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Heterocyclic Chemistry of Sulfur Chlorides – Fast Ways to Complex Heterocycles

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This microreview highlights the most important advances in the synthetic applications of sulfur dichloride and disulfur dichloride for the preparation of heterocycles. Sulfur chlorides can be considered some of the best sulfur-transfer reagents for the synthesis of heterocyclic systems. Their high reactivity towards nucleophilic organic compounds such as alkenes, alkynes, amines, nitriles, oximes, and their both chlorinating and sulfurating character explain the extensive use of these reagents. In many cases, the initial reactions give rise to reactive intermediates that can be trapped by nucleophiles in a tandem fashion, expanding the possibilities of the reactions. In this way, several new heterocyclic systems can be obtained by a careful selection of the appropriate combination of reagents.

Introduction

Sulfur-containing heterocyclic compounds have maintained the interest of researchers along decades of historical development of organic synthesis.[1] The grounds of this interest are their biological activities and unique structures that led to several applications in different areas of pharmaceutical and agrochemical research or, more recently, in materials science. However, the preparation of these compounds by conventional ways has usually implied many synthetic steps and expensive starting materials. Sulfur dichloride (SCl_2) and disulfur dichloride (S_2Cl_2), two common reagents of the sulfur halides series, are reactive electrophiles[1] but also can be considered some of the best sulfur-transfer reagents in heterocyclic synthesis. This review will focus on the reactions of these two sulfur chlorides and simple organic substrates for the synthesis of valuable sul-

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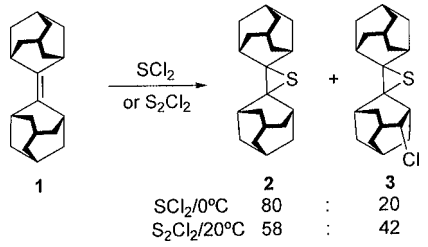
MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

fur-containing heterocycles. For most of the covered examples, a survey of their immediate transformations will be also given.

1. Small Ring Compounds

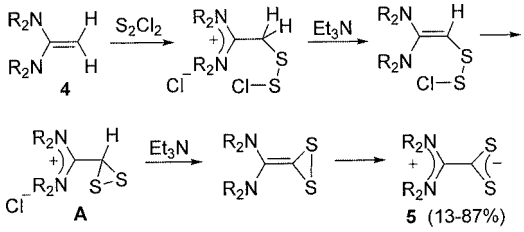
Nakayama and Ishii have reviewed the chemistry of dithiiranes, 1,2-dithietanes and 1,2-dithietes.[2] After it, new synthetic methods that employ the electrophilic addition of sulfur chlorides to multiple C–C bonds as the key in synthesis of small ring compounds have appeared.

The episulfidation of alkenes by addition of sulfur chlorides to double bonds has been described. Only alkenes carrying bulky alkyl substituents have been successfully episulfidized in good yields (Scheme 1). The easy desulfuration of thiiranes to alkenes by the action of sulfur chlorides explained the limitation of this method. Moreover, sulfur dichloride dissociated into chlorine that not only chlorinated the thiirane but also added to the alkene double bond. Another disadvantage of this methodology was the lack of selectivity of the process.[3]



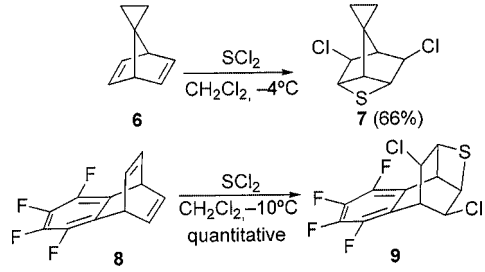
Scheme 1.

When the starting alkenes were 1,1-bis(dialkylamino)ethenes, the addition of S_2Cl_2 in the presence of triethylamine afforded the inner salts **5** by the intermediacy of dithiiranes **A** (Scheme 2).[4] The intermediacy of dithiiranes in the chemistry of sulfur chlorides has also been proposed to explain a number of reaction mechanisms leading to sulfur-rich heterocycles such as 1,2,4-trithiolanes, 1,2,4,5-tetrathianes, 1,2,3,5,6-pentathiepanes and hexathiepanes.[5]



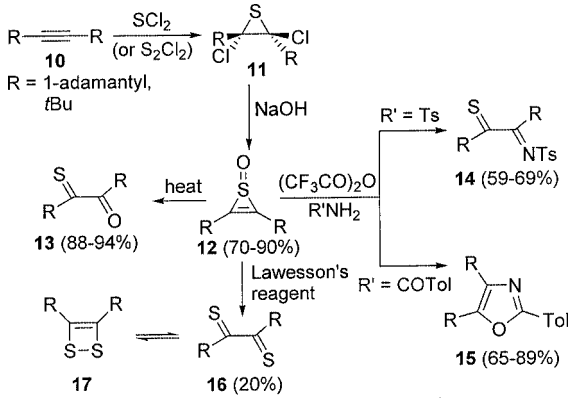
Scheme 2.

The electrophilic addition of SCl_2 to cyclic and acyclic bis-unsaturated substrates has been applied extensively to the synthesis of dihalosulfide rings of different sizes.[6] Although the formation of thietanes appears to be a disfavored process, the electrophilic addition of SCl_2 to specific doubly unsaturated substrates afforded them (Scheme 3). Episulfonium intermediates have been proposed in these syntheses.[7]

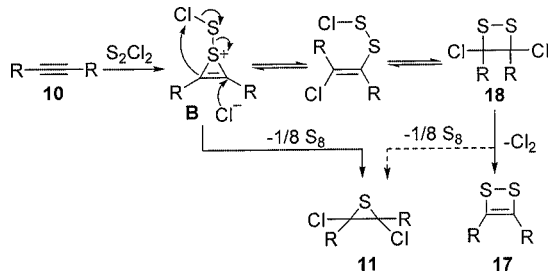


Scheme 3.

In contrast to alkenes, treatment of acetylenes with sulfur chlorides afforded 2,3-dichlorothiiranes near quantitatively and with high stereoselectivity. The alkaline hydrolysis of these thiiranes furnished thiirene 1-oxides in high yield.[8] By boiling in toluene, these compounds afforded α-oxothioketones **13**,[8b] by treatment of the thiirene 1-oxides with *p*-toluensulfonamide or *p*-toluamide, α-imino thioketones **14** and oxazoles **15**, respectively, were obtained,[9] and α-dithiones **16**[10] were prepared by their treatment with Lawesson's reagent (Scheme 4). The equilibrium that existed in solution between α-dithiones **16** and their valence tautomers, 1,2-dithietes **17**, explained the difficulty in the isolation of α-dithiones.[10]



Scheme 4.



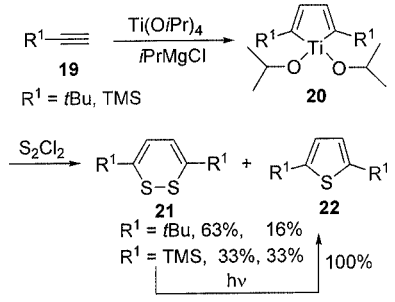
Scheme 5.

Moreover, 1,2-dithietes have been isolated as minor products in the reaction of alkynes and S_2Cl_2. Nakayama proposed that initial formation of a thiirenium intermediate ion **B** subsequently underwent two competitive reactions. First, the reorganization with loss of sulfur leaded to episulfides **11**, second, the completion of the addition of S_2Cl_2 produced adducts which provided 1,2-dithiethanes **18**. The thermal instability of 1,2-dithietanes **18** was remarkable and decomposed to give highly stable 1,2-dithietes **17** with dechlorination (Scheme 5).[8b]

2. Five-Membered Rings

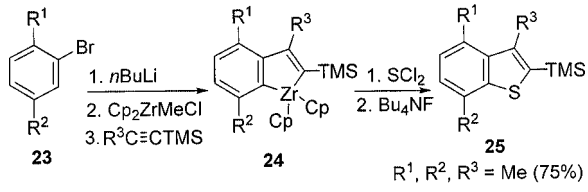
2.1. Five-Membered Rings with One Heteroatom

The addition of sulfur chlorides to doubly unsaturated compounds has been the traditional approach for the synthesis of thiophene derivatives.[11] Recently, the reaction of transition metal complexes and sulfur chlorides has been showed to be an effective method for the synthesis of heterocyclic compounds. Thus, the reaction of terminal alkynes, such as 3,3-dimethylbutyne and (trimethylsilyl)ethyne, and (η^2-propene)Ti(O*i*Pr)$_2$ afforded titanacyclopentadienes **20**, which were treated with S_2Cl_2 to give 1,2-dithiins **21** and thiophenes **22**. The facile light-induced extrusion of sulfur in 1,2-dithiins yielded thiophenes (Scheme 6).[12]



Scheme 6.

Starting from zirconocene complexes, fused aromatic systems have been obtained. The highly regioisomeric insertion of trialkylsilylacetylene on zirconocene complexes to get **24**, followed by consecutive reaction with SCl_2 and tetrabutylammonium fluoride yielded polysubstituted benzothiophenes **25** (Scheme 7).[13]

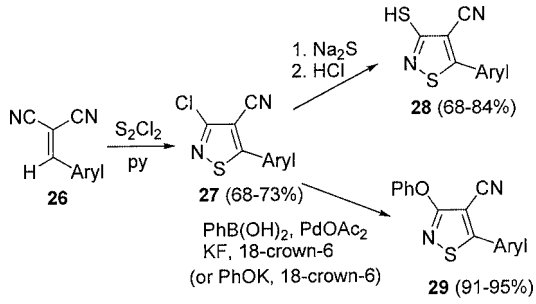


Scheme 7.

2.2. Five-Membered Rings with Two Heteroatoms

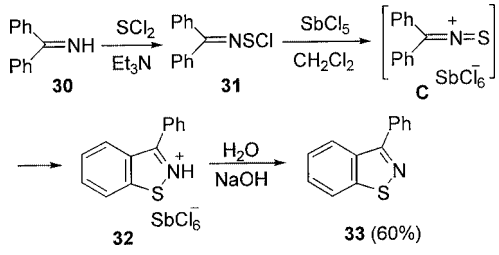
2.2.1. Isothiazoles

One of the most attractive characteristics in the chemistry of sulfur chlorides is the easy access to different heterocyclic systems that are available by a careful selection of the appropriate reagents. Nitriles have been efficiently used as starting materials for the synthesis of several heteroaromatic systems. Isothiazoles **27** were prepared by cyclization of (arylmethylene)malonitriles **26** with S_2Cl_2 in the presence of pyridine. The obtained isothiazoles **27** easily gave nucleophilic substitutions at C-3, but attempted phenylation by Suzuki couplings was unsuccessful, giving only the 3-phenoxy derivative **29** (Scheme 8).[14]



Scheme 8.

Although no direct cyclization was achieved, fused aromatic systems resulted in the reaction of diarylketimines **30** with SCl_2, followed by treatment with $SbCl_5$. The intermediate 1-thia-2-azoniaallene salts **C** evolved to isothiazolium salts **32** which, under aqueous NaOH treatment, afforded 1,2-benzisothiazoles **33** (Scheme 9).[15]



Scheme 9.

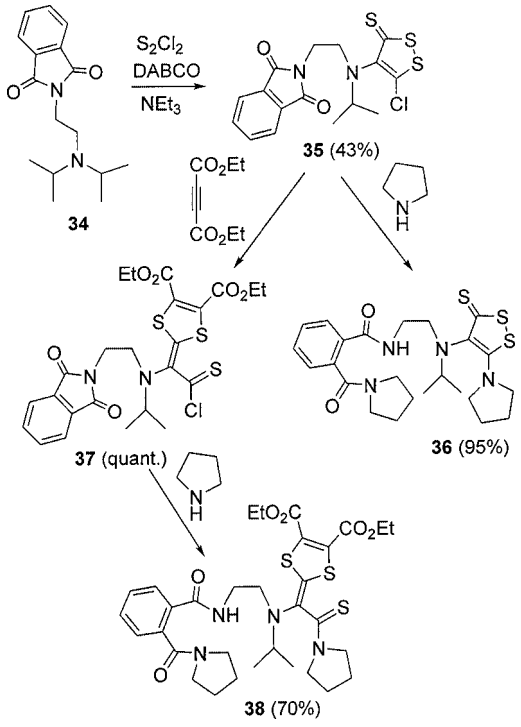
2.2.2. Dithioles

2.2.2.1. 1,2-Dithioles from Isopropylamines

Heterocycles can be synthesized either by ring synthesis or transformation of an existing ring, or by a combination of both methodologies. One of the best examples to illustrate this concept is given by the reactions of S_2Cl_2 with isopropylamines and subsequent transformations.

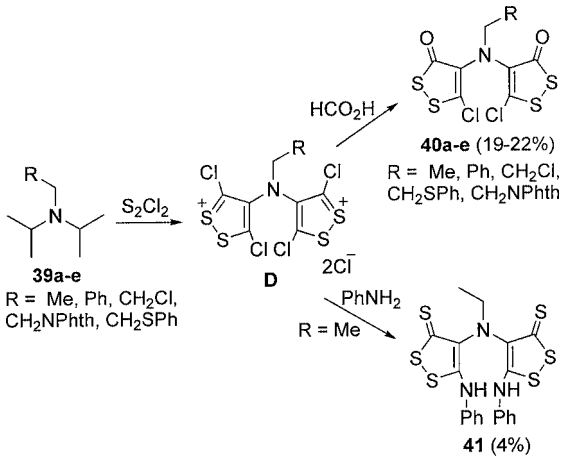
The reaction of *N*-ethyldiisopropylamine (Hünig's base) with S_2Cl_2[16] was able to give several different products, depending on the reaction conditions. Both ethyl groups can be sulfurated independently, giving rise to all final products. For example, sulfuration of a single isopropyl group afforded 5-chloro-1,2-dithiole-3-thiones **35**, stabilized by the presence of a phthalimidoethyl group (Scheme 10).[17] Chlorodithiolethione **35** reacted with 2 equivalents of pyrrolidine giving rise to **36**. On the other

hand, the cycloaddition of **35** to activated alkynes yielded the 1,3-dithiol derivative **37**, bearing a stable thioacid chloride that reacted with an excess of pyrrolidine giving rise to **38**. In this way, from simple isopropylamines, polyheterocyclic amides were obtained in only two reaction steps.



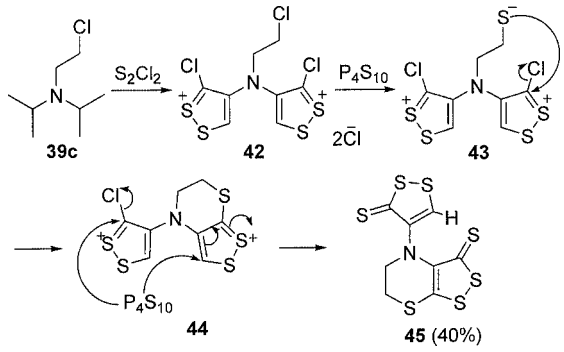
Scheme 10.

The sulfuration of both isopropyl groups of **39a**–**e** followed by extensive chlorination gave rise to a probable intermediate **D** that underwent reaction with formic acid or with amines added during the last period of the reaction, affording several derivatives **40a**–**e**, **41** of the *N*,*N*-bis(1,2-dithiol-4-yl)amine (Scheme 11).[18]



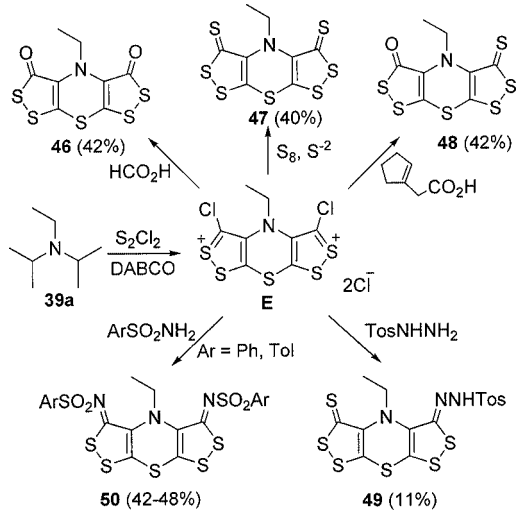
Scheme 11.

The substitution on the ethyl group had a pronounced effect on the evolution of this reaction. When the starting amine was the *N*-(2-chloroethyl)diisopropylamine, the addition of phosphorus pentasulfide at the last stage of the reaction changed the course of the reaction. In this case, the chlorine atom was replaced by sulfur both in the lateral chain and in the intermediate salt giving a new [1,2]dithiolo[1,4]thiazine ring system **45** (Scheme 12).[19]



Scheme 12.

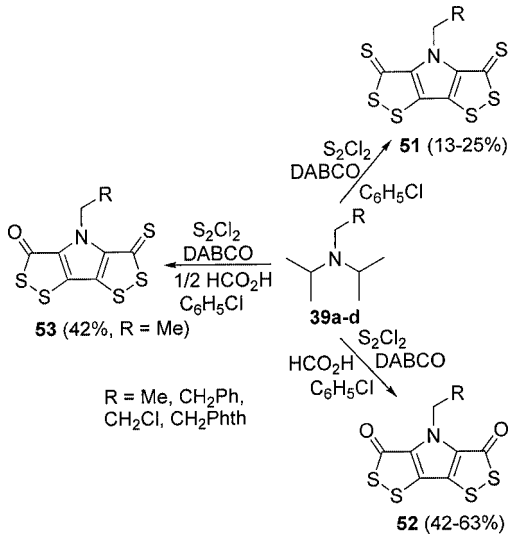
The complete sulfuration of the Hünig's base, affordable by extensive reaction with S_2Cl_2 and DABCO, gave rise to a expected intermediate disalt **E**, from which a complete range of di[1,2]dithiolo[1,4]thiazine derivatives could be obtained by trapping of the intermediate salts with sulfur and oxygen nucleophiles,[19,20] as well as nitrogen nucleophiles,[21] giving rise to several dithiole derivatives **46**–**50** (Scheme 13).



Scheme 13.

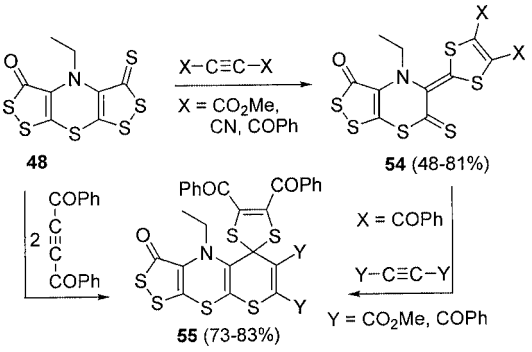
The sulfur atom of the 1,4-thiazine ring was easily extruded in all the *N*-substituted di[1,2]dithiolo-[1,4]thiazine derivatives (but not in the *N*-unsubstituted) yielding pyrrole derivatives **51**–**53** (Scheme 14).[20,22]

Dithiolthiones reacted as either dienophile[23] or dipolarophile[24] reagents in 1,3-dipolar cycloadditions, show-



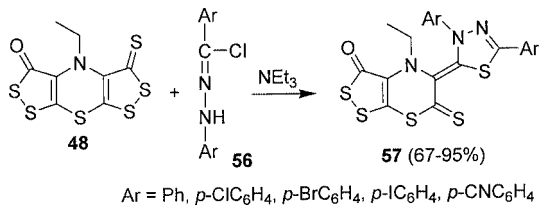
Scheme 14.

ing a very high reactivity. The initial 1,3-dipolar cycloaddition of di-dithiolo-thiazines), or di-dithiolo-pyrroles, and typical dipolarophiles generated heterodynes of type **54** that were the substrate of subsequent hetero-Diels–Alder cycloadditions to give **55** (Scheme 15).[23]



Scheme 15.

The reaction of di[1,2]dithiolo[1,4]thiazine **48** as dipolarophile with imines **56** was followed by spontaneous opening of the dithiole ring, with extrusion of sulfur, to give 1,3,4-thiadiazoles **57** (Scheme 16).[24b]

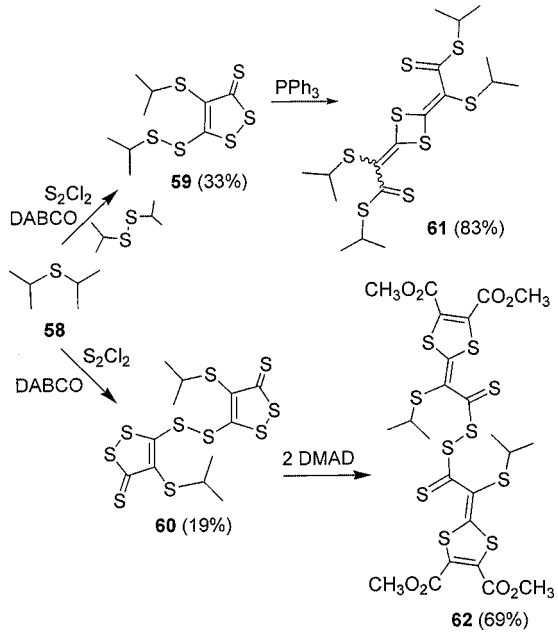


Scheme 16.

Taking into account that all starting heterocycles were obtained in one-pot reactions from tertiary amines, this method permitted the preparation of highly branched polysulfur-nitrogen heterocycles in only two steps from tertiary amines, S_2Cl_2 and doubly activated alkynes.[25]

2.2.2.2. 1,2-Dithioles from Thioethers

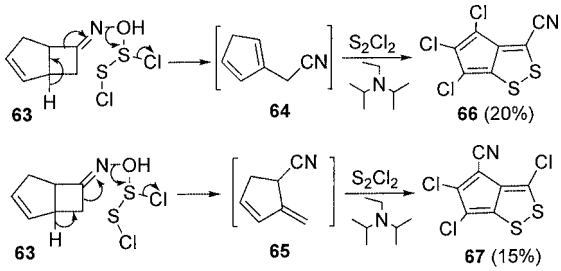
A similar role of nitrogen can be played by sulfur as the center of activation of isopropyl groups. 1,2-Dithiol-3-thione derivatives **59**–**60** were obtained by reaction of diisopropyl sulfide **58** with S_2Cl_2 under different conditions. The chemistry of these heterocycles permitted the synthesis of sulfur-rich molecules **61**–**62** (Scheme 17).[26]



Scheme 17.

2.2.2.3. 1,2-Dithioles from Oximes

Other nitrogenated groups used in the synthesis of 1,2-dithiole rings were bicyclic oximes. A sequence of second-order Beckmann rearrangements followed by trapping of intermediates by S_2Cl_2, dehydrogenation and chlorination from bicyclic cyclopentencyclobutanone oxime **63**, gave the 1,2-dithioles **66**–**67** (Scheme 18).



Scheme 18.

The rearrangement process, related to the Beckmann 2nd order opening reaction of oximes, gave rise to two different intermediates that were trapped in the reaction conditions

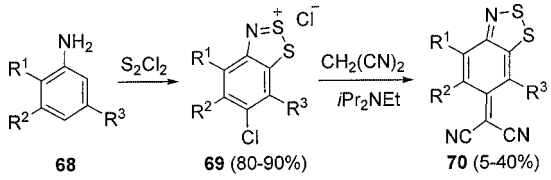
by the combined action of S_2Cl_2 and Hünig's base, resulting in a very fast route to isomeric cyclopenta-1,2-dithioles in a one-pot reaction.[27]

2.3. Five-Membered Rings with Three Heteroatoms

2.3.1. Dithiazoles

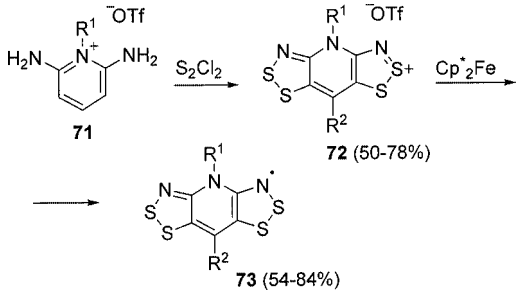
2.3.1.1. 1,2,3-Dithiazoles from Amines

The condensation of aromatic amines **68** and S_2Cl_2 accompanied by the *para*-chlorination of the starting aniline, known as the Herz reaction, afforded 6-chloro-1,2,3-benzodithiazolium chlorides **69** that were treated with malononitrile to form derivatives **70** (Scheme 19).[28]



Scheme 19.

Based on double Herz condensations of *N*-alkylated 2,6-diaminopyridinium salts, highly delocalized dithiazolodithiazolyl radicals have been synthesized. Starting from the diaminopiridine salt **71**, different derivatives were obtained depending on the reaction conditions (R^2 = H, Cl) (Scheme 20).[29] This method constituted a general approach to 4-substituted 2,6-aminopyridinium salts (4-Me, 4-Ph) starting from *N*-alkylated-4-substituted 2,6-diaminopyridine.[30] The salts **72** were reduced to the thermally stable radicals **73**.

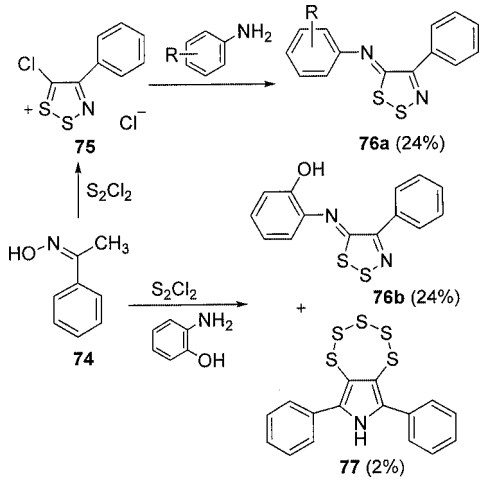


Scheme 20.

These systems constitute a new generation of molecular building blocks with potential applications in single-component magnetic and conductive materials.[29–31]

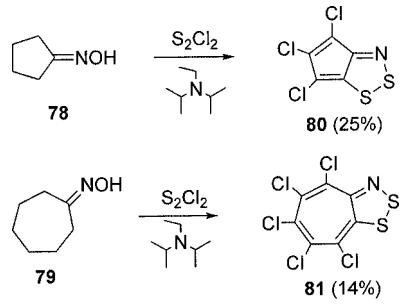
2.3.1.2. 1,2,3-Dithiazoles from Oximes

The possibility of obtaining new dithiazole derivatives via reaction of oximes with sulfur chlorides has been studied by Rees and co-workers. The reaction of acetophenone oxime **74** and S_2Cl_2 gave 5-chloro-4-phenyl-1,2,3-dithiazolium chloride **75** which on treatment with primary aromatic amines gave 4-aryl-5-arylimino-1,2,3-dithiazoles **76a**–**b** in fair yields, but the treatment of acetophenone oxime with S_2Cl_2 in the presence of 2-aminophenol also gave a minor amount of 6,8-diphenyl-1,2,3,4,5-pentathiepino[6,7-*c*]pyrrole **77** in an unusual new reaction (Scheme 21).[32]



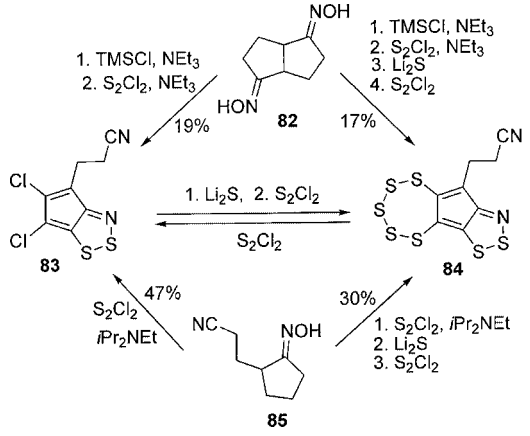
Scheme 21.

The construction of fused aromatic systems has been achieved in one-pot reactions from saturated cyclic oximes **78**–**79**, that represents a particularly efficient synthesis of complex heterocycles **80**–**81** (Scheme 22).[33]



Scheme 22.

In this way, the use of the aliphatic bicyclo[3.3.0]octan-2,6-dione dioxime **82** as the starting material for the one-pot synthesis of 4-(2-cyanoethyl)pentathiepinocyclopenta[1,2,3]dithiazole **84** is noteworthy. Alternatively, the

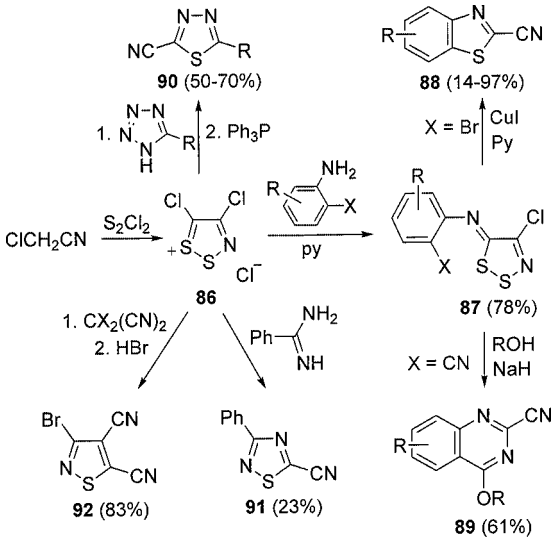


Scheme 23.

5,6-dichloro-4-(2-cyanoethyl)cyclopenta[1,2,3]dithiazole **83** could be obtained. The same products were obtained from 2-(2-cyanoethyl)cylopentanone oxime **85** (Scheme 23).[34]

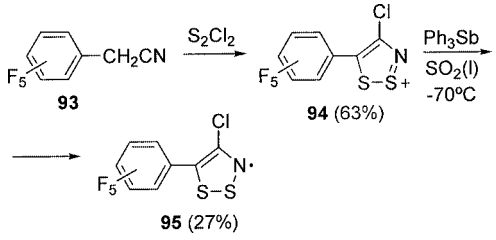
2.3.1.3. 1,2,3-Dithiazoles from Nitriles

The most common synthetic route to monocyclic 1,2,3-dithiazolium salts involved the Appel's cyclization of aliphatic nitriles with S_2Cl_2.[35] The ready preparation of Appel's salt **86** from chloroacetonitrile and its high reactivity has led to several new preparative procedures for the synthesis of heterocycles such as benzothiazoles **88**, quinazolines **89**,[36] 1,3,4-thiadiazoles **90**,[37] 1,2,4-thiadiazoles **91**[38] and isothiazoles **92**[39] (Scheme 24).



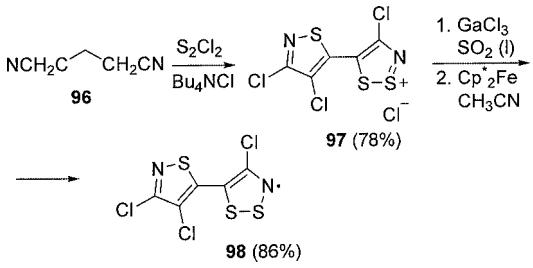
Scheme 24.

As in the case of the fused 1,2,3-dithiazolyl radicals **73** seen above, the association behaviour of 1,2,3-dithiazolyl radicals derived from monocyclic systems such as **94**, in turn obtained by Appel's cyclization, has been fully studied. Heavy spin density at the 5-position favored the dimerization at carbon, while sterically protected radicals at the 5-position facilitated the isolation and structural characterization of a simple monocyclic radical **95** as its S···S dimer (Scheme 25).[40]



Scheme 25.

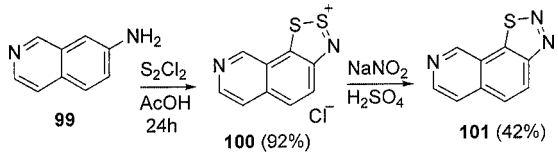
The Appel's cyclization carried out on glutaronitrile conducted to the isothiazolyl-dithiazolylium chloride **97**, which was reduced to the corresponding radical **98** (Scheme 26). The presence of the isothiazol group prevented the association, resulting in the first unassociated 1,2,3-dithiazolyl radical ever described.[41]



Scheme 26.

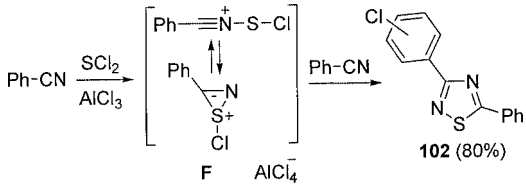
2.3.2. Thiadiazoles

The syntheses of thiadiazole systems are probably the best examples of the applicability of sulfur chlorides in the synthesis of sulfur containing heterocycles. The synthesis of the four possible thiadiazole isomers has been described using this methodology. By this chemistry, 1,2,3-benzothiadiazoles were obtained in two steps from amines by the reaction of aromatic amines with S_2Cl_2 (Herz reaction) and treatment of the resulting benzodithiazol salt with nitrous acid (Scheme 27).[42]



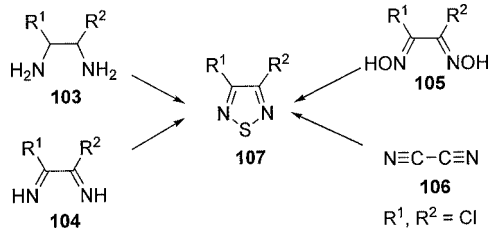
Scheme 27.

The reaction of benzonitrile with SCl_2 in the presence of Lewis acid catalyst yielded 3,5-diphenyl-1,2,4-thiadiazole **102**, along with the 3-chlorophenyl analog. The proposed mechanism is shown in Scheme 28 and proceeded via a cationic intermediate **F** that added a second molecule of nitrile to give **102**.[43]



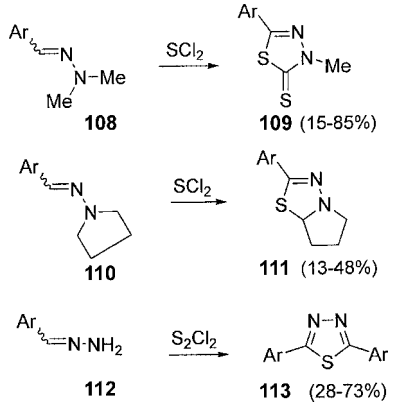
Scheme 28.

Compounds containing an acyclic NCCN system at any hybridization state reacted with sulfur chlorides to form the appropriately substituted 1,2,5-thiadiazoles (Scheme 29).[44]



Scheme 29.

Hydrazones **108**, **110** and **112** were the starting materials for the synthesis of 1,3,4-thiadiazole derivatives **109**, **111**, **113** (Scheme 30). The nature of the resulting thiadiazole depended on the *N*-substitution.[45]

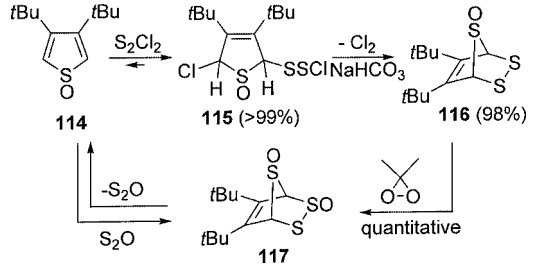


Scheme 30.

In contrast to the reactions of aldohydrazones, the reaction of non-substituted ketohydrazones with sulfur chlorides gave rise to a new range of different products, such as tetrathiolanes, pentathianes and hexathiepanes.[46]

2.3.3. Trithianorbornanes

Recently, Nakayama and co-workers have reported the synthesis and applications of a new heterocyclic system. Addition of S_2Cl_2 to 3,4-di-*tert*-butylthiophene 1-oxide (**114**) afforded quantitatively the highly labile 1,4 adduct **115** that, by treatment with aqueous $NaHCO_3$ solution, produced the trithiabicyclo system **116**. The oxidation of **116** with dimethyldioxyrane gave quantitatively an isomeric mixture of dioxides **117** that constituted a new and clean source for the generation of S_2O by a hetero retro-Diels–Alder reaction (Scheme 31).[47]

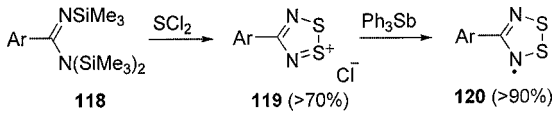


Scheme 31.

2.4. Five-Membered Rings with Four Heteroatoms

The potential applications of 1,2,3,5-dithiadiazolyl radicals in molecular magnets and conductors explained the increasing interest in these systems. The synthesis of these heterocycles from sulfur chlorides as sulfur transfer agents has been well developed from amidines[48] and analogues (*gem*-dinitrogenated compounds).[1]

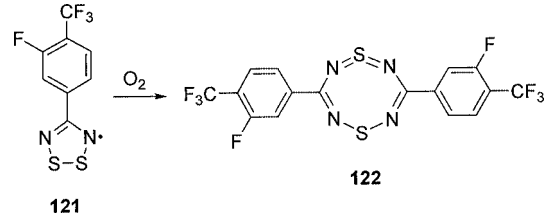
4-Aryl-1,2,3,5-dithiadiazolium salts **119** have been synthesized by condensation of silylated aryl amidines **118** or their *N*-lithium salts with excess of SCl_2, which were reduced to the corresponding radical species **120** (Scheme 32).[48]



Scheme 32.

The standard synthetic routes to *meta*- and *para*-substituted phenyl-1,2,3,5-dithiadiazolium salts are not generally applicable to *ortho*-substituted derivatives and this has been attributed to steric hindrance.[48a] Fluorination has led to some unusual structural features as compared to their hydrogenated analogues; for example, whilst the majority of dithiadiazolyl radicals dimerizes in the solid state, the perfluro derivatives are monomeric.[49]

The characteristics of dithiadiazolyl radical **121** are remarkable, thus while its sublimation in a partial atmosphere of oxygen resulted in the formation of the dithiatetrazocine **122** (Scheme 33), the sublimation of **121** under partial atmospheres of N_2, CO_2, and/or SO_2 formed inclusion structures.[50a] Dithiatetrazocines similar to **122** can be obtained in yields up to 60% by reaction of the corresponding dithiadiazolium chlorides with triphenylantimony and oxygen.[50b–50c]

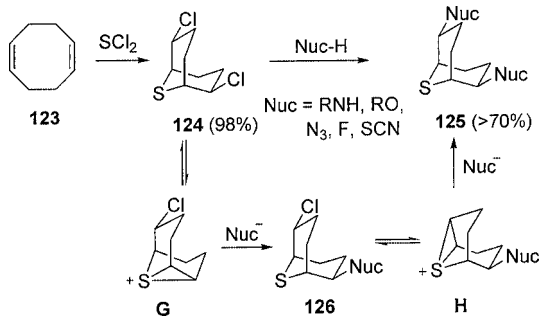


Scheme 33.

3. Six-Membered Rings

3.1. Six-Membered Rings with One Heteroatom

The transannular additions of SCl_2 to 1,5-cyclooctadiene provided an easy route to 2,6-dichloro-9-thiabicyclo[3.3.1]-nonane (**124**). This system is a reliable acceptor of a wide variety of heteroatom nucleophiles with high stereochemical control and participation of the neighboring sulfur atom.[51] Although the attack at either carbons of the intermediate episulfonium rings **G** and **H** was possible, the high regioselectivity observed was probably due to the higher energy of the 9-thiabicyclo[4.2.1] skeleton in comparison to the analogous [3.3.1] form (Scheme 34).

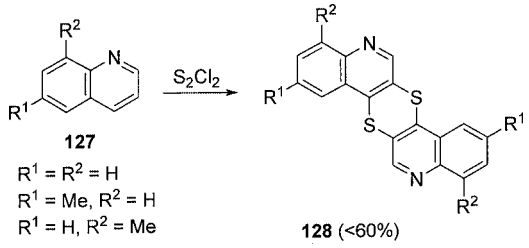


Scheme 34.

3.2. Six-Membered Rings with Two Heteroatoms

3.2.1. Dithiins

The detailed study of dithiins has been limited by the lack of convenient synthetic approaches. The reaction of disulfur dichloride with quinolines **127** to give 1,4-dithiins **128** has been known for more than 100 years, although the correct structure was assigned lately (Scheme 35).[52]



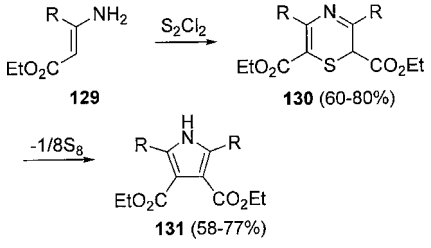
Scheme 35.

Recently, several methods that included titanacyclopentadienes as starting materials have been developed. Some of these substrates afforded dithiins as the major products in their reactions with S_2Cl_2, as shown in Scheme 6.[12]

3.2.2. Thiazines

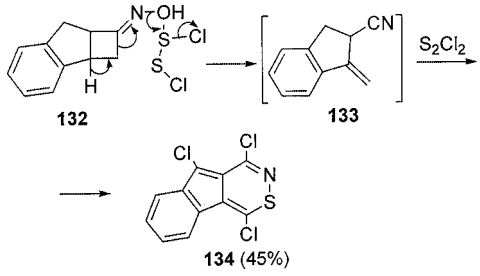
Thiazines are other representative heterocycles which have been obtained from different nitrogen-containing functional groups.

The synthesis of 1,4-thiazines **130** (or pyrroles **131**) has been achieved from simple enamines **129** (Scheme 36).[53]



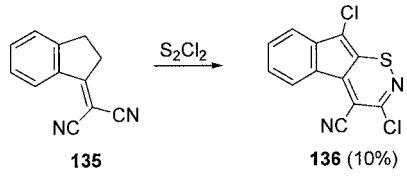
Scheme 36.

Section 2.2.2.1 described the preparation of fused 1,4-thiazine systems. Indenecyclobutanone oxime **132** gave the indenethiazine **134** in good yield (Scheme 37).[26]



Scheme 37.

Production of new heterocycles and chlorinated indene derivatives was not restricted to cyclobutanone oximes. In fact, indene acetonitrile or indene acetic acid derivatives also gave new indene[1,2]thiazines. Some of these products constituted a new class of discotic liquid crystals (Scheme 38).[54]

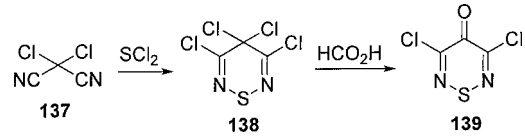


Scheme 38.

3.3. Six-Membered Rings with Three or More Heteroatoms

3.3.1. Thiadiazines

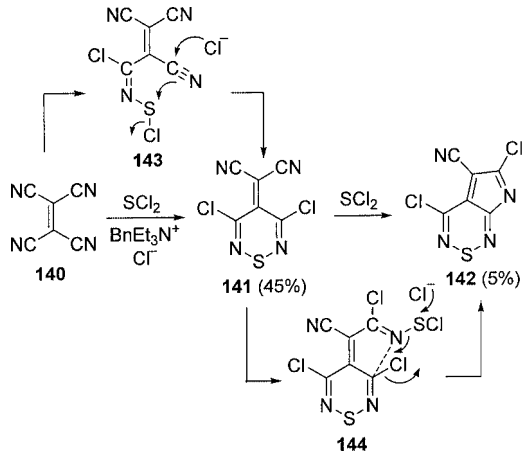
The method developed for the synthesis of 1,2,5-thiadiazoles has been extended to the synthesis of other heterocycles such as thiadiazines. Thus, the addition of SCl_2 to dichloromalononitrile **137** afforded 3,5-dichloro-1,2,6-thiadiazine **138** in good yield. 3,5-Dichloro-4*H*-1,2,6-thiadiazin-4-one (**139**) was prepared quantitatively by treatment with formic acid (Scheme 39).[55]



Scheme 39.

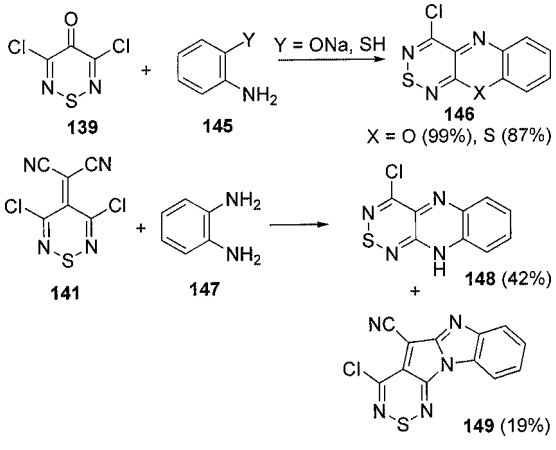
The chlorine atoms in **139** can be successively displaced by a range of nitrogen, oxygen and sulfur nucleophiles. Displacement of the first chlorine atom occurred readily but the second one required harder conditions. To overcome this problem, Rees and Koutentis replaced the keto group by a stronger electron-withdrawing group. Treatment of tetracyanoethylene **140** with SCl_2 afforded 3,5-dichloro-4-dicyanomethylene-4*H*-1,2,6-thiadiazine (**141**) as the major product (Scheme 40).[55b] When the thiadiazine **141** was treated with SCl_2, the second dicyanomethylene group did not react further to give the symmetrical dimer, but gave

4,6-dichloro-5-cyanopyrrolo[2,3-*c*][1,2,6]thiadiazine **142**. Presumably the first step in the mechanism was the same in both syntheses, but in the second reaction the generated intermediate cyclized with displacement of an activated chlorine atom on the thiadiazine to form the pyrrole ring.



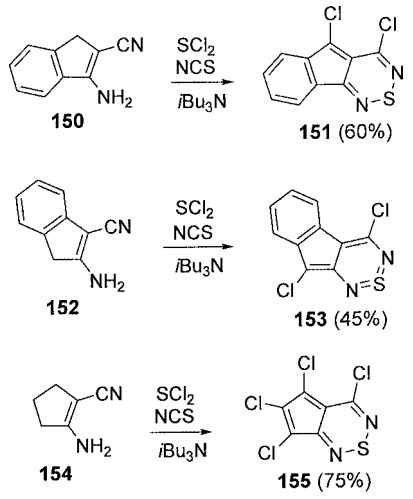
Scheme 40.

Although the thiadiazine **141** usually showed enhanced susceptibility towards displacement of the second chlorine atom over thiadiazinone **139**, the reactions of **139** were cleaner since there was little reactivity other than chlorine displacement, whereas **141** could also undergo hydrolysis of the dicyanomethylene group or cyclisation onto a cyano group, resulting in more complex reactions.[56] Illustrative examples were the reactions of these systems with dinucleophiles used for the synthesis of thiadiazine derivatives **146**, **148** and **149** (Scheme 41).[56b]



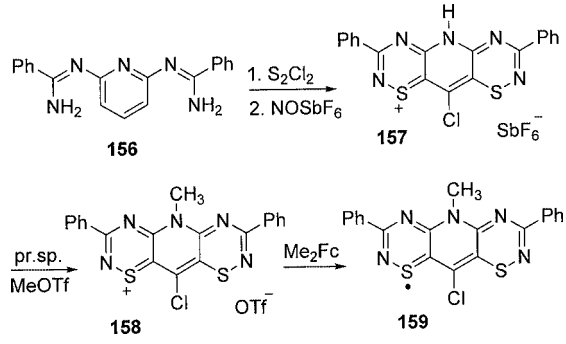
Scheme 41.

Recently, the reactions of indene and cyclopentene enaminonitriles **150**, **152** and **154** with SCl_2, triisobutylamine and *N*-chlorosuccinimide (NCS), to give the first cyclopenta[1,2,6]thiadiazines **151**, **153** and **155**, have been reported (Scheme 42).[57] Some of these thiadiazines showed unusual characteristics, thus **153** was a near-infrared dye and **155** was a liquid crystal.



Scheme 42.

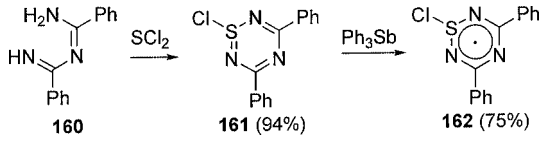
Resonance-stabilized bis(thiadiazinyl) radicals were obtained by the synthetic sequence shown (Scheme 43). Thus cyclocondensation of the bifunctional amidine **156**, with S_2Cl_2 followed by metathesis of the protonated chloride salt (>70% yield) with $NOSbF_6$ generated the corresponding hexafluoroantimonate salt **157**. Treatment of this salt with Proton Sponge and methyl triflate furnished the *N*-methyl salt **158**. Chemical reduction of solutions of **158** with dimethylferrocene afforded the corresponding [1,2,4]thiadiazino[6′,5′:5,6]pyrido[2,3-*e*][1,2,4]thiadiazin-2-yl radical **159**. The material was remarkably stable, both in solution and in the solid state, towards aerial oxidation and heat.[58]



Scheme 43.

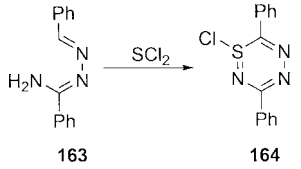
3.3.2. Thiatriazines

Although all thiatriazines can, in principle, form 7π-electron radicals, only 1,2,4,6- and 1,2,4,5-thiatriazines have been investigated in this context. However, the results obtained from every one of these two derivatives were different. The reaction of *N*-imidoylamidines **160** and SCl_2 afforded the *S*-chloro-1,2,4,6-thiatriazines **161** in good yields and the thiatriazine ring was easily reduced by Ph_3Sb to the 1,2,4,6-thiatriazinyl radical **162**. This was a persistent and thermally stable radical which was a cofacial diamagnetic dimer in the solid state (Scheme 44).[59]



Scheme 44.

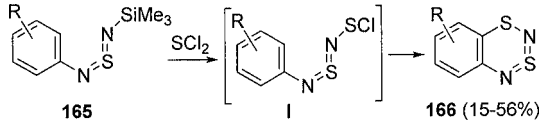
The 1,2,4,5-thiatriazine **164** was prepared by a condensation reaction of 1-amino-2,3-diaza-1,3-butadiene **163** with SCl_2, but attempts to generate the corresponding 1,2,4,5-thiatriazinyl radical were not successful, although a weak ESR signal was observed in the experiment (Scheme 45).[60]



Scheme 45.

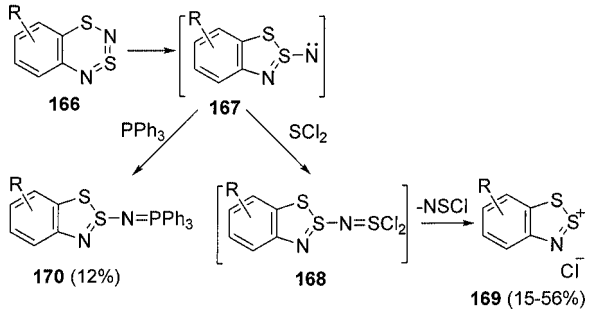
3.3.3. Dithiadiazines

The synthesis of benzo-1,3-dithia-2,4-diazines **166** was achieved by condensation of silylated sulfur diimides **165** with SCl_2 followed by intramolecular *ortho*-cyclization of the intermediates **I** (Scheme 46).[61]



Scheme 46.

This synthesis was complicated by further reaction of **166** with SCl_2 to give Herz salts **169**. A thermodynamic stability of an antiaromatic system into an aromatic system seemed to be the driving force of the reaction. The key intermediates were singlet 1,2,3-benzodithiazol-2-yl nitrenes identified under matrix isolation conditions. The reaction of **166** with Ph_3P to give **170** probably proceeded in a similar way (Scheme 47).[61b]

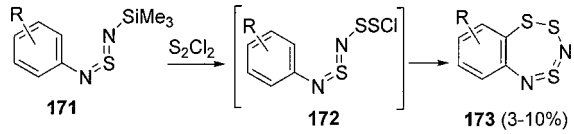


Scheme 47.

4. Seven-, Eight-Membered and Macrocyclic Systems

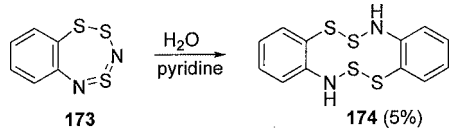
The reaction of different substrates and sulfur chlorides has been considered one of the best methodologies for the preparation of highly sulfurated heterocycles. A review on the chemistry of organic polysulfanes, including cyclic polysulfanes, has recently appeared.[62] The synthesis, reactivity and properties of pentathiepins have received a specific attention in a recent review.[63]

Other seven-membered ring systems have been investigated; thus Zibarev and co-workers, in continuation with their work on silylated sulfur diimides, have described the synthesis of 1,2,4,3,5-benzotrithiadiazepines of type **173** by intramolecular electrophilic cyclization of Ar–N=S=N–$SiMe_3$ (**171**) under the action of S_2Cl_2 (Scheme 48).[64]



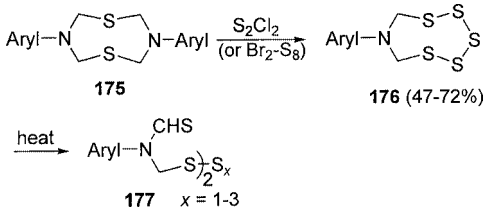
Scheme 48.

The heteroatom reactivity of 1,2,4,3,5-benzotrithiadiazepine differed from its known symmetric isomer 1,3,5,2,4-benzotrithiadiazepine.[1] Whilst the last isomer was stable towards hydrolysis in weak bases and acids, the hydrolysis of **173** in pyridine afforded the unusual macrocyclic 7*H*,14*H*-dibenzo[*d*,*i*][1,2,6,7,3,8]tetrathiadiazocine (**174**) (Scheme 49).[64]



Scheme 49.

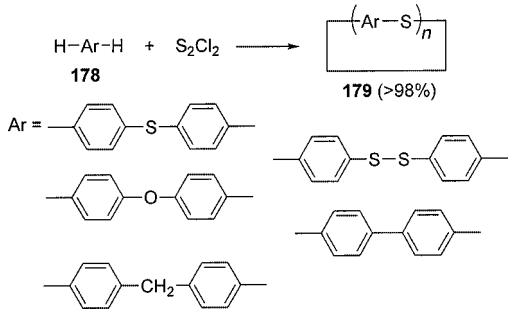
Rings of similar size were obtained by treatment of 1,5,3,7-dithiadiazocanes **175** with S_2Cl_2. The thermal reaction of 1,2,3,4,5,7-pentathiazocanes **176** caused ring fission to give polysulfides **177** in low yields (Scheme 50).[65]



Scheme 50.

Sulfur chlorides are also useful reagents for the synthesis of macrocyclic oxathiacrown and thiacrown ethers from bis-unsaturated compounds[66] or (thio-arylene) oligomers by oxidative polymerization of aromatic compounds (Scheme 51).[67] The intramolecular head-to-tail reaction of

the oligomeric sulfonium species occurred under high dilution conditions leading to the selective formation of the cyclic products. These macrocyclic oligomers have attracted considerable attention in view of their significance as reactive precursors for the synthesis of high-performance polymers via free-radical ring-opening polymerization.



Scheme 51.

Conclusions

The reactions here described permit the preparation of new heterocyclic systems characterized by the high number of heteroatoms included in their structures. This methodology constitutes a very fast and safe way to get highly interesting heterocyclic systems that in several cases are not easy to obtain by conventional ways. The limits of this chemistry are difficult to foresee. The interesting characteristics found in many of these heterocycles, the development of rapid synthetic methods from easily available materials in multicomponent reactions, and the huge number of products obtainable by these methods offer a wide scope for the synthesis of new polysulfur-containing heterocycles.

Acknowledgments

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