reaction products of cyclopentadienone oxime **64,** stabilised by two *tert*-butyl groups, with sulfur monochloride in tetrahydrofuran at room temperature.[43]



64 **63** (58%)

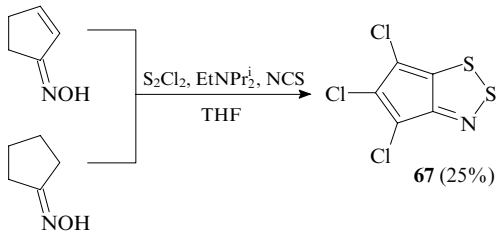
All other transformations of cyclic ketone oximes generally gave only 1,2,3-dithiazoles. These products are possibly formed upon deoxygenation of the intermediate *N*-oxides with S_2Cl_2. Thus 1-hydroxyimino-3-phenylindene (**65**) reacts with sulfur monochloride to form dithiazole **66**.[34,44] Since the five-membered carbocycles contain substituents, no chlorination of this ring occurs in the syntheses of **63** and **66**.[34]



65 **66** (60%)

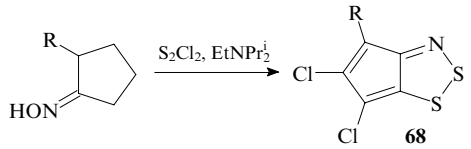
This reaction was extended to cyclopentenone and cyclopentanone oximes.[34] The highest yields of dithiazoles **66** and **67** were obtained when the process was conducted in the presence of *N*-ethyl-*N*,*N*-diisopropylamine (the Hunig base). Numerous chlorination, dehydrochlorination and oxidation reactions suggested by the authors as a rationale of the complex multistep mechanism of formation **67** make this transformation

sensitive to subtle changes in the conditions and lead to a moderate yield of the final product.



67 (25%)

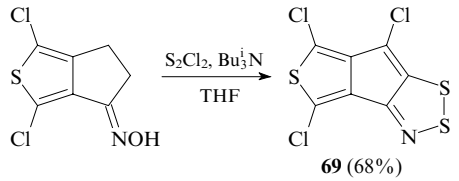
Cyclopenta-1,2,3-dithiazoles **68** are formed upon the reactions of 2-substituted cyclopentanone oximes and sulfur monochloride.[45,46] As in the case of other cyclopentadithiazoles, this reaction occurs with exhaustive chlorination of the aromatic C—H bonds (see above).



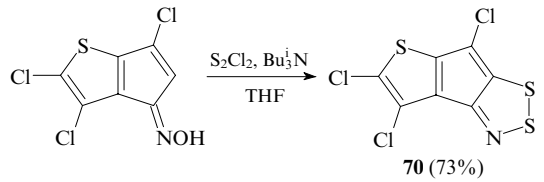
68

R = CH_2CH_2CN (47%), $CH_2CH_2CO_2Et$ (16%), CO_2Et (65%), CO_2Me (67%).

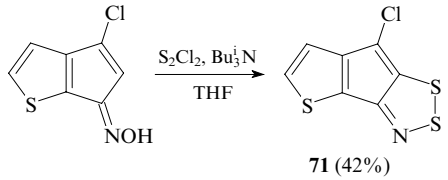
Chlorine-substituted cyclopentanone oximes fused with the thiophene ring react with sulfur monochloride and triisobutylamine in tetrahydrofuran at 4 °C for three days.[46] This affords a number of the corresponding thienocyclopentadithiazoles **69**–**71** in moderate to high yields.



69 (68%)

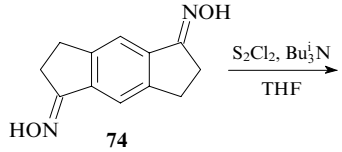


70 (73%)

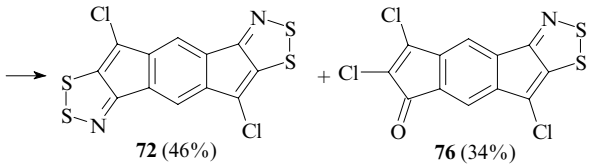


71 (42%)

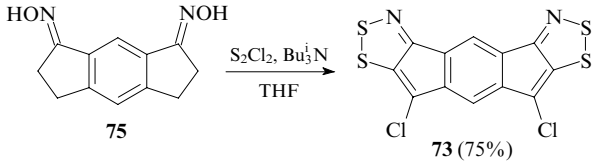
The same approach was used for the synthesis of pentacyclic bis(1,2,3-dithiazolo)-*s*-indacenes **72** and **73** from 1,5- and 1,7-hydroindacenedione dioximes **74** and **75**, respectively.[46] In the former case, the process was complicated by hydrolysis of one of the oxime groups leading to monodithiazole **76**.



74

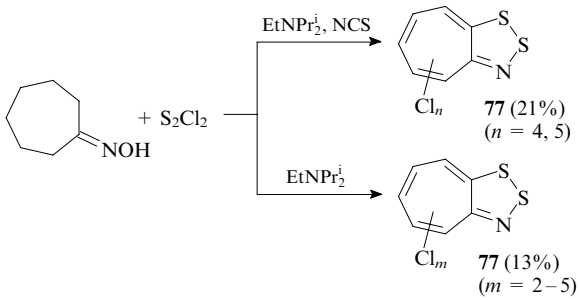


72 (46%) **76** (34%)



75 **73** (75%)

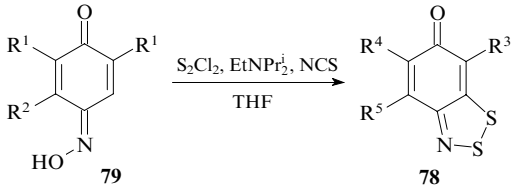
The reaction of the oxime of the seven-membered cyclic ketone with S_2Cl_2 occurs in the same way and leads to a mixture of chlorinated cyclohepta-1,2,3-dithiazoles **77**.[34] In order to achieve high degrees of chlorination, one can use a 15-fold excess of sulfur monochloride; the highest yield of polychlorination products is observed in the presence of *N*-chlorosuccinimide.



77 (21%) (n = 4, 5)

77 (13%) (m = 2–5)

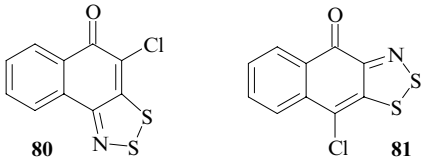
6*H*-Benzo-1,2,3-dithiazol-6-ones **78** can be obtained from benzoquinone-4-oximes **79** and S_2Cl_2 in the presence of *N*-ethyl-*N*,*N*-diisopropylamine and NCS.[47] The formation of a dithiazole ring from the oxime is accompanied, as usual, by chlorination. Note that the substituents in the positions 2 and 6 of benzoquinone are preserved in the reaction products except the *tert*-butyl group, which is replaced by the chlorine atom.



79 **78**

Compound **79**		Compound **78**		
R^1	R^2	R^3	R^4	R^5
H or Cl	H	Cl	Cl	H
Bu^t	H	Bu^t	Cl	Cl
Me	H	Me or $ClCH_2$	Me	H or Cl
Pr^i	H	Pr^i	Pr^i	H
Me	Me	Me	Me	Me

1,4-Naphthoquinone-4-oxime and 1,2-naphthoquinone-2-oxime form dithiazoles **80** and **81** in a similar reaction.[47]

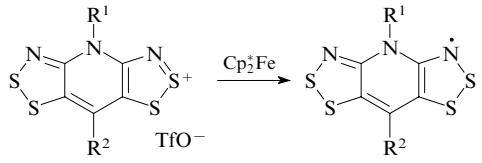


80 **81**

7. 1,2,3-Dithiazole-derived radicals

Stable 1,2,3-dithiazolyl radicals are regarded as promising conductors; therefore, much attention has recently been paid to their synthesis. These radicals are usually generated by reduction of readily accessible Hertz salts.

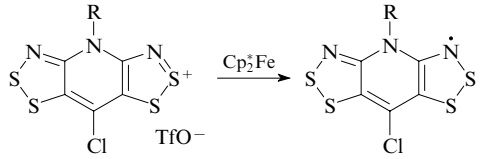
Bis(1,2,3-dithiazolo)pyridinyl radicals **82** were synthesised from salts **11** under the action of decamethylferrocene (Cp^*_2Fe).[15]



11a–d **82a–d** (56%–58%)

Cp* = η^5-C_5Me_5; R^1 = Me: R^2 = Me (**a**), Ph (**b**); R^1 = Et: R^2 = Me (**c**), Ph (**d**).

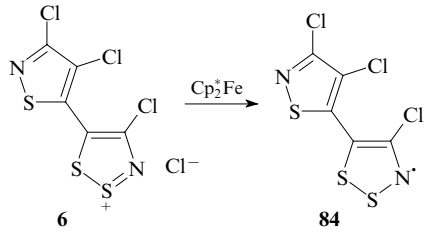
Chlorine-containing salts **13a**,**b**, under these conditions, also form the corresponding radicals **83a**,**b**.[16, 17]



13a,**b** **83a**,**b** (64%–83%)

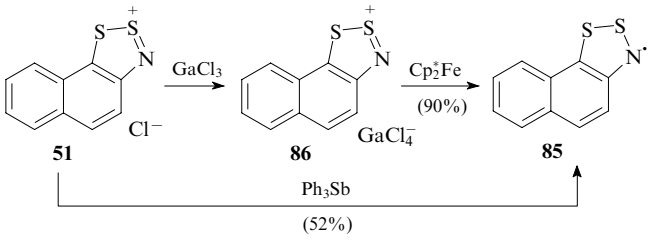
R = Me (**a**), Et (**b**).

The same reducing agent was used for generating radical **84** from isothiazolyldithiazolium chloride **6**.[9]



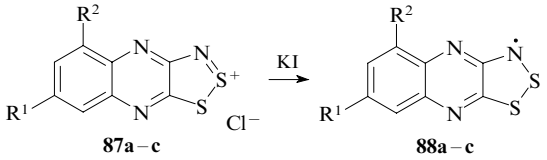
6 **84**

Other reducing agents are also used for the preparation of the 1,2,3-dithiazolyl radicals. Thus naphtho-1,2,3-dithiazolium chloride **51** is transformed by triphenylantimony into the corresponding radical **85**; the highest yield of the latter was obtained in the reaction of tetrachlorogallate **86** with decamethylferrocene.[35]



51 **86** **85**

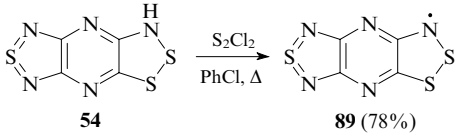
For quinoxaline-1,2,3-dithiazolium salts **87a–c**, various reducing agents were assayed (KI, Bu_4NI, Ph_3Sb, Zn).[20] Potassium iodide in acetonitrile or in liquid SO_2 was the reagent of choice, but the yields of radicals **88a–c** were low (~10%) because of the complex purification procedure.



87a–c **88a–c**

R^1 = R^2 = H (**a**); R^1 = Cl, R^2 = H (**b**); R^1 = R^2 = I (**c**).

Radicals are also formed in the oxidation of 1,2,5-thiadiazolo-1,2,3-dithiazolopyrazine imide **54**.[36] The reaction route, however, depends on the nature of the oxidant. Bromine and sulfuryl chloride do not react with imide **54**; in the case of chlorine, the S—S bond of the dithiazole ring is broken; and in boiling benzene, sulfur monochloride forms radical **89** in good yield.



54 **89** (78%)

III. Chemical properties

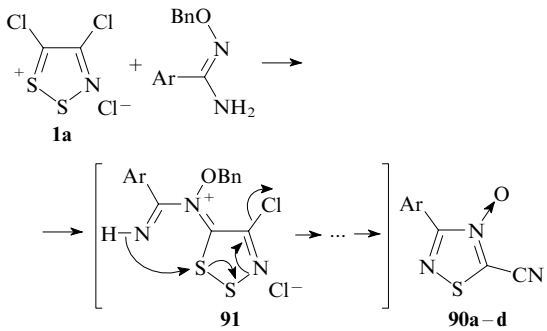
In the group of non-fused 1,2,3-dithiazoles, the chemical properties are well investigated only for the Appel salt derivatives, in particular, 5-arylimino-4-chloro-5*H*-1,2,3-dithiazoles. The reactions of these compounds with nucleophilic reagents involve the attacks on the carbon and sulfur atoms leading to cleavage of the dithiazole ring with elimination of one or two sulfur atoms. Similar transformations result from thermal treatment. The reactions of 1,2,3-dithiazol-5-ones, -5-thiones, and -5-alkylidenes are less studied. Below we present recent data on the reactivities of fused 1,2,3-dithiazoles.

1. Reactions of 5-arylimino-4-chloro-5*H*-1,2,3-dithiazoles

a. Nucleophilic attack on the sulfur atom of the dithiazole ring

Various nucleophilic reagents can attack the sulfur atoms of the 1,2,3-dithiazole ring. These reactions result in the formation of sulfur-containing heterocycles [when the S(1) atom is attacked] or compounds with a thione group [when the S(2) atom is attacked].

Condensation of benzamide oximes or their derivatives with the Appel salt **1a** gave, for the first time, 1,2,4-thiadiazole 4-oxides **90a–d**.[48] The reaction mechanism involves an attack of the imino group in the intermediate iminodithiazole **91** on the S(1) atom of the heterocycle.

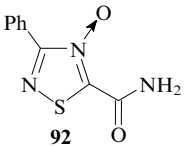


1a **91** **90a–d**

Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-$Me_2NC_6H_4$ (**d**).

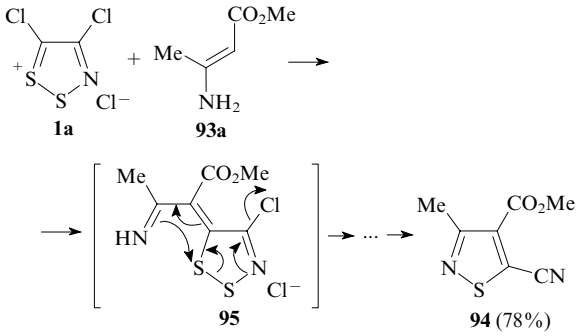
The structures of 4-oxides **90a–d** were confirmed by analysing mass spectra and NMR spectra of the ^{15}N-enriched

and usual reaction products, and also by X-ray diffraction data for carboxamide **92** obtained by hydrolysis of nitrile **90a**.[49]



92

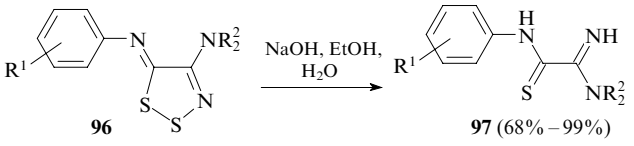
Methyl 3-aminocrotonate **93a** reacts with the Appel salt to form isothiazole **94** in high yield.[50] The spontaneous transformation of the hypothetical intermediate **95** into isothiazole also involves a nucleophilic attack on the S(1) atom of the heterocycle.



1a **93a** **95** **94** (78%)

This reaction is regarded as a version of the Boulton–Katritzky rearrangement where the triatomic side chain attacks the five-membered heterocycle, resulting in ring cleavage and formation of a new five-membered ring. Note that this recyclisation occurs under the extraordinarily mild conditions due to the easy cleavage of the S–S bond in 1,2,3-dithiazole and the formation of an aromatic isothiazole ring and a stable nitrile group.[50]

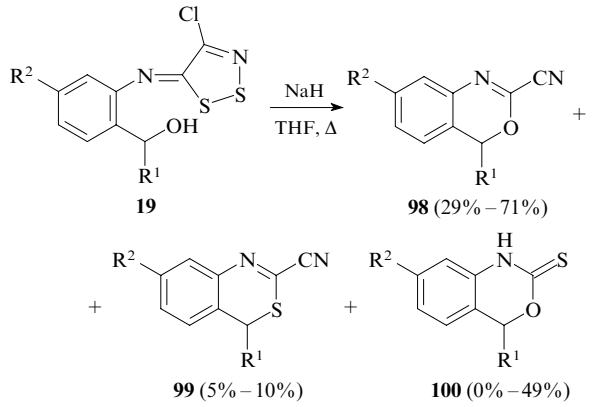
Various nucleophiles or reducing agents can attack the S(2) atom of the dithiazole ring. Thus treatment of arylimines **96** with sodium hydroxide in aqueous ethanol leads to thiocarbamoylformamidines **97** with high yields.[51] The formation of amidines is explained by the nucleophilic attack of the hydroxide anion on the S(2) atom with subsequent S–S bond cleavage of the dithiazole ring.



96 **97** (68%–99%)

R^1 = 4-NO_2, 4-Cl, 4-Br, 4-Me, 4-OMe, 3-NO_2; R^2 = Et, Pr^n, Bu^n.

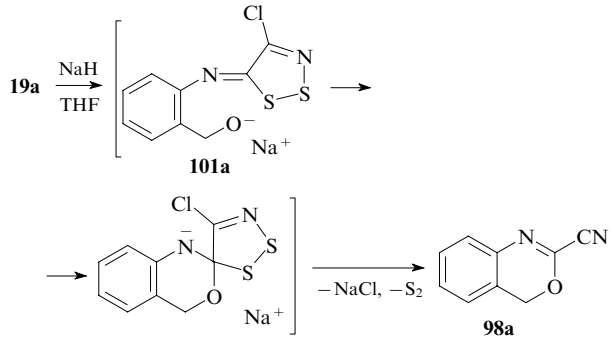
Refluxing of 5-[2-(hydroxymethyl)phenylimino]-4-chloro-5*H*-1,2,3-dithiazoles **19** (Ar = 2-HOCH(R^1)-5-$R^2C_6H_3$) with sodium hydride in tetrahydrofuran leads to a mixture of benzoxazines **98**, benzothiazines **99**, and benzoxazine-2-thiones **100**.[52]



19 **98** (29%–71%) **99** (5%–10%) **100** (0%–49%)

R^1 = H, Me; R^2 = H, Me, Cl.

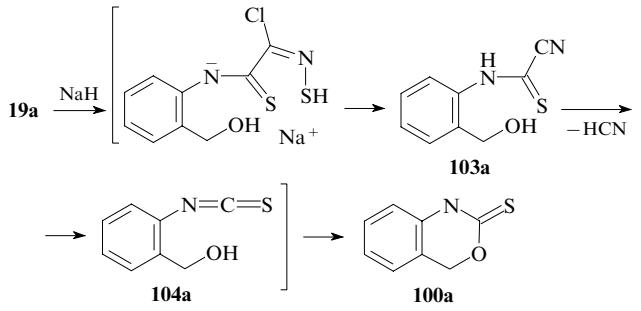
The mechanisms of all reaction routes are given below for compound **19a** (Ar = 2-$HOCH_2C_6H_4$) used as an example. The formation of the major reaction product benzoxazine **98a** may be represented as a nucleophilic attack of the alkoxide anion **101a**, generated from substituted benzyl alcohol under the action of sodium hydride, at the imine carbon atom with subsequent elimination of the diatomic sulfur molecule.



101a **98a**

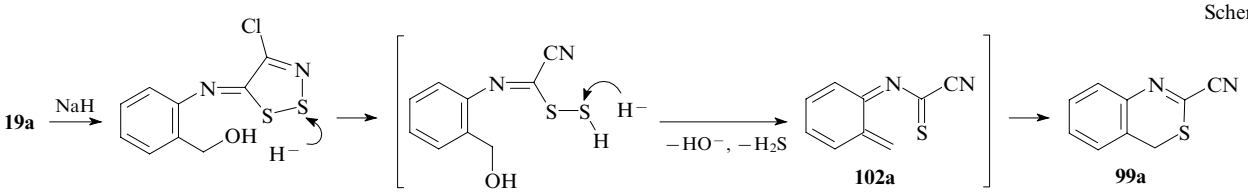
It was assumed that benzothiazine **99a** formed as a result of a nucleophilic attack of the hydride ion on the S(2) atom with cleavage of the dithiazole ring, followed by the elimination of hydrogen sulfide and water molecules and the intramolecular cyclisation of intermediate **102a** (Scheme 1).

The nucleophilic attack of the hydride ion on the S(2) atom and further opening of the dithiazole ring lead to *N*-[2-(hydroxymethyl)phenyl]cyanothioformamide (**103a**),



103a **104a** **100a**

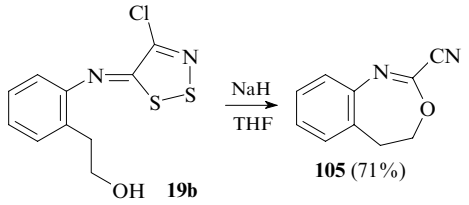
Scheme 1



102a **99a**

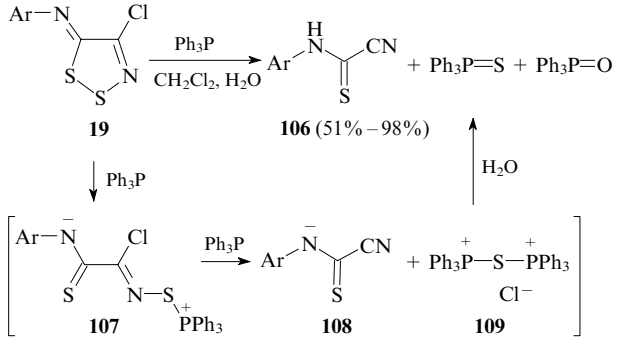
which forms 2-(hydroxymethyl)phenyl isothiocyanate **104a** after elimination of HCN. Intramolecular cyclisation of the latter gives benzoxazine-2-thione **100a**.

Dihydro-3,1-benzoxazepine **105**, a homologue of benzoxazine **98a**, was synthesised from imine **19b** by treatment of the latter with sodium hydride.[53]



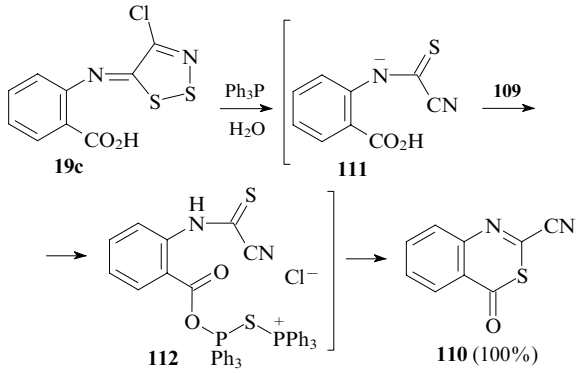
19b **105** (71%)

Triphenylphosphine and phosphorus ylides are known as convenient reagents for the removal of the sulfur atom from organic compounds. The reaction of 5-arylimino-4-chloro-1,2,3-dithiazoles **19** with two equivalents of triphenylphosphine in moist dichloromethane leads to *N*-arylcyanothioformamides **106** and triphenylphosphine sulfide and oxide.[54, 55] This transformation was explained as a nucleophilic attack of the triphenylphosphine molecule on the S(2) atom of imine **19** to form zwitterion **107**, which is attacked by another triphenylphosphine molecule on the same sulfur atom. This results in a stabilised cyanothioformamide ion **108** and dication **109**; hydrolysis of the latter leads to Ph_3PS and Ph_3PO.



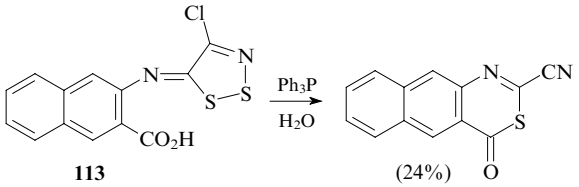
Ar = 2-$MeO_2CC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 2-NC-4,5-$(MeO)_2C_6H_2$, 2-MeO_2C-4,5-$(MeO)_2C_6H_2$.

Imine **19c** obtained from the Appel salt **1a** and anthranilic acid (without addition of pyridine at the final stage), reacts with triphenylphosphine to form 2-cyano-3,1-benzothiazin-4-one (**110**) in quantitative yield.[55] Presumably, imine **19c** generates thioamide anion **111**, which can add dication **109**. Intermediate **112** then undergoes cyclisation into benzothiazinone **110**.



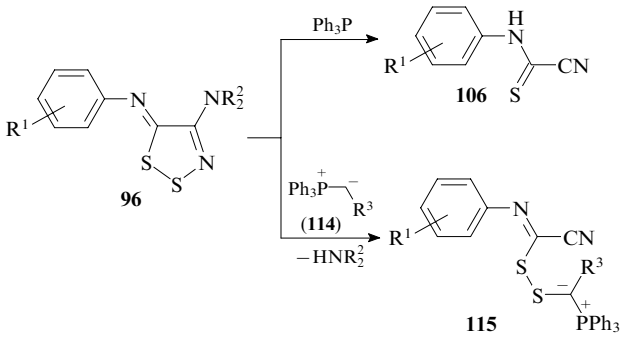
19c **111** **112** **110** (100%)

Imine **113** synthesised from 3-aminonaphthalene-2-carboxylic acid reacts with Ph_3P in a similar way.[55]



113 (24%)

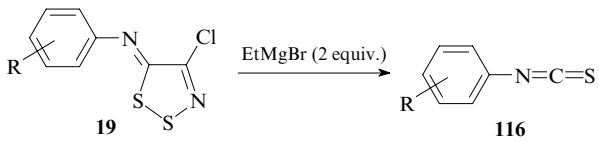
In their reactions with triphenylphosphine in moist dichloromethane, 4-amino-5-imino-1,2,3-dithiazoles **96**, like imines **19**, form *N*-arylcyanothioformamides **106**.[56]



R^1 = 2-OMe, 4-OMe, 2-CO_2Me, 3,4-$(OMe)_2$;
R^3 = CO_2Me, Ac, CN, 4-$ClC_6H_4C(O)$.

Compounds **106** can also be obtained from the appropriate imines and stabilised phosphoranes **114**. However, the major products of the latter reaction are dithiomethylenephosphoranes **115**, which unambiguously confirms the primary attack of the *P*-nucleophile on the S(2) atom of the heterocycle.[57]

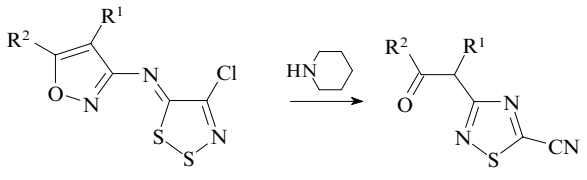
In the reaction of the Grignard reagents with imines **19** (Ar = RC_6H_4), the 1,2,3-dithiazole ring is opened probably upon the attack of the reagent on the S(2) atom. Addition of another equivalent of the Grignard reagent to the reaction mixture leads to aryl isothiocyanates **116**.[58]



19 **116**

R = H, 2-F, 2-CN, 4-OMe, 4-CN, *etc.*

Secondary amines can easily lead to the opening of the dithiazole ring as a result of an attack on a sulfur atom. One of the examples of this reaction is the rearrangement of isoxazolylimino-1,2,3-dithiazoles **117** into cyanothiadiazoles **118** under the action of piperidine.[59]

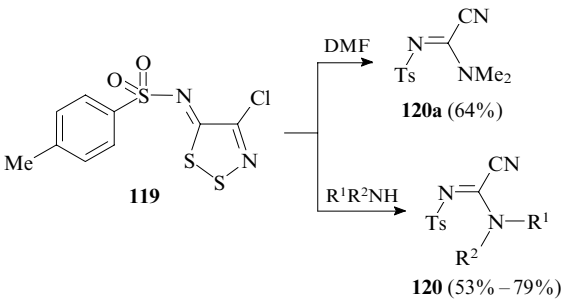


117 **118** (52%–80%)

R^1 = Me, Pr^i, Bu^n, Bu^t, Ph; R^2 = H, Me.

Boiling of 4-chloro-5-(4-tolylsulfonylimino)-5*H*-1,2,3-dithiazole (**119**) in dimethylformamide formed elementary

sulfur (19%) and *N′*-(4-tolylsulfonyl)-*N,N*-dimethylcyanoformamidine **120a** (64%).[60]

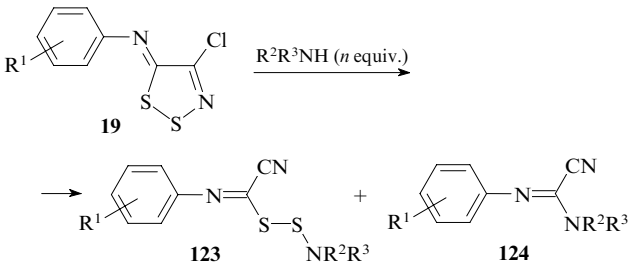


$R^1 = R^2 = Et$; $R^1 = H$: $R^2 = Pr^i$, Bu^i, $n\text{-}C_5H_{11}$;
$R^1 – R^2 = (CH_2)_4$, $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$; Ts = $4\text{-}MeC_6H_4SO_2$.

The formation of product **120a** suggested that dimethylamine formed as a result of the decomposition of DMF at high temperatures was directly involved in the reaction. Indeed, it was found that in reactions with imine **119** at room temperature, primary and secondary amines formed cyanoformamidines **120** in good yields.[61]

The mechanism of the reactions that form amidines **120** involves an amine attack on the S(2) atom of the 1,2,3-dithiazole ring, leading to disulfide **121**; further addition of the second amine molecule to the imine carbon atom; and elimination of S_2 molecules and one amine molecule (the one that was added to the sulfur atom) from intermediate **122** (Scheme 2).

The intermediate formation of disulfides **122** was confirmed by the isolation of similar compounds in the reactions of aryliminodithiazoles **19** (Ar = $R^1C_6H_4$) with various alkylamines. Thus mixtures of disulfides **123** and formamidines **124** were obtained from primary and secondary alkylamines at room temperature.[61] The product yields in these reactions are presented in Table 1.



As can be seen in Table 1, the reactions of imines **19** with amines proved sensitive to steric effects. For example, about half of the amount of the starting imine was recovered when isopropylamine was used (examples 4 and 8), and in the reaction with *tert*-butylamine, disulfide **123** did not form at all (example 14). In several cases, disulfide **123** was not detected in the reaction mixture because of its quick transformation into amidine **124** (see examples 6, 7, 9). The conclusion that disulfides **123** are intermediates in the reaction that forms

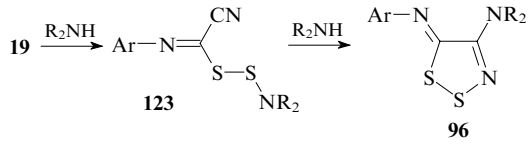
Table 1. Reaction products of 5-arylimino-1,2,3-dithiazoles **19** (Ar = $R^1C_6H_4$) with alkylamines.[61]

R^1	Example No.	Amine R^2	Amine R^3	*n* (see [a])	Yield (%) **19** [b]	**123**	**124**
4-OMe	1	$(CH_2)_5$		2.05	0	53	32
	2	$(CH_2)_4$		2.02	0	65	0
	3	$(CH_2)_4$		3.84	0	0	88
	4	Pr^i	H	2.02	55	14	0
	5	$(CH_2)_2O(CH_2)_2$		4.50	0	0	87
4-Me	6	$(CH_2)_5$		2.96	0	0	49
	7	$(CH_2)_4$		2.90	0	0	84
	8	Pr^i	H	2.21	49	23	0
	9	$(CH_2)_2O(CH_2)_2$		2.94	0	0	77
4-NO_2	10	$(CH_2)_5$		4.10	0	47	47
	11	$(CH_2)_4$		2.20	0	0	18
	12	Et	Et	7.92	0	0	48
	13	Pr^i	H	2.13	47	0	0
	14	Bu^t	H	3.92	14	0	0
3-NO_2	15	$(CH_2)_5$		5.84	0	0	26

[a] The number of equivalents of the amine; [b] the content of the unchanged substrate in the end mixture is indicated.

amidines **124** is confirmed by the fact that the yields of the latter increase when the amount of the isolated disulfide decreases. This hypothesis was finally confirmed by the reactions of disulfides **123** with primary and secondary amines, from which the corresponding amidines **124** were isolated in yields of up to 97%.

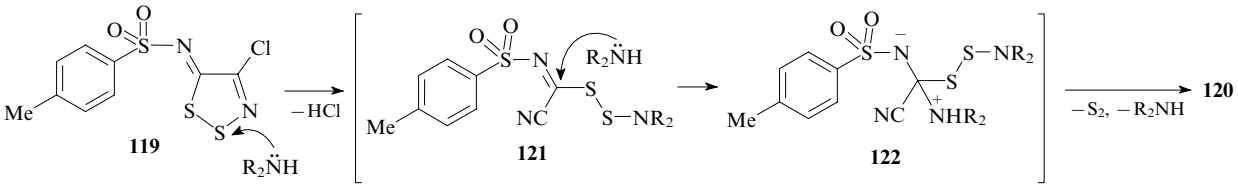
The reactions of 5-arylimino-1,2,3-dithiazoles **19** with a large excess of dialkylamines (diethyl-, dipropyl- and dibutylamines) at room temperature lead to 4-dialkylamino-5-arylimino-5*H*-1,2,3-dithiazoles **96**, which are the products of the formal replacement of the chlorine atom by the amino group.[62] The reactions evidently occur through cleavage of the heterocycle with intermediate formation of disulfides **123**.



Ar = Ph, $4\text{-}MeC_6H_4$, $2\text{-}ClC_6H_4$, $4\text{-}BrC_6H_4$, $3\text{-}O_2NC_6H_4$, $4\text{-}O_2NC_6H_4$, $2\text{-Cl-}5\text{-}O_2NC_6H_3$; R = Et, Pr^n, Bu^n.

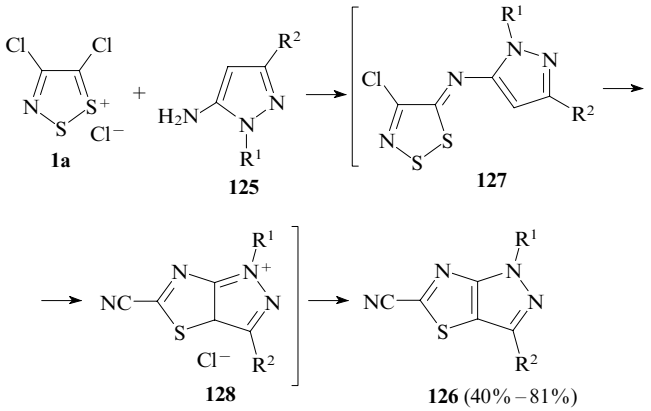
The yields of dithiazoles **96** depend on both the nature of the aryl substituent and the length of the alkyl chain of the amine. Disulfide **123** formed from compound **19** (Ar = $2\text{-Cl-}5\text{-}O_2NC_6H_3$) and diethylamine (R = Et) was isolated in pure form and reacted with an excess of diethylamine at room temperature. A UV study of the reaction mixture showed that the transformation of imine **19** (Ar = $2\text{-Cl-}5\text{-}O_2NC_6H_3$) into disulfide **123** occurred quickly and was followed by slow

Scheme 2



closure of the new dithiazole ring and formation of 4-dialkylamino derivative **96** (yield 26%).

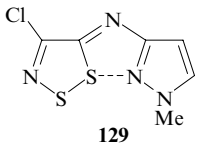
The Appel salt **1a** reacts with 5-aminopyrazoles **125** at room temperature in the presence of 2,6-dimethylpyridine unexpectedly leading to condensed 1*H*-pyrazolo[3,4-*d*]thiazoles **126**.[63] The authors assumed that these bicyclic compounds formed as a result of spontaneous intramolecular cyclisation of imines **127** *via* intermediates **128**.



1a **125** **127** **128** **126** (40%–81%)

R^1 = R^2 = Me, Ph; R^1 = Ph, R^2 = Me.

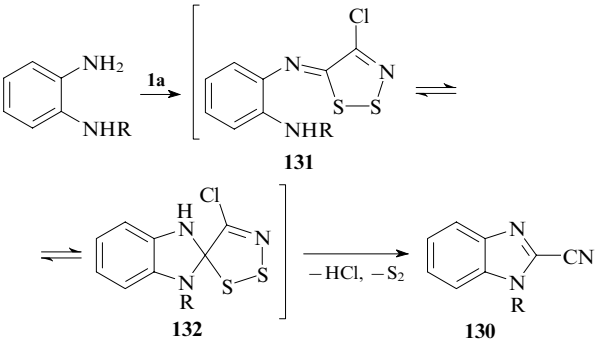
Evidently, the enamine fragment in intermediate **127** facilitates intramolecular cyclisation. Thus imine **129** formed from the Appel salt and 3-amino-1-methylpyrazole does not form bicyclic 2*H*-pyrazolo[3,4-*d*]thiazole by a similar mechanism. The thermal stability of imine **129** is explained by the S···N intramolecular interaction stabilising the molecule in the conformation that hinders the intramolecular cyclisation.[63]



129

b. Nucleophilic attack on the carbon atom of the heterocycle

N-Monosubstituted *o*-phenylenediamines react with the Appel salt **1a** in dichloromethane at room temperature to give 2-cyanobenzimidazoles **130**. The major stage of the reaction is thermal or acid-catalysed rearrangement of intermediate imino-1,2,3-dithiazoles **131**, which can be isolated from the reaction mixture.[64] The mechanism of this rearrangement involves a reversible attack of the *ortho*-amino group on the carbon atom of the heterocycle; spiro product **132** is aromatised with elimination of HCl and the diatomic sulfur molecule.

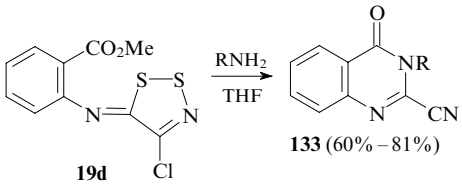


131 **132** **130**

R = Me, cyclo-C_6H_{11}, Ph, 4-ClC_6H_4, 2,4-$(O_2N)_2C_6H_3$, 4-methylpyridin-2-yl.

The formation of S_2 followed from the isolation of the corresponding cycloadducts with norbornene and 2,3-diphenylbuta-1,3-diene.[64]

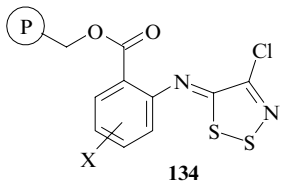
The reactions of compounds **19** containing fragments of methyl anthranylate derivatives as aryl substituents with amines[65–68] afford various heterocyclic systems. Thus the reactions of imine **19d**, obtained from methyl anthranylate and the Appel salt, with primary alkylamines in tetrahydrofuran at room temperature lead to 3-alkyl-2-cyanoquinazolin-4(3*H*)-ones **133**.[65]



19d **133** (60%–81%)

R = Me, Et, Pr^i, n-C_5H_{11}, Bn.

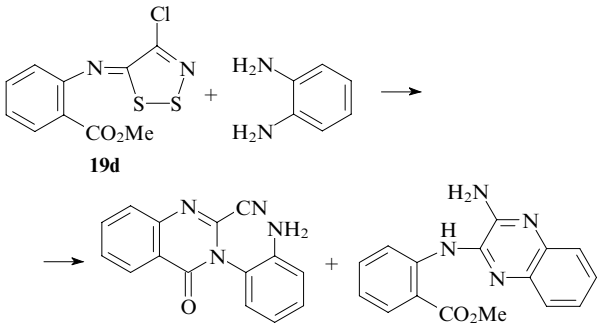
The derivatives of anthranilic acids linked by an ester bond with a polymeric matrix were converted into immobilised 5-arylimino-1,2,3-dithiazoles **134** by reactions with the Appel salt and then into 2-cyanoquinazolin-4(3*H*)-ones **133** upon subsequent treatment with various aliphatic amines.[66]



134

X = H, Cl, Me; (P) is polymer (Wang resin).

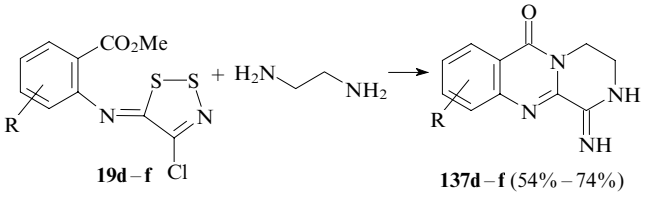
The reaction of imine **19d** with *o*-phenylenediamine in tetrahydrofuran at room temperature forms a mixture of the expected 2-cyanoquinazolinone **135d** and a 2-aminoquinoxaline derivative **136d**.[67]



19d **135d** (32%) **136d** (21%)

Both reaction products result from the attack of the diamine molecule on the C(5) atom of the dithiazole ring, which affords quinazoline **135d** and cyanothioformamide **106d** (Ar = 2-$MeO_2CC_6H_4$). The latter undergoes cyclisation into pyrazine **136d** under the action of another *o*-phenylenediamine molecule.

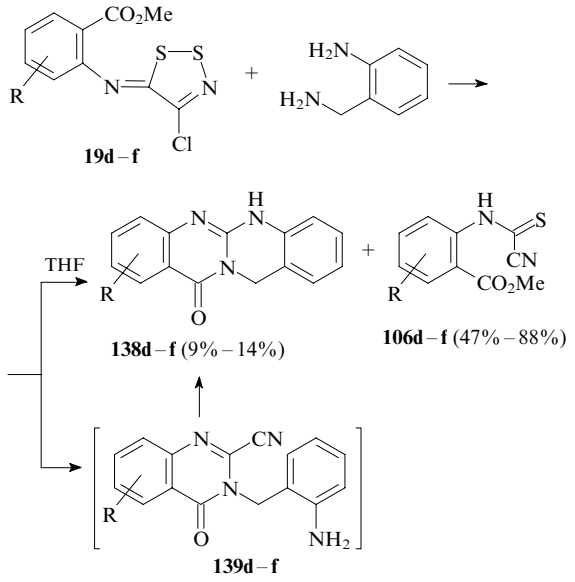
The reactions of imines **19d–f**, obtained from substituted anthranilic acid, with ethylenediamine lead to rare but biologically important tricyclic 3,3-dihydro-2*H*-pyrazino[2,1-*b*]-quinazolines **137d–f**.[68]



R = H (**d**), 5-Br (**e**), 4-Cl (**f**).

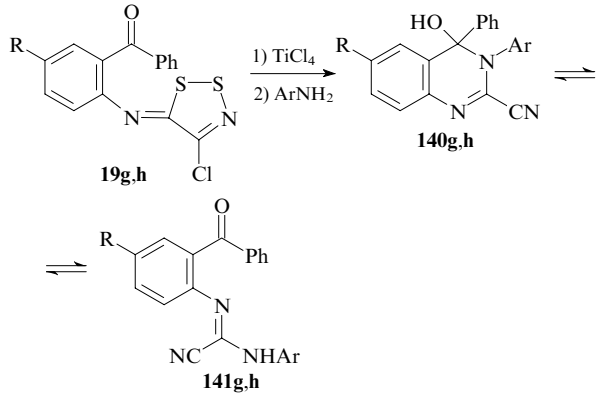
(Hereinafter, the positions of substituents in the benzene ring of the starting imine are indicated.)

Reactions of the same substrates with *o*-aminobenzylamine start with an attack of the aliphatic amino group predominantly on the sulfur atom of the 1,2,3-dithiazole ring (to form cyanothioformamides **106d**–**f**) and only partially on the carbon atom. In the latter case, new tetracyclic systems **138d**–**f** are formed. The process evidently occurs *via* intermediate 2-cyanoquinazolinones **139d**–**f**, which are analogues of compound **135d**.[67]



R = H (**d**), 5-Br (**e**), 4-Cl (**f**).

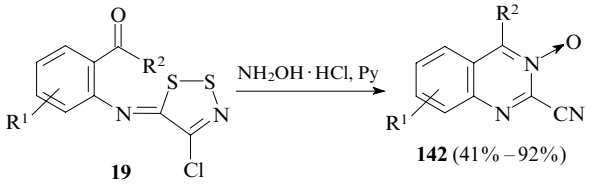
Aromatic amines do not react with arylamines **19g**,**h** even at the boiling point of the solvent (tetrahydrofuran). However, activation of the C(5) position of the dithiazole ring with a Lewis acid such as $TiCl_4$ leads to 4-hydroxy-4-phenylquinazolines **140g**,**h** in high yields.[68] An NMR spectroscopic study showed that in a deuterochloroform solution, compounds **140g**,**h** exist as an equilibrium mixture with the corresponding *N*-(2-benzoylaryl)cyanoformamidines **141g**,**h**.



R = H (**g**), Me (**h**); Ar = 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-ClC_6H_4, 4-$O_2NC_6H_4$, 2-ClC_6H_4, 3-ClC_6H_4.

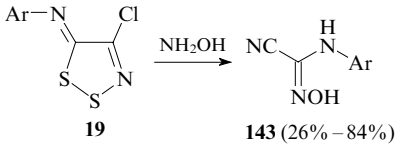
The mechanism of the transformation of **19g**,**h** involves a nucleophilic attack of the primary amino group on the C(5) atom of imine followed by elimination of HCl and S_2 molecules. An attack of the amidine fragment on the carbonyl group results in a quinazoline ring.[69]

The reactions of 5-arylimino-1,2,3-dithiazoles **19** with another *N*-nucleophile, namely, hydroxylamine occur readily. In the case of the *ortho*-acyl-substituted compounds **19**, 2-cyanoquinazoline 3-oxides **142** are formed in moderate to high yields.[70]



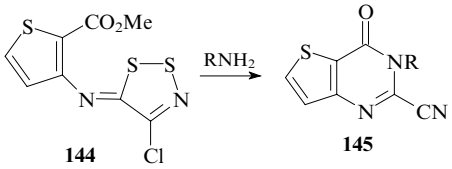
R^1 = H, 5-Me, 4-Cl; R^2 = Me, Ph.

If there is no acyl group in the *ortho*-position of the aromatic ring of **19**, the reactions produce *N*-arylcyanoformamide oximes **143**, which can be used as substrates for the synthesis of 4-substituted 2-cyanoquinazolines and 4-aryl-3-cyano-1,2,4-oxadiazin-5(6*H*)-ones.[70]



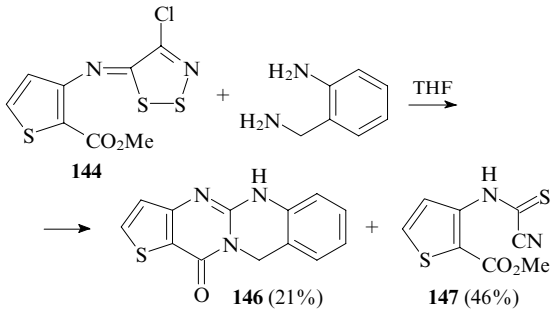
Ar = Ph, 4-BrC_6H_4, 4-ClC_6H_4, 4-$O_2NC_6H_4$, 2-$MeO_2CC_6H_4$, *etc*.

5-Imino-1,2,3-dithiazole **144**, prepared from the Appel salt and methyl 3-aminothiophene-2-carboxylate, reacts with various amines in the same way as compounds **19**. Its reactions with primary aliphatic amines yield 3-alkyl-2-cyanothieno[3,2-*d*]pyrimidin-4(3*H*)-ones **145**.[65, 71]



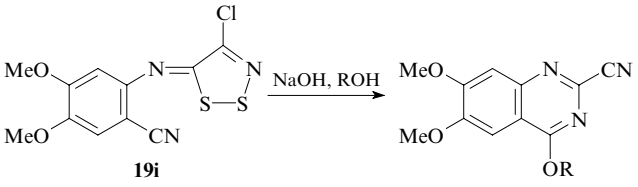
R = Me, Et, Pr^i, n-C_5H_{11}, Bn.

The reaction of compound **144** with *o*-aminobenzylamine in terahydrofuran led to a new heterocyclic system, **146**, in which the thienopyrimidine ring is fused with the quinazoline fragment.[72] However, the major reaction product was cyanothioformamide **147** formed, according to the above mechanism, as a result of two nucleophilic attacks of the aliphatic amino group on the sulfur atom of the iminodithiazole ring.



o-Phenylenediamine, which is less nucleophilic, does not react with imine **144**.

Reactions of dithiazoles with *O*-nucleophiles are also known. Thus treatment of iminodithiazole **19i** containing a nitrile group in the *ortho*-position to the imino group with an alkali in an aliphatic alcohol leads to quinazoline-2-carbonitriles **148**.[73] The probable mechanism of this transformation involves the addition of the alkoxide anion to the nitrile group and subsequent cyclisation and elimination of HCl and S_2 molecules.

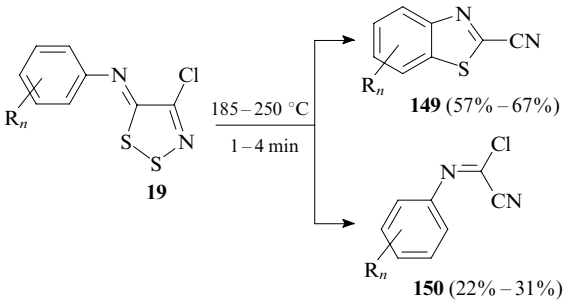


19i **148** (29% – 82%)

R = Me, Et, Pr^n, Pr^i, Bu^n, *etc.*

c. Thermolysis

5-Arylimino-1,2,3-dithiazoles **19** are readily converted into 2-cyanobenzothiazoles **149** on heating. This reaction underlies a simple two-stage method for the synthesis of these heterocycles from the corresponding aromatic amines.[21,30] The electron-donating substituents in the aniline ring favour this transformation, while the electron-withdrawing substituents hinder it; in the latter case, a side reaction occurs with a loss of both sulfur atoms of the dithiazole ring and formation of cyanoformimidoyl chlorides **150**.



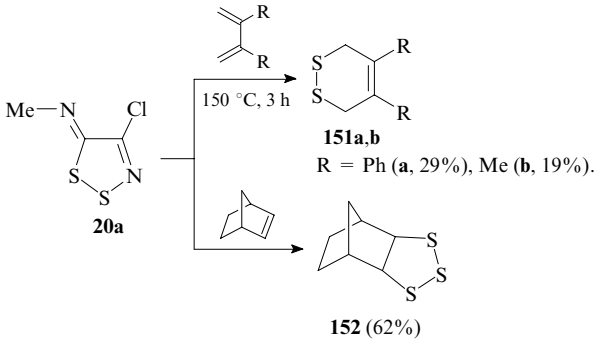
19 **149** (57% – 67%) **150** (22% – 31%)

R_n = H, 4-Me, 2,4-Me_2, 2,4,6-Me_3, 2,4,6-Et_3, 2-F, 2,4-F_2, 3,4-F_2, *etc.*

If both *ortho*-positions of the benzene ring contain substituents, compounds **150** become the sole reaction products (the yield is 22% for R_n = 2,4,6-Me_3 and 31% for R_n = 2,4,6-Et_3).[21] Arylimines **19** containing fluorine atoms in the aromatic ring also form mixtures of benzothiazoles **149** and imidoyl chlorides **150**.[74] The fluorine atoms are insufficiently strong electron-withdrawing substituents for the formation of imidoyl chlorides **150** to become the major reaction route; their yields are up to 20% (for R_n = 4-F, 2,4-F_2, 3,4-F_2).

Cyclisation of imines **19** into 2-cyanobenzothiazoles **149** occurs upon irradiation in a microwave oven in a high-boiling solvent such as *N*-methylpyrrolidin-2-one at 150 °C or if the reaction is performed without a solvent in the presence of graphite at the same temperature.[75] The product yields are moderate under these conditions (45% – 52%).

5-Alkyliminodithiazoles **20** often decompose at lower temperatures than the aryl derivatives.[21] For example, when heated to 150 °C in a sealed tube with 2,3-diphenyl- and 2,3-dimethylbuta-1,3-dienes, methylimine **20a** forms 1,2-dithiines **151a**,**b**, which are the known products of the Diels – Alder reaction involving the diatomic sulfur molecule in the singlet state. Under the same conditions, norbornene affords trisulfide **152**. Note that compounds **151** and **152** are not formed when elementary sulfur is heated with alkene under the same conditions.

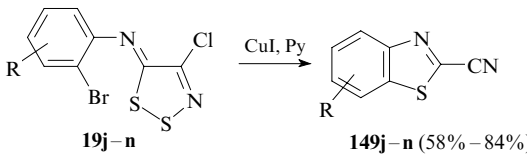


20a **151a**,**b**

R = Ph (**a**, 29%), Me (**b**, 19%).

152 (62%)

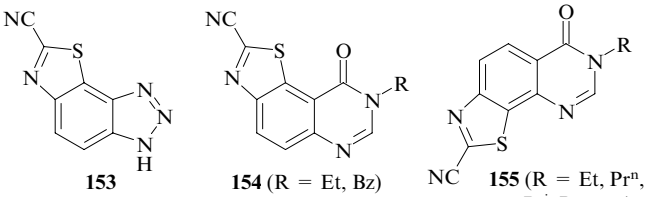
The reactions of *o*-bromophenyl derivatives of imines **19j** – **n** in the presence of copper(I) iodide in boiling pyridine lead to 2-cyanobenzothiazoles **149j** – **n** in good yields.[76] Performing this reaction in a microwave reactor decreased the reaction time, but not the yields of the final products (61% – 87%). It is assumed that elimination of the sulfur atom and cyclisation into the thiazole ring are favoured by the formation of a complex of the bromine atom with univalent copper.



19j – **n** **149j** – **n** (58% – 84%)

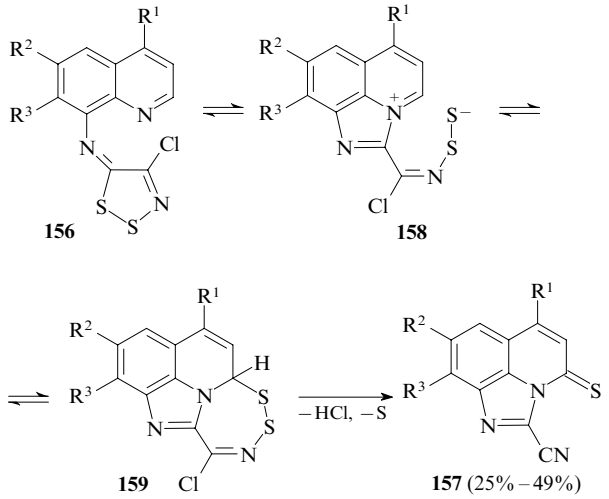
R = H (**j**), 4-F (**k**), 4-Me (**l**), 4-NO_2 (**m**), 5-CF_3 (**n**).

Using a similar procedure, a number of cyano-substituted thiazolobenzotriazoles **153**[77] and isomeric thiazoloquinazolinones **154**, **155** have been obtained,[78] which inhibit growth of tumour cells.[79]



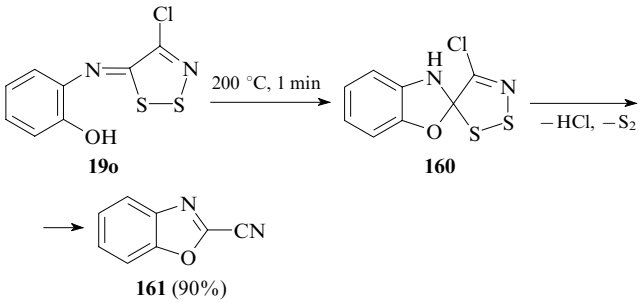
153 **154** (R = Et, Bz) **155** (R = Et, Pr^n, Pr^i, Bn, *etc.*)

Thermolysis of imino-1,2,3-dithiazoles **156** prepared from the Appel salt (**1a**) and 8-aminoquinolines for 1 min at 200 °C unexpectedly leads to imidazoquinolinethiones **157**.[80,81] The mechanism of this unusual rearrangement suggests that the nitrogen atom of the quinoline ring is involved in the formation of imidazoquinoline **158**, cyclised into tetracyclic structure **159**. After liberation of HCl and elimination of one sulfur atom from the seven-membered ring of **159**, the final product **157** is formed.



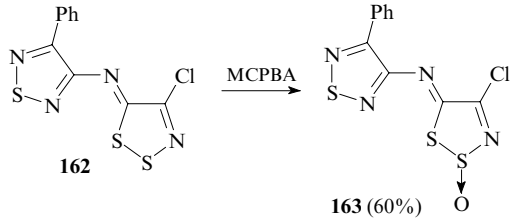
R^1 = H, Ph; R^2 = H, OMe; R^3 = H, Me.

Thermolysis of (*o*-hydroxyphenyl)imine **19o** occurs with elimination of the diatomic sulfur molecule and hydrogen chloride presumably *via* the intermediate spiro compound **160**, and leads to 2-cyanobenzoxazole **161** in a high yield.[30]

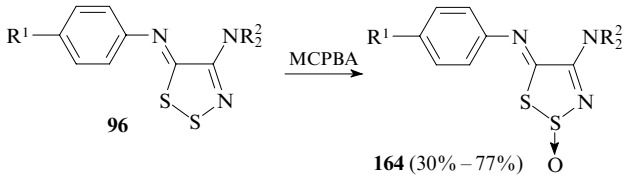


d. Oxidation and reduction

Oxidation of imine **162** with *m*-chloroperoxybenzoic acid (MCPBA) in dichloromethane forms *S*-oxide **163**.[27] The S(1) atom in molecule **162** is evidently less nucleophilic than the S(2) atom because of the displacement of electron density towards the imine nitrogen atom.

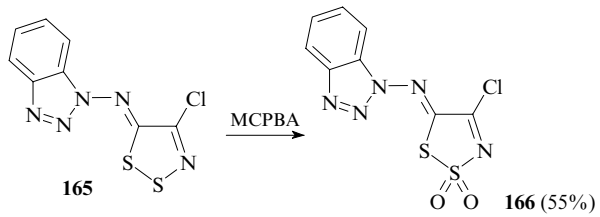


More recently, a number of 4-dialkylamino-5-imino-1,2,3-dithiazoles **96** were oxidised to 2-*S*-oxides **164** under the same conditions.[51]

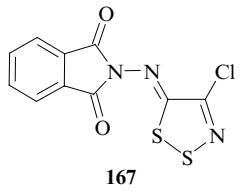


R^1 = Me, Br, OMe, NO_2; R^2 = Et, Pr^n, Bu^n.

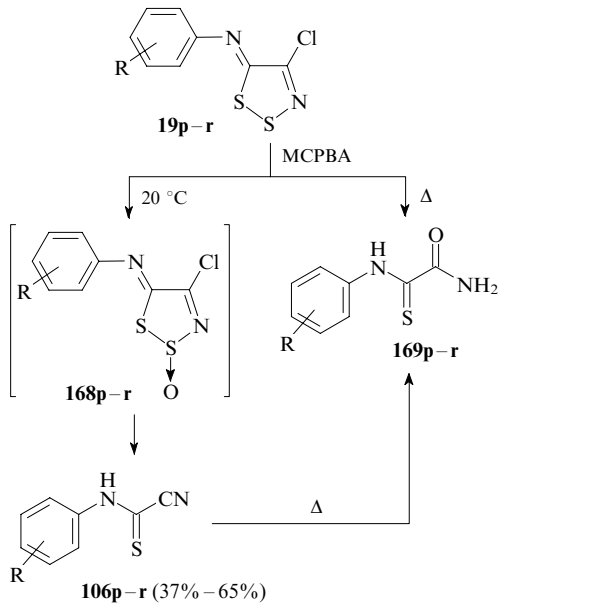
Prolonged storage of imine **165** with *m*-chloroperoxybenzoic acid at room temperature leads to *S*,*S*-dioxide **166** in moderate yield.[82]



However, the similar phthalimide derivative **167** was not oxidised under mild conditions. Thus 82% of the starting compound was recovered in the reaction with MCPBA, 62% in the reaction with potassium permanganate in acetone, and 80% in the reaction with nitrogen dioxide in dichloromethane.[82]



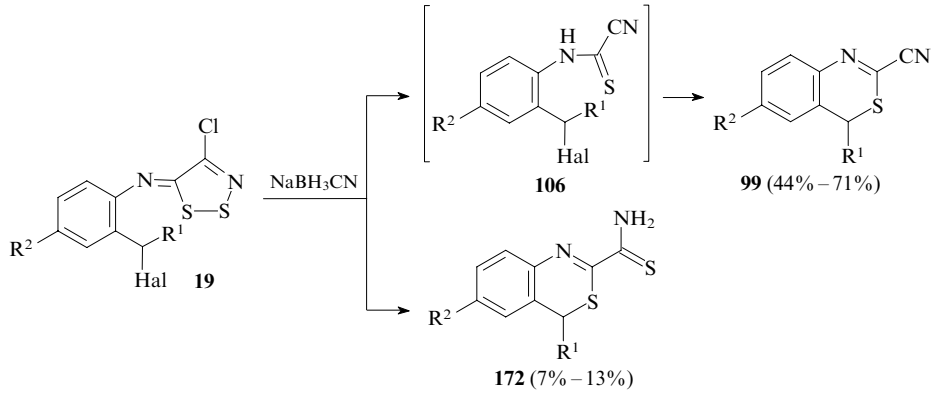
Oxidation of the dithiazole derivatives with MCPBA occasionally was more profound. In all cases, however, the intermediate is supposed to be mono-2-*S*-oxide. Thus the reaction of arylimines **19** with MCPBA at room temperature leads to cyanothioformamides **106** obviously *via* *S*-oxide **168**. Oxidation of the same substrate with excess reagent in boiling dichloromethane affords thioamide **169**. The latter results from oxidative hydration of the nitrile group of compound **106**, which occurs in 80% yield.[74]



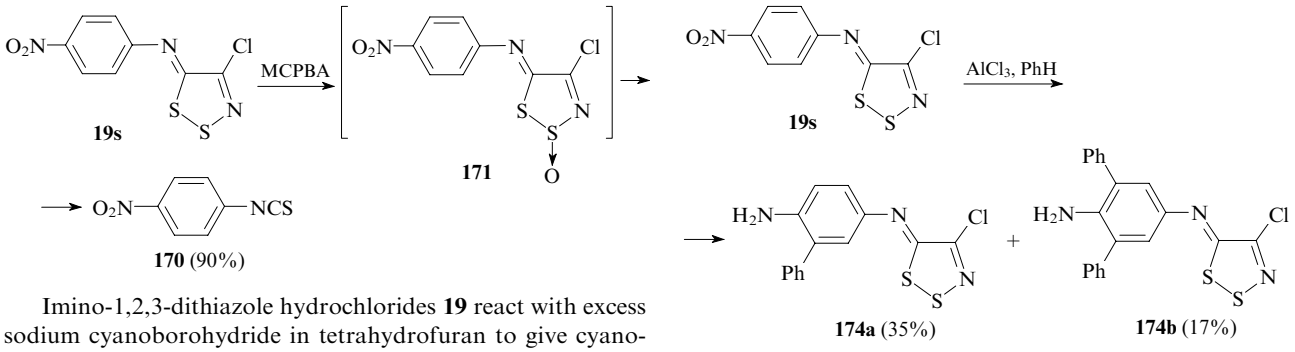
R = 4-Me (**p**), 4-F (**q**), 2-F (**r**).

When oxidised with MCPBA, 4-nitrophenylimine **19s** is unexpectedly quantitatively converted into 4-nitrophenyl isothiocyanate **170**.[74] In this case again it is assumed that the reaction occurs *via* *S*-oxide **171**.

Scheme 3



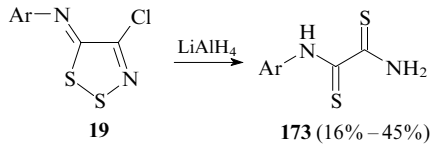
R^1 = H, Me; R^2 = H, Cl; Hal = Cl, Br.



Imino-1,2,3-dithiazole hydrochlorides **19** react with excess sodium cyanoborohydride in tetrahydrofuran to give cyanothioformamides **106** in high yields.[83] Note that the same products were obtained in the oxidation of 1,2,3-dithiazole imines with bases (see above).

With sodium cyanoborohydride, *ortho*-halomethyl derivatives of arylimines **19** [Ar = 2-(HalCHR^1)-4-R^{2}C$_6$H$_3$] form a mixture of 2-cyano- (**99**) and 2-thiocarbamoylbenzothiazines (**172**).[52] The thiazine ring in these molecules is probably formed upon cyclisation of the intermediate cyanothioformamide **106** (Scheme 3).

5-Arylimino-1,2,3-dithiazoles **19** can be transformed into *N*-aryldithiooxamides **173** by reactions with lithium aluminium hydride.[84] Although the yields of the end products are moderate, this is a convenient two-stage procedure for the synthesis of the non-symmetrical derivatives of rubeanic acid from aromatic amines.

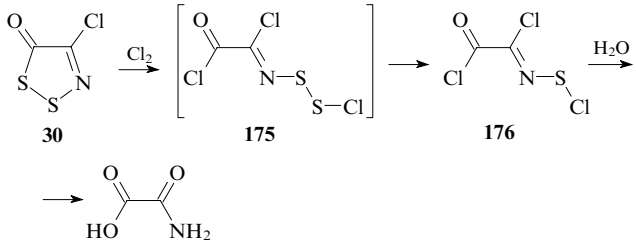


Ar = Ph, 4-MeOC$_6$H$_4$, 2-ClC$_6$H$_4$, 3,4-F$_2$C$_6$H$_3$, 3,4,5-(MeO)$_3$C$_6$H$_2$, *etc.*

Arylation of 4-nitrophenylimine **19s** with benzene in the presence of anhydrous $AlCl_3$ leads to compounds **174a**,**b** containing an amino group in the benzene ring. The best product yields were obtained by refluxing the reactants in benzene in the presence of a 14-fold excess of $AlCl_3$.[85] Notably, the 1,2,3-dithiazole ring remains intact in this transformation.

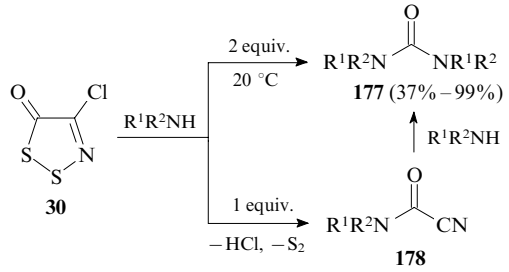
2. Reactions of 1,2,3-dithiazol-5-ones

Interaction of 4-chloro-5*H*-1,2,3-dithiazol-5-one (**30**) with chlorine at room temperature in dichloromethane is a sluggish reaction that gives a mixture of unchanged dithiazolone **30** with chlorodisulfide **175** and sulfenyl chloride **176**.[1] Intermediate **175** is thermally unstable and is converted, on gentle heating, into a more stable compound, **176** (90% yield). The latter is readily hydrolysed to oxalic acid monoamide when stored in a moist atmosphere for 5 days.



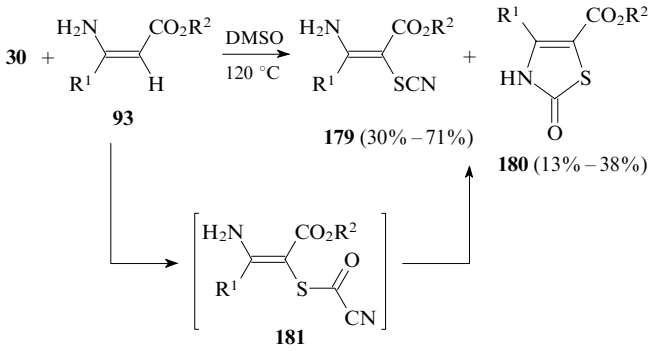
The reactions of primary or secondary amines with dithiazolone **30** lead to symmetrical *N*,*N*′-disubstituted or *N*,*N*,*N*′,*N*′-tetrasubstituted ureas **177** in moderate to high yields.[86] In the case of the less nucleophilic amino acid esters, activation with a more than a twofold excess of triethylamine is required; this reaction forms cyanoformamides **178** in addition to disubstituted ureas. Compounds **178** can be converted into substituted ureas **177** by reactions with amines. The ureas are probably formed upon the nucleophilic attack of the alkylamine molecule on the carbonyl carbon atom of dithiazolone

30 with subsequent elimination of S_2 and HCl molecules and formation of cyanoformamide **178**. Replacement of the cyano group by an alkylamino group in the latter leads to ureas **177**.



R^1 = Et, Pr^n, Pr^i, Bu^t, n-C_5H_{11}, n-C_6H_{13}, CH_2—CH=CH_2, *etc.*;
R^2 = H, Et, Pr^n, CH_2—CH=CH_2.

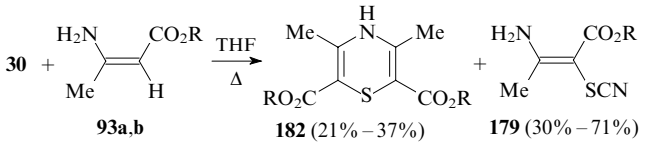
Treatment of dithiazolone **30** with α,β-unsaturated β-amino acid esters in dimethyl sulfoxide at 120 °C leads to mixtures of unsaturated thiocyanates **179** and thiazolin-2-ones **180**,[87] the former being the major reaction products.



R^1 = Me, Pr^n, n-C_5H_{11}, CH_2Bn; R^2 = Me, Et, Bu^t, CH_2—CH=CH_2.

It is conceivable that the reaction starts with a nucleophilic attack of the enamine carbon atom on the S(1) atom of dithiazolone **30**, and intermediate **181** is formed after the elimination of the sulfur atom and HCl. The latter can lead to both thiocyanate **179** (*via* an intramolecular rearrangement with elimination of carbon monoxide) and thiazolinone **180** (*via* cyclisation with elimination of the HCN molecule).[87]

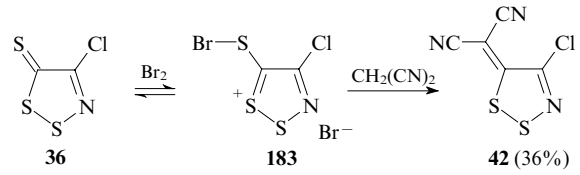
Note that the reaction route depends considerably on the solvent used. Thus, if the reaction is conducted in boiling tetrahydrofuran, 1,4-thiazines **182** are formed along with compounds **179**.[87]



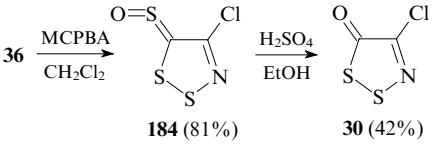
R = Me (**a**), Et (**b**).

3. Reactions of 1,2,3-dithiazole-5-thiones

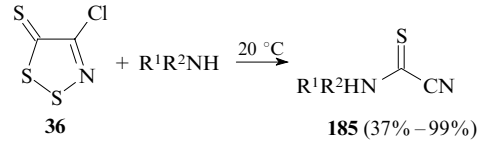
4-Chloro-5*H*-1,2,3-dithiazole-5-thione (**36**) reacts with bromine to form 5-bromosulfanyl-4-chloro-1,2,3-dithiazolium bromide **183**.[31] This salt is relatively stable at room temperature in an inert atmsophere, but is converted back to thione **36** when stored in air. The structure of **183** was proved by spectroscopic and elemental analyses and confirmed by the reaction with malononitrile, leading to ylidene derivative **42**.



Oxidation of thione **36** with *m*-chloroperoxybenzoic acid in cooled dichloromethane leads to sulfine **184**,[30] which is readily hydrolysed with sulfuric acid in ethanol to form dithiazolone **30**.

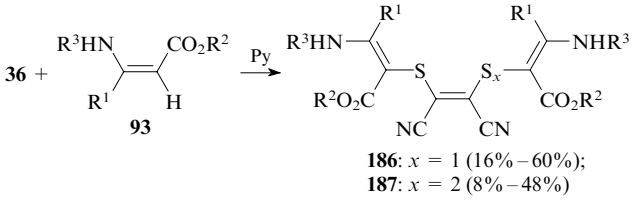


Interaction of compound **36** with primary and secondary alkylamines leads to mono- and dialkylcyanothioformamides **185**, respectively.[88] Two possible mechanisms are suggested for these reactions, namely, nucleophilic attack on the C(5) atom of alkylamine or on the S(2) atom of dithiazole with subsequent elimination of S_2 and HCl molecules. It was not discussed which mechanism was preferable.[88]



R^1, R^2 = H, Me, Et, Bn, Pr^n, Pr^i, Bu^t, n-C_5H_{11}, *etc.*

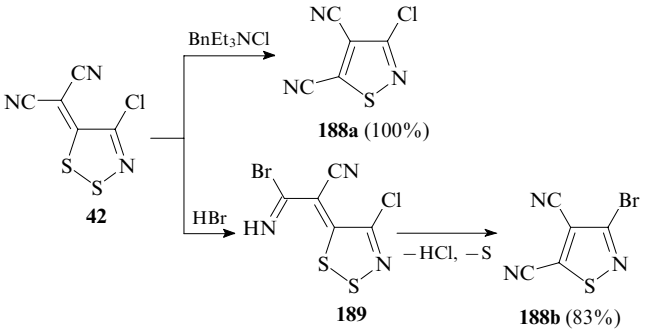
In the presence of pyridine, thione **36** reacts with 3-alkyl-(aryl)-3-aminoacrylates **93** to form a mixture of dicyanovinylsulfanyl- (**186**) and -disulfanyl derivatives (**187**) generally in moderate yields.[89] The original work presented the complex mechanism of these reactions that includes a nucleophilic attack on the S(1) and S(2) atoms of the heterocycle followed by dimerisation of the intermediates.



R^1 = Me, Et, CF_3, Ph; R^2 = Me, Et; R^3 = H, Pr^i, Bn, 4-ClC_6H_4.

4. Reactions of 5-alkylidene-5*H*-1,2,3-dithiazoles

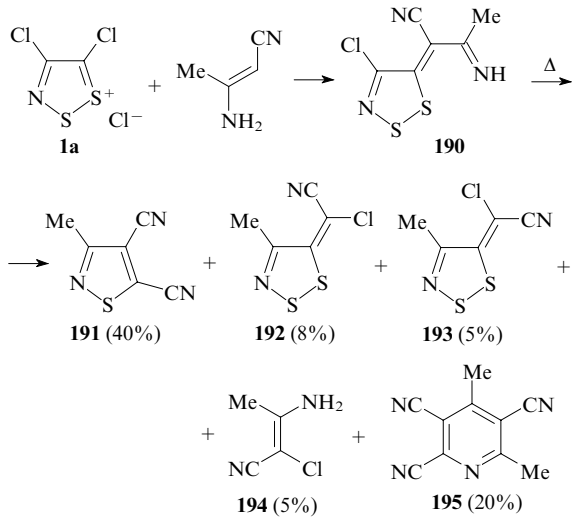
It was shown [29] that dicyanomethylidenedithiazole **42** reacted with compounds containing the chloride ion (for example, with quaternary ammonium salts) to form 3-chloro-4,5-dicyanoisothiazole **188a**. A similar bromo derivative, **188b**, was synthesised by a reaction of dithiazole **42** with hydrobromic acid.[31]



42 **188a** (100%) **189** **188b** (83%)

In the latter case, the formation of the isothiazole ring probably involves an attack of the imine nitrogen atom of the intermediate imidoyl bromide **189** on the S(1) atom of 1,2,3-dithiazole.[31]

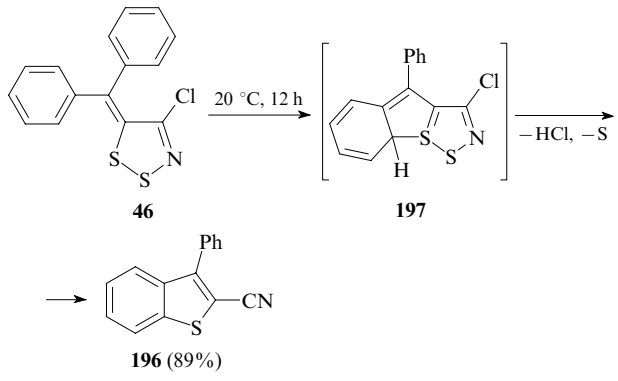
The ylidene derivative **190**, obtained from the Appel salt and β-aminocrotononitrile, decomposes into five products, namely, dicyanoisothiazole **191**, ylidenedithiazoles **192** and **193**, the chlorination product of the starting nitrile **194** and 2,3,5-tricyano-4,6-dimethylpyridine **195**.[50]



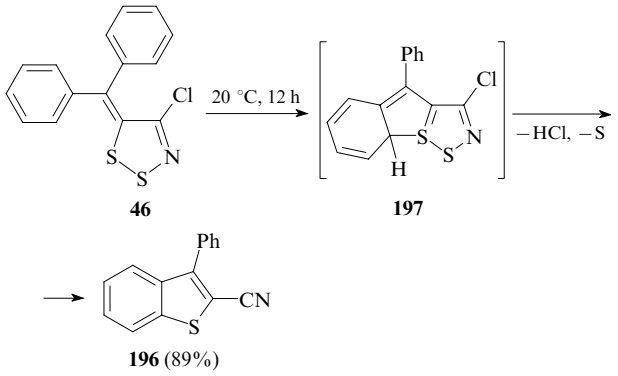
1a **190** **191** (40%) **192** (8%) **193** (5%) **194** (5%) **195** (20%)

It was assumed [50] that the most unusual reaction product, substituted pyridine **195**, formed as a result of the addition of another enamine molecule to ylidene **190**; then cyclisation into a pyridine ring occurred with elimination of S_2, HCl, and NH_3 molecules.

At room temperature dithiazole **46** is unstable and, after being stored overnight, is quantitatively rearranged into benzothiophene **196** with elimination of sulfur and hydrogen chloride presumably from intermediate **197**.[29] This reaction is a new route to the thiophene ring, and its easy occurrence is explained by the high stability of the benzothiophene system and the presence of a nitrile group.

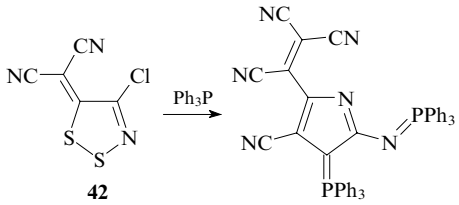


46 **197** **196** (89%)



46 **197** **196** (89%)

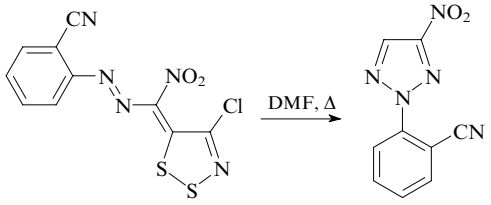
Ylidene **42** reacts with triphenylphosphine to form 3*H*-pyrrolo-3-ylidenophosphorane **198**; its structure



42 **198** (24%)

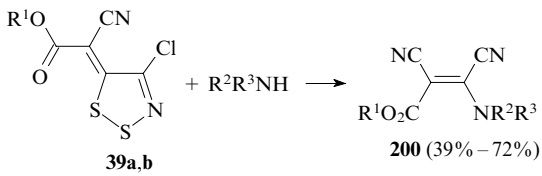
was established by X-ray diffraction.[90] The complex mechanism of this reaction includes the primary attack of triphenylphosphine on the S(2) atom of the 1,2,3-dithiazole ring and is discussed in detail elsewhere.[90]

After being refluxed in DMF for a short period of time, 1,2,3-dithiazole **44a** leads to triazole **199**.[33] The major stage of this unusual transformation is probably the reaction of dithiazole with dimethylamine formed from DMF during heating. The structure of triazole **199** was proved by X-ray diffraction.



44a **199** (48%)

The reactions of (4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-cyanoacetates **39a**,**b** with primary and secondary amines yield (*Z*)-3-alkylamino-2,3-dicyanoacrylates **200** in moderate to high yields.[91] The latter is formed by the nucleophilic attack of alkylamine on the C(5) atom of the dithiazole ring, liberating S_2 and HCl and forming the stable nitrile group.

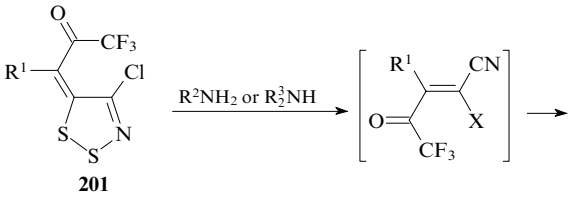


39a,**b** **200** (39%–72%)

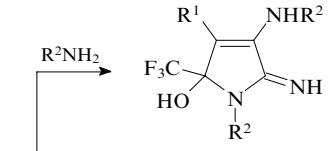
R^1 = Me, Et; R^2, R^3 = Me, Et, Pr^n, Pr^i, Bu^n, n-C_5H_{11}, CH_2—CH=CH_2.

Reactions of trifluoroacetylmethylidene derivatives of 1,2,3-dithiazoles **201** with alkylamines differ substantially from the above reaction. Thus primary amines are transformed

into hydroxyiminopyrroles **202** under these conditions, and secondary amines form iminodihydrofurans **203**.[91] The key intermediates in the synthesis of these heterocycles are assumed to be cyanoenamino ketones, which are analogues of **200**.

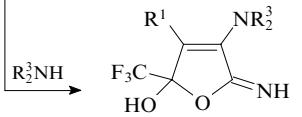


201



202 (22% – 55%)

R^1 = H, CO_2Et, C(O)Ph;
R^2 = Me, Et, Pr^i, n-C_5H_{11}.

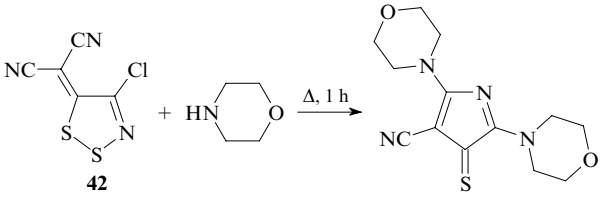


203 (18% – 62%)

R^1 = CO_2Et, C(O)Ph;
R^3 = Et, Pr^n; $R^3 - R^3$ = $(CH_2)_2O(CH_2)_2$.

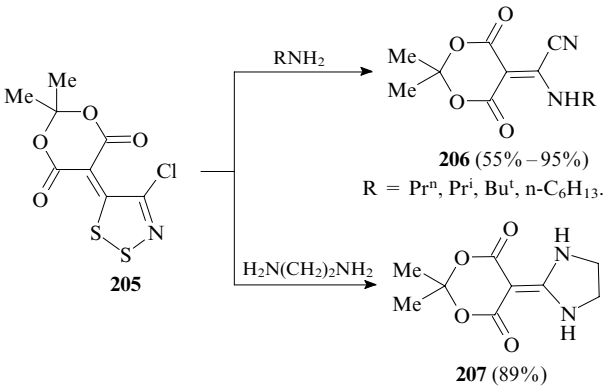
X = NHR^2 or NR^3_2.

The formation of the pyrrole ring from the 1,2,3-dithiazole ring was also observed in the reaction of dicyanomethylidene derivative **42** with an excess of morpholine.[90] After the reaction mixture was refluxed for 1 h, 4-cyano-2,5-dimorpholino-3*H*-pyrrole-3-thione (**204**) was isolated.



42 **204** (31%)

The reaction of ylidene **205**, obtained from the Appel salt (**1a**) and Meldrum's acid, with primary amines terminates after the formation of (alkylamino)cyanomethylidene derivative **206**.[92] Ethylenediamine forms imidazolidin-2-ylidene **207** under these conditions as a result of the replacement of the nitrile group by the amino group of the diamine. Similar products were also obtained from other diamines.

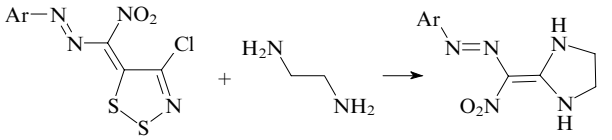


205 **206** (55% – 95%)

R = Pr^n, Pr^i, Bu^t, n-C_6H_{13}.

207 (89%)

Interaction of the azo derivatives of 1,2,3-dithiazole **44a**,**b** with ethylenediamine leads to dihydroimidazoles **208a**,**b**, which are structurally related to compound **207**.[33]

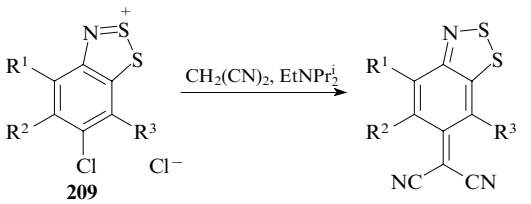


44a,**b** **208a**,**b** (53% – 55%)

Ar = 2-NCC_6H_4 (**a**), 4-FC_6H_4 (**b**).

5. Reactions of fused 1,2,3-dithiazoles

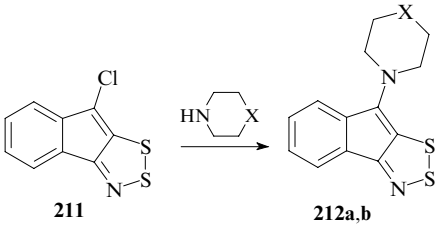
The Hertz salts **209** containing chlorine atoms in the position 6 of the benzodithiazole ring react with malononitrile to form deep-coloured ylidenes **210**.[93] This is a general reaction for all Hertz salts studied, which is, though, occasionally complicated by side processes. The respective products, 2-cyanobenzothiazoles and benzo-1,2,3-dithiazole 2-oxides, were isolated and identified (see Ref. 93).



209 **210** (5% – 40%)

R^1, R^2, R^3 = H, Me, OMe.

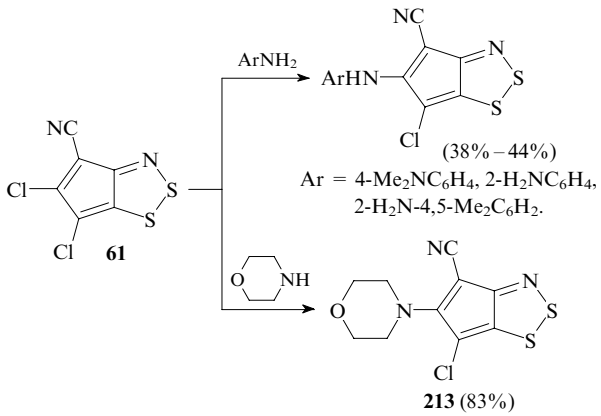
Chlorinated cyclopenta-1,2,3-dithiazoles can easily exchange chlorine atoms with the amino group. Thus 8-chloroindenodithiazole **211** reacts with morpholine and piperidine in tetrahydrofuran.[34] However, the yields of the corresponding products **212a**,**b** were moderate evidently because of the insufficient mobility of the chlorine atom in the substrate.



211 **212a**,**b**

X = O (**a**, 14%), CH_2 (**b**, 42%).

The more active chlorine atom in the position 5 of the 5,6-dichloro-4-cyanocyclopenta-1,2,3-dithiazole molecule (**61**) is



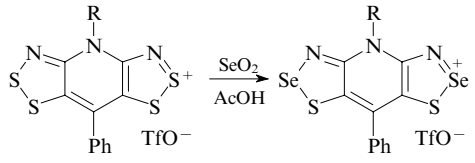
61 **213** (83%)

(38% – 44%)

Ar = 4-$Me_2NC_6H_4$, 2-$H_2NC_6H_4$, 2-H_2N-4,5-$Me_2C_6H_2$.

readily replaced under the action of morpholine (forming compound **213**) or aromatic amines.[42] The selectivity of these reactions (substitution only at the position 5) is explained by the effect of the vicinal nitrile group on the mobility of this chlorine atom.

The sulfur atoms were replaced by selenium atoms by refluxing salts **11a**,**d** with selenium dioxide in acetic acid.[94]



11a,**d**

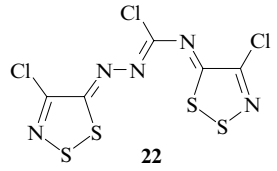
R = Me (**a**, 83%), Et (**d**, 96%).

IV. Spectral studies

1. X-Ray diffraction analysis

One of the most outstanding achievements in the field of X-ray diffraction analysis of 1,2,3-dithiazoles is investigation of 4,5-dichloro-1,2,3-dithiazolium chloride or the Appel salt (**1a**).[22] In this compound, the positive charge is not concentrated on the S(1) atom, but is delocalised. This leads to a shortening of the S−S bond [2.034(2) Å] compared with the ordinary single S−S bond, the length of the former being only slightly larger than its analogue in a completely delocalised 1,2,3-dithiazole ring [2.023 Å]. The Cl^- anion in the Appel salt (**1a**) is almost equidistant from both sulfur atoms of the 1,2,3-dithiazole ring; the distance is 2.932(2) Å to the S(1) atom and 2.974(2) Å to the S(2) atom. The chloride anion is shifted by only 0.34 Å from the plane of the dithiazole ring and lies at a distance of electrostatic interaction with another 1,2,3-dithiazole molecule (Fig. 1).

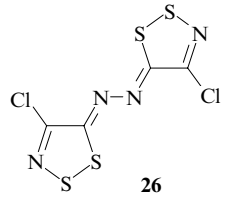
The bis(1,2,3-dithiazole) molecules **22** are planar and lie on the mirror crystallographic planes.[22]



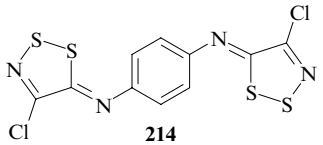
22

The two heterocycles have almost identical geometric parameters; the bond lengths differ significantly from the corresponding parameters of **1a**. Nearly all ring bonds except the C=N bonds, which are clearly double bonds [1.276(3) and 1.278(3) Å], are considerably longer than the same bonds in **1a** (1.319 Å), and their values are closer to the lengths of single bonds.

The crystal structures of bis(1,2,3-dithiazoles) **26** and **214** were determined by X-ray diffraction.[24]



26



214

The bis(dithiazole) molecules **26** lie at the crystallographic inversion centres and are nearly planar (within 0.03 Å). The bond lengths in compound **26** are close to those in bis(dithiazoles) **43** (see below) and are quite consistent (as well as the length of the N−N single bond) with an azine resonance structure. The bis(dithiazolyl)benzene molecule **214** is also centrosymmetric but nonplanar. To avoid steric hindrances between the S(1) and H−C(3) atoms, the dithiazole ring (which is planar within 0.07 Å) is rotated around the N(1)−C(4) bond, forming a dihedral angle of 137.30(7)° with the plane of the benzene ring. As a result of this torsional rotation, conjugation with the benzene ring is considerably weakened.

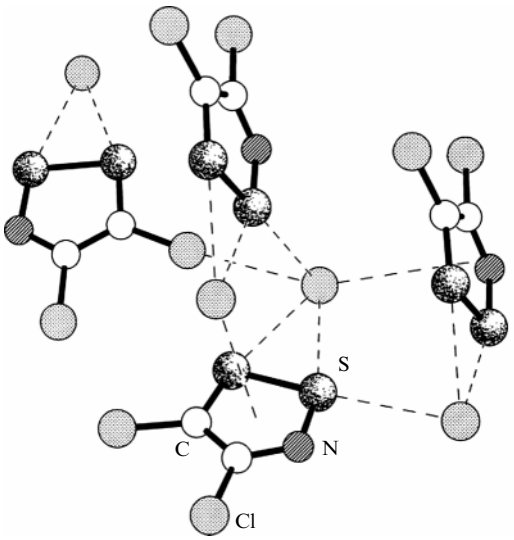
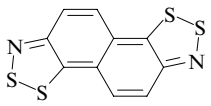
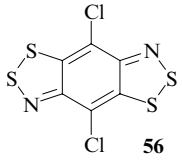


Figure 1. Packing of molecules **1a** in crystal (X-ray diffraction data).[22]

The molecules of fused bis(1,2,3-dithiazoles) **53**[14] and **56**[37] also lie at the crystallographic inversion centres and are planar within 0.02 Å. The crystal structures of these compounds typically have slipped π-stacks parallel to the *x* axis, with adjacent molecules linked with one another according to the 'head-to-head' or 'head-to-side' motif.

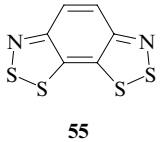


53

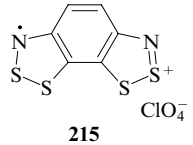


56

X-Ray analyses were performed for charged dithiazoles. The ion packing of radical cation **215** has several S···S intermolecular contacts between cations; the shortest contact (3.740 Å) exceeds the sum of the van der Waals radii of two sulfur atoms (3.6 Å).[38] A comparison of the bond lengths in the neutral bis(dithiazole) molecule **55** and its radical cation **215** shows that as a result of one-electron oxidation, the S−S, S−N, and S−C bonds are shortened, while the C−N bonds are lengthened.

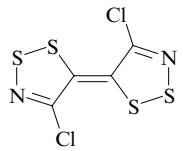


55

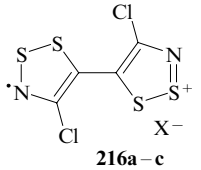


215

X-Ray diffraction studies were also carried out for *trans*-dichlorotetrathiadiazafulvalene **43** and its radical cation salts **216a**−**c**.



43

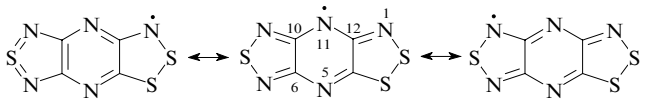


216a–c

X = BF_4 (**a**), ClO_4 (**b**), FSO_3 (**c**).

The S–S, S–N, and S–C bond lengths in molecule **43** are only slightly larger than in 1,2,3-dithiazolium salts,[95] in agreement with the values obtained by *ab initio* calculations.[32] The crystal structures of **216a–c** have larger unit cells (than the neutral compound **43**) because they include the corresponding anions. The molecules in crystal are stacked in layers, and adjacent layers are linked by S···S intermolecular contacts; their lengths are close to the sum of the van der Waals radii of the sulfur atoms.

In crystals, tricyclic radicals **89**, which are planar within 0.07 Å, are nonrigidly associated into centrosymmetric or 'head-to-tail' dimers with S···S short contacts (3.233 Å) between dimers. The intermolecular orbital interactions of these radicals are weak, but strong enough in order to quench paramagnetism due to the formation of weak chemical bonds between two radical species. In radical **89**, the bond lengths between atoms differ from those in the neutral molecule, which points to delocalisation of the odd electron of the radical over the entire molecule. The shortening of the N(1)–C(12) bond indicates that this is a multiple bond, while the shortening of the N(11)–C(10) and N(5)–C(6) bonds and lengthening of the N(11)–C(12) bond can be attributed to the presence of a number of resonance structures.[36]

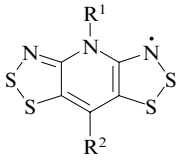


89

The planar (within 0.03 Å) dithiazolyl radicals **84** in crystals form 'stacks' parallel to the *x* axis due to π interactions.[9] There are no S···S contacts between them. The shortest S···S distances were recorded for radicals arranged according to the 'head-to-head' (3.843 Å) and 'head-to-tail' (3.626 Å) motifs and also between neighbouring radicals in a stack (3.707 Å).

The crystal structures of bis(dithiazolyl) radicals **82e–g**, **83a–c** consist of the π stacks of monomer radicals lying parallel to the *z* (for **83b**,**c**) or *x* (**83a**) axes.[96] All crystals studied have many short (shorter than the sum of the van der Waals radii in length) S···S contacts between adjacent dithiazole rings. For these non-dimerised heterocyclic sulfur–nitrogen radicals, the shortest non-binding S···S contacts were found (3.234 Å).

According to EPR data, radical **85** is diamagnetic. Its unit cell consists of four dimers linked according to the 'head-to-head' type. The dimers are linked with one another by two different S–S intraannular bonds.[35] This type of association was not previously observed for 1,2,3-dithiazoles. Unlike other 1,2,3-dithiazolium radicals, the dimers of radicals **85** do not form π stacks; instead, they are assembled into 'herring-bone' type structures; the packing of radicals is such that the S and N atoms are separated by the largest possible distance from each other.

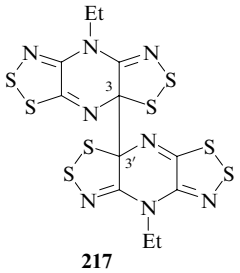


82e–g, **83a–c**

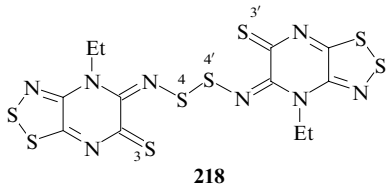
R^2 = H: R^1 = Me (**82e**), Et (**82f**), Pr^n (**82g**);
R^2 = Cl: R^1 = Me (**83a**), Et (**83b**), Pr^n (**83c**).

The structure of two dimers of the bis(1,2,3-dithiazolyl)-pyrazinyl radical formed by the C–C (**217**) or S–S (**218**) bond was finally established in an X-ray diffraction study.[40] In the centrosymmetric dimer **217**, two radicals are linked by the C(3)–C(3′) σ bond [1.607(4) Å], which is considerably longer than the ordinary $C(sp^3)–C(sp^3)$ bond (1.54 Å) and is comparable in length to the bonds of strained π systems. The concurrent rehybridisation of the C(3) atoms leads to drastic distortions of the planar heterocycles, transforming them into 'butterfly' conformations with longer intramolecular bonds.

Crystals **218** consist of centrosymmetric dimers linked by the S(4)–S(4′) σ bond. The nearly coplanar association of radicals is accompanied by ring cleavage and the formation of an exocyclic thione group; its sulfur atom interacts with the S(4) atom [the distance is 2.817(4) Å].



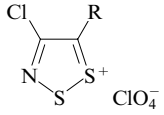
217



218

2. NMR spectroscopy

In the ^{13}C NMR spectrum of compound **30**, the signal of the C(4) atom lies at δ 146.72; the signal of the C(5) atom, at δ 180.81 (Ref. 30). The chemical shifts in the ^{13}C NMR spectra were measured for a number of 1,2,3-dithiazolium perchlorates **1i–l** (Table 2).[7]



1i–l

Table 2. ^{13}C NMR spectroscopic data for 1,2,3-dithiazolium perchlorates **1i–l**.

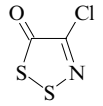
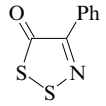
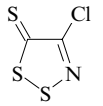
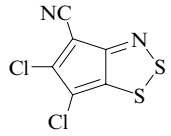
Compound **1**	R	Chemical shifts (δ)/ppm	
		C(4)	C(5)
i	MeS	150.6	193.2
j	4-$MeOC_6H_4$	154.6	181.3
k	Ph	156.4	182.1
l	4-$NO_2C_6H_4$	157.7	178.7

The carbon atom in the position 5 of salts **1i–l** resonates in a weaker field compared with the neutral dithiazole molecule due to a considerable positive charge on the S(1) and S(2)

atoms. The upfield shift of the C(5) signals on passing from R = MeS, Ph to R = 4-$NO_2C_6H_4$ points to the reduced ability of these compounds to stabilise the positive charge on the sulfur atoms. In the case of compound **1i**, however, the donor methoxy group has a reverse effect. Thus, the chemical shifts of the ^{13}C atoms afford a qualitative picture of charge distribution in 1,2,3-dithiazolium perchlorates.

Table 3 gives ^{14}N NMR spectral data for several 1,2,3-dithiazoles.[10] The data revealed a slight difference in the chemical shifts of the nitrogen atom between monocyclic and fused 1,2,3-dithiazoles.

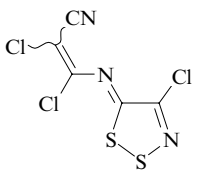
Table 3. ^{14}N NMR spectroscopic data for 1,2,3-dithiazoles ($CDCl_3$, 0 °C).

Compound	Structure	δ /ppm [a]	ν /Hz [b]
30		319	315
33		332	487
36		321	365
61		320	420

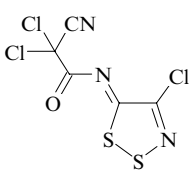
[a] The chemical shifts are given relative to the signal of anhydrous ammonia; [b] the full width at half height.

3. Mass spectrometry

The presence of a 1,2,3-dithiazole ring in a molecule is often revealed by mass spectrometry. Thus the mass spectrum of a mixture of the geometrical isomers of **219** contains fragmentation ions with m/z 137 (C_2ClNS_2), 125 ($CClNS_2$), 102 (C_2NS_2), 93 (Cl–C=N–S), 70 (C_2NS), and 64 (S_2) formed by fragmentation of the molecule.[30] These conclusions were confirmed by high-resolution mass spectrometry (HRMS), which made it possible to identify the extra ions with m/z 120 (C_3Cl_2N) and 85 (C_3ClN), formed from the substituents of the dithiazole ring. Fragmentation of the dithiazole molecule **220** occurs so easily that the intense molecular ion peak (m/z 287) can be obtained only by the fast atom bombardment (FAB) method.[31]



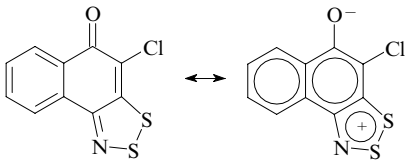
219



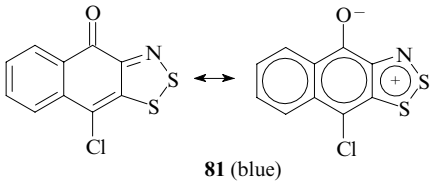
220

4. UV and IR spectroscopy

The unusual effects that take place in dithiazoles were investigated by electron spectroscopy. For example, naphthodithiazolone isomers **80** and **81** are formally considered to be heteroaromatic 14π systems with similar electron density distributions.[47] The large difference in colour and electronic spectra between the CH_2Cl_2 solutions of compounds **80** (red solution with λ_{max} = 461 nm, $\log\varepsilon$ = 4.03) and **81** (blue solution with λ_{max} = 602 nm, $\log\varepsilon$ = 3.63) is explained by the differences in their structure. The electronic transitions in the angular structure of **80** have lower energies than in the linear structure of **81**. This effect was previously observed for phenanthrene- and anthracene-type carbocyclic systems and also for their aza derivatives.



80 (red)

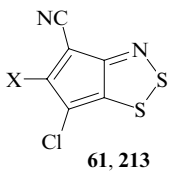


81 (blue)

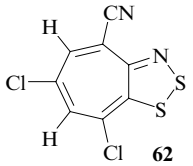
The intense bands of the π–π transitions in the spectra of bis(dithiazole) **53** are observed in a longer wave region (622 nm)[14] than the corresponding absorption bands in the spectra of dithiazoles **56** (522 nm) and **43** (565 nm).[95]

The UV spectra of 4-chloro-1,2,3-dithiazoles **36** and **184** typically show strong absorption in the range 423–431 nm ($\log\varepsilon$ = 3.8–4.0) and weaker absorption around 330 nm ($\log\varepsilon$ = 3.2–3.3).[30]

The UV spectrum of fused morpholinodithiazole **213** (λ_{max} = 412 nm, ε = 23 928) differs significantly from the spectrum of its chloro derivative **61** (λ_{max} = 546 nm, ε = 2618).[42] The morpholine group in dithiazole **213** obviously hinders the charge transfer between the two rings because of conjugation between the amino and nitrile groups. In the electronic spectrum of related dithiazole **62** fused with a seven-membered ring, there is a wide absorption band in the near IR region (λ_{max} = 700 nm, ε = 864).



61, **213**



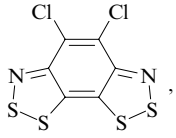
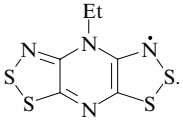
62

X = Cl (**61**), N O (**213**).

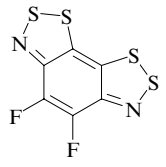
Fused dithiazoles **221** with two five- and one six-membered rings and dithiazoles **222** and **223** with one five- and three six-membered rings have an angular structure. The electronic spectra of these compounds contain strong ($\log\varepsilon$ = 3.9–4.2) absorption bands at 570–635 nm, while the similar linear system, **224**, absorbs in a shorter wave region (λ_{max} = 533 nm, $\log\varepsilon$ = 4.7). The difference between the bands of the π–π transitions of the non-fluorinated heterocycles and their fluorinated analogues is small. In addition, polycyclic systems

Table 4. Electrochemical characteristics and EPR spectral data for 1,2,3-dithiazoles.

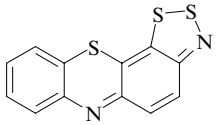
Compound	Potential /V			EPR spectrum parameters		Ref.
	$E_{1/2}^{(0/+)}$	$E_{1/2}^{(0/2+)}$	$E_{pc}^{(0/-)}$	*g* factor	a_N /mT	
11b	−0.104	1.305	−0.956	2.0086	0.32; 0.06	94
11d	−0.118	1.295	−0.970	2.0086	0.317; 0.06	94
26	1.36	1.60	−0.91 [a]	2.0102	0.236	24
43	0.80	1.25	−0.95	2.0117	0.096	24
53	0.41	0.66	−1.06	2.0106	0.235	14
55	0.61	1.10	−0.98	2.0117	0.161	38
56	0.93	1.5 [a]	−0.95	2.0114	0.201	37
See [b]	0.81	1.37	−0.96	2.0117	0.143	38
82a	−0.136	1.278	−0.94	2.0084	0.317	15
82b	−0.104	1.305	−0.956	2.0086	0.320	15
82e	−0.130	1.294	−0.952 [a]	2.0082	0.317	15
82f	–	–	–	2.0082	0.318	17
82g	–	–	–	2.0082	0.310	96
83a	0.005	1.415	−0.835	2.0083	0.310	15
See [c]	−0.029			2.0087	0.313; 0.267	40
84	0.565	–	−0.389 [a]	2.00875	0.498	9
85	0.207	–	−0.91 [a]	2.0081	0.748	35
89	1.14	–	0.15	2.009	0.514	36

[a] Irreversible process, [b] compound , [c] radical .

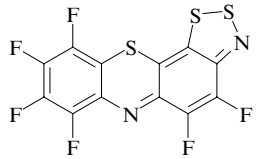
222–**224** demonstrate fluorescence in the range ~660–680 nm.[97]



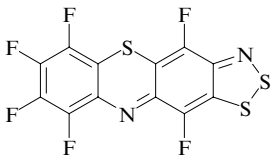
221



222



223



224

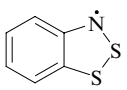
The 1120 cm^{-1} absorption band in the IR spectrum of tricyclic dithiazole **66** is assigned[98] to the vibrations of the N−S bond of the ring. The spectrum of 4-chloro-5*H*-1,2,3-dithiazole-5-thione oxide (**184**) shows intense absorption bands at 1041, 1029, and 1013 cm^{-1} corresponding to the symmetric and asymmetric vibrations of the sulfine group.[30]

5. Electrochemical methods

The electrochemical behaviour of dithiazoles was investigated in order to examine the redox properties of the 1,2,3-dithiazole ring. For example, a cyclic voltammetry study for bis(dithiazole) **56** in acetonitrile on a platinum electrode with a 0.1 M solution of $Bu_4^nNPF_6$ as a supporting electrolyte revealed[37] two redox potentials. The first wave with $E_{1/2}(ox) = 0.93$ V corresponds to reversible oxidation; the second wave with a peak of anode potential $E_{pa} = 1.5$ V, to irreversible oxidation. Attempts to suppress the irreversible oxidation of the singly charged cation to the doubly charged one by varying the scan frequency of electric voltage and the substrate concentration failed. The reduction of compound **56** is accompanied by the appearance of a single broad and irreversible wave with a cathode peak potential of $E_{pc} = -0.95$ V. The half-wave potentials for the first and second stages of oxidation [$E_{1/2}^{(0/+)}$ and $E_{1/2}^{(+/2+)}$, respectively] and the cathode peak potentials ($E_{pc}^{(0/-)}$) for the reduction of 1,2,3-dithiazoles are listed in Table 4.

6. EPR spectroscopy

The EPR spectrum of a liquid SO_2 solution of the radical cation obtained from chlorine-containing bis(dithiazolyl)benzene **56** shows a very strong and stable quintet with an intensity ratio of 1 : 2 : 3 : 2 : 1. This confirms that spin density is completely delocalised on both nitrogen atoms of the dithiazole rings.[37] The effect of the spin–orbit interaction on the sulfur atoms on the value of the *g* factor is much more pronounced in the tricyclic bis(dithiazole) radical cation $[\mathbf{56}]^{+\bullet}$ ($g = 2.0114$) than in simple monofunctional dithiazolyl radicals or benzo-1,2,3-dithiazolyl **225** ($g = 2.008$).



225

Likewise, more pronounced delocalisation of spin density in radical cation $[\mathbf{56}]^{+\bullet}$ compared with delocalisation in simple 1,2,3-dithiazolyl radicals leads to smaller hyperfine coupling constants on the nitrogen atom ($a_N = 0.201$ mT) in the EPR spectra. One can also observe additional splitting under the

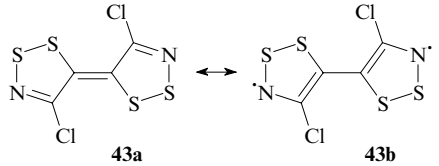
action of two protons with a_H = 0.079 and 0.048 mT in radical cation [**53**]$^{+\bullet}$ (Ref. 14). The EPR spectrum of radical **89** is much more complex than the spectra of the above-mentioned systems; however, calculations made it possible to reveal hyperfine splitting on all five nitrogen atoms. The spin density is partially shifted from the carbon atom in the position 5 of dithiazole and redistributed not only to the nitrogen atom of the dithiazole ring, but also over all other nitrogen atoms of the thiadiazolopyrazine system. As a result of this rearrangement, radical **89** cannot be dimerised by forming a C–C bond.[36]

In addition to the triplet (a_N = 0.498 mT) arising from hyperfine splitting of the signal of the dithiazole nitrogen atom, the EPR spectrum of radical **84** contains a splitting (a_N = 0.135 mT) from the isothiazole nitrogen atom and also splitting with smaller constants from two of the three chlorine atoms in the molecule. This points to a considerable spin delocalisation outside the dithiazole ring.[9]

The *g* factors and a_N constants of the 1,2,3-dithiazolyl radicals are presented in Table 4.

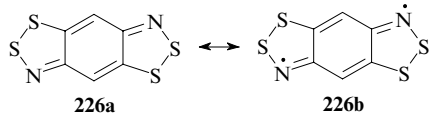
V. Quantum chemical calculations of 1,2,3-dithiazole molecules

Calculations for the tetrathiadiazafulvalene molecule **43**, carried out by the density functional theory (DFT) method at the B3LYP/6-31G** level showed[32] that the ground state of the molecule corresponded to structure **43a**, but not to biradical **43b**, although there was a strong interaction between the rings *via* the C=C bridging bond.



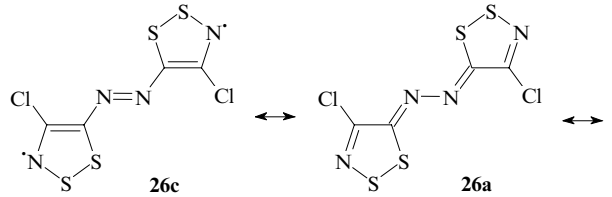
43a **43b**

DFT calculations including electron correlation for benzobis(dithiazole) **226** are reported.[37] The asymmetry of a pair of molecular orbitals having one electron per orbital and mixed with the benzene orbitals leads to a considerable difference in energy between the a_u and b_g frontier orbitals and hence to the quinoid singlet state of **226a**. The biradical singlet state of **226b** should have an energy 0.72 eV higher than that of the ground state of **226a**.

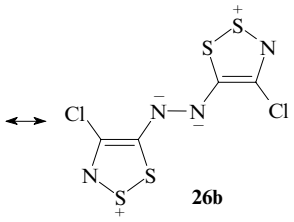


226a **226b**

Calculations of the interactions of the frontier molecular orbitals (FMOs) in bis(1,2,3-dithiazole) **26** show[24] that the high electronegativity of the N–N bridge is not critical to the electron density distribution; it stabilises the ground singlet state of **26a** relative to the biradical triplet state of **26c** by lowering the energy of the highest occupied molecular orbital (HOMO) and polarises the two π bonds in the azine bridge.



26c **26a**



26b

The charge distribution also indicates that the structure of bis(1,2,3-dithiazole) **26** with a diazine bridge corresponds to the covalent (**26a**) rather than polar (**26b**) form.

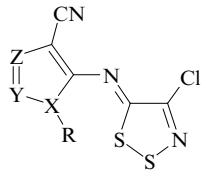
The band structure of the crystalline bis(1,2,3-dithiazolyl) radicals **89**[36] and **82**, **83**[15,17] possessing high conductivity was calculated by the extended Hückel method. High conductivity is provided by the polylayer structure of the radicals with layers imitating the atomic lattice of the traditional metals. Strictly speaking, none of these compounds is a metal; nevertheless, the calculated dispersion curves allow one to evaluate the extent of the intermolecular interaction along the π stacks and in the perpendicular direction.

The spin density distribution in radicals **89** and **225** was calculated by the UB3LYP/6-31G* method.[99] 1,2,3-Dithiazole fused with benzene **225** showed a significant spin density delocalisation. Allyl type nonpolar resonance forms are inherent in this molecule in addition to the polar resonance forms; they are formed due to the involvement of the benzene ring in the spin density distribution. It is shown that the disproportionation energies of radicals **89** and **225** calculated by the same method quantitatively correlate with the conductivity data for these radicals. Extensive π systems containing an N–S–S group (for example, radical **89**) possess low disproportionation energies and hence high conductivities.[100]

VI. Biological activity and applications of 1,2,3-dithiazoles

5-Arylimino-1,2,3-dithiazoles **19** (Ar = RC_6H_4) and **113** have a significant antibacterial activity against gram-positive bacteria.[56,101] The unsubstituted compound **19** (R = H) and its *ortho*-methoxy derivative (R = 2-OMe) were most active among the tested compounds. For four types of fungi, the minimum fungicidal concentrations of 1,2,3-dithiazoles **19** and **113** were at most twice higher than the minimum inhibiting concentration (MIC), which confirms the high fungicidal activity of these compounds.[101] The aromatic moiety of the molecule has no significant effect on the antimicrobial activity. Evidently, the biological action of these derivatives is associated with the presence of the 1,2,3-dithiazole ring, which acts as a powerful inhibitor of several enzymes that are structurally related to serine proteases.

The fungicidal activity of dithiazoles was examined *in vitro* on yeast microorganisms of the type *Candida albicans* ATCC 10231, *Candida utilis* ATCC 9950, *Candida lipolytica* CBS 6124, *Saccharomyces cerevisiae* ATCC 26785, and *Pichia stipitis* CBS 5776 and mould of the type *Aspergillus niger* L32 and *Penicillium* sp.[102,103] All of the 1,2,3-dithiazoles tested, **227**–**229**, showed high fungicidal activity against the yeast types studied. Compounds **227e**–**g**, **228**, **229** exhibited MIC from 10 to 50 μg ml^{-1}. These substances are comparable in efficiency to amphotericin B, which is used as a reference compound in determining the fungus growth inhibiting activity.



227a–g, **228**, **229**

X = Y = N, Z = CH: R = Me (**a**), Ph (**b**), Bn (**c**), CH_2Bn (**d**), $(CH_2)_2Bn$ (**e**), CMe_3 (**f**), 2,4-$Cl_2C_6H_3(CH_2)_2$ (**g**); X = Z = N, Y = CH, R = CH_2Bn (**228**); X = Y = Z = N, R = 2-MeC_6H_4 (**229**).

The antitumour activity of 1,2,3-dithiazoles **227**–**229** was investigated *in vitro* on K562 human myeloid leucemia and L1210 mice leucemia lines. These imines actively inhibited growth of tumour cells at concentrations from 3 to 10 μg ml^{-1}; *i.e.*, their activity was comparable to that of the natural compound distamycin A.

The heterocyclic π electron donor benzobis(1,2,3-dithiazole) **55** was proposed as a donor component for the creation of conducting materials.[38] Neutral heterocyclic radicals, including the derivatives of 1,2,3-dithiazoles, are now being considered as an attractive alternative of charge transfer complexes, which are the traditional synthetic conductors. Dithiazolyl radicals such as (thiadiazolo)dithiazolopyrazinyl **89**,[36] chlorobis(dithiazolo)pyridinyls **83**,[9,16] perchloroisothiazolo-1,2,3-dithiazolyl **84**,[9] and substituted bis-1,2,3-dithiazolopyridinyls **82**[15] were investigated in detail by Oakley and co-workers.

* * *

To summarise, 1,2,3-dithiazoles are one of the best studied classes of five-membered heterocycles containing sulfur and nitrogen atoms. Dithiazoles fused with benzene (mainly in the form of the Hertz salts) have been known for more than 80 years. Considerable progress in synthesis of fused 1,2,3-dithiazoles started in 1970, when it was shown that readily accessible oximes could be promising substrates for this class of heterocycles. This approach was actively developed over the last 15 years by Rees and co-workers.

Considerable interest in non-fused 1,2,3-dithiazoles is explained by the accessibility and also high and various reactivity of 4,5-dichloro-1,2,3-dithiazolium chloride obtained by Appel and his co-authors in 1985. Today the literature contains over 100 references to studies of the Appel salt, and more than 700 new compounds were synthesised from it. Other 5-substituted analogues of the salt, however, have not yet been investigated.

In recent years, much attention has been paid to the synthesis of organic radicals with a 1,2,3-dithiazole fragment and investigation of their properties. This is due to prospects for the application of these systems in the design of organic magnets, conductors, and molecular switches in technology.

Thus, further investigation of the properties and potential applications of 1,2,3-dithiazoles is a promising field of heterocyclic chemistry.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 08-03-00003-a).

References

1. R Appel, H Janssen, M Siray, F Knoch *Chem. Ber.* **118** 1632 (1985)
2. L I Khmelnitski, O A Rakitin, in *Comprehensive Heterocyclic Chemistry II* Vol. 4 (Ed. R C Storr) (Oxford: Elsevier, 1996) p. 409
3. K Kim *J. Sulfur Chem. (Sulfur Rep.)* **21** 147 (1998)
4. U Wannagat, G Schindler *Angew. Chem.* **69** 784 (1957)
5. R Mayer *Phosphorus, Sulfur, Silicon Relat. Elem.* **23** 277 (1985)
6. T M Barclay, A W Cordes, L Beer, R T Oakley, K E Preuss, N J Taylor, R W Reed *Chem. Commun.* 531 (1999)
7. P A Koutentis *Molecules* **10** 346 (2005)
8. V V Korshak, A F Liseenko *Zh. Obshch. Khim.* **9** 1329 (1939) [a]
9. L Beer, A W Cordes, R C Haddon, M E Itkis, R T Oakley, R W Reed, C M Robertson *Chem. Commun.* 1872 (2002)
10. M A Gray, C W Rees, D J Williams *Heterocycles* **37** 1827 (1994)
11. K Emayan, C W Rees *Bull. Soc. Chim. Belg.* **106** 605 (1997)
12. L N Markovskii, T N Dubinina, G G Barashchenkov, E A Romanenko, Yu G Shermolovich *Zh. Org. Khim.* **29** 491 (1993) [b]
13. W K Warburton *Chem. Rev.* **57** 1011 (1957)
14. T M Barclay, A W Cordes, I J Burgess, R T Oakley, R W Reed *Chem. Commun.* 1939 (1998)
15. L Beer, J F Britten, O P Clements, R C Haddon, M E Itkis, K M Matkovich, R T Oakley, R W Reed *Chem. Mater.* **16** 1564 (2004)
16. L Beer, J L Brusso, A W Cordes, E Godde, R C Haddon, M E Itkis, R T Oakley, R W Reed *Chem. Commun.* 2562 (2002)
17. L Beer, J F Britten, J L Brusso, A W Cordes, R C Haddon, M E Itkis, D S MacGregor, R T Oakley, R W Reed, C M Robertson *J. Am. Chem. Soc.* **125** 14394 (2003)
18. N I Astrakhantseva, V G Zhiryakov, P I Abramenko *Khim. Geterotsikl. Soedin.* 1355 (1976) [c]
19. P I Abramenko, T K Ponomareva, G I Priklonskikh *Khim. Geterotsikl. Soedin.* 447 (1979) [c]
20. A W Cordes, J R Mingie, R T Oakley, R W Reed, H Zhang *Can. J. Chem.* **79** 1352 (2001)
21. R F English, O A Rakitin, C W Rees, O G Vlasova *J. Chem. Soc., Perkin Trans. 1* 201 (1997)
22. C W Rees, S Sivadasan, A J P White, D J Williams *J. Chem. Soc., Perkin Trans. 1* 1535 (2002)
23. V N Yarovenko, A A Es'kov, P A Kondrashev, A V Ignatenko, I V Zavarzin, L G Vorontsova, I P Sedishev, M M Krayushkin, Z A Starikova *Heterocycles* **65** 1601 (2005)
24. T M Barclay, L Beer, A W Cordes, R T Oakley, K E Preuss, R W Reed, N J Taylor *Inorg. Chem.* **40** 2709 (2001)
25. H W Roesky, J Sundermeyer, J Schimkowiak, T Gries, M Noltemeyer, G M Sheldrick *Z. Naturforsch., B* **41** 162 (1986)
26. J J Folmer, S M Weinreb *Tetrahedron Lett.* **34** 2737 (1993)
27. P J Dunn, C W Rees *J. Chem. Soc., Perkin Trans. 1* 2489 (1989)
28. M-K Jeon, K Kim *Tetrahedron* **55** 9651 (1999)
29. K Emayan, R F English, P A Koutentis, C W Rees *J. Chem. Soc., Perkin Trans. 1* 3345 (1997)
30. P A Koutentis, C W Rees *J. Chem. Soc., Perkin Trans. 1* 2505 (1998)
31. I C Christoforou, P A Koutentis, C W Rees *J. Chem. Soc., Perkin Trans. 1* 1236 (2002)
32. T M Barclay, L Beer, A W Cordes, R C Haddon, M E Itkis, R T Oakley, K E Preuss, R W Reed *J. Am. Chem. Soc.* **121** 6657 (1999)
33. V N Yarovenko, A A Es'kov, G V Zatonsky, I V Zavarzin, M M Krayushkin, B B Averkiev, M Yu Antipin *J. Heterocycl. Chem.* **41** 37 (2004)
34. M J Plater, C W Rees, D G Roe, T Torroba *J. Chem. Soc., Perkin Trans. 1* 769 (1993)

35. R T Oakley, R W Reed, C M Robertson, J F Richardson *Inorg. Chem.* **44** 1837 (2005)
36. T M Barclay, A W Cordes, R C Haddon, M E Itkis, R T Oakley, R W Reed, H Zhang *J. Am. Chem. Soc.* **121** 969 (1999)
37. T M Barclay, A W Cordes, J D Goddard, R C Mawhinney, R T Oakley, K E Preuss, R W Reed *J. Am. Chem. Soc.* **119** 12136 (1997)
38. T M Barclay, A W Cordes, R T Oakley, K E Preuss, R W Reed *Chem. Mater.* **11** 164 (1999)
39. L Beer, R T Oakley, J R Mingie, K E Preuss, N J Taylor, A W Cordes *J. Am. Chem. Soc.* **122** 7602 (2000)
40. A A Leitch, C E McKenzie, R T Oakley, R W Reed, J F Richardson, L D Sawyer *Chem. Commun.* 1088 (2006)
41. A A Leitch, R W Reed, C M Robertson, J F Britten, X Yu, R A Secco, R T Oakley *J. Am. Chem. Soc.* **129** 7903 (2007)
42. T Gomez, S Macho, D Miguel, A G Neo, T Rodriguez, T Torroba *Eur. J. Org. Chem.* 5055 (2005)
43. K Hafner, B Stowasser, V Sturm *Tetrahedron Lett.* **26** 189 (1985)
44. C W Rees *J. Heterocycl. Chem.* **29** 639 (1992)
45. S Macho, C W Rees, T Rodriguez, T Torroba *Chem. Commun.* 403 (2001)
46. S Macho, D Miguel, T Gomez, T Rodriguez, T Torroba *J. Org. Chem.* **70** 9314 (2005)
47. C Polo, V Ramos, T Torroba, O A Rakitin, C W Rees *Tetrahedron* **54** 223 (1998)
48. O A Rakitin, C W Rees, O G Vlasova *Chem. Commun.* 1273 (1996)
49. L S Konstantinova, O A Rakitin, C W Rees, T Torroba, A J P White, D J Williams *J. Chem. Soc., Perkin Trans. 1* 2243 (1999)
50. D Clarke, K Emayan, C W Rees *J. Chem. Soc., Perkin Trans. 1* 77 (1998)
51. S-H Choi, K Kim *Tetrahedron* **52** 8413 (1996)
52. H Lee, K Kim *Heteroat. Chem.* **4** 263 (1993)
53. T Besson, G Guillaumet, C Lamazzi, C W Rees *Synlett* 704 (1997)
54. T Besson, K Emayan, C W Rees *J. Chem. Soc., Chem. Commun.* 1419 (1995)
55. T Besson, K Emayan, C W Rees *J. Chem. Soc., Perkin Trans. 1* 2097 (1995)
56. G Cottenceau, T Besson, V Gautier, C W Rees, A-M Pons *Bioorg. Med. Chem. Lett.* **6** 529 (1996)
57. H-S Lee, K Kim *Tetrahedron Lett.* **37** 869 (1996)
58. T Besson, J Guillard, C W Rees, V Thiery *J. Chem. Soc., Perkin Trans. 1* 889 (1998)
59. T Iwakawa, A Murabayashi *Heterocycles* **51** 811 (1999)
60. K C Oh, H Lee, K Kim *Tetrahedron Lett.* **33** 4963 (1992)
61. H Lee, K Kim *J. Org. Chem.* **58** 7001 (1993)
62. H Lee, Ky Kim, D Whang, Ki Kim *J. Org. Chem.* **59** 6179 (1994)
63. G L'abbe, B D'hooge, W Dehaen *J. Chem. Soc., Perkin Trans. 1* 2379 (1995)
64. L S Konstantinova, O A Rakitin, C W Rees, S Sivadasan, T Torroba *Tetrahedron* **54** 9639 (1998)
65. H-S Lee, Y-G Chang, K Kim *J. Heterocycl. Chem.* **35** 659 (1998)
66. M-K Jeon, D-S Kim, H J La, D-C Ha, Y-D Gong *Tetrahedron Lett.* **46** 7477 (2005)
67. M de F Pereira, V Thiery, T Besson *Tetrahedron* **63** 847 (2007)
68. M de F Pereira, F R Alexandre, V Thiery, T Besson *Tetrahedron Lett.* **45** 3097 (2004)
69. Y-G Chang, K Kim *Synlett* 1423 (2002)
70. Y-G Chang, K Kim *Heterocycles* **51** 2653 (1999)
71. P K Mohanta, K Kim *Heterocycles* **57** 1471 (2002)
72. M de F Pereira, V Thiery, T Besson *J. Sulfur Chem.* **27** 49 (2006)
73. T Besson, M-J Dozias, J Guillard, P Jacquault, M-D Legoy, C W Rees *Tetrahedron* **54** 6475 (1998)
74. T Besson, C W Rees *J. Chem. Soc., Perkin Trans. 1* 1659 (1995)
75. S Frere, V Thiery, T Besson *Synth. Commun.* **33** 3795 (2003)
76. T Besson, M-J Dozias, J Guillard, C W Rees *J. Chem. Soc., Perkin Trans. 1* 3925 (1998)
77. A Beauchard, H Chabane, S Sinbandhit, P Guenot, V Thiery, T Besson *Tetrahedron* **62** 1895 (2006)
78. A Testard, C Loge, B Leger, J-M Robert, O Lozach, M Blairvacq, L Meijer, V Thiery, T Besson *Bioorg. Med. Chem. Lett.* **16** 3419 (2006)
79. A Testard, L Picot, O Lozach, M Blairvacq, L Meijer, L Murillo, J-M Piot, V Thiery, T Besson *J. Enzyme Inhibition Med. Chem.* **20** 557 (2005)
80. C W Rees, D G Roe, V Thiery *Chem. Commun.* 2775 (1996)
81. T Besson, C W Rees, D G Roe, V Thiery *J. Chem. Soc., Perkin Trans. 1* 555 (2000)
82. A M Cuadro, J Alvarez-Buila *Tetrahedron* **50** 10037 (1994)
83. H Lee, K Kim *Bull. Korean Chem. Soc.* **13** 107 (1992)
84. T Besson, C W Rees, V Thiery *Synthesis* 1345 (1999)
85. K Kim *Phosphorus, Sulfur, Silicon Relat. Elem.* **120 – 121** 229 (1997)
86. Y-G Chang, H-S Lee, K Kim *Tetrahedron Lett.* **42** 8197 (2001)
87. Y S Park, K Kim *Tetrahedron Lett.* **40** 6439 (1999)
88. H-S Lee, K Kim *Tetrahedron Lett.* **37** 3709 (1996)
89. Y-G Chang, K Kim, Y S Park *J. Heterocycl. Chem.* **39** 29 (2002)
90. P A Koutentis, C W Rees, A J P White, D J Williams *J. Chem. Soc., Perkin Trans. 1* 2765 (1998)
91. H-S Lee, K Kim *Tetrahedron Lett.* **39** 6895 (1998)
92. M-K Jeon, K Kim *J. Chem. Soc., Perkin Trans. 1* 3107 (2000)
93. P A Koutentis, C W Rees *J. Chem. Soc., Perkin Trans. 1* 315 (2002)
94. J L Brusso, S Derakhshan, M E Itkis, H Kleinke, R C Haddon, R T Oakley, R W Reed, J F Richardson, C M Robertson, L K Thompson *Inorg. Chem.* **45** 10958 (2006)
95. T M Barclay, A W Cordes, R T Oakley, K E Preuss, R W Reed *Chem. Commun.* 1039 (1998)
96. L Beer, J L Brusso, A W Cordes, R C Haddon, M E Itkis, K Kirschbaum, D S MacGregor, R T Oakley, A A Pinkerton, R W Reed *J. Am. Chem. Soc.* **124** 9498 (2002)
97. V V Zhivonitko, A Yu Makarov, I Yu Bagryanskaya, Yu V Gatilov, M M Shakirov, A V Zibarev *Eur. J. Inorg. Chem.* 4099 (2005)
98. M J Plater, C W Rees *J. Chem. Soc., Perkin Trans. 1* 311 (1991)
99. P Kaszynski *J. Phys. Chem. A* **105** 7615 (2001)
100. P Kaszynski *J. Phys. Chem. A* **105** 7626 (2001)
101. V Thiery, C W Rees, T Besson, G Cottenceau, A-M Pons *Eur. J. Med. Chem.* **33** 149 (1998)
102. P G Baraldi, M G Pavani, M del C Nunez, P Brigidi, B Vitali, R Gambari, R Romagnoli *Bioorg. Med. Chem.* **10** 449 (2002)
103. T Besson, C W Rees, G Cottenceau, A-M Pons *Bioorg. Med. Chem. Lett.* **6** 2343 (1996)

[a] — *Russ. J. Gen. Chem. (Engl. Transl.)*
[b] — *Russ. J. Org. Chem. (Engl. Transl.)*
[c] — *Chem. Heterocycl. Compd. (Engl. Transl.)*