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α,β-UNSATURATED ISOTHIOCYANATES

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The synthesis and the properties of α,β-unsaturated isothiocyanates are described with 276 literature references.

Key words: Heterocumulenes, isocyanides, isothiocyanates, thiocyanates, thiophosgene.

CONTENTS

1. INTRODUCTION

Organic isothiocyanates (mustard oils, organic isorhodanides) are biologically active compounds[1-10] and important starting materials and intermediates for the synthesis of various organic compounds,[1-3,8,9,11-21] including pharmaceuticals and agricultural chemicals.[1-3] Isothiocyanates attract special interest as convenient building blocks in heterocyclic syntheses.[9,22-24] The high reactivity of isothiocyanates towards nucleophiles made possible their widespread utilization in analytical practice[10,25] (Edman reaction[26,27]).

Among the isothiocyanates are volatile natural products known as mustard oils.[4,28-31] They are ingredients of oils of roots and seeds of various plants.

By the present time a variety of saturated and unsaturated isothiocyanates (alkyl, aryl, alkenyl mono- and diisothiocyanates), also polyenes and aliphatic aldehydes with a terminal vinylisothiocyanato function, have been isolated from (as free species or as derivatives)

or identified in the seeds of various kinds of the *Brassica* family *Cruciferae*, in rape, in the roots and seeds of *Brassicae* and *Conringia orientalis*,[4] in the marine sponges *Acanthella acuta*,[32] *Axinella cannabina*,[33] and *Halichondria sp.*,[29] in marine seaweeds (*Pseudaxinyssa sp.*), *Manduca sexta*[4,5,28,34,35] and others. Allyl isothiocyanate, for example, is a main component of mustard oil, prepared from *Sinapis nigra* or roots of *Cochlearia armoracea*.[2] The same isothiocyanate was isolated from the degradation products of the β-thioglucoside sinigrin.[36,37]

Many isothiocyanates possess high biological activity,[38-42] including pesticidal (fungicidal and herbicidal) properties. This allows one to employ some of them as soil sterilants, fungicides, nematocides, and herbicides.[6,7,43] Methyl isothiocyanate (with the trade names Trapex and Vorlex), for example, is a soil fumigant and is applied for controlling nematodes, soil fungus, insects and weeds.[6,7,44,45] Strong ovicidic properties of this compound have also been reported.[44] Allyl isothiocyanate is used for the preparation of ointments and mustard plasters.[7] Some natural and synthetic isothiocyanates have cytotoxic (on *HeLa* cells) and cancerostatic effects.[39-42]

During the last years, numerous patents[46-56] concerning the application of isothiocyanates as components of liquid-crystal compositions and their use in electro-optical elements have been published.

Recently a review,[57] covering the homo- and copolymerization of heterocumulenes, including isothiocyanates, to give functional polymers, has appeared.

A new type of heterodienes with an isothiocyanate group conjugated with another multiple bond, *e.g.* a carbon-carbon, carbon-nitrogen, carbon-oxygen, carbon-sulfur double bond, or a carbon-carbon triple bond, is of high synthetic and practical potential. These novel bifunctional compounds may well be promising starting materials for heterocyclic compounds.[23,58]

This review deals with the basic methods of synthesis and with the structure and reactivity of α,β-unsaturated isothiocyanates (mainly vinyl isothiocyanates) and covers original papers mostly of the period from 1967 to 1989.[59-61]

These examples just illustrate some typical and important properties and applications of isothiocyanates and by no means constitute an exhausting coverage.

2. SYNTHESIS OF α,β-UNSATURATED ISOTHIOCYANATES

The classic procedures for the synthesis of isothiocyanates, including some α,β-unsaturated isothiocyanates, require the corresponding primary amines.[1,2,8,59] However, isothiocyanates with the NCS group bound directly to a C=C bond, as a rule, cannot be prepared in the usual manner. A number of general and special methods for the preparation of α,β-unsaturated isothiocyanates have been described.

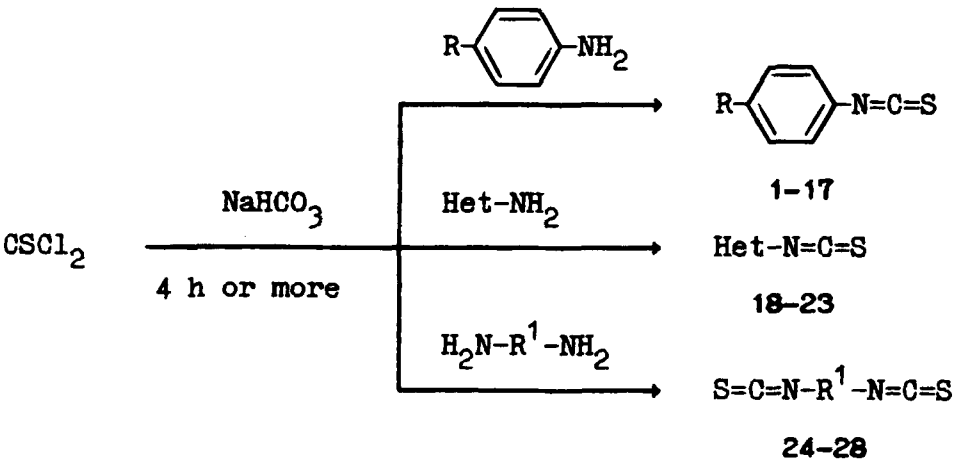
Some of the known isothiocyanate syntheses are of limited applicability, *e.g.*, the preparation of 2- and 3-thienyl isothiocyanate.[62]

Below, most general synthetic approaches to α,β-unsaturated isothiocyanates are discussed (the term "α,β-unsaturated isothiocyanates" comprises those formally containing C=C-NCS, C≡C-NCS, and N=C-NCS moieties).

2.1. *From Thiophosgene and Nitrogen Compounds*

2.1.1. *Reactions of amines with thiophosgene*

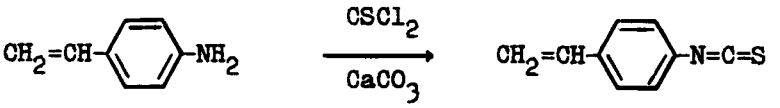
2.1.1.1. *Reactions of aryl amines and heterocyclic amines with thiophosgene* A number of 4-substituted phenyl isothiocyanates **1–17** [R = 4-morpholinyl (**1**), 1-methyl-4-piperazinyl (**2**), 1-methyl-4-piperazinyl methiodide (**3**), H_2NSO_2 (**4**), 4-chlorophenylthio (**5**), 4-nitrophenylthio (**6**), 4-methyl-2-thiazolyl (**7**), 2-methyl-4-thiazolyl (**8**), 5-nitro-2-thiazolylthio (**9**), 2-benzothiazolyl (**10**), 2-benzothiazolylthio (**11**), 2-benzoxazolylthio (**12**), 2-benzimidazolyl (**13**), 5-chloro-2-benzimidazolyl (**14**), 1-methyl-2-benzimidazolyl (**15**), (2-benzimidazolyl)methoxy (**16**), (1-methyl-2-benzimidazolyl)methoxy (**17**)] (yields 21–95%), heterocyclic isothiocyanates **18–23** [Het = 3-quinolyl (**18**), 6-quinolyl (**19**), 2-benzothiazolyl (**20**), 4-benzo[2.1.3]thiadiazolyl (**21**), 3-chloro-7-phenothiazinyl (**22**), 3-trifluoromethyl-7-phenothiazinyl (**23**)] (yields 32–92%) and arylene bisisothiocyanates **24–28** [R^1 = 2,6-pyridylene (**24**), 1,4-naphthylene (**25**), 1,5-naphthylene (**26**), 4,4-C_6H_4-SO_2-C_6H_4 (**27**), 4,4′-C_6H_4-S-S-C_6H_4 (**28**)] (yields 85–96%) have been synthesised by reaction of the corresponding amines with thiophosgene in chloroform or dioxane or acetone in the presence of aqueous sodium bicarbonate (Scheme 1).[63]



SCHEME 1

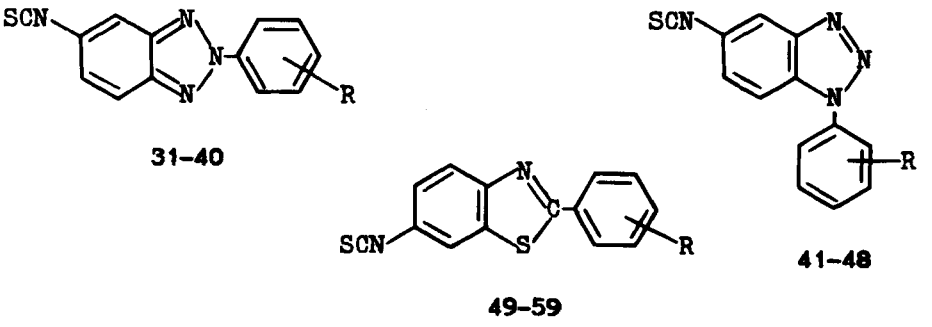
In the same manner, 4-vinylphenyl isothiocyanate **30** (yield 37.3%)[64] has been prepared from 4-aminostyrene **29** and thiophosgene in the presence of calcium carbonate in 1,2-dichloroethane/water (Scheme 2).

1-(R-Phenyl)-5-benzotriazolyl isothiocyanates **31–40**, 2-(R-phenyl)-5-benzotriazolyl isothiocyanates **41–48**, and 2-(R-phenyl)-6-benzothiazolyl isothiocyanates **49–59** have been prepared by the thiophosgene method from the corresponding substituted amines (Scheme 3).[65–69]



29 30

SCHEME 2

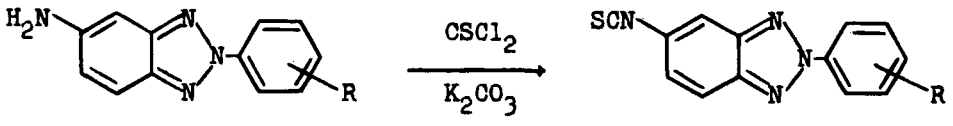


31–40 41–48 49–59

R = H (31,41,49), 3-Cl (32,42), 3-Br (33,50), 3-Me (34,43,51), 3-OMe (35), 3-NCS (52), 4-Cl (36,44,53), 4-Br (37,45,54), 4-I (55), 4-Me (38,46,57), 4-OMe (39,47,58), 4-CO_2Et (40,48), 4-NCS (56), 4-NMe_2 (59).

SCHEME 3

Thus, 5-amino-2-phenylbenzotriazole **60** reacts with thiophosgene in $CHCl_3/H_2O$ [1:2] in the presence of potassium carbonate for 2 h to give 5-isothiocyanato-2-phenylbenzotriazole **31** in 67% yield (Scheme 4).[69]

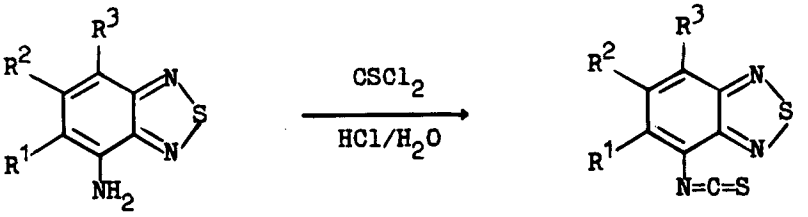


60–64 31,34,36,38,39

R = H (60,31), 3-Me (61,34), 4-Cl (62,36), 4-Me (63,38), 4-OMe (64,39).

SCHEME 4

4-Amino-2,1,3-benzothiadiazoles **65** have been converted to 4-isothiocyanato-2,1-3-benzothiadiazoles **21** and **66–83** by reaction with thiophosgene in 4 N aqueous HCl at room temperature for 24 h (Scheme 5).[70]

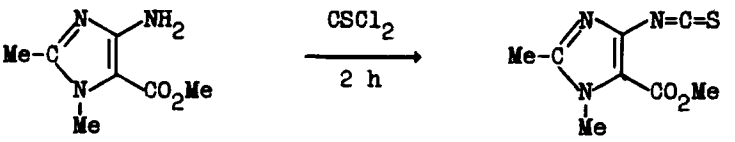


65 **21,66–83**

$R^1 = R^2 = R^3 = H$ (**21**); $R^1 = R^2 = H$, $R^3 =$ Me (**66**), OMe (**67**), NO_2 (**68**), OH (**69**); $R^1 = H$, $R^2 = R^3 =$ Cl (**70**); $R^1 =$ Me, $R^2 = R^3 = H$ (**71**), $R^2 = H$, $R^3 =$ Cl (**72**); $R^1 = R^2 =$ Me, $R^3 = H$ (**73**); $R^1 = R^3 =$ Me, $R^2 = H$ (**74**); $R^1 =$ Et, $R^2 = R^3 = H$ (**75**); $R^1 =$ OMe, $R^2 = R^3 = H$ (**76**); $R^1 =$ Cl, $R^2 = R^3 = H$ (**77**); $R^1 =$ Cl, $R^2 = H$, $R^3 =$ Me (**78**), Br (**79**); $R^1 = R^2 =$ Cl, $R^3 = H$ (**80**); $R^1 = R^3 =$ Cl, $R^2 = H$ (**81**); $R^1 =$ Br, $R^2 = R^3 = H$ (**82**); $R^1 =$ Br, $R^2 = H$, $R^3 =$ Cl (**83**).

SCHEME 5

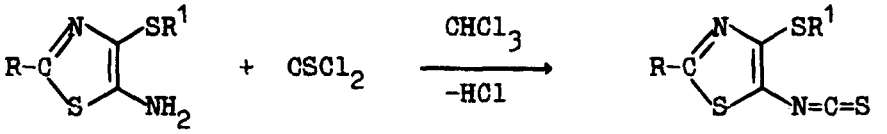
4-Aminoimidazole-5-carboxylic acid methyl ester **84** (in HCl) has been converted to the corresponding isothiocyanate **85** by reaction with thiophosgene in dichloromethane in the presence of aqueous calcium carbonate (Scheme 6).[71]



84 **85** (70%)

SCHEME 6

5-Amino-4-alkylthio-2-arylthiazoles **86** react with thiophosgene in water (15 °C, 30 min) to form 4-alkylthio-2-arylthiazol-5-yl isothiocyanates **87–89** in 50–72% yield (Scheme 7).[72]

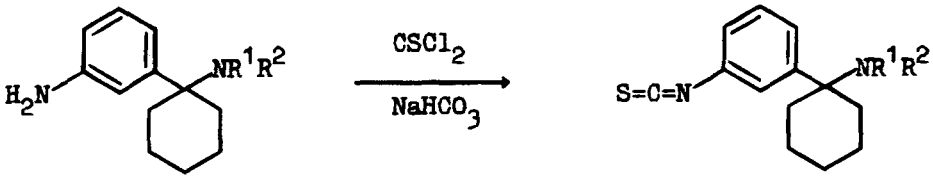


86 **87–89**

R = Ph, R^1 = Me (**87**), $PhCH_2$ (**88**); R = 4-ClC_6H_4, R^1 = Me (**89**).

SCHEME 7

Treatment of 1-[1-(3-aminophenyl)cyclohexyl]piperidine **90** with a solution of thiophosgene in a two-phase system consisting of chloroform and aqueous sodium bicarbonate and subsequent salt formation with methanesulfonic acid or HCl leads to the corresponding isothiocyanate **93** (Scheme 8).[73]



90–92 **93–95**

R^1-R^2 = $(CH_2)_5$ (**90,93**), R^1 = H, R^2 = Et (**91,94**), *t*-Pr (**92,95**).

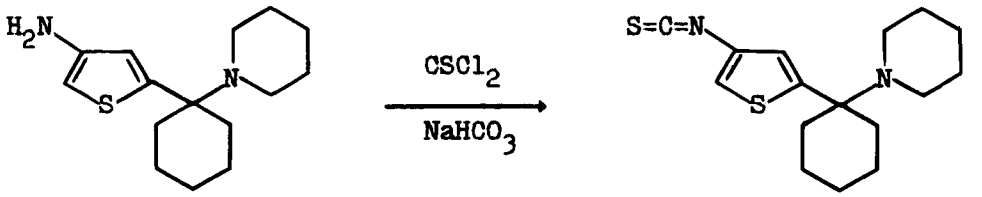
SCHEME 8

Analogously, 1-[1-(3-aminophenyl)cyclohexyl]ethylamine **91**, 1-[1-(3-aminophenyl)cyclohexyl]isopropyl amine **92** and 1-[1-(4-aminothiophen-2-yl)cyclohexyl]piperidine **96** have been converted to the corresponding isothiocyanates **94**, **95**, and **97** (Schemes 8 and 9).[74]

The methyl 3-amino-2-thiophenecarboxylate hydrochlorides **98** and **99** have been converted to the isothiocyanates **101** and **102** by treatment with thiophosgene in chloroform/water in the presence of sodium carbonate at room temperature for 1.5 h (Scheme 10).[75]

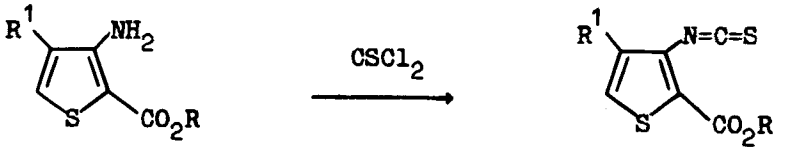
Under the same reaction conditions, but in the presence of sodium bicarbonate, ethyl 3-isothiocyanato-2-thiophenecarboxylate **103** has been prepared from ethyl 3-amino-2-thiophenecarboxylate **100**.[76]

Treatment of the ethyl 2-amino-3-thiophenecarboxylates **104** with thiophosgene in chloroform/water in the presence of sodium bicarbonate at room temperature for 1 h leads to corresponding isothiocyanates **105–109** (Scheme 11).[76]



96 97

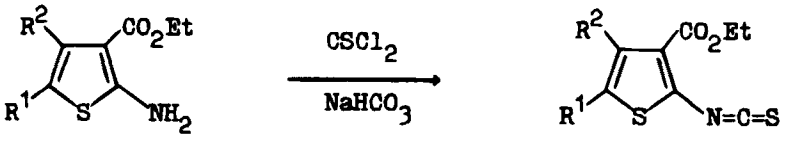
SCHEME 9



98–100 101–103

R = Me, R^1 = (98,101), Me (99,102); R = Et, R^1 = H (100,103).

SCHEME 10



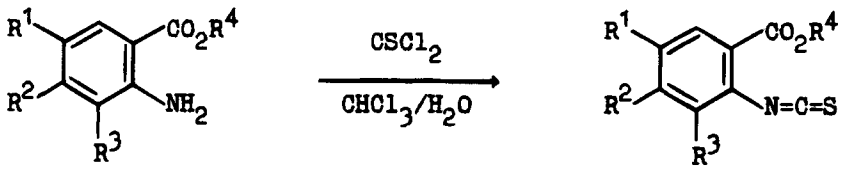
104 105–109

R^1 = R^2 = H (105), Me (106); R^1 = Me, R^2 = H (107); R^1 = Ph, R^2 = H (108); R^1–R^2 = $(CH_2)_4$ (109).

SCHEME 11

Analogously, the methyl (or ethyl) 1-isothiocyanato-2-benzenecarboxylates **111–121** have been prepared from the corresponding 1-amino derivatives **110** (Scheme 12).[76]

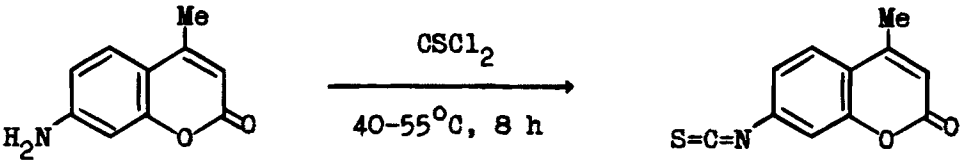
4-Methyl-coumarin-7-yl isothiocyanate **123** and 7-dimethylamino-4-methylcoumarin-3-yl isothiocyanate **125** have been synthesized from the corresponding amines **122** and **124** by reaction with thiophosgene (Schemes 13 and 14).[77]



110 111–121

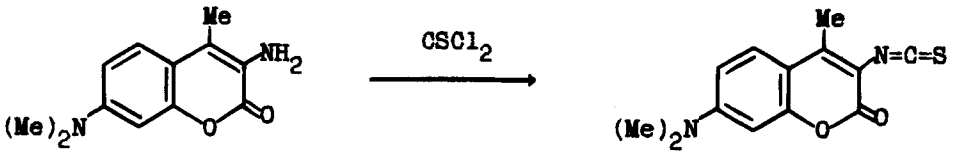
R^4 = Me: R^1 = R^2 = R^3 = H (111); R^2 = R^3 = H, R^1 = Cl (112), Me (113), *t*-Bu (114), MeO (115), CO_2Me (116); R^1 = R^3 = H, R^2 = Cl (117), Me (118); R^1 = H, R^2 = Cl, R^3 = Me (119); R^1 = R^2 = H, R^3 = Me (120); R^4 = Et: R^1 = H, R^2 = Cl, R^3 = Me (121).

SCHEME 12



122 123

SCHEME 13

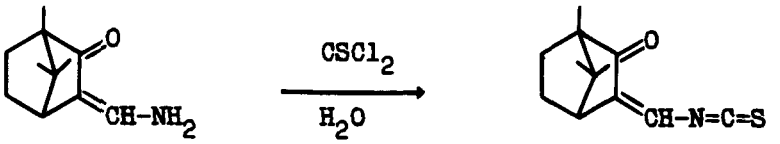


124 125

SCHEME 14

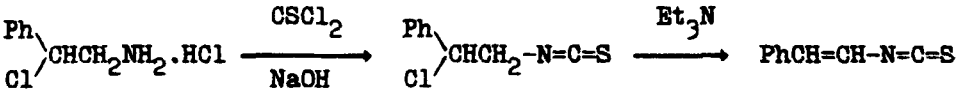
2.1.1.2. *Reaction of 3-aminomethylene-DL-camphor with thiophosgene* 3-Aminomethylene-*DL*-camphor **126** reacts with thiophosgene in water for 2 h to form the 3-(isothiocyanatomethylene)-*DL*-camphor **127** in 45% yield (Scheme 15).[78]

2.1.1.3. *Reactions of haloamines with thiophosgene* As a starting compound for the synthesis of β-styryl isothiocyanate **130**, 1-phenyl-1-chloroethylammonium chloride **128** has been used.[79] From this compound, 1-phenyl-1-chloroethyl isothiocyanate **129** has been ob-



126 127

SCHEME 15



128 129 130

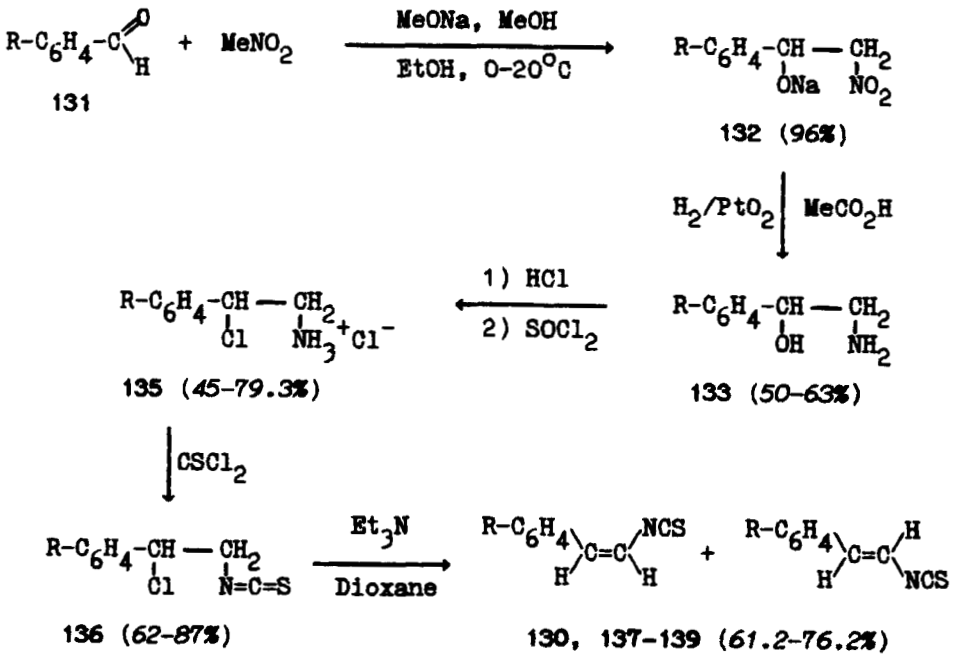
SCHEME 16

tained by the thiophosgene method in a yield of 79.5%.[79] Dehydrohalogenation of this compound with triethylamine gave β-styryl isothiocyanate **130** (in a yield of 67%) as a mixture of *cis*- and *trans*-isomers (1:4). This mixture was separated by preparative gas chromatography and the structures of the individual isomers were unambiguously proven by spectroscopic methods.[79]

A synthesis of the 4-substituted 2-phenylethenyl isothiocyanates **130** and **137–139** from the appropriate benzaldehydes **131** and nitromethane has been worked out (Scheme 17).[80] The intermediate nitro alcohols **133** were catalytically reduced at atmospheric pressure and transformed to the 4-substituted 2-chloro-2-phenylethylammonium chlorides **135** by reaction of the corresponding 2-hydroxy-2-phenylethylamine hydrochlorides **134** with thionyl chloride. The latter were thiophosgenated[79,80] and dehydrohalogenated with triethylamine (under nitrogen atmosphere at 100 °C, 8–50 h) to form the 4-substituted 2-phenylethenyl isothiocyanates **130** and **137–139** as mixtures of geometric isomers (Scheme 16).[80] Their configurations and ratios were determined by ^{1}H NMR spectroscopy and gas chromatography.[80] 2-(4-Nitrophenyl)ethenyl isothiocyanate **139** was isolated exclusively in the *trans form.*

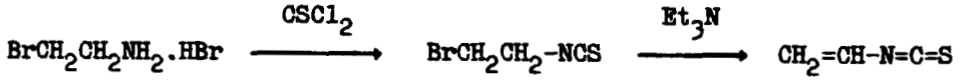
Vinyl isothiocyanate **142** has been prepared by the following procedure.[60,64,81] From 2-bromoethylamine hydrobromide **140** and thiophosgene in 1,2-dichloroethane/water 2-bromoethyl isothiocyanate **141** was obtained (yield 75%). Treatment of the isothiocyanate **141** with triethylamine gave vinyl isothiocyanate **142** in a yield of 61% (Scheme 18).

2.1.2. *Reactions of imines with thiophosgene* The alk-1-enyl isothiocyanates **145–147** have been prepared in 62–77% yield by the reaction of the ketimines **143** with thiophosgene in dry toluene (2–3 h) (Scheme 19).[82,83]



R = H (130), 4-Me (137), 4-Cl (138), 4-NO_2 (139).

SCHEME 17

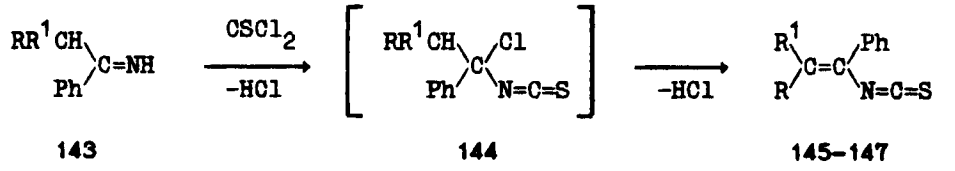


SCHEME 18

2.1.3. *Reactions of nitrogen heterocycles with thiophosgene*

2.1.3.1. *Reactions of azoles with thiophosgene* The preparation of 1,2-di(isothiocyanato)ethene **152** by cleavage of imidazole **148** with thiophosgene in the presence of calcium carbonate in dichloromethane and aqueous acetonitrile (under nitrogen at 5–10 °C, 1 h) has been described in Ref.[84] (Scheme 20).

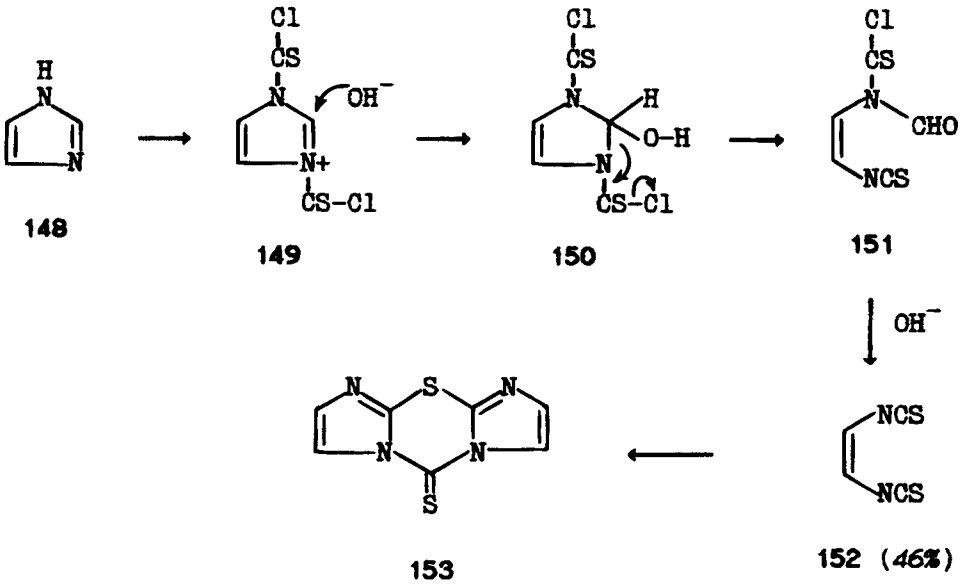
Although a solution of 1,2-di(isothiocyanato)ethene **152** may be stored (in a refrigerator) for a long period, attempts to isolate 1,2-di(isothiocyanato)ethene **152** have been un-



143 144 145–147

R = R^1 = Me (145); R = H, R^1 = *n*-Pr (146); R = H, R^1 = *i*-Pr (147).

SCHEME 19



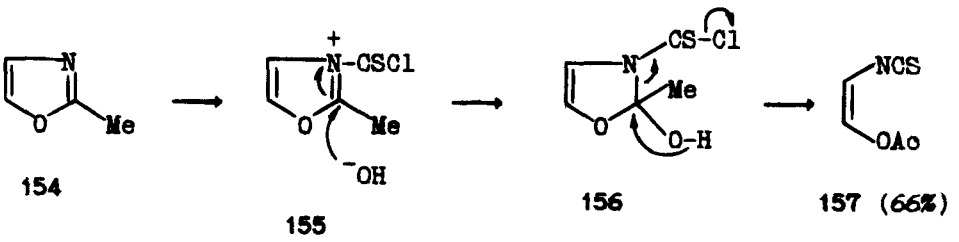
SCHEME 20

successful. Evaporation of the solution gave an oil which slowly decomposed on standing, with loss of carbon disulfide, into the tricyclic thione **153** (Scheme 20).[84]

The reaction of 2-methyloxazole **154** with thiophosgene (dichloromethane/water, $CaCO_3$, room temperature, 16 h) presumably proceeds according to Scheme 21. 2-Isothiocyanatovinyl acetate **157** was obtained as a colorless oil.[85]

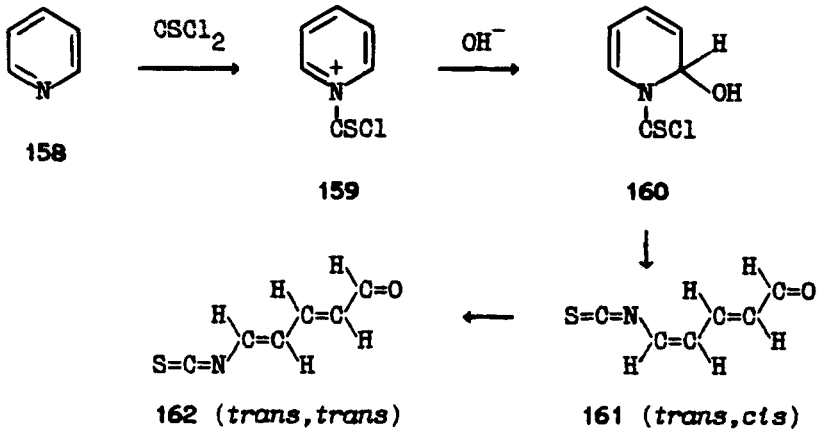
2.1.3.2. *Reactions of pyridine, quinolines and isoquinolines with thiophosgene* The study of Ref.[85] shows that thiophosgene and calcium carbonate in a two-phase water/dichloromethane system quite generally open the rings of nitrogen heterocyclic compounds.

Pyridine **158** reacts smoothly with thiophosgene and alkali in dichloromethane/water at 15 °C.[86] Extraction with ether yields *trans,cis*-1-formyl-4-isothiocyanatobuta-1,3-diene



SCHEME 21

161 (Scheme 22). The NMR spectrum of **161** exhibits considerable solvent dependence. Recrystallization (cyclohexane) of the crude reaction mixture gave the *trans,trans*-isomer of 1-formyl-4-isothiocyanatobuta-1,3-diene **162**. Its NMR spectrum also exhibits solvent dependence.[87]



SCHEME 22

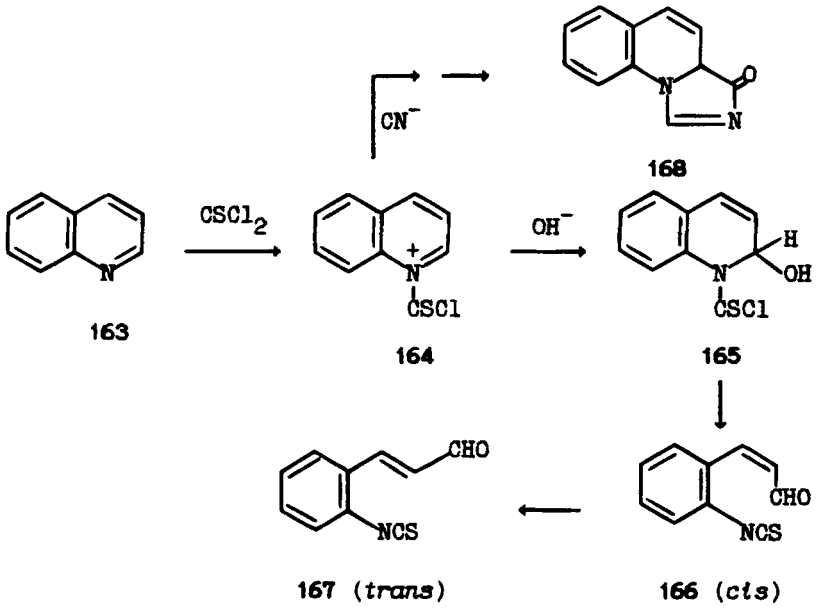
Less than 5% of a product, identified possibly as the *trans,trans*-isomer of 1-formyl-4-isothiocyanatobuta-1,3-diene **162**, has been obtained from the reaction of pyridine and thiophosgene with 2 N aqueous sodium hydroxide.[88] The yield was later raised to 18% by the use of barium carbonate (0 °C, 15 min). The reaction pathway requires addition of OH^- to the intermediate **159** which can then undergo ring scission to the diene **161** and isomerization to the diene isomer **162** (Scheme 22).[87,88]

In a repeat reaction of thiophosgene and barium carbonate with pyridine and immediate work-up of the reaction mixture, an isomeric compound was obtained as needles, m.p. 55

°C, tentatively identified as the *trans,cis*-isomer of 1-formyl-4-isothiocyanatobuta-1,3-diene **161**.[88]

Hull *et al.* reported a novel synthesis of 2-isothiocyanato-*trans*-cinnamaldehydes and 2-(*cis*-isothiocyanatovinyl)benzaldehyde by fission of quinolines and of isoquinoline, respectively, with thiophosgene in the presence of base (hydroxide ion).[88-91]

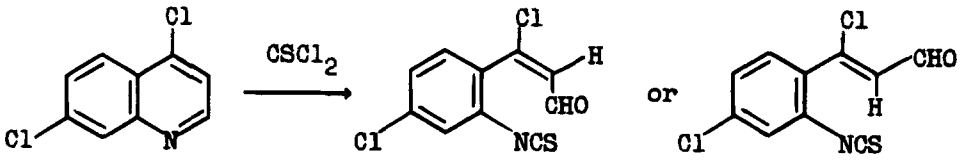
The reaction of quinoline **163** with thiophosgene and potassium cyanide in dichloromethane/water gave mainly two products: 2-isothiocyanato-*trans*-cinnamaldehyde **167** in 4% yield, and 3-oxoimidazo[1,5-*a*]quinoline **168** in 22% yield, separated by preparative TLC (Scheme 23).[85,88,92,93]



SCHEME 23

This means that the yield of the trans-aldehyde **167** should increase as the OH^- concentration increases. In fact, reaction of quinoline with thiophosgene and dilute sodium hydroxide in CH_2Cl_2/H_2O gave 2-isothiocyanato-*trans*-cinnamaldehyde **167** in 36% yield. Substitution of sodium hydroxide by barium carbonate gave the cis-isomer **166** as an oil. After standing overnight, 30% conversion had occurred to the *trans*-isomer **167**. A spectrum of the product after 3 days standing showed complete isomerization to the *trans*-isomer **167**.[88]

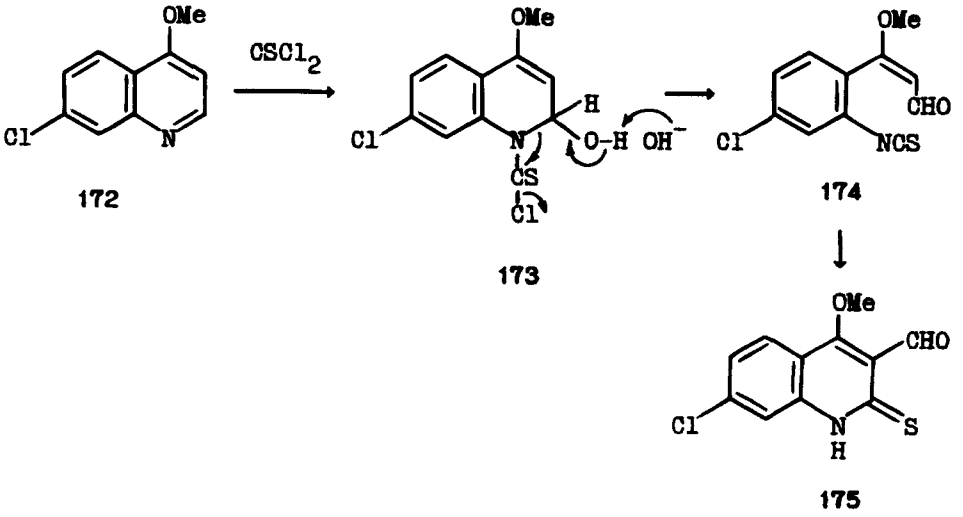
4,7-Dichloroquinoline **169** reacts smoothly with thiophosgene and $BaCO_3$ in dichloromethane/water (for 4 h at 0 °C, then overnight at room temperature) and yields (58%) the β,4-dichloro-2-isothiocyanatocinnamaldehydes **170** and **171** as reasonably stable compounds (Scheme 24).[91]



169 **170** **171**

SCHEME 24

The same procedure has been applied to 7-chloro-4-methoxyquinoline (**172**) (Scheme 25).[90] The reaction mixture was stirred in the presence of $BaCO_3$ for 2 h at 0 °C, then for 1 h at room temperature (H_2O/CH_2Cl_2). Ring fission took place, probably via the dihydroquinoline **173**, to yield the rather unstable 4-chloro-2-isothiocyanato-β-methoxycinnamaldehyde **174**.



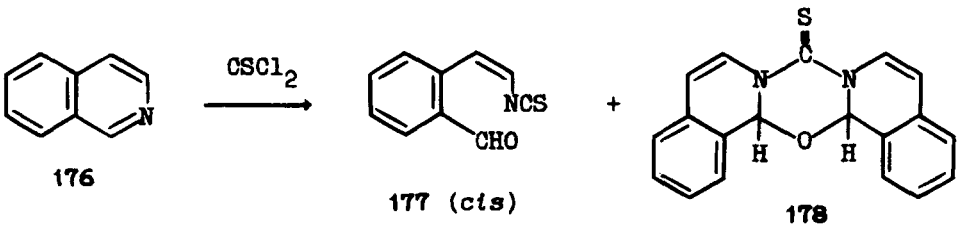
172 **173** **174** **175**

SCHEME 25

The product **174** could be observed by TLC and was identified by IR spectroscopy. The stereochemistry is unknown. Attempted isolation of **174** by evaporation of the dichloromethane solution led to violent decomposition. However, **174** in dichloromethane

underwent spontaneous ring closure to the alkali soluble methoxyquinolinecarbaldehyde **175**. Attempts to induce attack by an external nucleophile on the isothiocyanato group of 4-chloro-2-isothiocyanato-β-methoxycinnamaldehyde **174** led to complex mixtures which were not further investigated.[90]

By action of thiophosgene on isoquinoline **176** in the presence of dilute alkali two products, cis-4-isothiocyanatovinyl benzaldehyde **177** as a pale yellow oil and 15b,16a-dihydro-8*H*-diisoquinolino[1,2-*b*:2′,1′-*e*]-[1,3,5]oxadiazine-8-thione (**178**) as needles, have been obtained (Scheme 26).[88,92]



176 **177** (*cis*) **178**

SCHEME 26

As an extension of this work the authors of Ref.[89] prepared 3-(2-isothiocyanato-5-methoxyphenyl)prop-2-enal **181** (yield 62%) and 3-(2-isothiocyanatophenyl)but-2-enal **182** (an unstable dark oil) from 6-methoxyquinoline **179** and 4-methylquinoline **180**, respectively. The reaction was carried out in dichloromethane/water in the presence of calcium carbonate in an ice-bath for 4 h.

2-Isothiocyanato-trans-cinnamaldehyde **167** (yield 76%) has been prepared similarly from quinoline.[89]

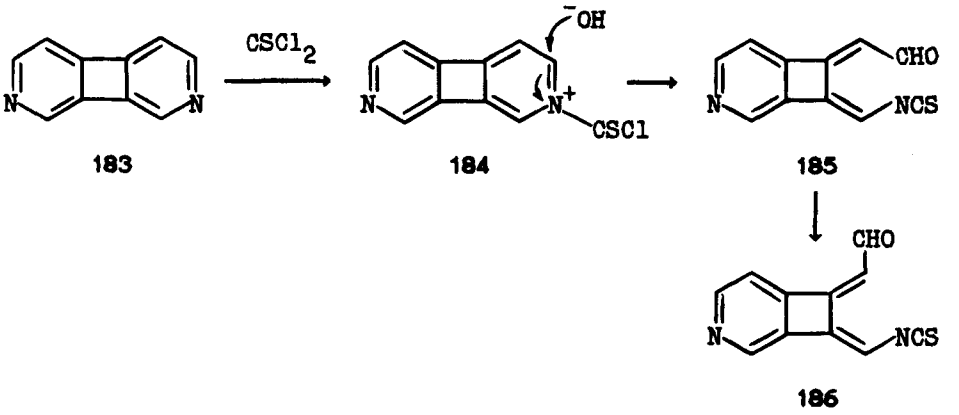
2.1.3.3. *Reactions of diazabiphenylenes with thiophosgene* Treatment of a dilute (10 mg/ml) solution of 2,7-diazabiphenylene **183** in dichloromethane with a corresponding solution of thiophosgene (1 mol) at 0 °C in the presence of suspended barium carbonate (5 mol) and an equal volume of water gave a single product **186** in 60% yield (after filtration, evaporation of the organic phase, and vacuum sublimation) (Scheme 27).[92,94]

The formation of the isothiocyanate **185** can be explained if initial electrophilic quaternization of a ring nitrogen is followed by nucleophilic addition to C-3. The reaction product is stable to air but discolors rapidly upon exposure to light.

1,8-Diazabiphenylene reacts with thiophosgene under similar conditions but no well-defined product could be isolated or detected by TLC.

2.2. *From Amines, Carbon Disulfide and Alkyl Chloroformates*

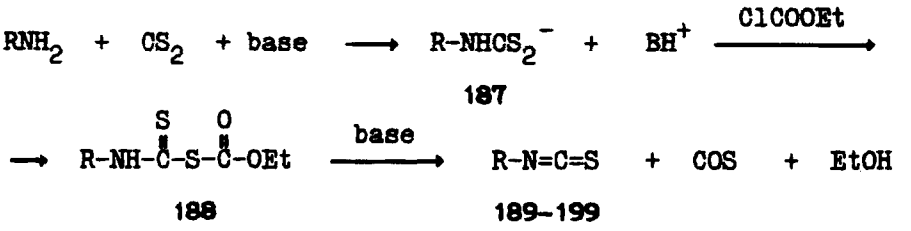
Aliphatic and aromatic isothiocyanates are conveniently formed by dehydrosulfurization of dithiocarbamates.[1,2,8] There are several methods by which this can be accomplished. The best route to alkyl isothiocyanates is considered to be the alkoxycarbonylation of dithio-



SCHEME 27

carbamates, followed by thermal decomposition of the resulting thiocarbonates.[95] This method can also be used to prepare alkenyl isothiocyanates.[95]

2.2.1. *Reactions of aromatic amines* The synthesis of the isothiocyanates **189–199** by the modified Kaluza method may be divided into three parts (Scheme 28): first, the formation of the dithiocarbamate salt **187** from an amine, carbon disulfide, and a base; secondly, the formation of the carbethoxy dithiocarbamate **188** by treatment of **187** with ethyl chloroformate and thirdly, decomposition of **188** with base to the isothiocyanate.[96]



R = Ar (see Table 1).

SCHEME 28

The first step of this synthesis proved to be more difficult with aromatic amines than with aliphatic amines owing to their lower basicity. In order to prepare the aryldithiocarbamates **187** (R = aryl), it was necessary to use nonaqueous solvents such as benzene or ether and a strong organic base such as triethylamine.[96] Under these conditions the aryldithiocarbamates precipitate from solution. With aniline and higher base strength amines, precipitation of the dithiocarbamate begins within about 5 min at 0 °C.[96] The lower base strength

amines, e.g., 4-chloroaniline, require several hours under the same conditions before the appearance of the dithiocarbamate derivative. Yields of this first step range from 83 to greater than 90%.[96]

Carbethoxylation of **187** has been accomplished in chloroform solution without difficulty. The decomposition of the intermediate carbethoxy aryldithiocarbamates **188** has been carried out in the same solution with triethylamine. The yields of the isothiocyanates **189–199** range from 70 to 92%.[96] That results obtained with various aromatic amines are summarized in Table 1.[96]

TABLE 1 Modified Kaluza synthesis[96] of aryl isothiocyanates, Ar-NCS (**189–199**)

Cpd. No.	Ar	Formation time for dithiocarbamate	Yield of dithiocarbamate, %	Yield of Ar-NCS, %
189	Ph	24 h	90	81
190	2-MeC_6H_4	24 h	89	80
191	3-MeC_6H_4	24 h	94	78
192	4-MeC_6H_4	24 h	92	81
193	4-ClC_6H_4	72 h	83	70
194	4-BrC_6H_4	3–4 d	88	73
195	2-$MeOC_6H_4$	3 h	88	82
196	4-$EtOC_6H_4$	3 h	89	88
197	4-$(Me)_2NC_6H_4$	15 min	95	60[a]
198	β-$C_{10}H_7$	7 d	90	73
199	4-$MeOC_6H_4$	3 h	95	92
	4-CNC_6H_4	No reaction	0	0
	4-$NO_2C_6H_4$	No reaction	0	0

[a]This is the only entry in the table based on a single reaction.

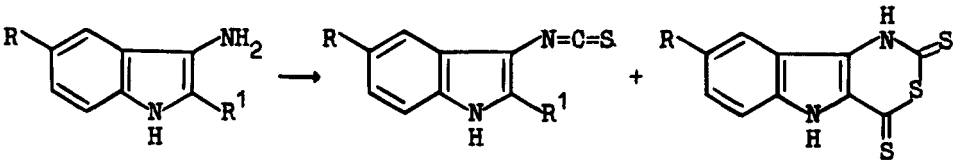
This method is not applicable, in its present form, to the synthesis of isothiocyanates containing strongly electron-withdrawing groups.

2.2.2. *Reactions of heterocyclic amines* It has been shown[97] that reaction of 3-aminoindole (**200**, R = R' = H) with carbon disulfide under conditions typical for the preparation of dithiocarbamate salts (amine, CS_2, KOH, EtOH) leads to 3-indolyl isothiocyanate **201** and 5*H*-2-mercapto-4-thioxoindolo[2,3-*d*]-1,3-thiazine **204** in 3% and 32% yield, respectively (Scheme 29).

Introduction of acetic anhydride into the reaction mixture (after 5 min) also gave isothiocyanate **201** (6%) together with 3-acetylaminoindole (**206**) (61%).[97]

The use of sodium ethoxide in ethyl alcohol instead of KOH allowed the conversion of the 3-aminoindoles **200** to the corresponding isothiocyanates **201–203** in 40–64% yield.[97] A proposed mechanism of this reaction is shown in Scheme 30.

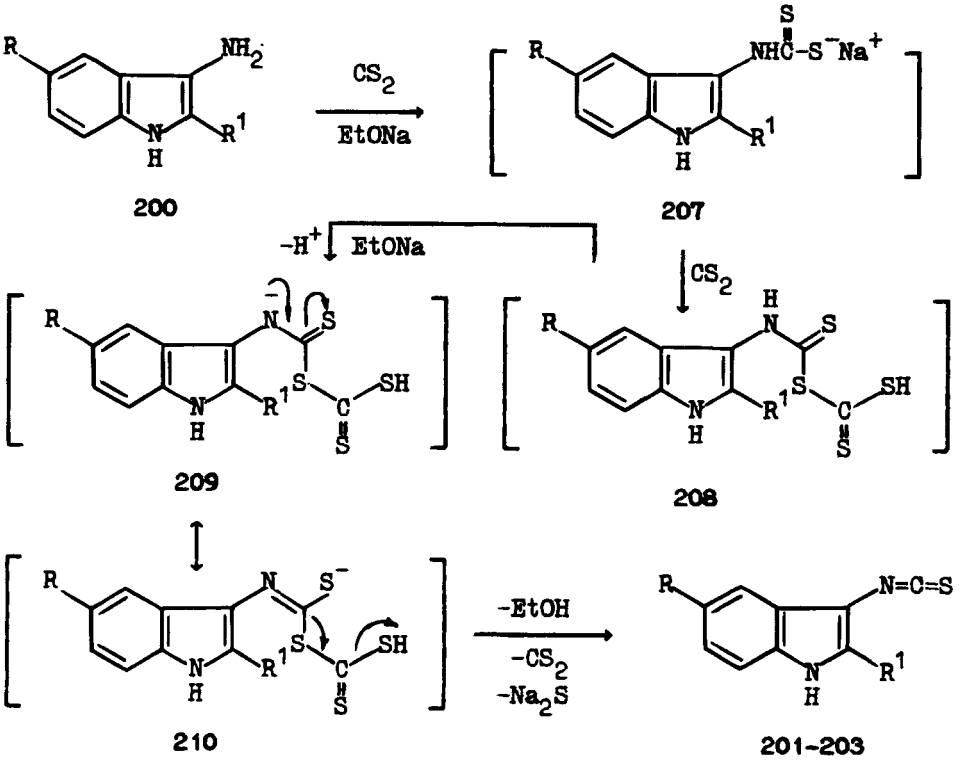
2-Aminobenzo[*b*]thiophene **211** with carbon disulfide in anhydrous toluene in the presence of triethylamine at 0–5 °C for 3 days under nitrogen and upon subsequent treatment with ethyl chloroformate at ambient temperature for 1 h gave 2-isothiocyanatobenzo[*b*]thiophene **212** as an oil (Scheme 31).[98]



200 201-203 204,205

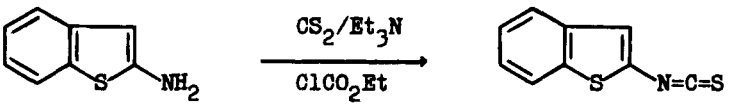
$R = R^1 = H$ (201,204); $R = Br$, $R^1 = H$ (202,205); $R = H$, $R^1 = Me$ (203).

SCHEME 29



200 207 209 208 210 201-203

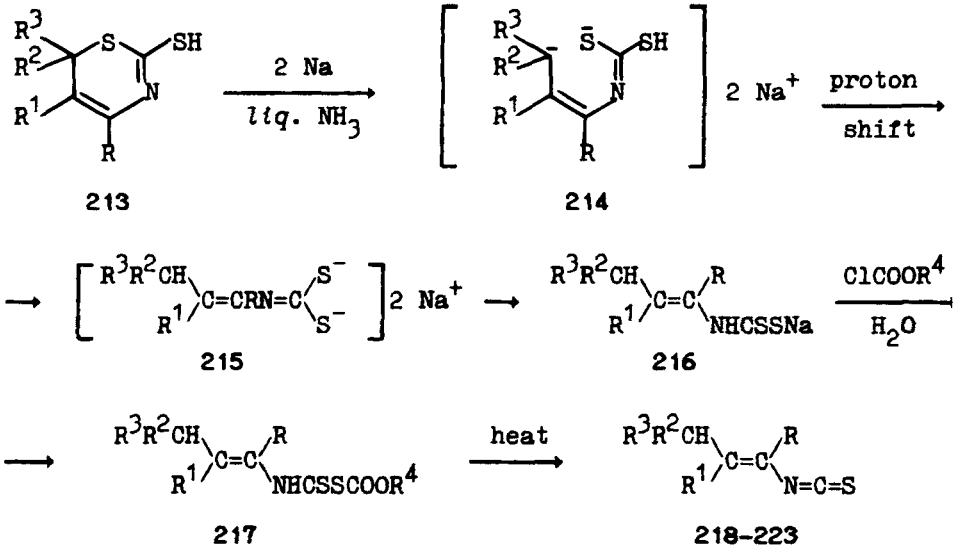
SCHEME 30



211 212

SCHEME 31

2.2.3. *Reactions of 1-alkenyl dithiocarbamates with alkyl chloroformates* An aqueous solution of the monosodium salt **216**, obtained by reductive cleavage of the alkyl- or aryl-substituted 2-mercapto-6*H*-1,3-thiazines **213** (with small pieces of sodium metal in anhydrous liquid ammonia)[99] and addition of one equivalent of ammonium chloride, is treated with an alkyl chloroformate at 0 °C (Scheme 32).[95] The intermediate *S*-alkoxycarbonyl *N*-1-alkenyldithiocarbamate **217** precipitates and can be isolated; however, heating of the heterogenous reaction mixture at about 50 °C induces decomposition of **217** to the 1-alkenyl isothiocyanates **218–223**, carbon oxysulfide and the corresponding alcohol. The isothiocyanates **218–223** can be isolated by distillation in yields of 54–88%.[95]



213 214 215 216 217 218–223

R = R^1 = R^2 = H, R^3 = Me (218); R = Me, R^1 = R^2 = R^3 = H (219); R = Me, R^1 = R^2 = H, R^3 = Ph (220); R = R^2 = R^3 = Me, R^1 = H (221); R = R^1 = Me, R^2 = R^3 = H (222); R = R^1 = R^2 = Me, R^3 = H (223).

SCHEME 32

The use of methyl or ethyl chloroformate leads to the formation of the bis(alkoxycarbonyl) sulfides **224**, $(R^4COO)_2S$ (R^4 = Me or Et), owing to the fact that the basic reaction

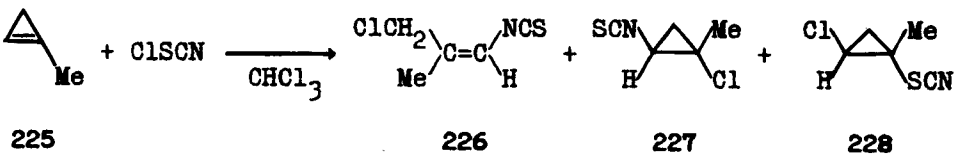
conditions are conducive to decomposition of the thioanhydride **217** to sodium thiocarbonate. Coupling of these carbonates with chloroformate gives rise to the formation of the bis(alkoxycarbonyl) sulfides **224**. These sulfides affect both the yield and the purity of the alk-1-enyl isothiocyanates **218–223**.[95] When isopropyl chloroformate is used as the carbalkoxylating agent, no sulfides **224** are formed.

The structure of the alk-1-enyl isothiocyanates **218–223** has been confirmed by elemental analysis and by spectroscopic data (IR, MS, ^{1}H NMR).

Irradiation of **218** and **220** with ultraviolet light in the presence of benzophenone as photosensitizer (benzene, 12 h) leads to photostationary states with *cis/trans* ratios of 1/1 and 3/1, respectively.[95]

2.3. *From Alkenes, Enamines, Alkynes and Inorganic Thiocyanates*

2.3.1. *Reactions with thiocyanogen halides* The reaction of 1-methylcyclopropene **225** with thiocyanogen chloride in the presence of di-*tert*-butyl-4-cresol at H −15 °C gave 2-methyl-2-chlorocyclopropyl isothiocyanate **227**, the isomeric 1-methyl-2-chlorocyclopropyl thiocyanate **228**, and 2-methyl-3-chloro-1-propenyl isothiocyanate **226** as the product of cyclopropane ring cleavage (Scheme 33).[100] The ratio of isothiocyanate **226**, Markovnikov and *anti*-Markovnikov adducts was determined by ^{1}H NMR spectroscopy as 5:3:2.[100]



225 **226** **227** **228**

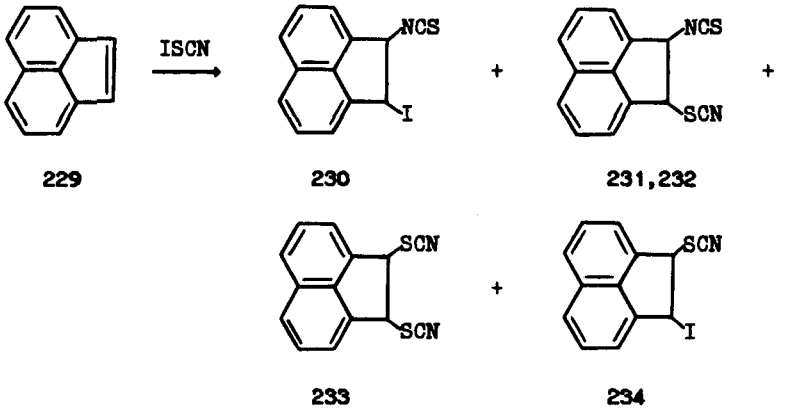
SCHEME 33

Reaction of acenaphthylene **229** with a mixture of thallium thiocyanate and iodine in chloroform at 0 °C for 2 h gave an oil which after HPLC afforded *trans*-1-iodo-2-isothiocyanatoacenaphthene **230** (16%), unstable oil, *trans*-1-isothiocyanato-2-thiocyanatoacenaphthene **231** (21%), pale yellow crystals, *cis*-1-isothiocyanato-2-thiocyanatoacenaphthene **232** (1.6%), unstable yellow solid, *trans*-1,2-dithiocyanatoacenaphthene **233** (4%), pale yellow needles, *trans*-1-iodo-2-thiocyanatoacenaphthene **234** (27%), unstable oil, and two unidentified compounds (traces) (Scheme 34).[101]

cis-1-Isothiocyanato-2-thiocyanatoacenaphthene **232** is also unstable, undergoing partial conversion to the ketone **237** during HPLC (Scheme 35).

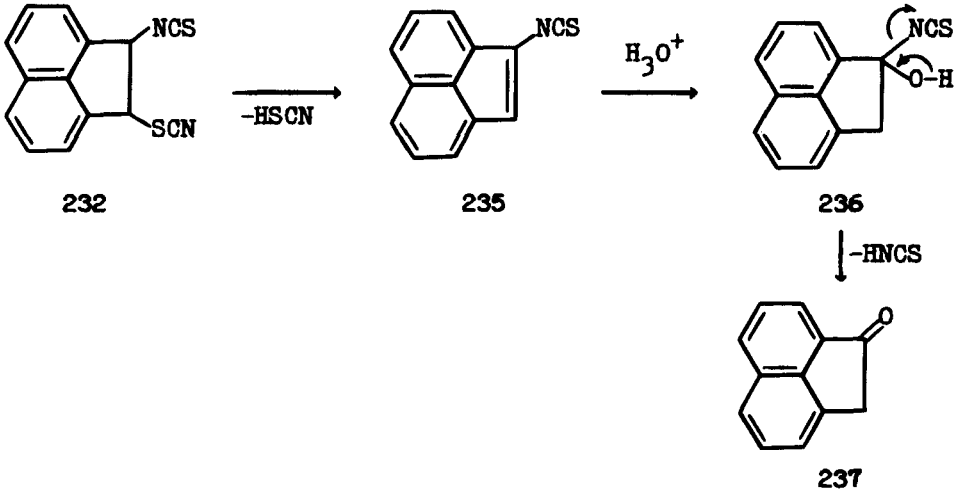
2.3.2. *Reactions of haloalkenes, enamines, and alkynes with thiocyanates*

2.3.2.1. *Reactions of vinyl halides* Photolysis of α-aryl-β,β-dimethylvinyl bromides **238** in the presence of thiocyanate anion in a two-phase system (CH_2Cl_2/H_2O) gives the vinyl isothiocyanates **145** and **240** (27–29%) together with the vinyl thiocyanates **241** (18–42%) (Scheme 36).[102]



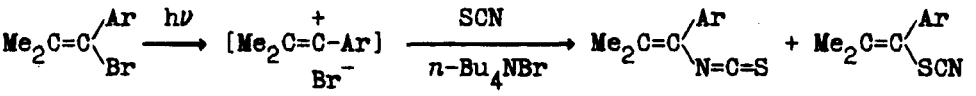
229 230 231,232 233 234

SCHEME 34



232 235 236 237

SCHEME 35



238 239 145, 240 241

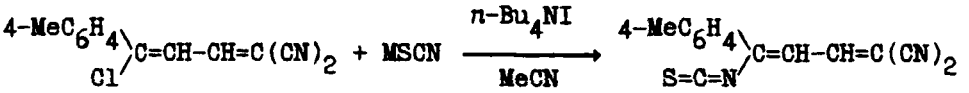
Ar = Ph (145), 4-$MeOC_6H_4$ (240).

SCHEME 36

Irradiation of the reaction mixture was performed with stirring and a Pyrex-filtered high-pressure Hg lamp (100 W) under N_2 atmosphere at 10 °C.[102]

Thus, the thiocyanate anion can react with the photogenerated vinyl cation **239** both at the sulfur and the nitrogen atom.[102]

Reaction of 3-(β-chlorovinyl)acrylonitrile **242** with potassium or sodium thiocyanate in the presence of tetrabutylammonium iodide gives 3-(β-isothiocyanatovinyl)acrylonitrile **250** (43–52%) (Scheme 37).[103]

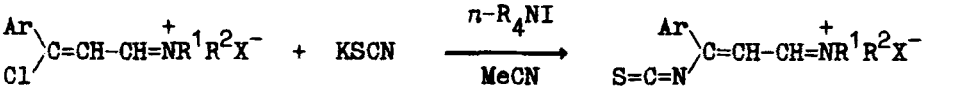


242 **243**

M = K, Na.

SCHEME 37

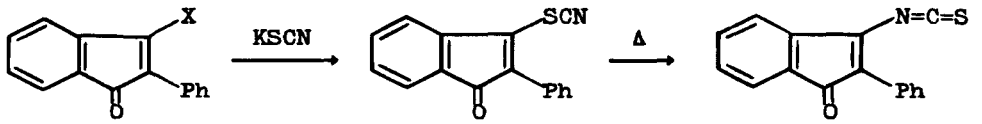
Analogously, reaction of the 3-chloro-2-propeneiminium salts **244** with KSCN or NaSCN in the presence of R_4NI (R = Et, *n*-Bu) and MCl (M = K, Na) in MeCN or DMF gives 3-isothiocyanato-2-propeneiminium salts **245–252**, were X = Cl^-, ClO_4^- or $PO_2Cl_2^-$ (Scheme 38).[104,105]



244 **245–252**

SCHEME 38

3,4-Dioxo-2-phenylcyclobut-1-enyl isothiocyanate **255** is prepared from 3-bromo- or 3-chloro-4-phenyl-3-cyclobutene-1,2-dione **253** and potassium thiocyanate in dry acetonitrile at 40 °C in 28% yield (Scheme 39).[106]

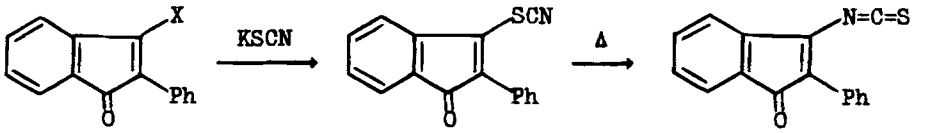


256 **257** **258**

X = Cl, Br.

SCHEME 39

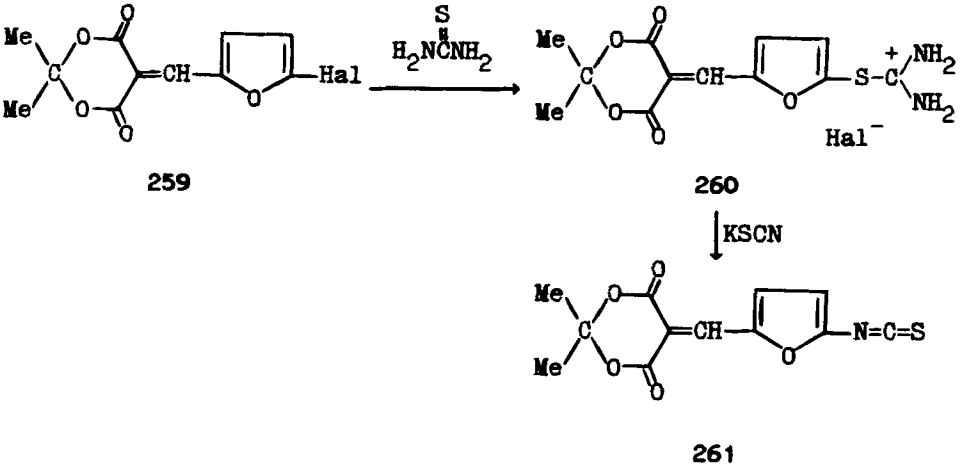
3-Halo-2-phenyl-1-indenones **256** in benzene react with a solution of potassium thiocyanate in methanol (ambient temperature, 1.5 h) to afford 3-thiocyanato-2-phenyl-1-indenone **257** in 87% yield (Scheme 40).[107] A facile thermal rearrangement (*absol.* DMF, 60 °C, 4 h) gives the corresponding isothiocyanate **258** in 99% yield.



256 **257** **258**

SCHEME 40

The reaction of 2,2-dimethyl-5-(5-halofurfurylidene-2)-1,3-dioxane-4,6-diones **259** with thiourea leads to *S*-thiouronium salts **260** in quantitative yield (Scheme 41). The following treatment of **260** with KSCN gives the corresponding isothiocyanate **261**.[108]



259 **260**

261

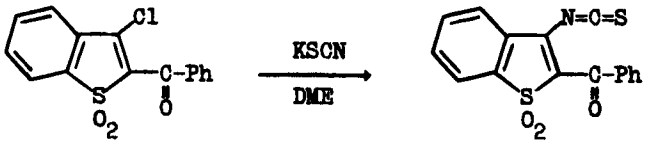
SCHEME 41

It has been noted that the isomeric thiocyanate is not formed.

2-Benzoyl-3-chlorobenzo[*b*]thiophene 1,1-dioxide **262** reacts with KSCN to give 2-benzoyl-3-isothiocyanatobenzo[*b*]thiophene 1,1-dioxide **263** (yield 80%) (Scheme 42).[109]

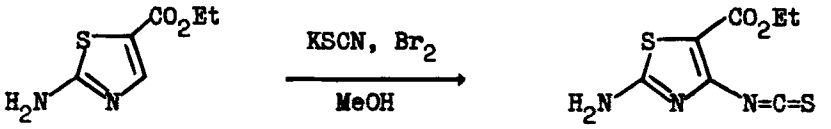
Treatment of ethyl 2-amino-4-thiazolecarboxylate **264** with potassium thiocyanate and bromine in methanol saturated with NaBr at –5 to 0 °C for 30 min and left overnight at 6–10 °C yields ethyl 2-amino-5-isothiocyanato-4-thiazolecarboxylate **265** (Scheme 43).[110]

Reaction of 2-(4-methylphenyl)-3-chloro-*N*-phenylmaleinimide **266** with potassium thiocyanate in DMSO at room temperature for 15 h leads to 2-(4-methylphenyl)-3-thio-



262 **263**

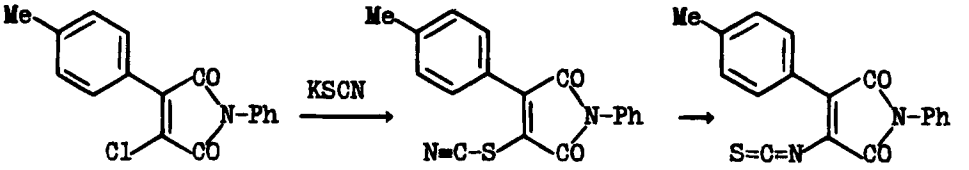
SCHEME 42



264 **265**

SCHEME 43

cyanato-*N*-phenylmaleinimide **267** in 93% yield (Scheme 44).[111] Refluxing thiocyanate **267** in acetonitrile in the presence of a catalytic amount of potassium thiocyanate for 10 h gave 2-(4-methylphenyl)-3-isothiocyanato-*N*-phenylmaleinimide **268** in 42% yield.[111]



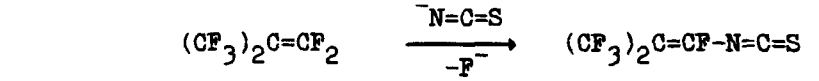
266 **267** **268**

SCHEME 44

The infrared spectrum of **268** in the region of the fundamental C=O stretching vibrations in carbon tetrachloride and chloroform has been recorded.[112]

By the reaction of perfluoroisobutylene (**269**) with potassium thiocyanate (sulfolane, steel autoclave, 100 °C, 20 h) the corresponding isothiocyanate **270** was obtained (yield 6%) together with dimeric bis(trifluoromethyl)thioketene (**272**) (Scheme 45).[113]

Perfluoroisobutylene (**269**) vigorously reacts with potassium thiocyanate in polar solvents, for example, *absol.* benzonitrile (–78 °C, atmospheric pressure) to give perfluroisobutenyl isothiocyanate (**264**) in 66% yield.[114]

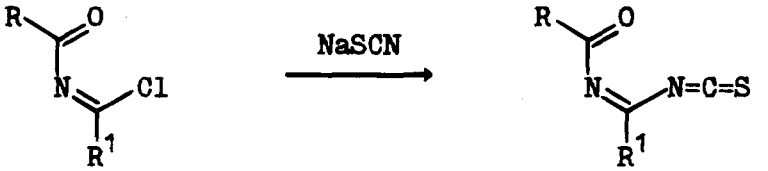


269 270

269 271 272 (20%)

SCHEME 45

2.3.2.2. *Reactions of imidoyl chlorides with sodium thiocyanate* *N*-Benzoylimidoyl chlorides **273** and sodium thiocyanate in *absol.* acetone give the *N*-benzoylimidoyl isothiocyanates **274** and **275** (Scheme 46).[115]

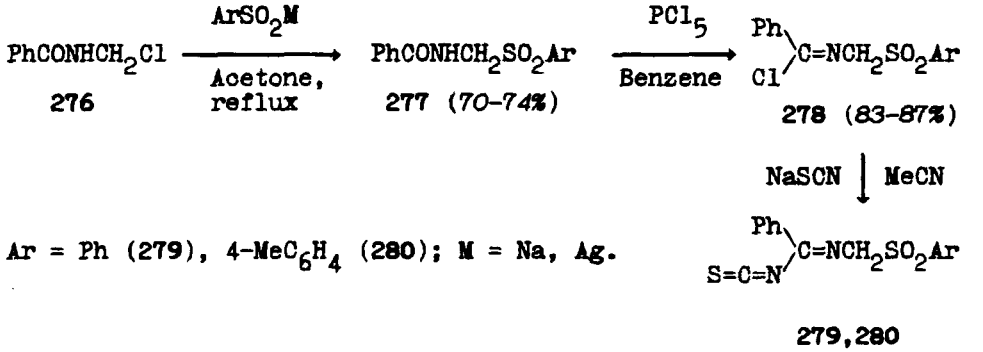


273 274,275

R = R^1 = Ph (274); R = Ph, R^1 = OPh (275).

SCHEME 46

Promising reagents, containing an imidoyl isothiocyanate fragment, an activated methylene group, and a good leaving group, i.e. arylsulfonyl, have been obtained as shown below (Scheme 47).[116-118]



Ar = Ph (279), 4-MeC_6H_4 (280); M = Na, Ag.

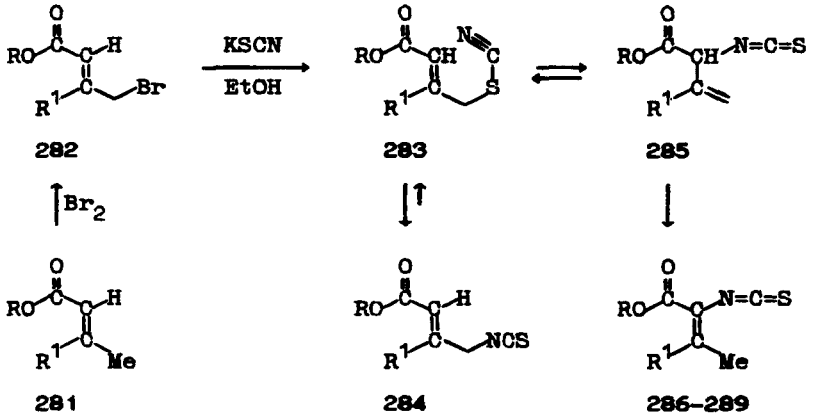
279,280

SCHEME 47

The reaction of the *N*-(arylsulfonylmethyl)benzimidoyl chlorides **276** with sodium thiocyanate was carried out in anhydrous acetonitrile at room temperature for 24 h. The *N*-(arylsulfonylmethyl)benzimidoyl isothiocyanates **279** and **280** were formed in 80% yield.[117]

2.3.2.3. *Reactions of allyl halides with potassium thiocyanate* Although allylic thiocyanates undergo a facile thermal [3,3] isomerization to form the more stable allylic isothiocyanates, this transformation has played a surprisingly minor role in organic synthesis.[119] It has been found that the α,β-unsaturated esters **281** can be converted to the α-isothiocyanatoacrylic esters **286–289** *via* an allylic [3,3] thiocyanate isomerization.[119]

The authors of Ref.[119] rationalized that γ-thiocyanate substituted α,β-unsaturated esters **283**, once formed, should undergo a thermal [3,3] isomerization to generate the intermediates **285**, which should further isomerize to give the desired α-isothiocyanatoacrylic esters **286–289** (Scheme 48).



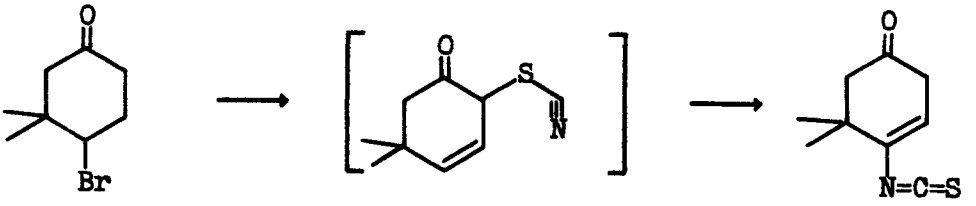
R = Et, R^1 = H (*E*) (**286**); R = Me: R^1 = Me (*E*) (**287**), Ph (*Z*) (**288**), CO_2Me (*E*) (**289**).

SCHEME 48

The synthesis of the allylic thiocyanates **283** has been achieved by bromination of the appropriate α,β-unsaturated esters **281** in carbon tetrachloride, followed by potassium thiocyanate treatment. Distillation of the thiocyanate **283** at appropriate temperatures afforded, after silica gel chromatography, the α-isothiocyanatoacrylic esters **286–289** in 10–76% yield. While the reaction appears general, yields vary since this [3,3] isomerization is substantially influenced by substituents in the α,β-unsaturated esters **281**.

The extension of this method to α,β-unsaturated cyclic ketones resulted in an unexpected, yet interesting reaction which reflects the role of alkene conjugation in the [3,3] isomer-

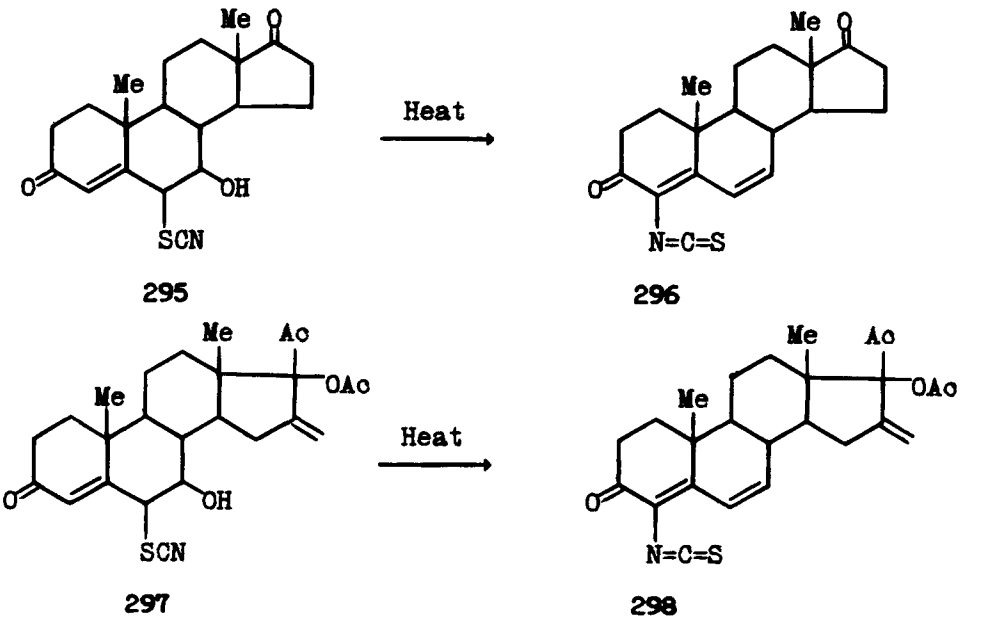
izations.[119] Treatment of 4-bromo-5,5-dimethyl-2-cyclohexene-1-one (**290**) with potassium thiocyanate in refluxing acetonitrile in the presence of dibenzo-18-crown-6 afforded, after silica gel chromatography, directly 4-isothiocyanato-5,5-dimethyl-3-cyclohexene-1-one (**292**) in 43% yield (Scheme 49).[119]



290 **291** **292**

SCHEME 49

Reaction of 6β-bromo-7α-acetoxyprogestin (**293**) or its C19 analog **294** with KSCN in DMF for 2–4 days at 25 °C afforded only the 6β-thiocyanato-3-oxo-$\Delta^{4,6}$-steroids **295** and **297** in 75–85% yield (Scheme 50).[120] The 4-isothiocyanato-3-oxo-$\Delta^{4,6}$-steroids **296** and **298** have been prepared in good yield by the thermally induced allylic rearrangement of the corresponding 6β-thiocyanato-3-oxo-$\Delta^{4,6}$-steroids **295** and **297** in DMF, benzene, or toluene.[120]

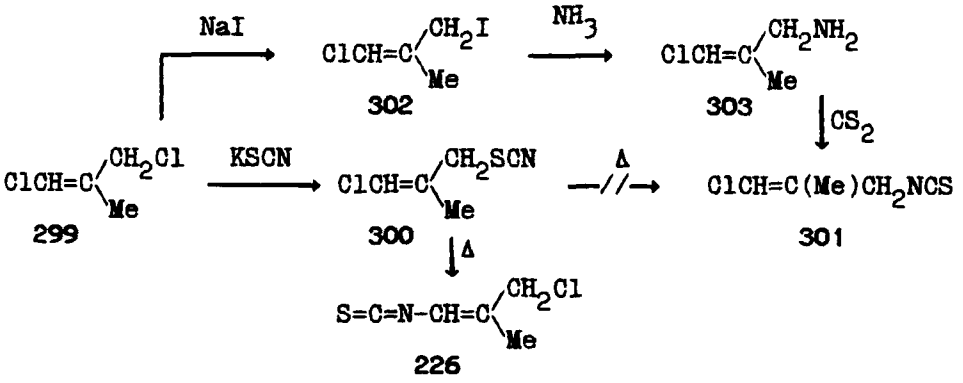


295 **296**

297 **298**

SCHEME 50

Reaction of 1,3-dichloro-2-methylprop-1-ene (**299**) with potassium or ammonium thiocyanate in DMSO (room temperature, 3 h) affords 1-chloro-2-methyl-3-thiocyanato-prop-1-ene (**300**) in 60% yield (Scheme 51).[121] Subsequent reflux of **300** (dioxane, 6 h) gave 3-chloro-1-isothiocyanato-2-methylprop-1-ene (**226**) in 50% yield.[121,122]



SCHEME 51

Analogously, the γ-chloroallyl chlorides **304** react with potassium or ammonium thiocyanate in dimethyl sulfoxide or acetone (room temperature, 3 h) to give the corresponding thiocyanates **305** (Scheme 52).[123] The latter after reflux (dioxane, 4–7 h, mainly 6 h) gave the isothiocyanates **226** and **306–315**.[122–125]

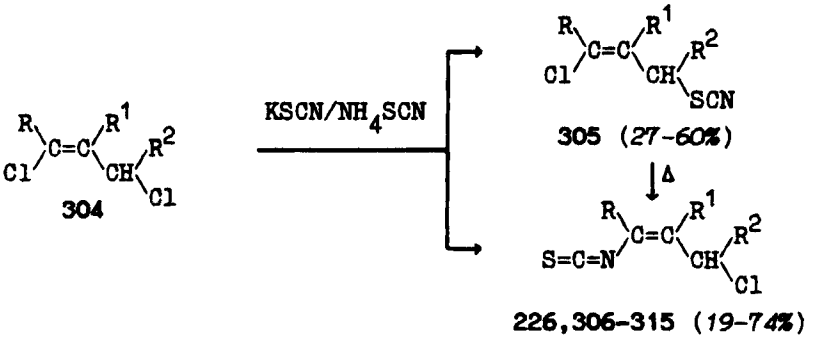
With R = R¹ = R² = H; R = R¹ = Me, R² = H or R–R¹ = $(CH_2)_n$, R² = H, the corresponding isothiocyanates **306**, **309**, and **313–315**, respectively, have been prepared by direct reaction of γ-chloroallyl chlorides **304** with potassium thiocyanate.[123]

The cyclic γ-chloroallyl chlorides **316** [1-chloro-2-(chloromethyl)cyclohexene and 1-chloro-2-(chloromethyl)cycloheptene] have been treated with KSCN in DMSO at 50–70 °C to give the 2-isothiocyanato-3-methylenecycloalkenes **317** and **318** in 35–50% yield (Scheme 53).[126,127]

When the 1-chloro-2-(chloromethyl)cycloalkenes **316** were allowed to react with potassium thiocyanate in DMSO at room temperature the 1-isothiocyanato-(2-chloromethyl)cycloalkenes **314**, **315**, and **320** were obtained (*via* the unisolated geminally substituted intermediates **319**) in 50–70% yield (Scheme 54).[127,128]

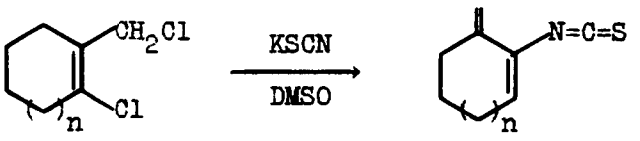
The reaction of 4-*tert*-butyl-2-(chloromethyl)furan (**321**) with aqueous potassium thiocyanate at ambient temperature required over 24 h and gave a mixture of normal and abnormal products (total yield 65.9%): 2-isothiocyanatomethyl-4-*tert*-butylfuran (**322**), 2-methylthiocyanato-4-*tert*-butylfuran (**323**) and 2-thiocyanato- (**324**) or 2-isothiocyanato-4-*tert*-butyl-5-methylfuran (**325**) (Scheme 55).[129]

The following isomer ratios were observed at 37 °C: normal thiocyanate, 43%; normal isothiocyanate, 43%; abnormal product, 14%.



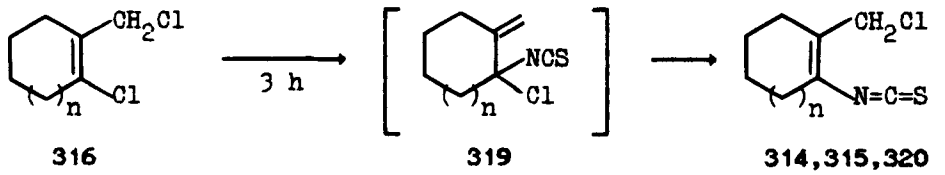
R = R^1 = R^2 = H (306); R = R^2 = H, R^1 = Me (226); R = Me, R^1 = R^2 = H (307); R = R^1 = H, R^2 = Me (308); R = R^1 = Me, R^2 = H (309); R = R^1 = R^2 = Me (310); R = *t*-Pr, R^1 = R^2 = H (311); R = Ph, R^1 = Me, R^2 = H (312); R^2 = H: R - R^1 = $(CH_2)_3$, (313), $(CH_2)_4$ (314), $(CH_2)_5$ (315).

SCHEME 52



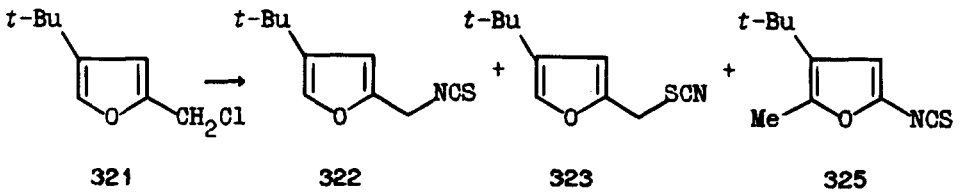
n = 1 (317), 2 (318).

SCHEME 53



n = 1 (314), 2 (315), 3 (320).

SCHEME 54



321 322 323 325

SCHEME 55

2.3.2.4. *Reactions of alkynyl halides with alkali metal thiocyanates* The isothiocyanatopropargyl ethers **327–330** have been prepared by reaction of the 1-halopropargyl ethers **326** with sodium or potassium thiocyanate (Scheme 56).[130,131] It was found[130,131] that the best yields of isothiocyanates **327–336** were obtained when the reaction was carried out at 55–60 °C for 2.5–3 h in a mixture of equal volumes of ethanol and acetone.

$$\underset{\mathbf{326}}{RO{-}CH_2{-}C{\equiv}C{-}X} + MSCN \longrightarrow \underset{\mathbf{327\text{-}336}\ (68\text{-}96\%)}{RO{-}CH_2{-}C{\equiv}C{-}N{=}C{=}S}$$

M = K, Na; X = I, Br; R = 2-ClC_6H_4 (**327**), 2,4-$Cl_2C_6H_3$ (**328**), 2,4,6-$Cl_3C_6H_2$ (**329**), 3,4,6-$Cl_3C_6H_2$ (**330**), C_6Cl_5 (**331**), 2-BrC_6H_4 (**332**), 2,4-$Br_2C_6H_3$ (**333**), 2,4,6-$Br_3C_6H_2$ (**334**), α-$C_{10}H_7$ (**335**), β-$C_{10}H_7$ (**336**).

SCHEME 56

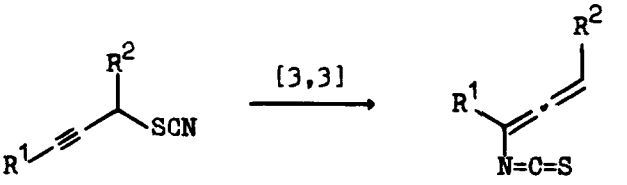
γ-Isothiocyanatopropargyl ethers of α- (**335**) and β-naphthol (**336**) have been prepared in 96–98% yield in the same way from γ-iodopropargyl ethers of α- and β-naphthol, respectively, and a methanol solution of sodium thiocyanate in benzene at 50–55 °C for 2.5 h.[132]

2.3.2.5. *Rearrangements of alkynyl and allenyl thiocyanates* The authors of Ref.[133–135] recently reported the preparation of the highly reactive allenyl isothiocyanate (**338**), which can be easily obtained from propargyl thiocyanate (**337**) by gas-phase thermolysis (conversion 98%) (Scheme 57).

$$\underset{\mathbf{337}}{HC{\equiv}CCH_2SCN} \xrightarrow[0.75\ Torr]{400^\circ C} \underset{\mathbf{338}\ (95\text{-}100\%)}{CH_2{=}C{=}CH{-}N{=}C{=}S}$$

SCHEME 57

The alkynyl thiocyanates **339** after [3,3] sigmatropic isomerization in dilute solution (60–100 °C) gave the isothiocyanato substituted allenes **338**, **340**, and **341** in 7–20% yield (Scheme 58).[133] The yields of **338**, **340**, and **341** are limited in this case by subsequent polymerization.

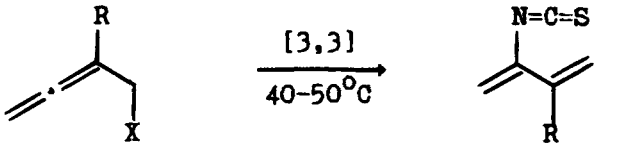


339 **338,340,341**

$R^1 = R^2 = H$ **(338)**; $R^1 = H$, $R^2 = Me$ **(340)**; $R^1 = Me$, $R^2 = H$ **(341)**.

SCHEME 58

Similar [3,3] sigmatropic rearrangements also allow the preparation of the isothiocyanato substituted 1,3-butadienes **344** and **345**, which can be further used for cycloaddition reactions (Scheme 59).[133,135]



342,343 **344,345**

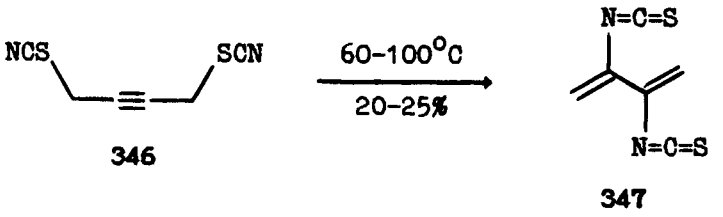
R = H, X = Br (SCN) **(342,344)**; R = Me, X = Cl (SCN) **(343,345)**.

SCHEME 59

The required 2,3-butadienyl thiocyanates **342** and **343** were prepared from the corresponding chloro or bromo derivatives and ammonium thiocyanate.

Heating of a dilute solution of the alkynyl thiocyanate **346** *via* double [3,3] sigmatropic isomerization gaves the isothiocyanate **347** (Scheme 60). The yield of **347** is also limited by its polymerization.[133]

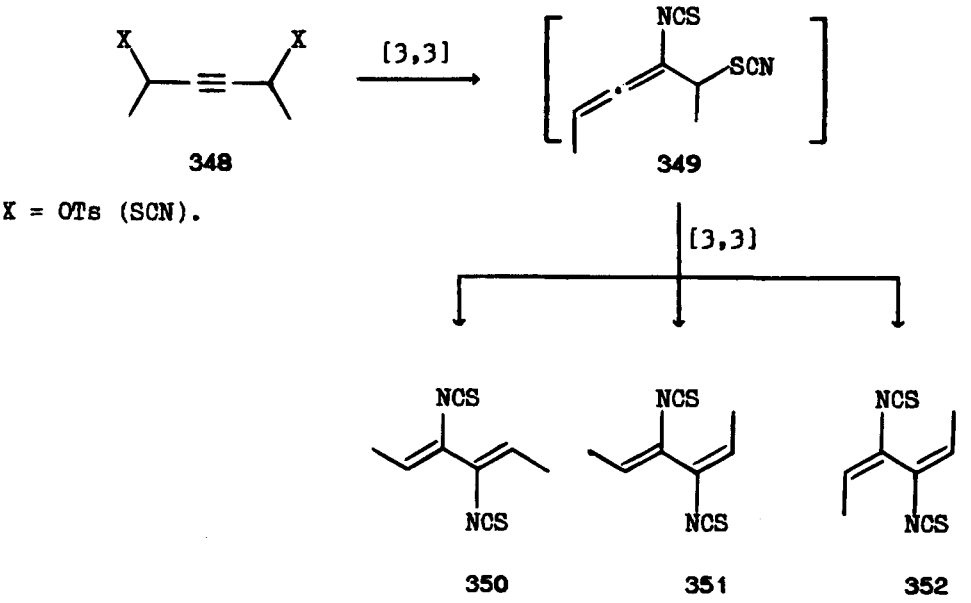
By distillation (90 °C/0.001 Torr) of the alkynyl thiocyanate **348** the isomeric hexadienyl isothiocyanates **350–352** (in the ratio 1:2:1) have been obtained in 67% yield



346 347

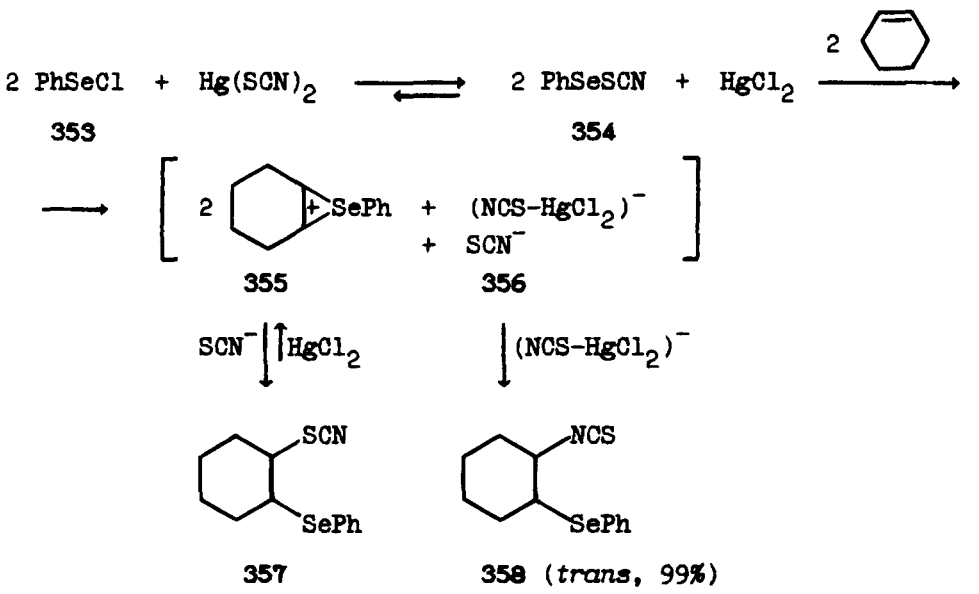
SCHEME 60

(Scheme 61).[133] Distillation of **348** at 180 °C/26 mbar leads to the thermodynamically more stable *Z,Z*-isothiocyanate **350** (56% yield, ratio of **350**:**351**:**352** = 8:1:1). The second step of the isomerization **349** → **350**–**352** is reversible at increased temperature.

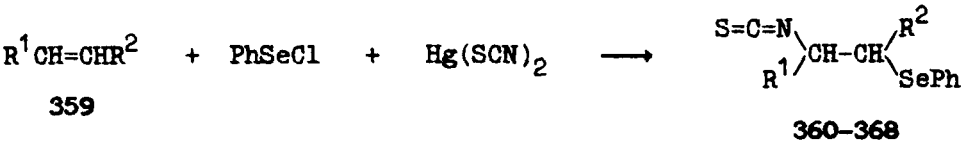


SCHEME 61

2.3.3. *Reactions of alkenes with benzeneselenenyl chloride and mercury (II) thiocyanate*/ The reaction of the mono- and 1,2-disubstituted alkenes **359** with a mixture of benzeneselenenyl chloride **353** and mercury(II) thiocyanate in benzene affords the β-(phenylseleno)alkyl isothiocyanates **358** and **360**–**368** selectively in good to excellent yields (Schemes 62 and 63).[136]



SCHEME 62



SCHEME 63

An investigation of the isomerization of thiocyanates to isothiocyanates under various reaction conditions in chloroform as the solvent showed that the mercury salt not only increases the N-selectivity in a kinetically controlled reaction, but also accelerates the isomerization of β-(phenylseleno)alkyl thiocyanates to the corresponding isothiocyanates **358** and **360–368**.[136]

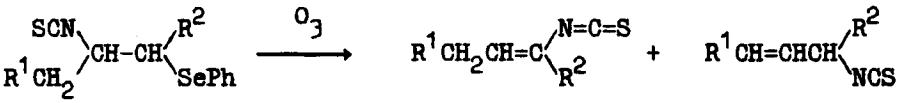
The remarkable effect of the mercury salt in the cyclohexenyl system, as described above, prompted the authors of Ref.[136] to apply the reaction to various cyclic as well as mono- and 1,2-disubstituted alkènes which were expected to afford various products convenient for the study of selenoxide elimination reactions. As shown in Table 2, β-(phenylseleno)alkyl isothiocyanates could be prepared in good to excellent yields in every case.

Oxidative elimination of the β-(phenylseleno)alkyl isothiocyanates **358** and **360–368** gives predominantly the vinylic isothiocyanates **369–374** and **376–378** together with a small amount of the allylic isothiocyanates **375** (Schemes 64 and 65). The ozonization of the isothiocyanates was carried out in dichloromethane at –78 °C, followed by addition of the resulting solution to refluxing carbon tetrachloride.[136]

TABLE 2 Preparation of various β-(phenylseleno)alkyl isothiocyanates **358** and **360–368**[a]

Olefin	Time, h	Yield, %[b] (isomer ratio)
Cyclopentene	14	99 (**360**)
Cyclohexene	20	99 (**358**)
Cycloheptene	0.5	97 (**361**)
Cyclooctene	5	91 (**362**)
Cyclooctene	20	92 (**362**)
Cyclododecene	96	93 (**363**)
cis-4-Octene	3	84 (**364**, *threo-7*)
cis-4-Octene	20	98 (**364**, *threo-7*)
trans-4-Octene	3	94 (**365**, *erythro-7*)
trans-4-Octene	20	99 (**365**, *erythro-7*)
1-Octene[c]	20	84 (**366**) (>95:<5)[d]
Styrene	2	72 (**367**)
Styrene	20	70 (**367**)
3,3-Dimethyl-1-butene	15	93 (**368**)

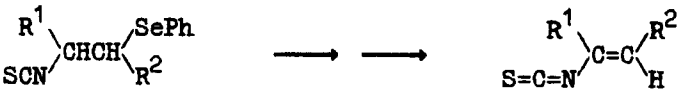
[a]Carried out with alkene (5 mmol), benzeneselenenyl chloride (5 mmol), and mercury(II) thiocyanate (2.5 mmol) in benzene (10 mL) at ambient temperature. [b]Isolated yield by column chromatography or preparative TLC. [c]Carried out at reflux temperature. [d]The isomer ratio was determined by comparison of the intensities of the ^{13}C NMR signals.



358, 360–365 **369–374** **375**

$R^1 - R^2 = (CH_2)_n$, n = 2 (**369**), 3 (**370**), 4 (**371**), 5 (**372**), 9 (**373**); R^1 = Et, R^2 = *n*-Pr (**374**).

SCHEME 64



366–368 **376–378**

R^1 = n-C_6H_{13}, R^2 = H (**376**); R^1 = Ph, R^2 = H (**377**); R^1 = H, R^2 = *t*-Bu (**378**).

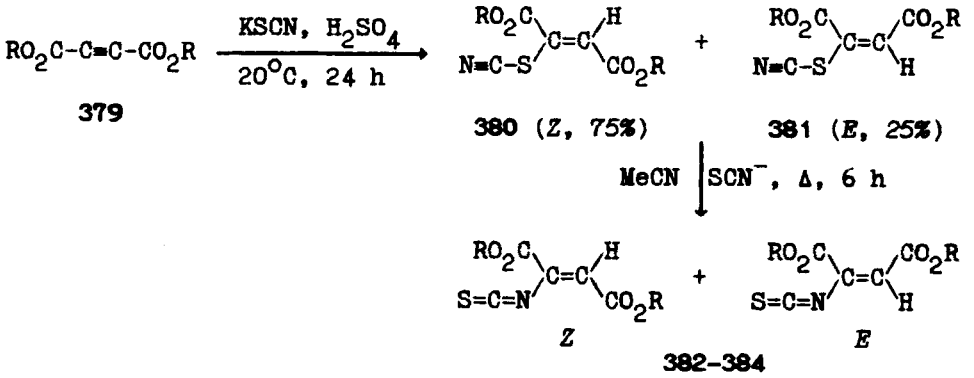
SCHEME 65

Oxidation with other reagents such as hydrogen peroxide and 3-chloroperbenzoic acid resulted in the formation of an unworkable mixture of resinous products.[136]

Since vinylic isothiocyanates can be easily separated from other products (allylic isothiocyanates, diphenyl diselenide, *etc.*), the formation of β-(phenylseleno)alkyl isothiocyanates, followed by selenoxide elimination, represents a convenient method for the conversion of alkenes to vinylic isothiocyanates.[136]

2.4. *Addition Reactions of Alkynes with Thiocyanates*

2.4.1. *With the system "thiocyanate-HA"* The potassium thiocyanate catalyzed isomerization of the mixture of the thiocyanatofumaric esters **380** and the corresponding thiocyanatomaleic esters **381**, obtained by treatment of the butynedioic acid dialkyl esters **379** with KSCN in the presence of H_2SO_4 in benzene, affords a mixture of the corresponding isothiocyanato esters, the *E*- and *Z*-vinylogous acyl isothiocyanates **382–384** (27–68%) (Scheme 66).[137]



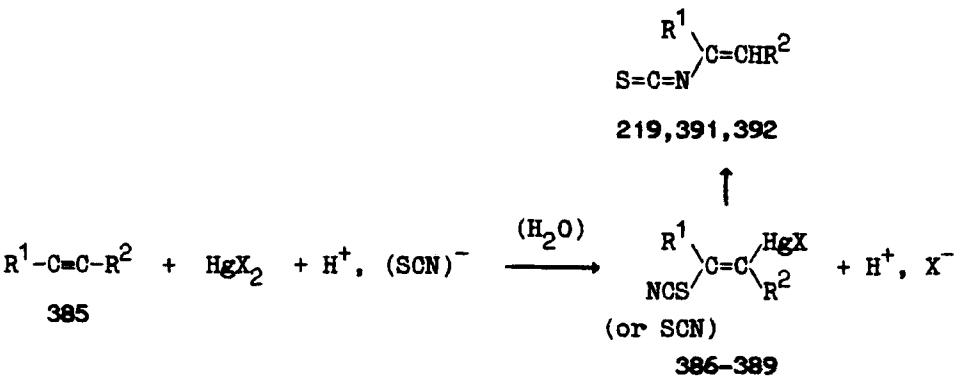
R = Me (**382**), Et (**383**), *i*-Pr (**384**).

SCHEME 66

Ionic addition of thiocyanic acid, catalyzed by Lewis acids, to non-activated alk-1-ynes has been described.[138] The reaction was studied with hex-1-yne, non-1-yne, and phenylacetylene. In this process, thiocyanic acid can be considered as being formed *in situ* in dichloromethane, from an equimolar mixture of *n*-$Bu_4N^+SCN^-$ and a strong acid HA ($K_{HA} > K_{HSCN}$) such as 96% H_2SO_4, dry HCl gas, or HBF_4 (54% solution in diethyl ether).[138] The HSCN addition obeys Markovnikov's rule and leads to 2-thiocyanatoalk-1-enes only, to the exclusion of the isothiocyanato isomers. 2-Isothiocyanatoalk-1-enes can be obtained by a slightly different addition process, described below.

2.4.2. *Thiocyanatomercuration* In the presence of SCN^- mercuric salts, HgX_2 (X = Cl, SCN) add to alkynes **385** affording in most cases the β-thiocyanatoalkenyl α-mercuro derivatives **386**, $R^1C(SCN)=C(R^2)HgX$, and if $R^1 = R^2$ = Et or *n*-Bu, the isothiocyanates **388** and **389**, $R^1C(NCS)=C(R^2)HgCl$ (Scheme 67).[139-141]

386, $R^1C(SCN)=C(R^2)HgX$ and if $R^1 = R^2$ = Et or *n*-Bu isothiocyanates **388**, **389**, $R^1C(NCS)=C(R^2)HgCl$ (Scheme 67).[139-141]



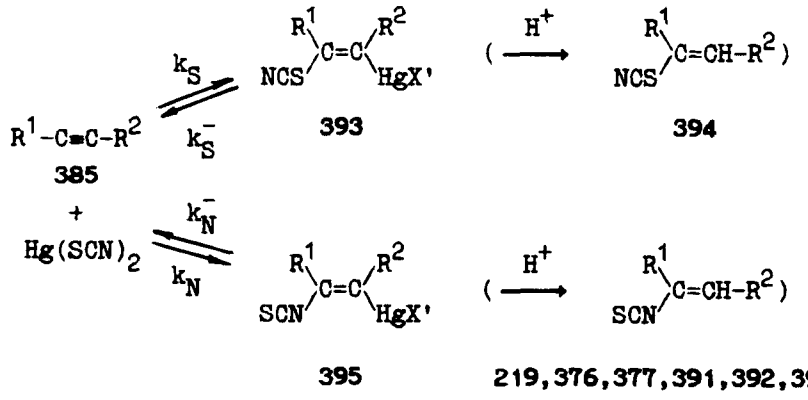
R^2 = H, R^1 = H, *n*-Pr, *n*-Bu, Ph, CH_2OMe, CH_2OBu-*t*; R^1 = H, R^2 = CH_2OMe, CH_2OBu-*t*, CO_2Me; $R^1 = R^2$ = Me (**219**, **387**), Et (**388**, **391**), *n*-Bu (**389**, **392**), CO_2Me.

SCHEME 67

The spontaneous isomerization of 1,2-dimethyl-2-thiocyanatovinylmercuric chloride (**390**) leads to the isothiocyanate **387**, protodemercuration of which gives the corresponding isothiocyanate **219**.[140] The isothiocyanate **219** has also been obtained by protodemercuration of the thiocyanate **390** (in 30% yield). Similarly, the isothiocyanates **391** and **392** have been obtained from the isothiocyanates **388** and **389**, respectively.

2.4.3. *With the system "thiocyanate-HgX_2-HA"* Thiocyanic acid can be added to some unactivated alkynes **385** in a two-step one-pot procedure which involves, first, the generation in dichloromethane of β-thiocyanato- (**393**) and/or β-isothiocyanato- (**395**) alkenylmercuric compounds by addition of mercury(II) thiocyanate to **385**, then the substitution of mercury by hydrogen by acid treatment (Scheme 68).[141-143]

The bonding of the SCN moiety to carbon is through sulfur or nitrogen, depending upon the influence of R^1 and R^2. The vinyl thiocyanates **394** (R^2 = H), $NCS\text{-}C(R^1)=CH_2$ are obtained specifically from alk-1-ynes, but some symmetrically disubstituted alkynes afford the vinyl isothiocyanates **390** and **391** ($R^1 = R^2$ = Et, *n*-Bu).[142] Other alkynes give mixtures of regio- and/or stereoisomers of thiocyanates and/or isothiocyanates.[142]



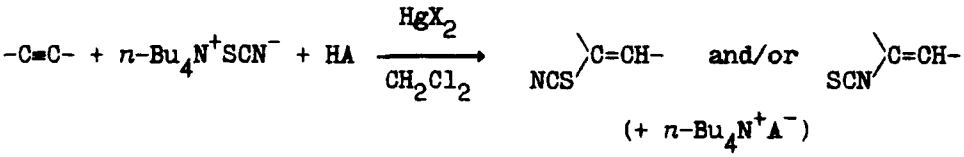
395 **219,376,377,391,392,396–405**

R^2 = H: R^1 = *n*-Pr (**396**), *n*-Bu (**397**), *n*-C_6H_{13} (**376**), *n*-C_7H_{15} (**398**), *t*-Bu (**399**), Ph (**377**), CH_2OMe (**400**); R^1 = R^2 = Me (**219**), Et (**391**), *n*-Bu (**392**); R^1 = *n*-Pr, R^2 = Me (**401**); R^1 = Me, R^2 = *n*-Pr (**402**), Ph (**403**); R^1 = Ph, R^2 = Me (**404**); R^1 = SMe, R^2 = *n*-C_5H_{11} (**405**).

SCHEME 68

With proper conditions of stoichiometry and reaction time the process is thermodynamically controlled and thus allows to obtain vinyl isothiocyanates even when the isomeric vinyl thiocyanates are kinetically favored.[141]

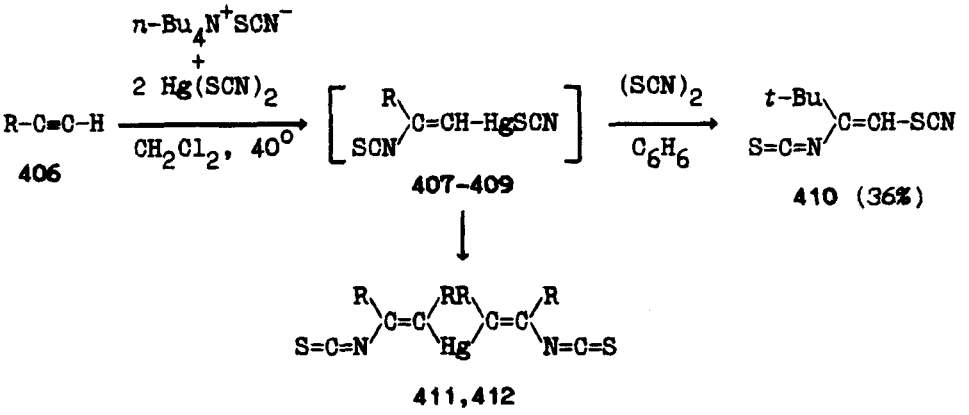
The reaction is carried out according to the general Scheme 69 in the presence of *n*-$Bu_4N^+SCN^-$ and HA ($K_{HA} \geq K_{HSCN}$) at 20–40 °C over 0.5–408 h. In addition to ~96% H_2SO_4, HCl or 54% solution of HBF_4 in Et_2O as HA[141,142] also organic acids such as CF_3CO_2H, Cl_2CHCO_2H, $ClCH_2CO_2H$, HCO_2H, CH_3CO_2H, 2,4,6-trinitrophenol and 2,4-dinitrophenol (for the hydrothiocyanation of 1-nonyne) have been employed.[141]



SCHEME 69

The preparation of 3,3-dimethyl-2-isothiocyanato-1-thiocyanato-1-butene **410** has also been reported (Scheme 70).[141]

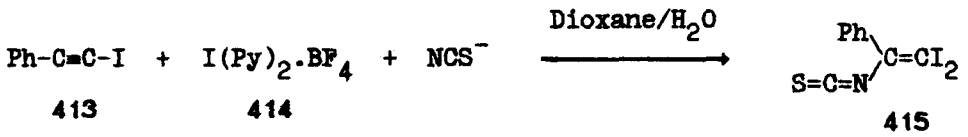
The symmetric organomercuric diisothiocyanate **412** has been isolated from the reaction products in 15% yield together with the isothiocyanate **408** (46%) (Scheme 70).[141] Di(isothiocyanato-4-hexene-3-yl)mercury **411** has been obtained in 57% yield by treatment of this reaction mixture with an aqueous solution of $NaBH_4$.[140,141]



R = Et (407,411), *n*-Bu (408,412), *t*-Bu (409).

SCHEME 70

2.4.4. *With bis(pyridine)iodine tetrafluoroborate and isothiocyanates* When bis(pyridine)iodine tetrafluoroborate **414** is allowed to react with 1-iodo-2-phenylacetylene **413** and thiocyanate ions at room temperature for 60 h 1,1-diiodo-2-phenyl-2-isothiocyanato-1-ethene **415** is produced in good yield (75%) (Scheme 71).[144]



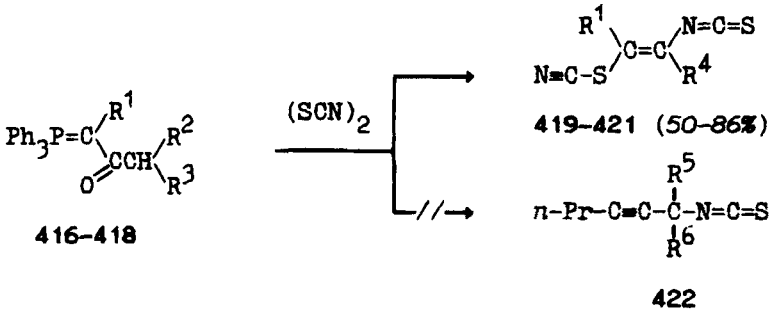
SCHEME 71

2.5. *Reactions of Phosphoranes*

2.5.1. *With thiocyanogen* Reaction of the triphenyl-β-oxoalkylenephosphoranes **416–418** with thiocyanogen gives the 1-thiocyanato-2-isothiocyanatoethylenes **419–421** (Scheme 72).[145] The mechanism of this reaction is shown in Scheme 73.

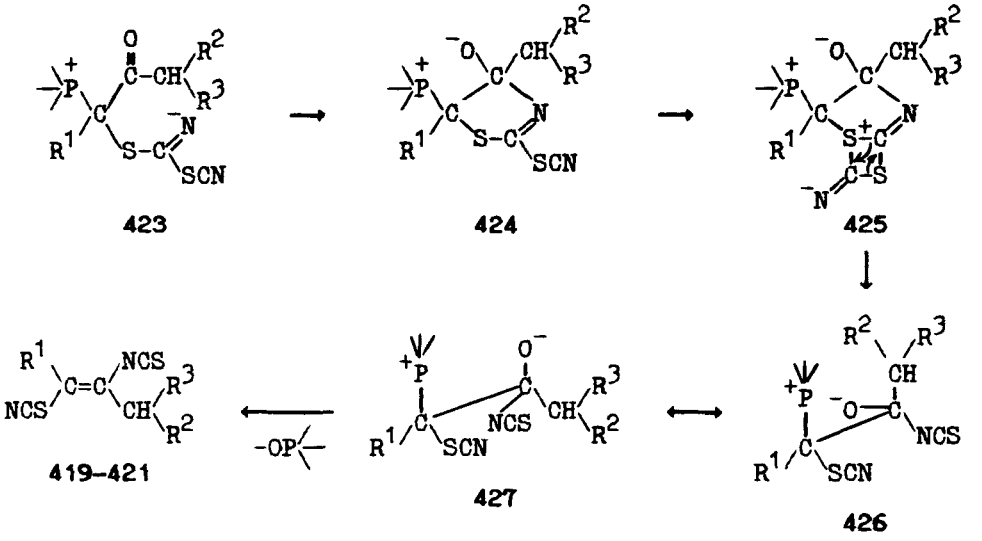
Reaction of 2-(triphenylphosphoranylidene)cycloheptanone **428** with $(SCN)_2$ in anhydrous benzene at room temperature for 3.5 h yields 1-isothiocyanato-2-thiocyanato cyclohept-1-ene **429** (Scheme 74).[146]

2.5.2. *With carbon disulfide* The aza-Wittig reaction of iminophosphoranes with heterocumulenes, *e.g.*, carbon dioxide, carbon disulfide, and isocyanates or isothiocyanates is a very useful reaction in synthetic heterocyclic chemistry.[147-151] Reaction the of 4-[(*N*-arylim-



R^1 = *n*-Pr, R^2 = R^3 = Me (416), R^4 = *t*-Pr (419); R^1 = *n*-Pr, R^2 = R^3 = $(CH_2)_3$ (417), R^4 = *cyclo*-Bu (420); R^1 = OMe, R^2 = R^3 = Me (418), R^4 = *t*-Pr (421); R^5 = R^6 = Me, R^5–R^6 = $(CH_2)_3$.

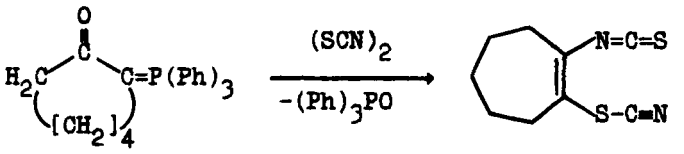
SCHEME 72



SCHEME 73

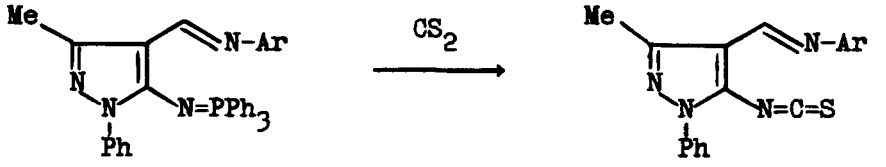
ino)methyl]-3-methyl-1-phenyl-5-[(triphenylphosphoranylidene)amino]-1*H*-pyrazoles **430** and **431** with carbon disulfide in dry dichloromethane (under nitrogen at room temperature for 2 h) yields the corresponding isothiocyanates **432** and **433**, respectively (Scheme 75).[152]

Analogously, ethyl 3-(1-methylindol-3-yl)-2-[(triphenylphosphoranylidene)amino]prop-2-enoate **437** reacts with carbon disulfide in dry toluene under reflux for 12 h to give the isothiocyanate **438** as a crystalline solid in 89% yield (Scheme 76).[153] [The starting ethyl 2-



428 429 (60%)

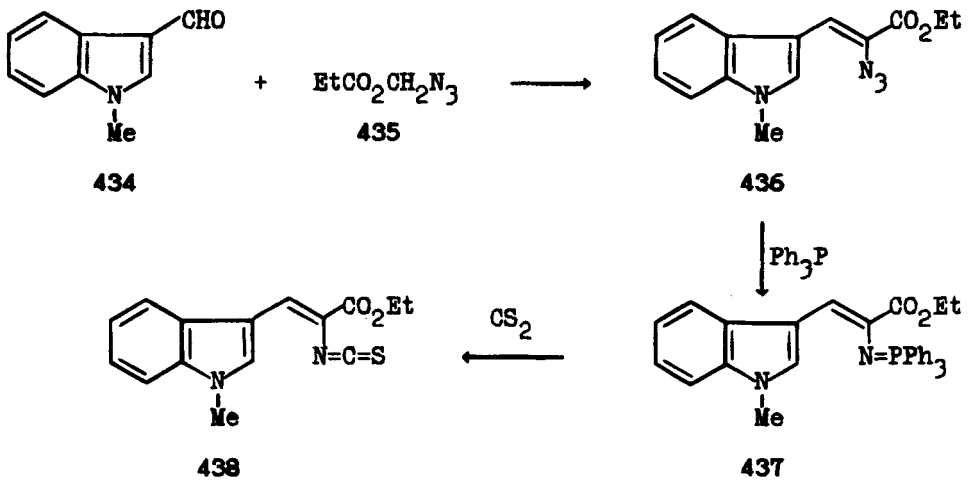
SCHEME 74



430,431 432,433

Ar = Ph (430,432), 4-MeC_6H_4 (431,433).

SCHEME 75

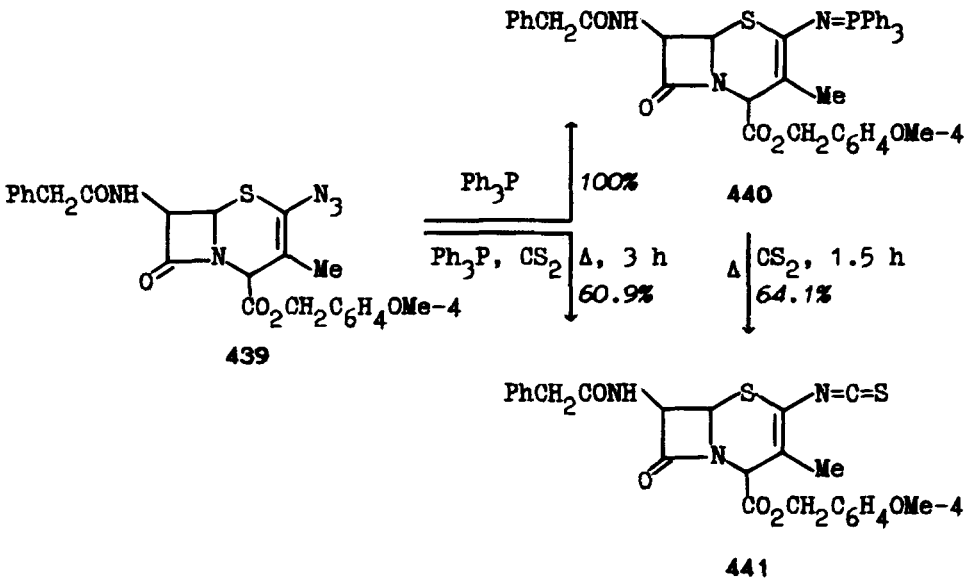


434 435 436 437 438

SCHEME 76

azido-3-(1-methylindol-3-yl)prop-2-enoate **436**, available from 3-formyl-1-methylindole **434** and ethyl azidoacetate **435**, reacts with triphenylphosphine in dry dichloromethane at 0 °C to give the iminophosphorane **437** in near quantitative yield].

Treatment of 4-methoxybenzyl 7β-phenylacetamido-2β-azido-2-cephem-4α-carboxylate **439** with triphenylphosphine and carbon disulfide (in one or two preparative steps) gave 4-methoxybenzyl 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4α-carboxylate **441** (Scheme 77).[154]

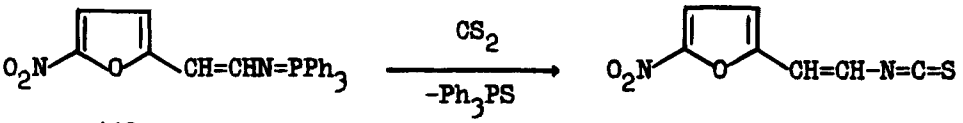


SCHEME 77

4-Methoxybenzyl 7β-phenylacetamido-2β-isothiocyanato-3-methyl-3-cephem-4α-carboxylate **442** has been prepared from the corresponding 3-cephem according to the same Scheme.[154]

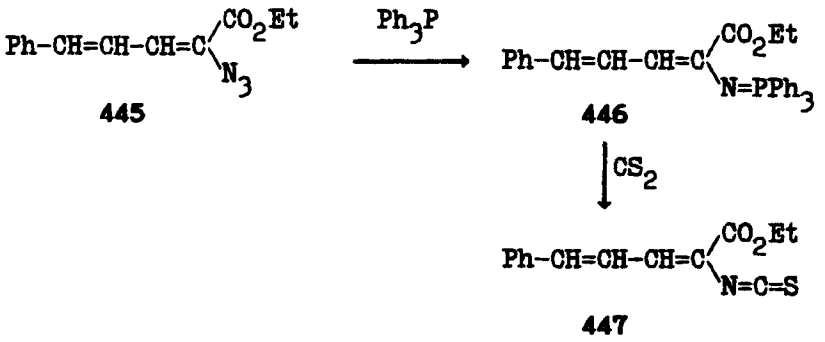
Treatment of 5-nitro-2-furylvinylene-*N*-iminotriphenylphosphorane **443** with CS_2 under an inert gas (optimally in toluene at 100 °C, argon) for 50–100 h gave 45–60% of 5-nitro-2-furylvinylene isothiocyanate **444** (Scheme 78).[155] Heating the above reaction mixture for 6 h at 100 °C and 1330 kPa increased the yield of **444** to 80%.

The classical Staudinger reaction of ethyl 2-azido-5-phenyl-2,4-butadienecarboxylate **445** with triphenylphosphine in ether gives the iminophosphorane **446** (Scheme 79). The latter reacts with carbon disulfide to give the corresponding isothiocyanate **447** in 73% yield as a crystalline solid.[156]



443 **444**

SCHEME 78



445 **446** **447**

SCHEME 79

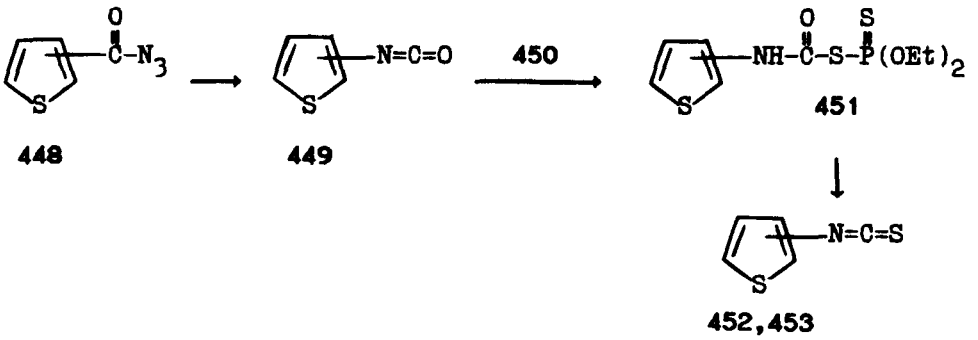
2.6. *Reactions of Isocyanates with Dithiophosphate*

Thienyl isocyanates **449** are readily available by Curtius rearrangement of thenoyl azides **448**,[157,158] but the "thio-Curtius" rearrangement does not take place. Attempted preparations of thioacyl azides invariably yielded the cyclized thiatriazoles, which thermally decompose to nitriles and sulfur,[159–161] although small amounts of isothiocyanates have been detected after UV photolysis of thiatriazoles.[162]

Ottmann and Hooks[163] prepared isothiocyanates by thermal decomposition of the reaction products obtained from isocyanates and *O,O*-diethyl hydrogen dithiophosphate **450**. The authors of Ref. [62] found that it is possible to apply this reaction in the thiophene series to prepare both 2- and 3-thienyl isothiocyanate **452** and **453**, respectively (Scheme 80).

2-Thenoyl and 3-thenoyl azide **448** have been thermally rearranged in boiling carbon tetrachloride to the corresponding thienyl isocyanates **449** (under anhydrous conditions for 17 h). These were then treated with *O,O*-diethyl hydrogen dithiophosphate **450**, and upon cooling, *S*-[*N*-(2- or 3-thienyl)carbamoyl]-*O,O*-diethyl dithiophosphate **451** crystallized out (yield 100%). The crude dithiophosphates **451** were then thermally rearranged (under reduced pressure at 135–150 °C) to the thienyl isothiocyanates **452** and **453**.[62]

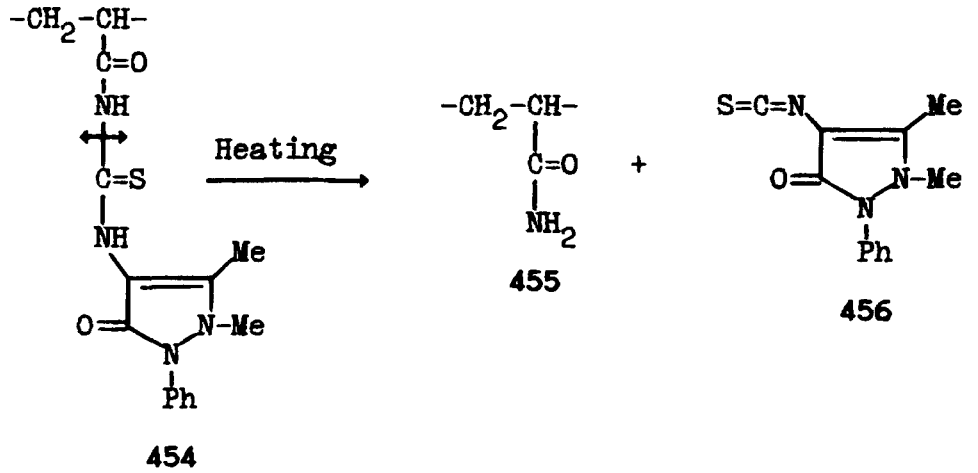
Because **452** and **453** are labile to acid it was found necessary to minimize their contact with the thiophosphoric acid coproducts which codistil from the reaction mixture. This was accomplished by chromatography after which the thienyl isothiocyanates could be successfully redistilled.[62]



SCHEME 80

2.7. *Decomposition of Sulfur-Containing Compounds*

The thermal behavior of poly[(*N*-(2,3-dimethyl-1-phenyl-5-oxo-3-pyrazolin-4-yl)-*N'*-acryloylthiourea] **454** was studied in detail by *El-Hamouly* and *El-Saied*.[164] The IR spectra show no change in most of the functional groups present upon heating up to 175 °C, except that a new band appears at 2040 cm^{-1}, assigned to the stretching vibrations of the isothiocyanate group, ν(-N=C=S). This indicates that a homolytic scission takes place in the C-N[-C(=S)-NH-] moiety in a similar manner as occurs in *N*-acyl-*N'*-arylthioureas[165] as shown in Scheme 81.



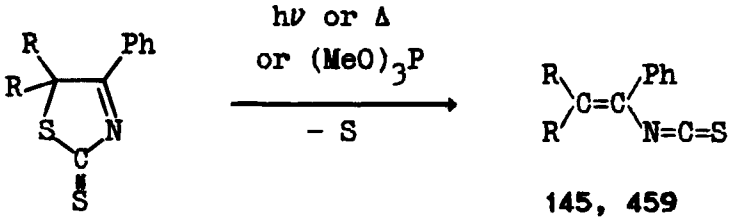
SCHEME 81

In contrast, the spectra of the samples heated up to 175 °C show a rapid decrease in the intensity of the bands characteristic of ν(NH), ν(C=O) and ν(C=S) and the band at 2040 cm^{-1} disappeared from the spectrum of a sample heated at 260 °C. The above arguments in-

dicate that the homopolymer in question is subject to depolymerization and decomposition.[164]

The Δ^3-thiazoline-2-thiones **457** and **458** eliminate sulfur thermally, photolytically, or with trimethyl phosphite to give the vinyl isothiocyanates **145** and **459** (Scheme 82).[166]

Thus, 5,5-dimethyl-4-phenyl-Δ^3-thiazoline-2-thione **457** in *absol.* benzene under argon after 7 h UV-irradiation gave 1-isothiocyanato-2-methyl-1-phenylprop-1-ene **145** in 68% yield.[166]



457, 458 **145, 459**

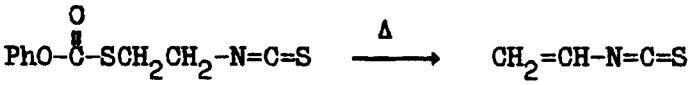
R = Me (457,145), Ph (458,459).

SCHEME 82

Isothiocyanatotriphenylethene **459** has been prepared in 72% yield from triphenyl-Δ^3-thiazoline-2-thione **458** by reflux in *absol.* xylol for 55 h in the dark.[166] The corresponding light reaction with trimethyl phosphite in refluxing *absol.* benzene for 7 h leads to the same isothiocyanate **459** in 92% yield.[166]

2.8. *Reactions of Isothiocyanates*

2.8.1. *Thermal decomposition* 2-(*S*-Phenyloxycarbonylthio)ethyl isothiocyanate **460** gave vinyl isothiocyanate **142** upon heating in 1,2-dichlorobenzene under nitrogen for 2 h in low yield (12%) (Scheme 83).[167]



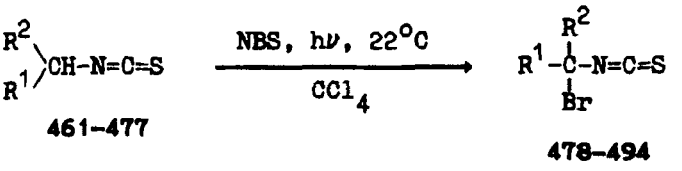
460 **142**

SCHEME 83

2.8.2. *Dehydrohalogenation* The dehydrohalogenation of haloalkyl isothiocyanates with bases is a widely used method for the preparation of conjugated isothiocyanates.[80,168]

The secondary isothiocyanates **470**, **472**, **475** and **477** as well as the primary isothiocyanates **466** and **467** with an activating group R' react with *N*-bromosuccinimide (NBS)

to form the α-brominated isothiocyanates **483**, **484**, **487**, **489**, **492**, and **494** in high yields (80–100%) (Scheme 84).[168] The non-activated primary isothiocyanate **463** slowly forms a stable α,α-dibromo derivative.

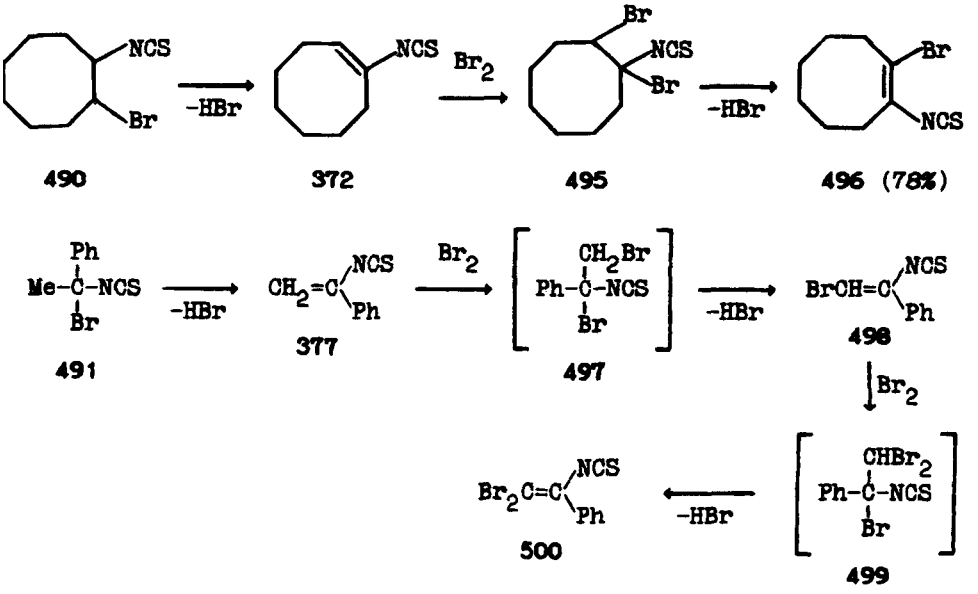


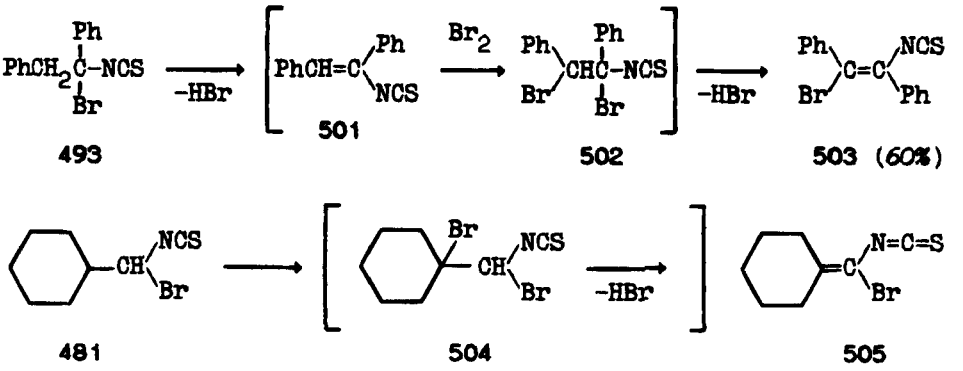
461–477 **478–494**

$R^1 = R^2 = H$ (**461,478**); $R^1 = H$, $R^2 = i\text{-Pr}$ (**462,479**), $t\text{-Bu}$ (**463,480**), $cyclo\text{-}C_6H_{11}$ (**464,481**), $PhCH_2$ (**465,482**), Ph (**466,483**), $EtCO_2$ (**467,484**), CN (**468,485**), $CH_2{=}CH$ (**469,486**); $R^1 = R^2 =$ Me (**470,487**), Ph (**471,488**); $R^1\text{-}R^2 = (CH_2)_5$ (**472,489**), $(CH_2)_7$ (**473,490**); R^1 = Me, R^2 = Ph (**474,491**); R^1 = t-Bu, R^2 = Ph (**475,492**); $R^1 = PhCH_2$, R^2 = Ph (**476,493**); $R^1 = i\text{-Pr}$, $R^2 = MeCO_2$ (**477,494**).

SCHEME 84

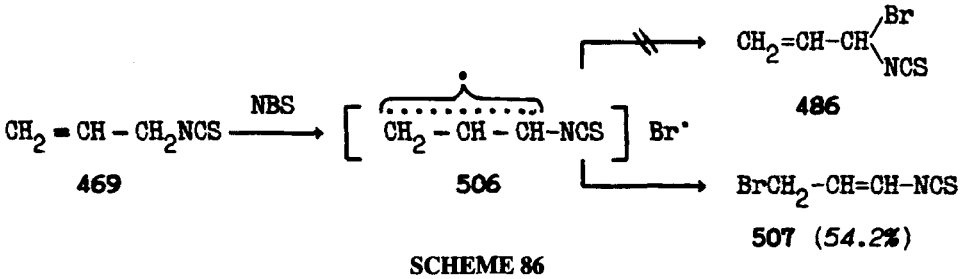
β-Hydrogen containing α-bromoalkyl isothiocyanates eliminate HBr spontaneously and also secondary products may be formed (Scheme 85).[168]





SCHEME 85

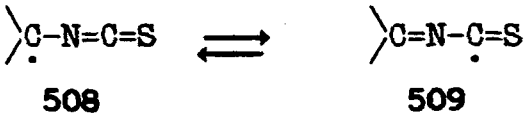
Radical bromination of allyl isothiocyanate **469** with NBS in dry carbon tetrachloride in the presence of dibenzoyl peroxide (under reflux for 1 h) results in a mixture of *cis*- and *trans*-3-bromo-1-propenyl isothiocyanate **507** in the ratio 3:1, from which the pure *trans*-isomer can be obtained by freezing (–30 °C, several hours) (Scheme 86).[169] The residue was composed of 81% *cis*-isomer and 19% *trans*-isomer. The mixture could not be separated by column or TLC on SiO_2 due to the almost identical R_f values of both isomers.[169]



SCHEME 86

This reaction represents a new method for the preparation of vinyl isothiocyanates with a reactive halogen, which cannot be obtained in the usual way. For example, the analogous 3-chloro-1-propenyl isothiocyanate **306** was prepared by *Schulze et al.*[121,123] from the difficultly accessible 1,3-dichloropropene and KSCN (Scheme 52).[169]

For the α-bromination of isothiocyanates with NBS the so-called Goldfinger mechanism has been suggested, where the intermediate radical is stabilized by the NCS group (Scheme 87).[168–171]

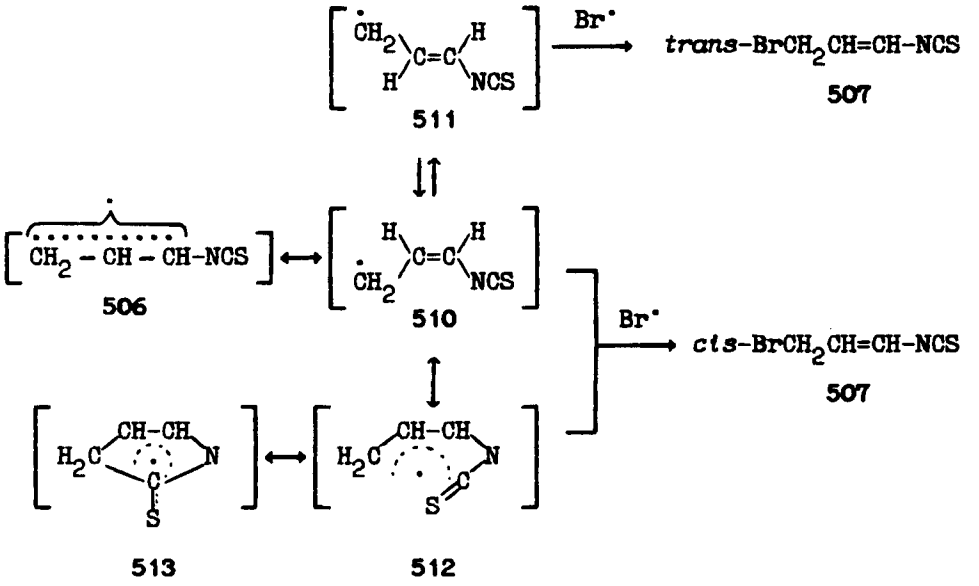


SCHEME 87

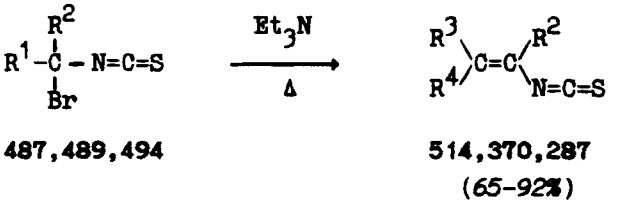
The authors of Ref.[169] assume that such a stabilization may operate also in the radical bromination of allyl isothiocyanate in consequence of which the delocalized radical **512** is formed, affording in turn preferentially the *cis*-derivative **507** (Scheme 88).

The α-bromoalkyl isothiocyanates **487**, **489**, and **494** with a hydrogen in the β-position eliminate HBr to form the vinyl isothiocyanates **514**, **370** and **287**, respectively (autoclave, *absol.* pentane or CCl_4, 100 °C, 1.5–3 h) (Scheme 89).[172]

The α-bromoalkyl isothiocyanates **487**, **489**, and **494** were prepared previously by photochemical reaction of the corresponding alkyl **470**, **477** or cycloalkyl **472** isothiocyanates with NBS in a solvent (pentane, CCl_4) over 3–4 h under N_2.[168,172]



SCHEME 88



$R^1 = R^2 =$ Me (**487**); R^1-$R^2 = (CH_2)_5$ (**489**); R^1 = *t*-Pr, R^2 = $MeCO_2$ (**494**); R^2 = Me, $R^3 = R^4$ = H (**514**); R^2-$R^3 = (CH_2)_4$, R^4 = H (**370**); $R^2 = MeCO_2$, $R^3 = R^4$ = Me (**287**).

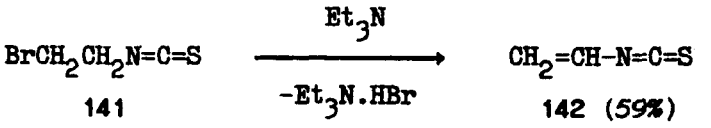
SCHEME 89

Vinyl isothiocyanate **142** has also been synthesised by reaction of 2-bromoethyl isothiocyanate **141** with triethylamine (Scheme 90).[173,174]

This reaction is carried out in the presence of a catalytic amount of hydroquinone; the solution was heated at 50 °C with stirring for an additional hour.[174]

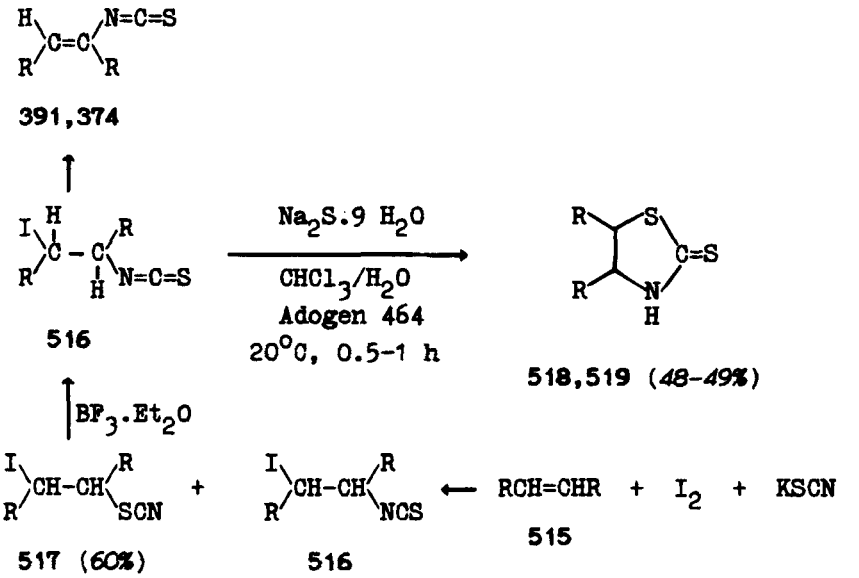
The reactions of the *vic*-iodo isothiocyanates **516** with hydrosulfide anion as the nucleophile in the presence of a phase-transfer catalyst form the substituted thiazolidine-2-thiones **518** and **519** (Scheme 91).[175] No reaction occurs in the absence of the phase-transfer catalyst. The formation of *trans*-4,5-diethylthiazolidine-2-thione **518** and *trans*-4,5-dipropylthiazolidine-2-thione **519** is accompanied by the elimination of hydrogen iodide to give low yields (trace for R = Et and 15% for R = *n*-Pr) of the corresponding (*E*)-vinyl isothiocyanates **391** and **374**.[175]

The starting *vic*-iodo isothiocyanates **516** were prepared as a mixture with the *vic*-iodo thiocyanates **517** (in a ratio *ca.* 1:2) by reaction of the corresponding alkene **515**, iodine, and potassium thiocyanate in $CHCl_3$ at room temperature in the dark for 24 h (Scheme 91).[101,175] The *erythro*-iodo thiocyanates **517**, after separation, were treated with boron tri-



141 142 (59%)

SCHEME 90

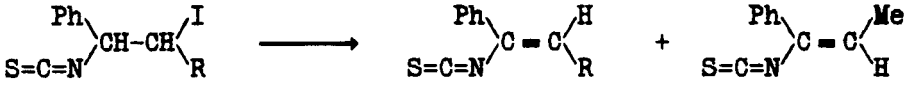


R = Et (391), *n*-Pr (374).

SCHEME 91

fluoride-ether at room temperature for 5 h. Work-up and chromatography on silica gel (hexane-chloroform, 2:1) gave the corresponding iodo isothiocyanates **516** (yield 65%).[175]

Treatment of the *vic*-iodo isothiocyanato derivatives of arylpropenes **520** and **521** with potassium *t*-butoxide in anhydrous ether at 20 °C for 2 h resulted in elimination to give the vinyl isothiocyanates **377** and **404** in moderate yields (54–66%) (Scheme 92).[176]



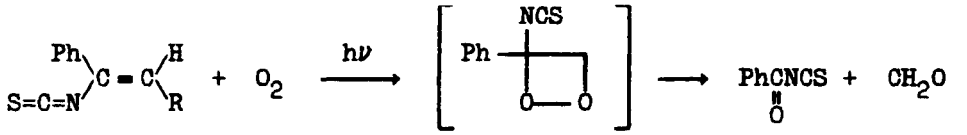
520,521 **377,404**

R = H (520,377), Me (521,404).

SCHEME 92

The initial product from the 1-isothiocyanato-1-phenyl-2-iodopropane **521** was entirely the *E*-isomer of 1-phenyl-1-isothiocyanatopropene **404** which partially isomerized to the *Z*-isomer during purification by PLC; almost complete isomerization occurred on standing at 20 °C for 24 h in > 90% yield.[176]

The vinyl isothiocyanates **377** and **404** undergo decomposition on standing to give benzoyl isothiocyanate **523**. The latter is thought to arise *via* an intermediate 1,2-dioxetane **522**, produced by the action of singlet oxygen on the activated double bond in the presence of light (Scheme 93).[176]



377,404 **522** **523**

R = H, Me.

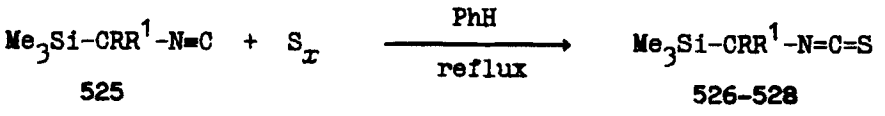
SCHEME 93

After 2 days at 20 °C 1-isothiocyanato-1-phenylethene **377** was converted (69%) to benzoyl isothiocyanate.**523**.[176]

2.8.3. *Reactions of trimethylsilyl isothiocyanates* The application of silicon reagents in organic synthesis has increased over time. Trimethylsilyl isothiocyanate **524** and mono- **526**, bis- **527** and tris(trimethylsilyl)methyl **528** isothiocyanate are such silyl reagents for the introduction of an NCS group into an organic molecule.[177–179]

Trimethylsilyl isothiocyanate **524** has been prepared by the reaction of sodium thiocyanate with chlorotrimethylsilane.[179,180]

Mono-, bis- and tris(trimethylsilyl)methyl isothiocyanate have been prepared from the corresponding isocyanides **525** and sulfur in 76%, 80% and 76% yield, respectively (Scheme 94).[177,178]

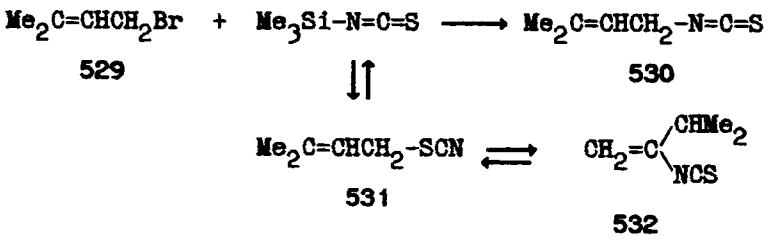


$R = R^1 = H$ (**526**), $R = H$, $R^1 = Me_3Si$ (**527**), $R = R^1 = Me_3Si$ (**528**).

SCHEME 94

2.8.3.1. *With organyl halides* The substitution of organic halides (mainly benzyl bromides) by trimethylsilyl isothiocyanate **524** and the rearrangement of thiocyanates to isothiocyanates has been described by the authors of Ref.[179]

1-Bromo-3-methybut-2-ene **529** is also reactive towards trimethylsilyl isothiocyanate, giving a mixture of three products: 3-isothiocyanato-3-methylbut-1-ene **532**, 1-thiocyanato-3-methylbut-2-ene **531**, and 1-isothiocyanato-3-methylbut-2-ene **530** (Scheme 95). This reaction pathway is corroborated by the time dependence of the product distribution (Table 3).[179] The intramolecular rearrangement between **532** and **531** is known,[181] and has been postulated to take place *via* a cyclic mechanism.[179]



SCHEME 95

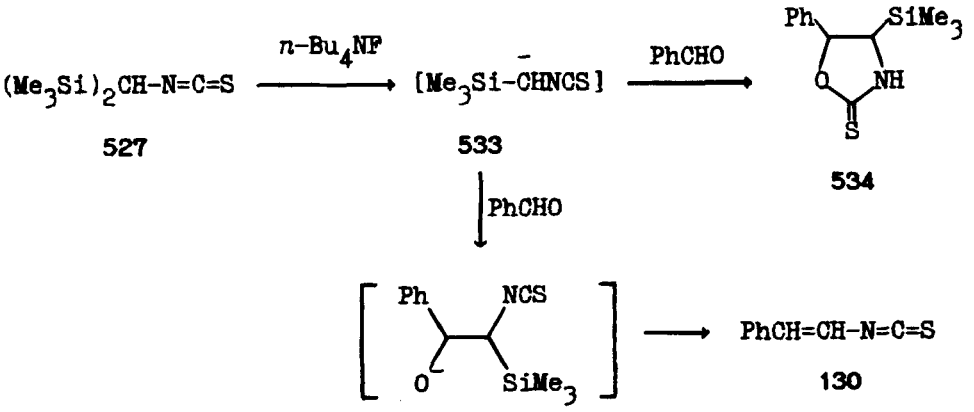
Each structure was confirmed by ^1H NMR and IR spectra.

TABLE 3 Reaction of 1-bromo-3-methylbut-2-ene **529** with trimethylsilyl isothiocyanate[a]

Time, h	Product, %[b]		
	532	**531**	**530**
24	37	34	29
48	27	25	48
72	23	23	54
120	15	22	63

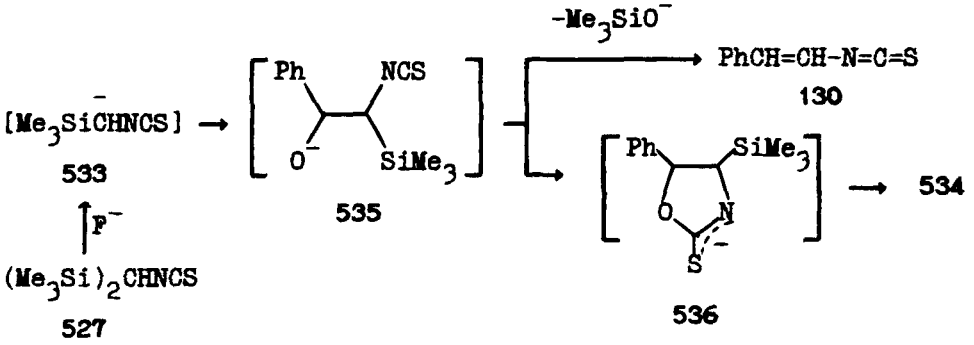
[a]The reaction was carried out in HMPA at room temperature. [b]The ratio of products was determined by ^1H NMR spectra.

2.8.3.2. *With benzaldehyde* The *n*-Bu_4NF-catalyzed reaction of bis(trimethylsilyl)methyl isothiocyanate **527** with benzaldehyde (THF, room temperature, nitrogen atmosphere) gives β-styryl isothiocyanate **130** and 5-phenyl-4-(trimethylsilyl)oxazolidine-2-thione **534** in 31% and 6% yield, respectively (Scheme 96).[177,178] The *trans:cis* ratio (56:44) **130** was determined by the ^1H NMR spectrum.[178]



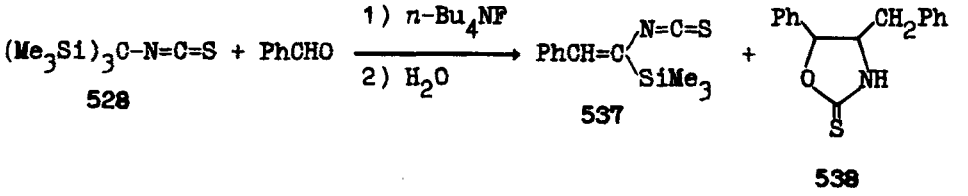
SCHEME 96

The mechanism of the formation of styryl isothiocyanate **130** is outlined in Scheme 97. The β-trimethylsilylalkoxide intermediate **535** undergoes elimination of Me_3SiO^- to give the isothiocyanate **130**. Both silyl groups of bis(trimethylsilyl)methyl isothiocyanate **527** participate in the synthesis of styryl isothiocyanate, the generation of the carbanion by fluoride ion and the Peterson olefination.[182] Ring closure of rotamer **535** leads to 5 phenyl-4-(trimethylsilyl)oxazolidine-2-thione **534**.[178]



SCHEME 97

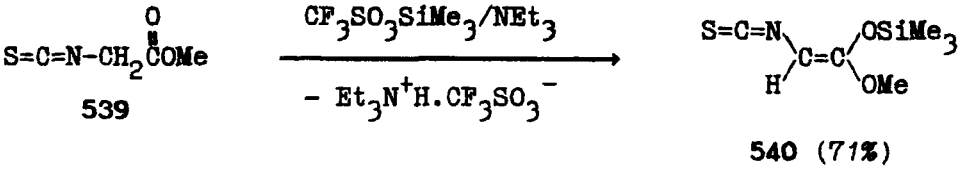
Tris(trimethylsilyl)methyl isothiocyanate **528** has been converted to α-(trimethylsilyl)styryl isothiocyanate **537** and 4-benzyl-5-phenyl-4-oxazoline-2-thione **538** in 26% and 7% yield, respectively, by treatment with benzaldehyde in the presence of a catalytic amount of *n*-Bu_4NF (THF, room temperature, nitrogen atmosphere) (Scheme 98).[178]



528 **537** **538**

SCHEME 98

2.8.4. *By reaction with trimethylsilyl trifluoromethanesulfonate* From the *N*-protected glycine methyl ester **539** the ketene acetal, 2-isothiocyanato-1-methoxy-1-(trimethylsiloxy)ethene **540**, was obtained by reaction with trimethylsilyl trifluoromethanesulfonate/triethylamine in *absol.* diethyl ether at 0–20 °C for 6 h (Scheme 99).[183]

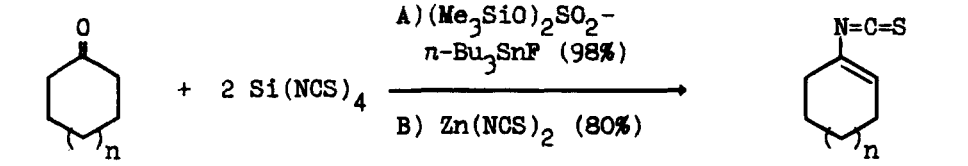


539 **540** (*71%*)

SCHEME 99

2.8.5. *By reaction of cyclic ketones with silicon tetraisothiocyanate* The reaction of the cycloalkanones **541–545** with silicon tetraisothiocyanate in the presence of $(Me_3SiO)_2SO_2$-*n*-Bu_3SnF or $Zn(NCS)_2$ provides the 1-cycloalkenyl isothiocyanates **369**, **370**, **372**, **373**, **546**, and **547** in good yields under mild conditions (Schemes 100 and 101).[184]

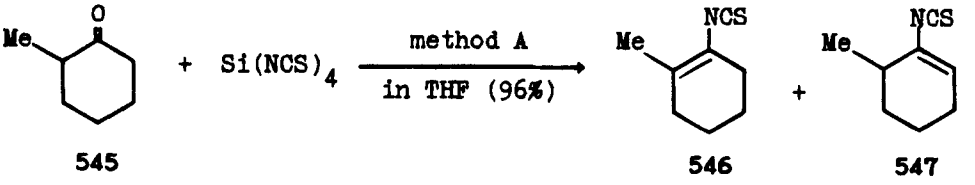
The analogous reagents $MeSi(NCS)_3$, $Me_2Si(NCS)_2$, and Me_3SiNCS proved to be less effective compared to $Si(NCS)_4$. Heating a solution of cyclohexanone **542** and $Si(NCS)_4$ in



541–544 **369,370,372,373**

n = 0 (**541,369**), 1 (**542,370**), 3 (**543,372**), 7 (**544,373**).

SCHEME 100



545 546 547

SCHEME 101

THF without catalyst gave none of the desired cyclohexenyl isothiocyanate **370** and the cyclohexanone was recovered unchanged.[184] Among many catalysts examined, a combination of $(Me_3SiO)_2SO_2$-*n*-Bu_3SnF (method A) and/or $Zn(NCS)_2$ (method B) was found[184] to be effective for the preparation of the title compounds. KF, CsF, or *n*-Bu_4NF could be used instead of *n*-Bu_3SnF in the former case. Lewis acids such as $ZnBr_2$ and $EtAlCl_2$ were marginal and $TiCl_4$ and $BF_3 \cdot OEt_2$ were ineffective.[184] The choice of the solvent was also critical for the successful reactions. Other cycloalkanones [cyclopentanone **541**, cyclooctanone **543**, cyclododecanone **544**] were converted by method B.

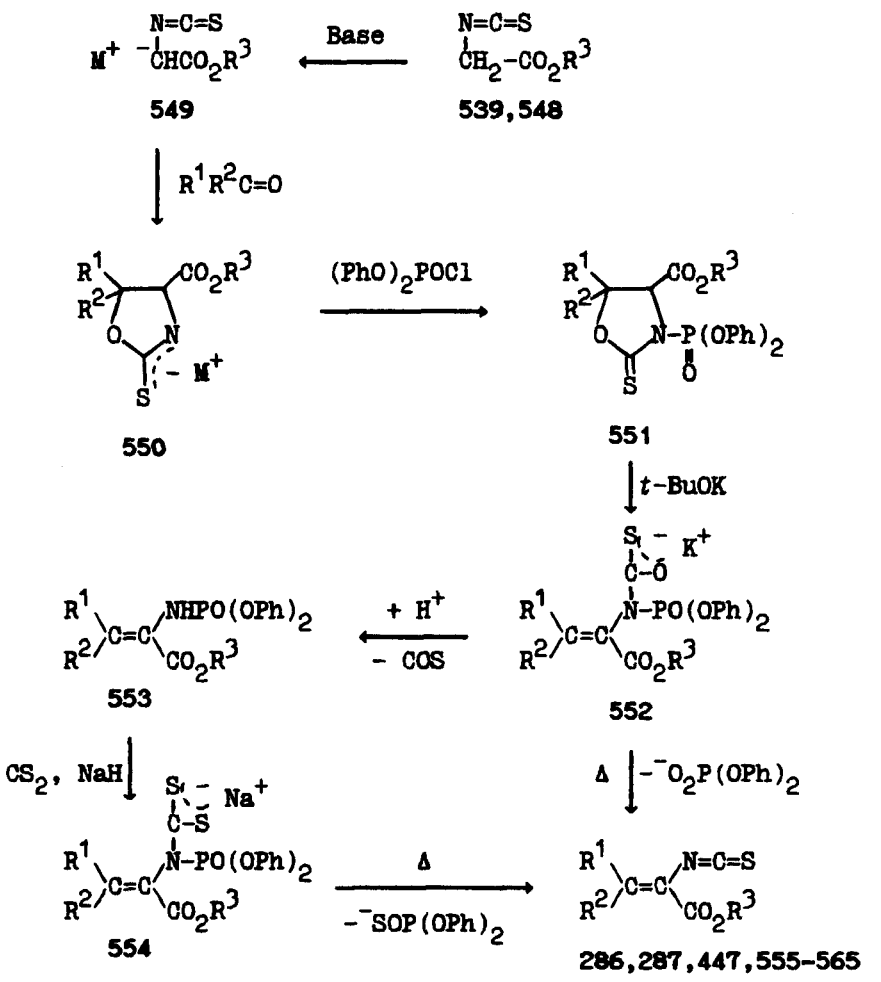
The stereoselectivity was examined with 2-methylcyclohexanone **545** as the substrate.[184] 2-Methyl-1-cyclohexyl isothiocyanate **546** was obtained as the major product along with a regioisomer, 6-methyl-1-cyclohexyl isothiocyanate **547** (90:10) (Scheme 101).

2.8.6. *From alkyl isothiocyanatoacetates, ketones and diphenyl phosphorochloridate* The β-substituted α-isothiocyanato acrylates **286**, **287**, **447**, and **555–565** have been prepared in 51–75% yield in a one-pot reaction starting from methyl **539** or ethyl **548** isothiocyanatoacetate and ketones: by phosphorylation of the base-induced alkali salts of 2-thioxo-4-oxazolidine-carboxylic esters **550** with diphenyl phosphorochloridate at 20–30 °C in tetrahydrofuran, treatment of the resulting 3-(diphenoxyphosphoryl)-2-thioxo-oxazolidine-4-carboxylic acid alkyl esters **551** with *t*-BuOK at –70 to –60 °C, and either warming up the *N*-(*O,O'*-diphenylphosphoryl)-*N*-vinylmonothiocarbamidates **552** to room temperature (with elimination of potassium *O,O'*-diphenylphosphate) (variant A), or neutralizing them with acetic acid at –60 °C and subsequent treatment of the resulting α-[*N*-(*O,O'*-phenoxyphosphoryl) amino]acrylates **553** with carbon disulfide-sodium hydride at 20–40 °C (with elimination of the *O,O'*-diphenylthiophosphate fragment) (variant B) (see Table 4) (Scheme 102).[185–187]

2.8.7. *Reactions of alkenyl isothiocyanates*

2.8.7.1. *With substituted acetonitriles* Treatment of 3-isothiocyanatoprop-2-eneiminium salts **566** with substituted acetonitriles in the presence of triethylamine gives the 3-(β-isothiocyanatovinyl)acrylonitriles **243** and **567–571** (12–96%) (Scheme 103).[103]

2.8.7.2. *With N-bromosuccinimide* The 2-isothiocyanatobut-2-enoates **287**, **289**, and **561** can be brominated with NBS [in CCl_4 in the presence of dibenzoyl peroxide (5 mol%) at 80 °C for 2.5 h] to yield 4-bromo-2-isothiocyanato-3-phenylbut-2-enoic acid methyl **573** (*E/Z* = 70:30) or ethyl **574** (*E/Z* = 65:35) ester and ethyl 4-bromo-2-isothiocyanato-3-(bromomethyl) but-2-enoate **572** (Scheme 104).[188]



R^3 = Me: R^1 = R^2 = Me (287); R^1 = H, R^2 = Ph (555); R^3 = Et: R^1 = H, R^2 = Me (286), *t*-Pr (556), Ph (557), 3,4-$(MeO)_2C_6H_3$ (558), PhCH=CH (447); R^1 = R^2 = Me (559); R^1 = Me, R^2 = Et (560), Ph (561); R^1 = R^2 = Ph (562), $PhCH_2$ (563); R^1 - R^2 = $(CH_2)_4$ (564), $(CH_2)_5$ (565).

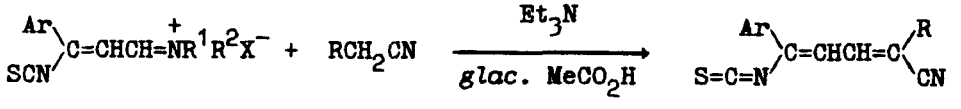
SCHEME 102

2.8.7.3. *With arylamines* *trans,cis*-1-Formyl-4-isothiocyanatobuta-1,3-diene **161** reacts with a range of nitrogen nucleophiles, *e.g.*, amines and hydrazines, forming thioamide derivatives.[87] However, primary arylamines do not yield the expected thioamides, these being thermally unstable. Presumably in this case initial attack by the arylamine occurs at the

TABLE 4 β-Substituted α-isothiocyanatoacrylates **286**, **287**, **447**, and **555–565**[167]

$SCNCH_2R^3$	Ketone	Variant	Yield, %[a]	Isomer ratio, *Z/E*
Et	Acetone	A	67[b], 54[c] (**559**)	—
Me	Acetone	A	41*c* (**287**)	—
Et	2-Butanone	A	75[b], 51[c] (**560**)	55:45
Et	Cyclopentanone	A	72[b], 63[c] (**564**)	—
Et	Cyclohexanone	A	62[b], 44[c] (**565**)	—
Et	Acetaldehyde	B	29[d] (**286**)	95:<5
Et	Isobutyraldehyde	B	60[d] (**556**)	95:<5
Et	Benzaldehyde	B	51[c] (**557**)	95:<5
Me	Benzaldehyde	B	48[c] (**555**)	95:<5
Et	3,4-Dimethoxybenzaldehyde	B	55[e] (**558**)	95:<5
Et	Cinnamaldehyde	B	54[c] (**447**)	75:25
Et	Acetophenone	B	61[c] (**561**)	57:43
			69[e]	35:65[f]
Et	Benzophenone	B	32[c] (**562**)	—
Et	1,3-Diphenylacetone	B	35[c] (**563**)	—

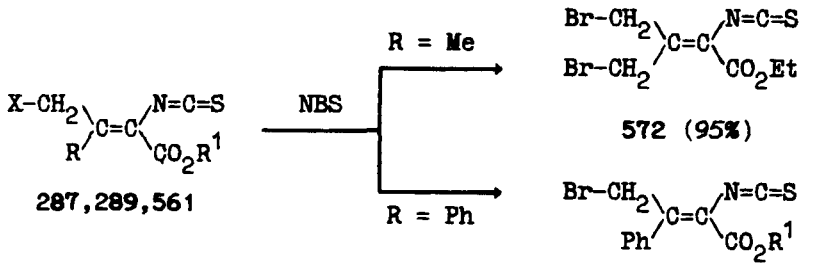
[a]Yield based on consumed $SCNCH_2R^3$. [b]95% crude product. [c]After chromatographic separation on kieselguhr. [d]Purified by distillation. [e]Purified by recrystallization. [f]Only 1 h at 30 °C.



566 **243,567-571**

X^- = Cl^-, ClO_4^-, $POCl_2^-$; $R^1 = R^2$ = Me, R^1-R^2 = $(CH_2)_4$; R = CN, Ar = Ph (**567**), 4-ClC_6H_4 (**568**), 4-MeC_6H_4 (**243**), β-$C_{10}H_7$ (**569**); Ar = 4-ClC_6H_4, R = $EtCO_2$ (**570**), benzimidazol-2-yl (**571**).

SCHEME 103

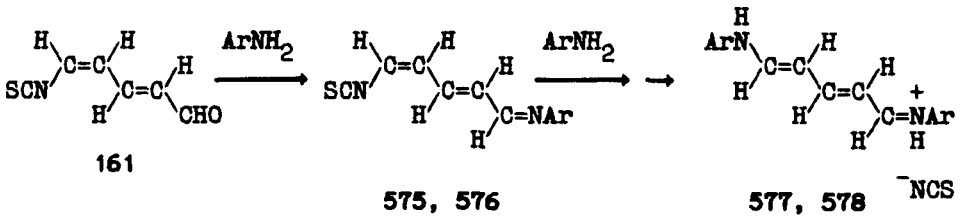


287,289,561 **572** (95%) **573,574** (89–92%)

X = H, R = R^1 = Me (**287,572**); R = Ph, R^1 = Me (**289,573**); Et (**561,574**).

SCHEME 104

aldehyde group to form the Schiff base **575** or **576**, with subsequent displacement of the isothiocyanato group by a second molecule of the arylamine, to yield the iminium isothiocyanates **577** and **578** (Scheme 105).[87]

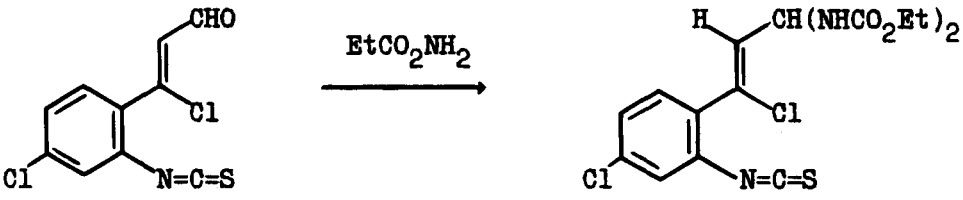


161 **575, 576** **577, 578**

Ar = 4-ClC$_6$H$_4$ (575,577), 4-MeC$_6$H$_4$ (576,578).

SCHEME 105

2.8.7.4. *With ethyl carbamate* Ethyl carbamate, in the presence of acid (trace of hydrogen chloride for 12 h in ethyl acetate), reacts with β,4-dichloro-2-isothiocyanatocinnamaldehyde **171** to yield 1-chloro-1-(4-chloro-2-isothiocyanatophenyl)-3,3-bis-(ethoxycarbonylamino)prop-1-ene **579** (Scheme 106).[91]



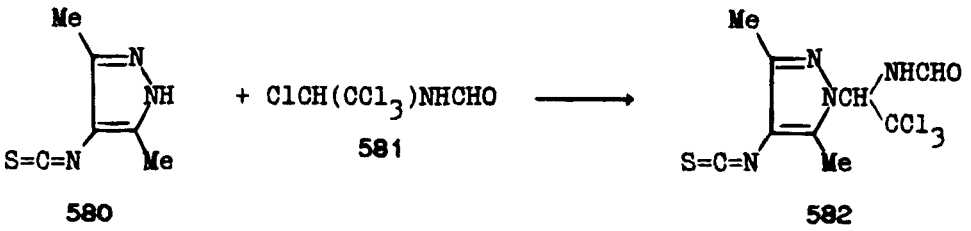
171 **579**

SCHEME 106

2.8.7.5. *With N-(1,2,2,2-tetrachloroethyl)formamide* Triethylamine was added to a mixture of chloro-*N*-(1,2,2,2-tetrachloroethyl)formamide **581** and 3,5-dimethyl-4-isothiocyanatopyrazole **580** in acetone at 0–5 °C and the mixture stirred for 1 h at room temperature to give the *N*-(1-substituted 2,2,2-trichloroethyl)formamide derivative **582** (Scheme 107).[189]

2.8.7.6. *With alcohols* The novel compounds paulomycinone A **585** and B **586** as well as paulinone **587**, have been obtained by degradation of the antibiotics paulomycin A **583** and paulomycin B **584** (Scheme 108).[190–192]

Paulomycin A **583** in a solution in MeOH (at room temperature for 5 days) is slowly converted to yellow solid paulomycinone A **585**, which can be purified by chromatography.[190–192]



580 582

SCHEME 107

The same reaction conditions can be used to obtain the paulomycinone B **586** when paulomycin B **584** is used as starting material.[190]

Acidic methanolysis of either paulomycin A **583** or B **584** (at room temperature for 3 days) leads to an orange, crystalline solid, 11-*O*-pauloylpaulinone **587**, and a colorless liquid, methyl 7-*O*-(2-methylbutyryl)paulomycoside **588**.[190–192] 11-*O*-Pauloylpaulinone **587** was purified by column chromatography and recrystallization.

The nucleosidyl isothiocyanates **590** and **592** have been prepared[193] by reaction of isocyanatoaryl isothiocyanates with 2′,3′-isopropylideneuridine **589** and 2′,3′-isopropylideneadenosine **591**. The 5′-hydroxy group of the nucleoside derivatives adds selectively to the isocyanate groups of the isocyanatoaryl isothiocyanates (Scheme 109).

2.8.7.7. *With carboxylic acids* Reaction of 4-methoxybenzyl 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4α-carboxylate **441** with trifluoroacetic acid in the presence of anisole for 30 min gives 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4a-carboxylic acid **593** in 51.9% yield (Scheme 110).[154]

Acetylation of 11-*O*-pauloylpaulinone **587** with a mixture of acetic acid and acetic anhydride in the presence of 4-toluenesulfonic acid at room temperature for 18 h gives 9,10,11-tri-*O*-acetyl-11-*O*-pauloylpaulinone **594** (Scheme 111).[192]

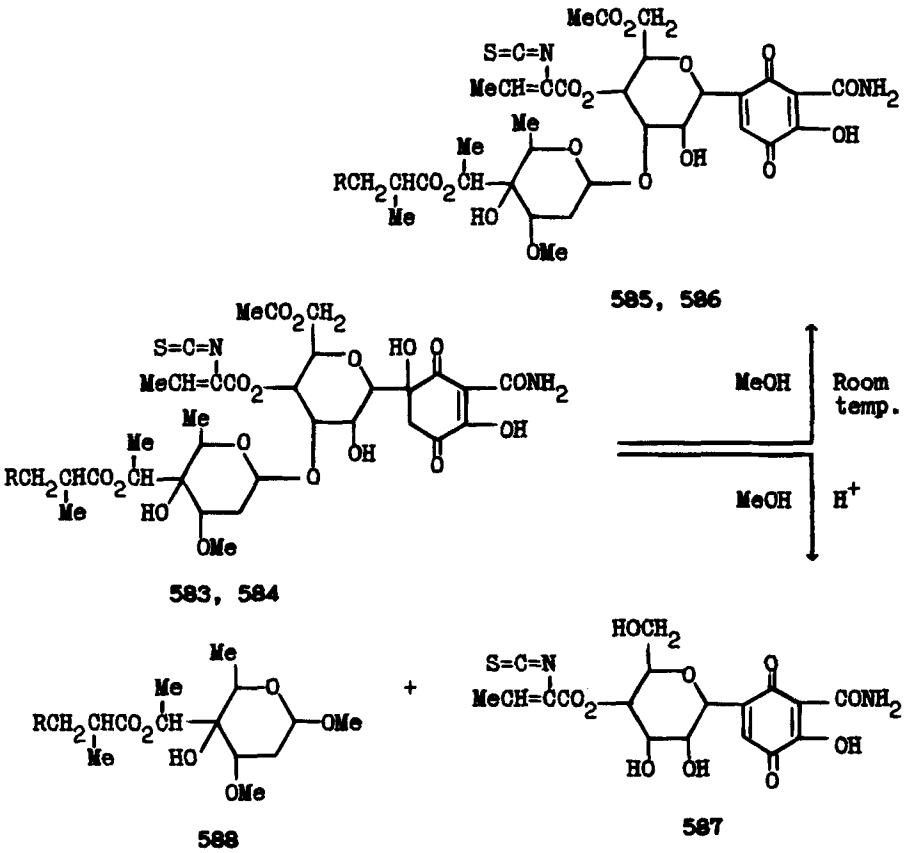
2.8.7.8. *Cycloadditions* Condensation of the isothiocyanato-buta-1,3-diene **345** and the isomeric isothiocyanatohexadienes **350** and **351** with tetracyanoethylene (TCNE) and dimethyl but-2-ynedioate gave the corresponding cycloolefinic isothiocyanates **595–598** in good yields (Scheme 112).[133]

The isothiocyanate **350** reacts with TCNE with more rapidly than its stereoisomer **351** to give the isomeric cycloadducts **595** and **596**, respectively.

2.8.7.9. *Haloalkenyl isothiocyanates*

2.8.7.9.1. *With sodium iodide* Reaction of 3-chloro-1-isothiocyanato-2-methylprop-1-ene **226** with sodium iodide in acetone at room temperature for 10 h leads to 1-isothiocyanato-3-iodo-2-methylprop-1-ene **599** (Scheme 113).[121,122]

2.8.7.9.2. *Reactions with thiocyanates* Reaction of 3-chloro-1-isothiocyanato-2-methylprop-1-ene **226** with ammonium thiocyanate in DMSO at room temperature for 5 h affords the



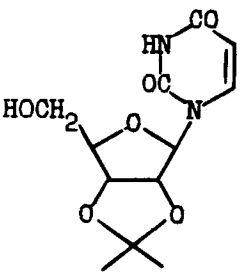
R = Me (583, 585), H (584, 586).

SCHEME 108

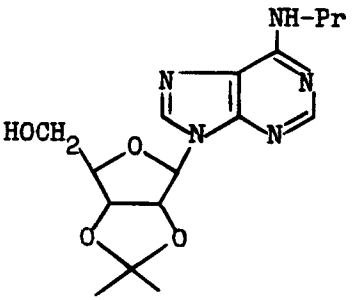
1-isothiocyanato-2-methyl-3-thiocyanatoprop-1-ene **600** which subsequently isomerizes to 1-isothiocyanato-2-methyl-3-isothiocyanatoprop-1-ene **601** (dioxane, 6 h) (Scheme 114).[121,122]

The known[169] 3-bromoprop-1-enyl isothiocyanate **507** represents a compound with highly reactive halogen of the allyl type which, by the reaction with KSCN (dry acetone, 1 h) and subsequent distillation of the crude product, affords *cis*-3-isothiocyanatoprop-1-enyl isothiocyanate **602** (Scheme 115).

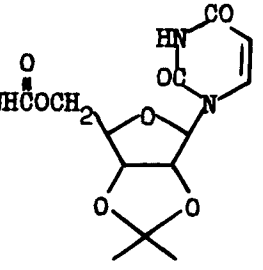
2.8.7.9.3. *Reactions with ammonium or potassium acetate* Treatment of 4-bromo-2-isothiocyanato-3-phenylbut-2-enoic acid ethyl ester **574** (*E/Z* = 65:35) with dicyclohexylethylammonium acetate (in acetone at 25 °C for 2 h) gave 4-acetoxy-2-isothiocyanato-3-phenylbut-2-enoic acid ethyl ester **603** (*E/Z* = 35:65) in 61% yield (Scheme 116).[188]



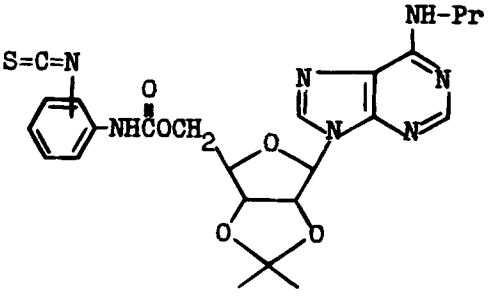
589



591

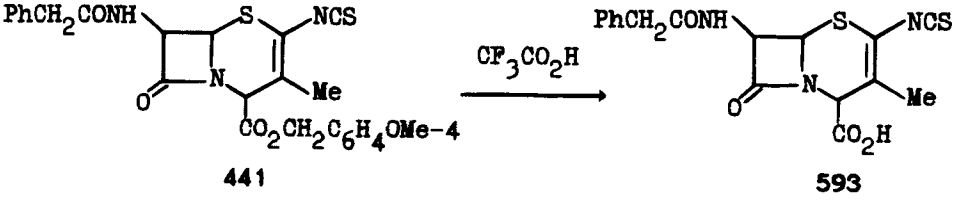


590



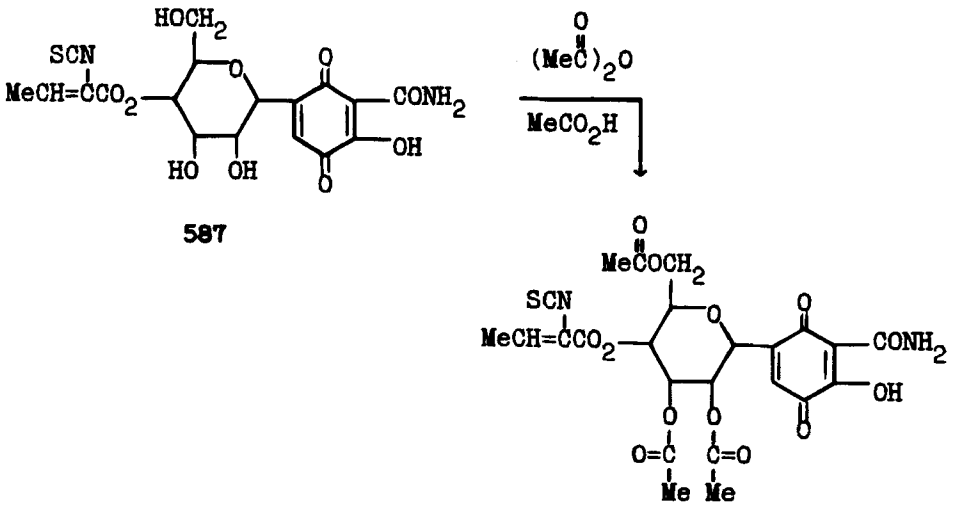
592

SCHEME 109

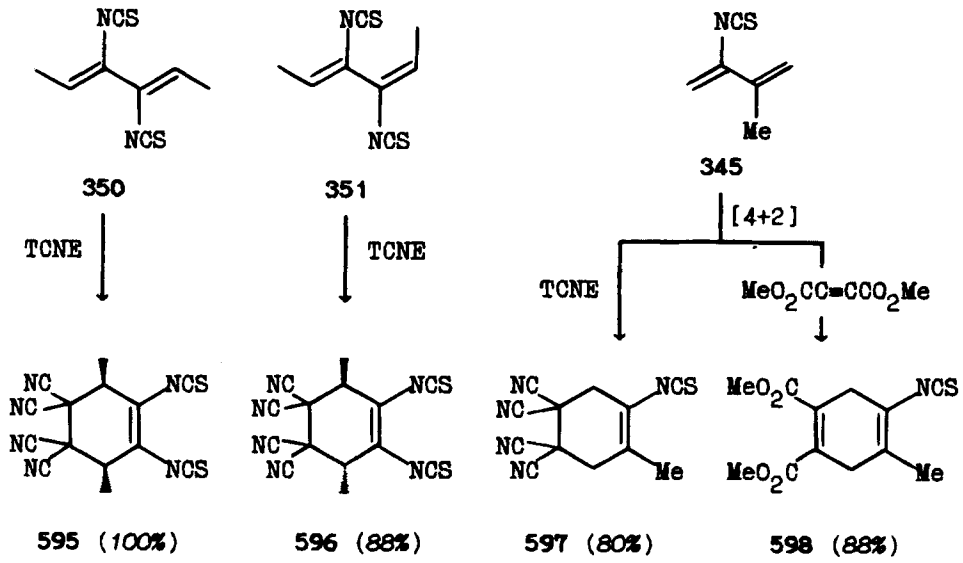


441 593

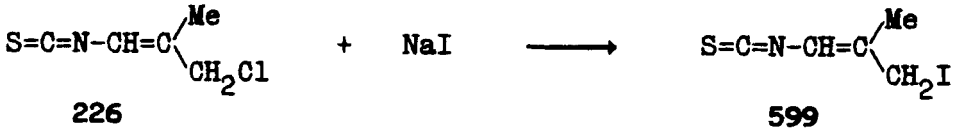
SCHEME 110



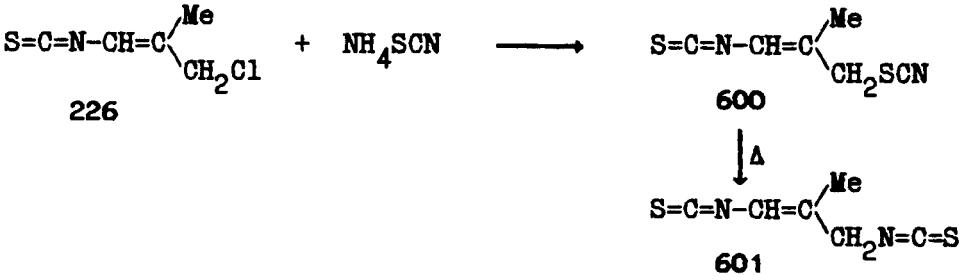
SCHEME 111



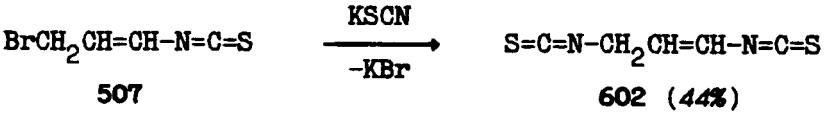
SCHEME 112



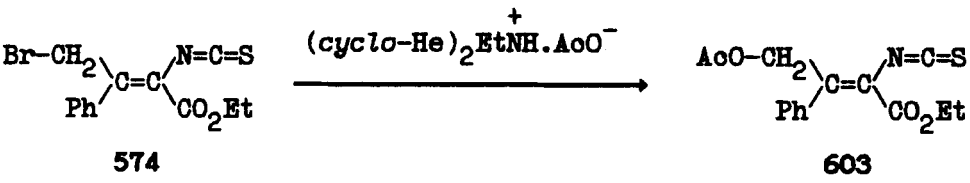
SCHEME 113



SCHEME 114



SCHEME 115



SCHEME 116

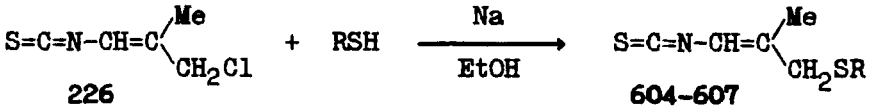
With potassium acetate (under the same reaction conditions) the isothiocyanate **603** was obtained in 25% yield.[188]

2.8.7.9.4. *Reactions with potassium hydridotetracarbonylferrate* 4-Bromo-2-isothiocyanato-3-phenylbut-2-enoic acid ethyl ester **574** has been converted to 2-isothiocyanato-3-phenylbut-2-enoic acid ethyl ester **561** by treatment with potassium hydridotetracarbonylferrate (DME, 30 °C, 3 h) (Scheme 117).[188]

574 561

SCHEME 117

2.8.7.9.5. *Reactions with thiols* 3-Chloro-1-isothiocyanato-2-methyl-prop-1-ene **226** in toluene reacts with aliphatic sodium thiolates in ethanol to form the 3-alkylmethylthio-1-isothiocyanato-2-methylpropenes **604–607** in 28–56% yield (Scheme 118).[121-123]

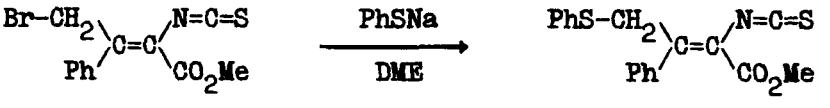


226 604–607

R = Et (**604**), *n*-Bu (**605**), $PhCH_2$ (**606**), Ph (**607**).

SCHEME 118

4-Bromo-2-isothiocyanato-3-phenylbut-2-enoic acid methyl ester **573** (*E/Z* = 70:30) with sodium benzenethiolate in 1,2-dimethoxyethane at 10 °C for 30 min gave 2-isothiocyanato-3-phenyl-4-(phenylthio)but-2-enoic acid methyl ester **608** (*E/Z* = 45:55) in 63% yield (Scheme 119).[188]



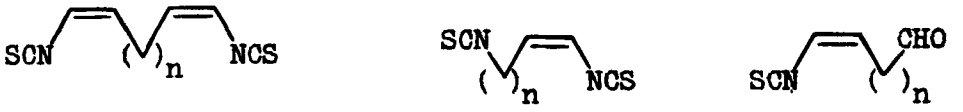
573 608

SCHEME 119

2.9. *α,β-Unsaturated Isothiocyanates from Natural Sources*

2.9.1. *From marine sponges* Isothiocyanates are well-known natural products which occur as glycosinolates of a few families of terrestrial plants, principally the *Cruciferae*, and are known as mustard oils.[30] At pH7 the glycosinolates decompose to isothiocyanates. Marine-derived isothiocyanates have been isolated from sponges, where they have been found as sesqui- or diterpenes, almost always accompanied by isocyanides and formamides.[29]

Eighteen long-chain aliphatic α,ω-bisisothiocyanates **609–626** have been isolated from a marine sponge, *Pseudaxinyssa* sp. from Fiji by the authors of Ref.[28,194] Eight compounds **609–616** are di-, ten **617–626** are monoolefinic. Three additional constituents are the α-isothiocyanato-ω–formyl compounds **627–629** (Scheme 120).[28,194]



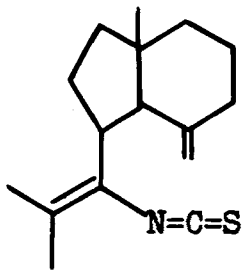
n = 8–14 n = 9–18 n = 9, 15, 16

609–616 **617–626** **627–629**

SCHEME 120

The biogenetic origin of the marine isothiocyanates is not known, but the presence in one animal of non-terpenoid aliphatic bisisothiocyanates and monoaldehydic isothiocyanates represents a significant departure from previously known secondary sponge metabolites.[28] It has been reported[34,35] that alkylene bisisothiocyanates selectively destroy the spiracle-forming cells in *Maduca sexta* which makes these compounds potential insect growth regulators.

A paper[33] reported the isolation and structure elucidation of axisothiocyanate-4 **630**, a novel axane sesquiterpenoid from the marine sponge *Axinella cannobina* (Scheme 121).



630

SCHEME 121

On the basis of X-ray and CD evidence the absolute configuration of this isothiocyanate was established.[195]

2.9.2. *From vegetable oils* It is known that the seeds of the Cruciferae in general, and thus rapeseed in particular, contain thioglucosides capable of hydrolysing through the action of the endogenous enzyme myrosinase, thus giving rise to the formation of sulfur and/or nitrogen compounds which are goitrogenic or in any case toxic for many animal species.[196] The fact that such enzymatic transformations, and still others of a chemical nature, can take place during the processing of the seeds for the production of oil, explains how some of these compounds can pass, according to their solubility, into the oil itself.

The presence of the four compounds vinyl, allyl, butenyl, and pentenyl isothiocyanate is determined by GLC analysis of the volatile fraction obtained by distillation of the olive oil as a mixture (prepared from rapeseed) in high vacuum; the fraction is collected in a low temperature trap.[196]

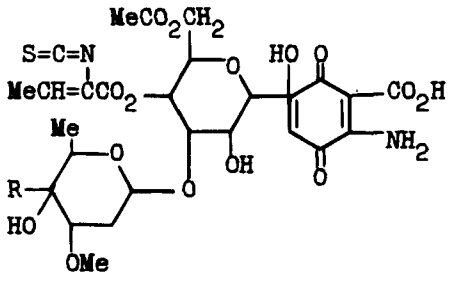
For the actual identification of the above-mentioned compounds, the authors of Ref.[196] examined some crude rapeseed oil, and the corresponding refined oil, produced industrially and with a normal erucic acid content of 50%. The results of the gas chromatographic examination show that in raw rapeseed oil these isothiocyanates, assumed to be vinyl isothiocyanate, are present, but absent in refined oil.

The isolation of various vinylic isothiocyanates (vinyl, allyl, butenyl, pentenyl) and aromatic isothiocyanates (phenyl, phenethyl) from colza oil has been described in Ref.[197]

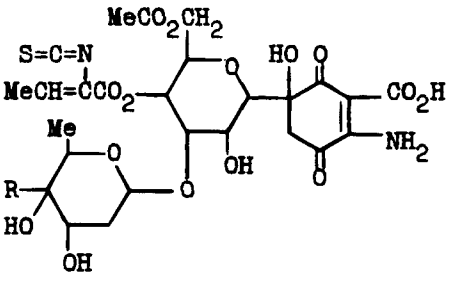
2.9.3. *Isothiocyanates produced by Streptomyces paulus* The production of the paulomycin complex by fermentation of *Streptomyces paulus*, strain 273, NRRL 12251, and the isolation and separation of paulomycin A **583** and B (**584**) (previously named as volonomycin A and volonomycin B), the main components of the mixture, has been reported by Argoudelis *et al.*[192,198–200] The structures of paulomycin A and B have been reported by Wiley *et al.*[191,192] and are shown in Scheme 122.[201]

An antibiotic complex active against multiply resistant strains of staphylococci and other Gram-positive bacteria has been isolated from cultures of *Streptomyces albus* G.[202] Silica gel and Sephadex LH-20 column chromatography gave two congeners with M_r values 786 and 772, thus differing by one methylene group. The two homologs contained an isothiocyanate group, and proved to be identical with paulomycin A **583** and B (**584**) produced by *Streptomyces paulus*; the FAB mass spectra, in addition, proved the same two congeners to be present in proceomycin obtained from *Streptomyces alboniger*.[202]

A paper[201] and two patents[199,200] describe the isolation, characterization and structure of several bioactive minor components produced by *Streptomyces paulus*. The biological properties of these new paulomycins, designated paulomycin A_2 **631** C (**632**), D (**633**), E (**634**), F (**635**) and demethylpaulomycin A **636** and B **637** are also briefly discussed (Scheme 122). The effect of various concentrations of methionine on paulomycin C **632** production by fermentation of *Streptomyces paulus* in a synthetic medium containing methionine has been reported.[203] These results indicate that methionine plays a central role in the biosynthesis of paulomycin C **632**. Since paulomycin C is an ester of propionic acid, it is presumably synthesized *via* catabolism of α-ketobutyric acid to propionyl-CoA.[203] The initial metabolism of methionine is known to yield α-ketobutyric acid.[204] The increased production of paulomycin A **583** is also the result of higher levels of α-ketobutyric acid generated in the presence of methionine.[203]



583,584,631-635



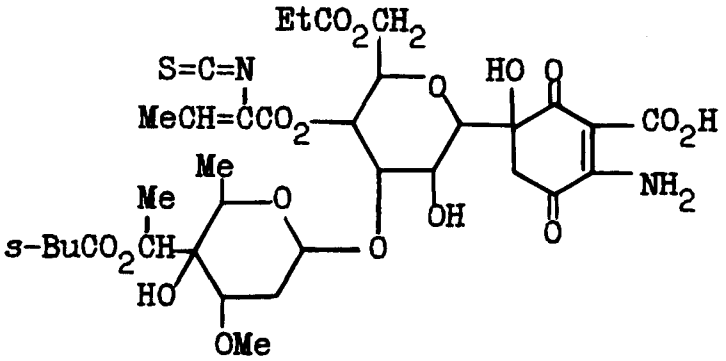
636,637

R = *s*-$BuCO_2CHMe$ (583), *t*-$PrCO_2CHMe$ (584), *t*-$BuCO_2CHMe$ (631), $EtCO_2CHMe$ (632), $MeCO_2CHMe$ (633), MeC(O) (634), HOCHMe (635), *s*-$BuCO_2CHMe$ (636), *t*-$PrCO_2CHMe$ (637).

SCHEME 122

The antibiotics paulomycin A and B can be produced selectively by precursor-directed biosynthesis.[205] By addition of 2-methylbutyric acid, isoleucine, α-ketobutyric acid, threonine or methionine to fermentations of *Streptomyces paulus*, a paulomycin complex containing 80–90% paulomycin A can be produced. The addition of isobutyric acid or valine results in the production of paulomycin containing 80–90% paulomycin B.[205,206]

The invention[207] concerns the production of the novel antibiotic paulomycin U **638** by growing *Streptomyces paulus*, strain 273, NRRL 12251, in the presence of L-α–aminobutyric acid as the nitrogen source (Scheme 123).



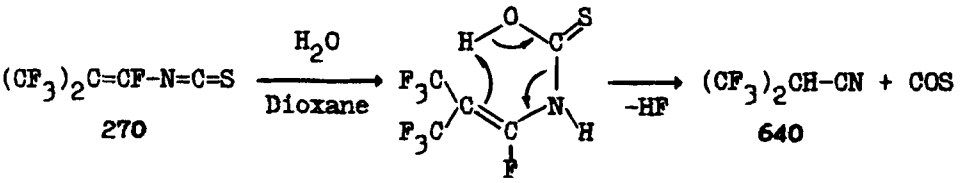
638

SCHEME 123

3. REACTIONS OF α,β-UNSATURATED ISOTHIOCYANATES

3.1. *Hydrolysis*

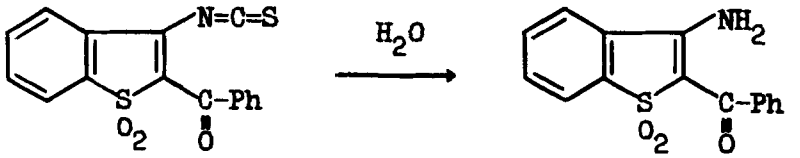
Perfluoroisobutenyl isothiocyanate **270** reacts easily with water to form α-hydroperfluoroisobutyronitrile **640** in 30% yield (Scheme 124).[114]



270 **639** **640**

SCHEME 124

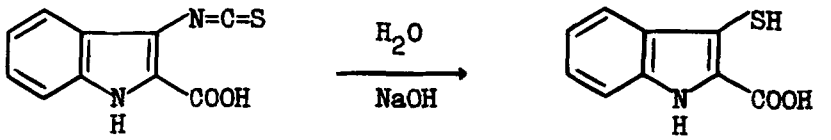
The hydrolysis of 2-benzoyl-3-isothiocyanatobenzo[*b*]thiophene 1,1-dioxide **263** leads to 3-amino-2-benzoylbenzo[*b*]thiophene 1,1-dioxide **641** (Scheme 125).[109]



263 **641**

SCHEME 125

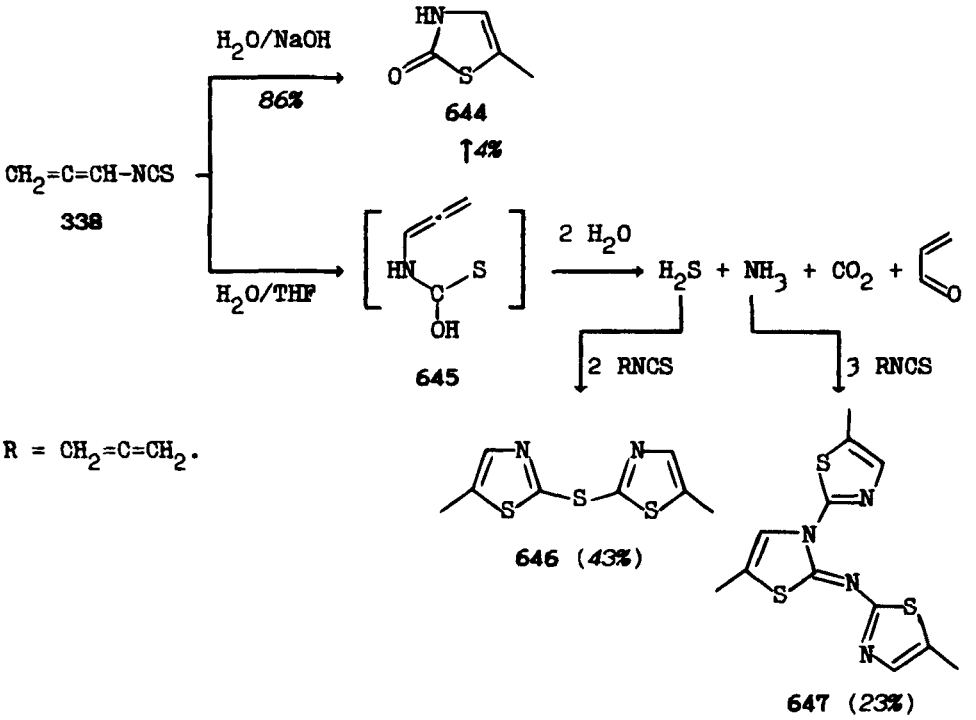
3-Mercapto-2-indolecarboxylic acid **643** is readily accessible by hydrolysis of 3-isothiocyanato-2-indolecarboxylic acid **642** with 2.5 N aqueous NaOH with reflux overnight under N_2 (Scheme 126).[110]



642 **643**

SCHEME 126

Allenyl isothiocyanate **338** with aqueous sodium hydroxide gave 5-methylthiazolidin-2-one **644** in 86% yield (Scheme 127).[133,135] Isothiocyanate **338** already at room temperature in H_2O/THF (1:2) gives the heterocycles **644**, **646** and **647**. The reaction proceeds via the intermediate **645** which not only cyclizes to **644** but also decomposes to acrolein, carbon dioxide, hydrogen sulfide and ammonia. The two latter compounds react with **338** to give **646** and **647**.



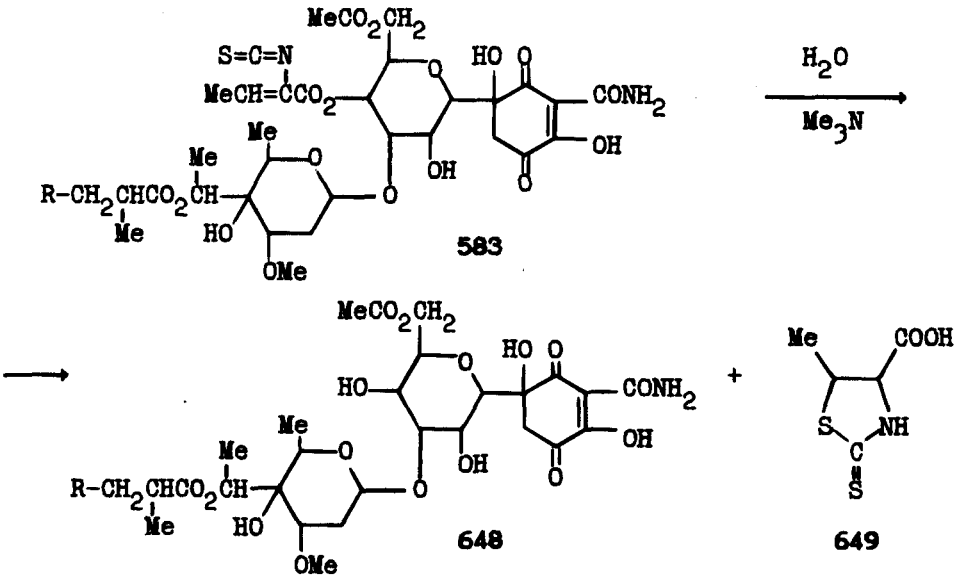
SCHEME 127

The action of dilute base (0.01 N trimethylamine) on paulomycin A **583** (R = Me) at room temperature for 2 days gives a colorless, crystalline solid, paulomenol A **648** (Scheme 128).[190-192]

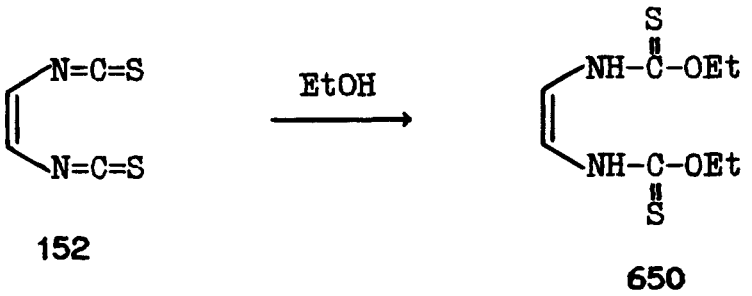
The five carbons lost were isolated as 5-methyl-2-thioxo-4-thiazolinecarboxylic acid **649**, which must arise from a MeCH=C(NCS)C=O moiety and H_2S being formed by hydrolysis of NCS and then reacting with the above pauloyl moiety.[192] 5-Methyl-2-thioxo-4-thiazolinecarboxylic acid **649** has been synthesised by reaction of a mixture of paulomycin A and B with 0.1 N Me_3N at room temperature for 12 h.[192]

3.2. *Reactions with alcohols*

Vinylene diisothiocyanate **152** reacts with ethanol at room temperature for 15 days to give the 2:1 thioester product, *O,O'*-diethyl-*N,N'*-vinylenebis(thiocarbamate) **650**, in 42% yield (Scheme 129).[208]



SCHEME 128



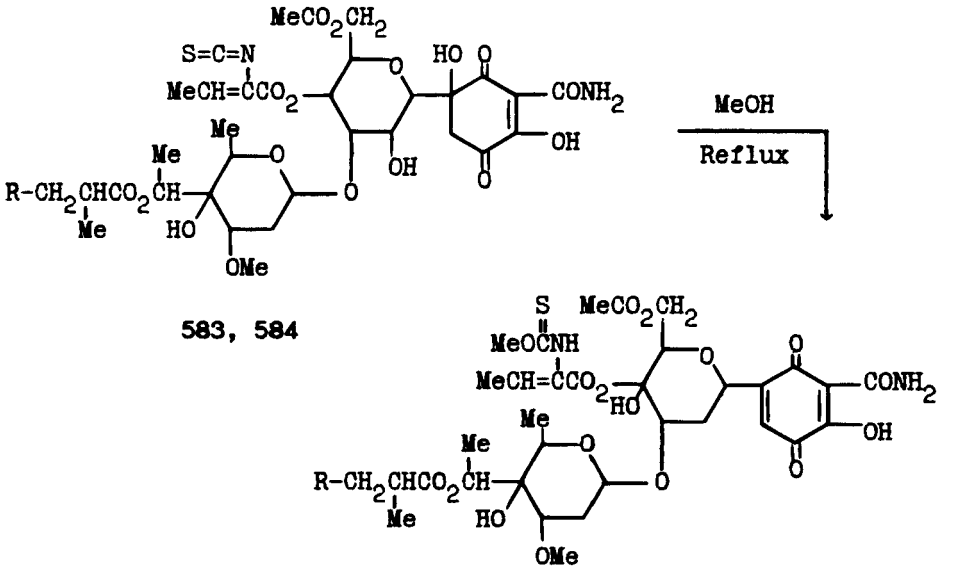
SCHEME 129

Methoxypaulomycinone A **651** and B **652** have been obtained by reflux for 22 h of a solution of paulomycin A **583** or B **584** in MeOH (Scheme 130).[190]

4-Methoxybenzyl 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4α-carboxylate **441** has been converted to 4-methoxybenzyl 7β-phenylacetamido-2-methoxythiocarbonylamino-3-methyl-2-cephem-4α-carboxylate **653** in 61% yield by reaction with refluxing methanol for 6 h (Scheme 131).[154]

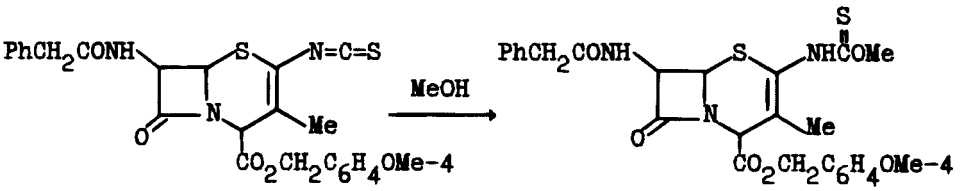
4-Isothiocyanato-2-morpholinoquinoline **654** reacts with methanol to give *N*-(2-morpholino-4-quinolyl)thiocarbamidocarboxylic acid *O*-methyl ester **655** in 85% yield (Scheme 132).[209]

Reaction of perfluoroisobutenyl isothiocyanate **270** with *absol.* alcohols gives the thiocarbamic acid derivatives **659** (Scheme 133).[114]



R = Me (583,651), H (584,652).

SCHEME 130

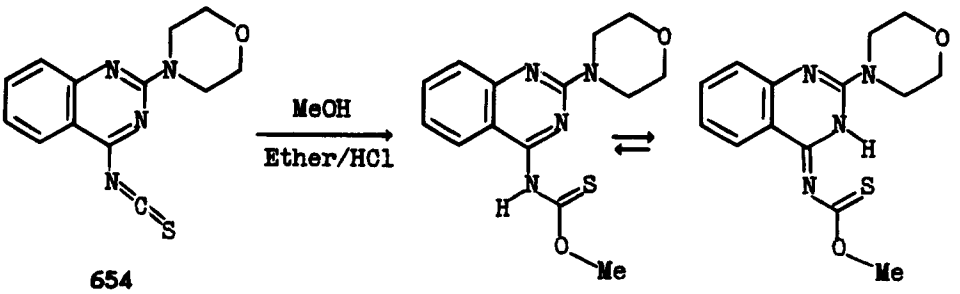


SCHEME 131

Alkanols add to the NCS group of α-isothiocyanatoacrylate **557** in the presence of base (sodium alkoxide) for 28–40 h to give 2-alkoxy-2-thiazoline-4-carboxylic acid ethyl esters **661** in 53–60% yield (Scheme 134).[23]

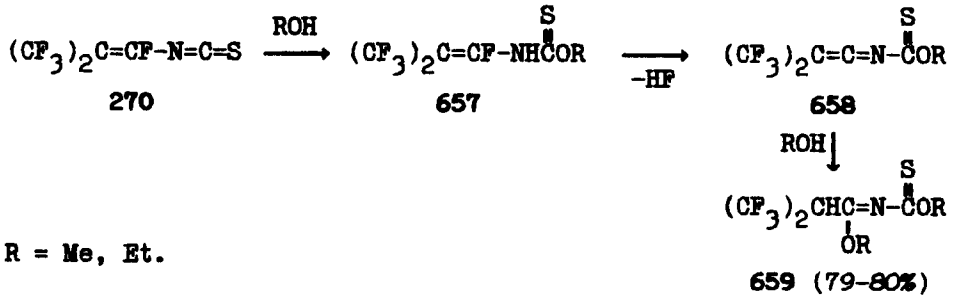
Reaction of the γ-isothiocyanatoallyl chlorides **226**, **313–315**, and **320** with alcohols catalyzed by *tert*-amines at 40 °C gives numerous 2-alkoxy-6*H*-1,3-thiazines 662 in 48–74% yield (Scheme 135).[124,128] Without triethylamine a mixture of γ-isothiocyanatoallyl ethers **663** and the bisadducts **664** was obtained.[124]

1-(Chloromethyl)-2-isothiocyanatocyclohexene **314** was stirred in methanol containing triethylamine while sodium methoxide in methanol was added dropwise (40 °C, 6 h) to give



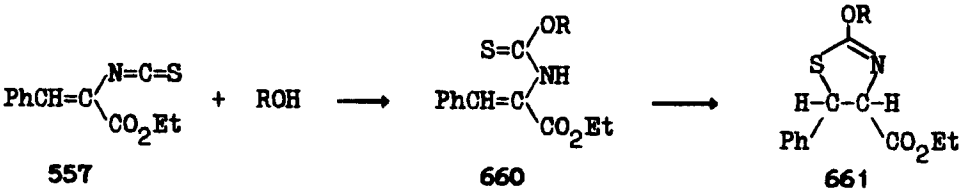
654 655 656

SCHEME 132



270 657 658 659 (79–80%)

SCHEME 133



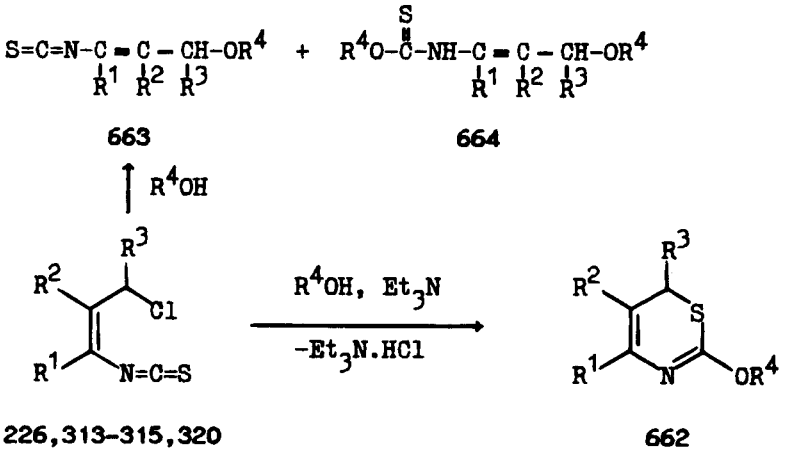
557 660 661

SCHEME 134

70% of 5,6,7,8-tetrahydro-2-methoxy-4*H*-3,1-benzothiazine **665**, an intermediate for pesticides (Scheme 136).[210]

Methanol and phenol react normally with β,4-dichloro-2-isothiocyanatocinnamaldehyde 171 in the presence of alkali (20–90 °C, few minutes) and yield 2-methoxy- **666** and 2-phenoxy-7-chloro-4-formylmethylene-4*H*-3,1-benzothiazine **667**, respectively (Scheme 137).[91]

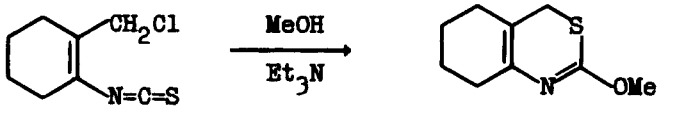
The reaction of prop-2-yn-1-ol with phenyl isothiocyanate **189** in the presence of a catalytic amount of sodium methoxide proceeds slowly and gives a mixture of the isomeric 1,3-oxathiolane **668** (46%) and 1,3-oxazolidine **669** (16%) (Scheme 138).[211]



663 664 226,313-315,320 662

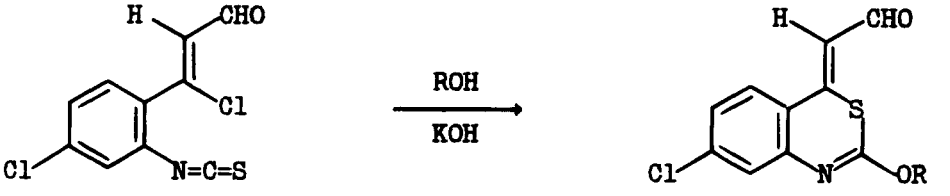
$R^1 = R^3 = H$, $R^2 = Me$ (226); $R^3 = H$, $R^1 - R^2 = (CH_2)_3$ (313), $(CH_2)_4$ (314), $(CH_2)_5$ (315), $(CH_2)_6$ (320); $R^4 = Me$, Et, *n*-Pr, *i*-Pr, *n*-Bu, $PhCH_2$.

SCHEME 135



314 665

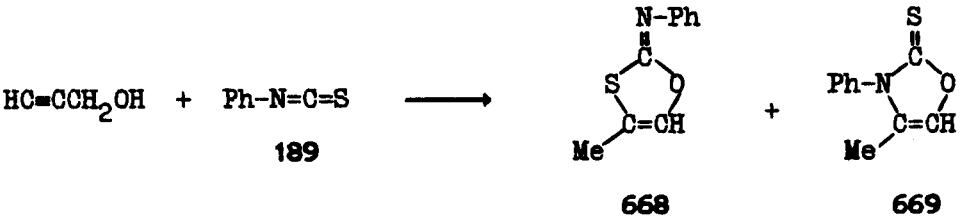
SCHEME 136



171 666,667

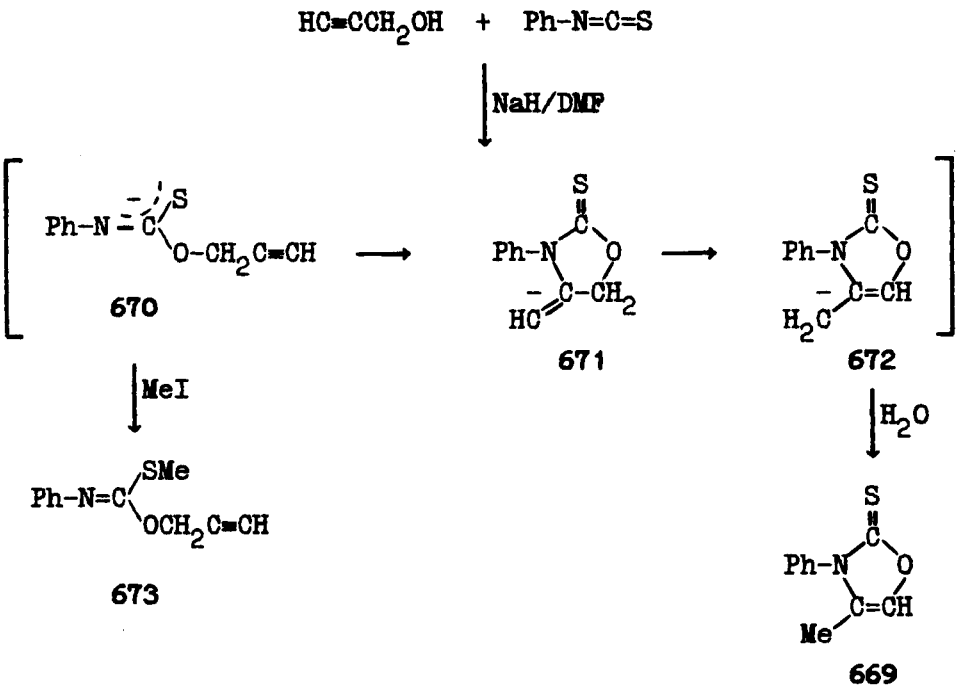
R = Me (666), Ph (667).

SCHEME 137



SCHEME 138

If the reaction is carried out in the presence of sodium hydride in absolute *N,N*-dimethylformamide 3-phenyl-4-methyl-1,3-oxazoline-2-thione **669** can be prepared in 80% yield (Scheme 139).[212]



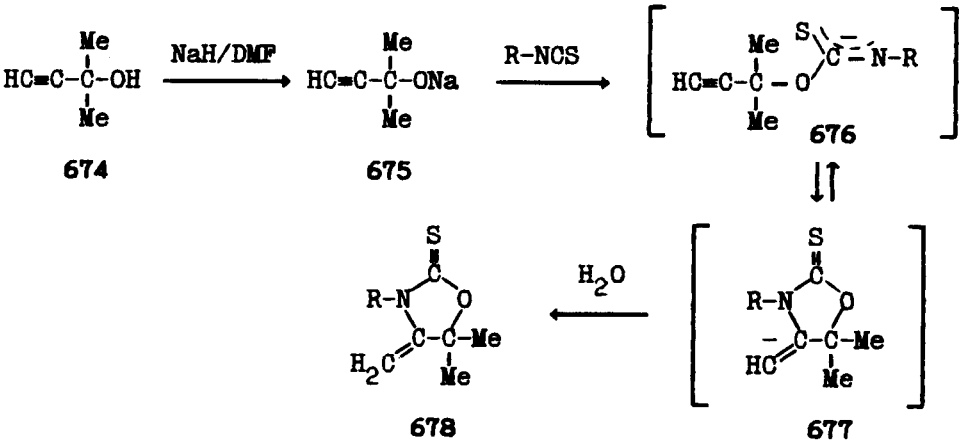
SCHEME 139

The formation of another product **668** as mentioned in Ref.[211] can be explained by different reaction conditions.[212] In the cited work[211] the reaction was catalyzed with sodium methoxide (5 mol %), so that the reaction mixture always contained free prop-2-yn-1-ol which can transfer the proton to the transient sodium salt of the monothiocarbamate ester **670**. The neutral ester thus formed is cyclized preferently at the sulfur atom to give the

oxathiolane derivative **668** as the main product. In the other case[212] obviously the proton migration leads to a high concentration of the anionic intermediates **671** and **672** which cannot be reached in the presence of prop-2-yn-1-ol as proton donor.

If the reaction is carried out in the presence of methyl iodide, the transient sodium salt of the *N*-phenyl-*O*-(prop-2-ynyl) ester of monothiocarbamic acid **670** undergoes *S*-methylation to give *N*-phenyl-*O*-(2-propynyl)-*S*-methyl iminomonothiocarbonate **673** (Scheme 139).[212]

It has been found[212] that 2-methylbut-3-yn-2-ol **674** reacts with isothiocyanates only in the form of the corresponding alkoxide ion (obtained *in situ* by action of sodium hydride on 2-methylbut-3-yn-2-ol in absolute *N,N*-dimethylformamide) to give various products depending on the structure of the isothiocyanate. Isothiocyanates with the NCS group bound to an sp^2 carbon atom [phenyl (**189**), 4-bromophenyl (**194**), and styryl isothiocyanate (**130**)] give the respective 3-substituted 4-methylidene-5,5-dimethyl-1,3-oxazolidine-2-thiones (**678**) in 50–68% yield (Scheme 140).[212]



R = Ph, 4-BrC_6H_4, PhCH=CH.

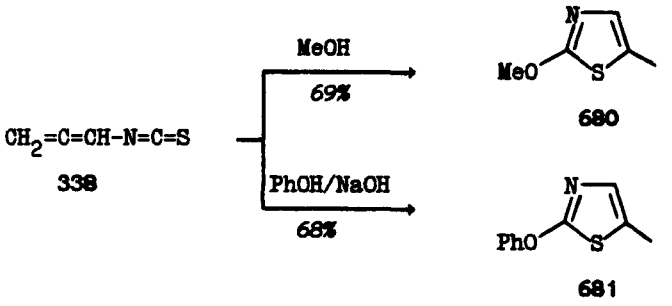
SCHEME 140

Isothiocyanates with their NCS group at an sp^3 carbon atom undergo cyclization *via* the sulfur atom to yield the 2-alkylimino-4-methylidene-5,5-dimethyl-1,3-oxathiolanes **679**.[212]

Allenyl isothiocyanate **338** with methanol and phenol gave a methoxy- (**680**) and phenoxy- (**681**) thiazole, respectively (Scheme 141).[133,135]

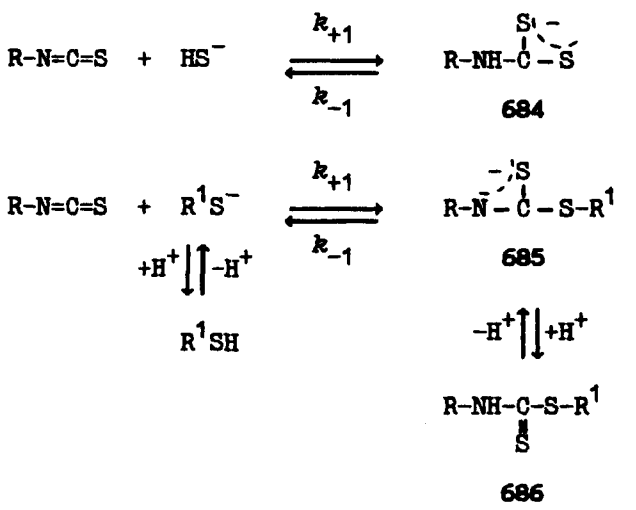
3.3. *Reactions with Thiols*

The kinetics of the reactions of phenyl isothiocyanate **189** and its 4-substituted derivatives **189**, **192**, **194**, **199**, **682**, and **683** with sodium sulfide, ethanethiol, mercaptoacetic acid, ethyl mercaptoacetate, 2-mercaptoethanol, 2-mercaptopropanoic acid,



SCHEME 141

methyl 2-mercaptopropanonate, dithiothreitol and benzenethiol have been studied (Scheme 142).[10]



R = Ph (189), 4-$MeOC_6H_4$ (199), 4-MeC_6H_4 (192), 4-BrC_6H_4 (194), 4-$MeCOC_6H_4$ (682), 4-$NO_2C_6H_4$ (683).

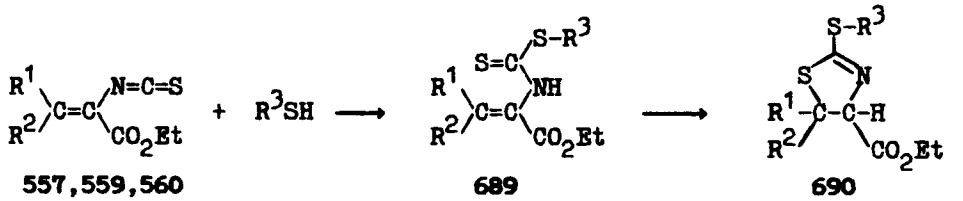
SCHEME 142

All these thiols react in their dissociated forms. Under the conditions described in paper[10] the isothiocyanates quantitatively react with HS^- or R^1S^- ions with formation of the dithio-

carbamates **685** and the *S*-esters of *N*-substituted dithiocarbamic acids **687**, respectively. Mercaptoacetic acid and its ethyl ester produce the 3-substituted thiocyanates **688**. The reactivity of phenyl isothiocyanate with HS^- ions and aliphatic thiols obeys the Hammett equation with positive slopes Q which vary in a narrow range. The reactivity of the thiols increases with their basicity.[10]

A comparison of the nucleophilities of OH^- ions, aliphatic alcohols, aliphatic amines, amino acids, HS^- ions, aliphatic thiols and benzenethiol towards phenyl isothiocyanate **189** indicates the enormous nucleophility of thiols as compared to other nucleophilic agents.[10]

Primary alkanethiols add, aided by base (triethylamine) to the α-isothiocyanatoacrylates **557**, **559**, and **560** in dry benzene or ethanol[119] under N_2 to yield the dithiocarbamates **689** (Scheme 143).[23] These cyclize on heating or in the presence of a catalyst (4-toluenesulfonic acid monohydrate) across the conjugated C=C bond to give the 2-alkylthio-2-thiazoline-4-carboxylic acid esters **690** in 49–87% yield.[23]



557,559,560 **689** **690**

$R^1 = R^2 = Me$ (**559**), $R^3 = PhCH_2$, $CH_2CH{=}CH_2$; $R^1 = Et$, $R^2 = Me$ (**560**), $R^3 = PhCH_2$; $R^1 = Ph$, $R^2 = H$ (**557**), $R^3 = PhCH_2$, *t*-Pr.

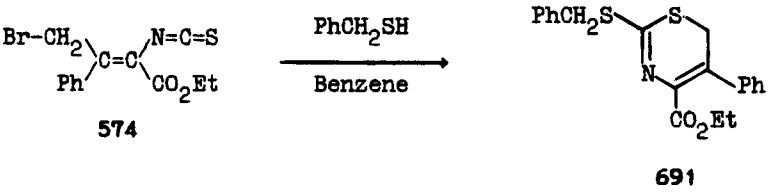
SCHEME 143

The reaction of isothiocyanate 557 with propane-2-thiol is carried out in the presence of 5 mol % 1,5-diazabicyclo[4.3.0]non-5-ene to yield 36% of *trans*-2-isopropylthio-5-phenyl-2-thiazoline-4-carboxylic acid ethyl ester **690** (R^1 = Ph, R^2 = H, R^3 = *i*-Pr).[23]

The reaction of 4-bromo-2-isothiocyanato-3-phenylbut-2-enoic acid ethyl ester **574** (*E*/*Z* = 65:35) with phenylmethanethiol/triethylamine in refluxing benzene for 2 h affords 2-benzylthio-5-phenyl-6*H*-1,3-thiazine-4-carboxylic acid ethyl ester **691** in 89% yield (Scheme 144).[188]

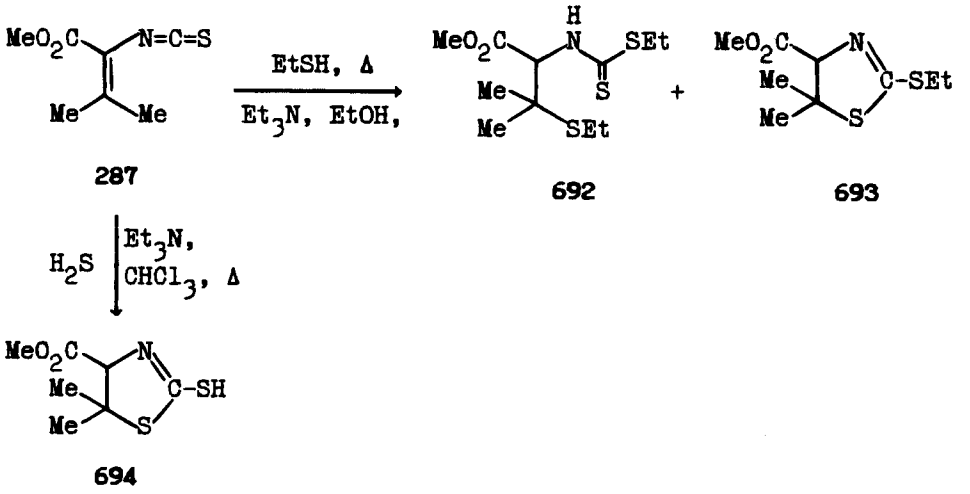
Treatment of methyl 2-isothiocyanato-1-methylcrotonate **287** with H_2S in the presence of triethylamine affords 2-mercapto-2-thiazoline-5,5-dimethyl-4-carboxylic acid methyl ester **694** in 90% yield (Scheme 145).[119]

That the formation of the 2-mercapto-2-thiazoline **694** involves H_2S addition to the isothiocyanate group, followed by intramolecular addition, is supported by the observation that treatment of methyl 2-isothiocyanato-1-methylcrotonate **287** with ethanethiol in the presence of triethylamine affords 9% dithiocarbamate **692** and 84% 2-ethylthio-2-thiazoline-5,5-dimethyl-4-carboxylic acid methyl ester **693** and by the observation that the



574 691

SCHEME 144



287 692 693 694

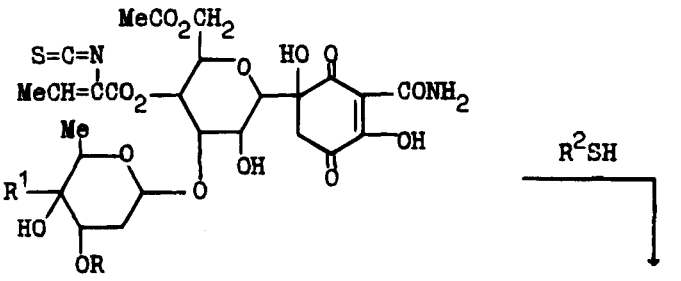
SCHEME 145

formation of thiazoline **693** from dithiocarbamate **692** fails to occur under the same reaction conditions.[119]

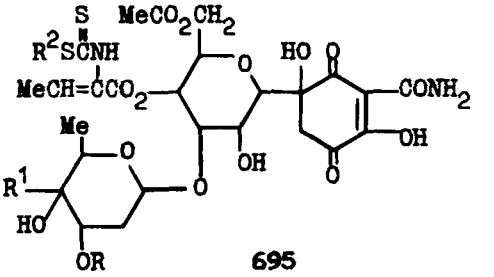
Paulomycin A **583**, A2 **631**, B **584**, D **633**, E **634** and *O*-demethylpaulomycin A **636** and B **637** can react with a variety of mercapto compounds, for example *N*-acetyl-L-cysteine and *N*-acetyl-L-cysteine esters (*e.g.*, methyl, ethyl, butyl, and octyl), mercaptoacetic acid, mercaptopropanoic acid, thiomalic acid, cysteine, homocysteine, glutathione, thioglucose, thioglycerol, 1-deoxy-1-thiopentitol, and 1-deoxy-1-thiohexitol to yield the antibacterially active compounds **695** as shown on Scheme 146.[199,200,213–215]

The reaction of paulomycin A, A_2, B, D, E and *O*-demethylpaulomycin A and B with *N*-acetyl-L-cysteine methyl, ethyl, butyl and octyl ester was carried out in tetrahydrofuran containing a catalytic amount of triethylamine at room temperature for 30 min.[199,200]

The antibiotics 273a_1*a* **695** (R = Me, R' = $MeCH_2CH(Me)CO_2$ CHMe, R^2 = $CH_2CHNH(MeCO)COOH$) and 273a_1*b* **695** (R = Me, R' = $(Me)_2CHCO_2CHMe$, R^2 = $CH_2CHNH(MeCO)COOH$) can be obtained by reaction of paulomycin A **583** and B **584**, respectively, with *N*-acetyl-L-cysteine (in phosphate buffer) at room temperature for



583,584,631,633,634,636,637



695

R = Me, R^1 = $MeCH_2CH(Me)CO_2CHMe$ (583), $(Me)_2CHCO_2CHMe$ (584), $(Me)_2CHCH_2CO_2CHMe$ (631), $MeCO_2CHMe$ (633), MeC(O) (634); R = H, R^1 = $MeCH_2CH(Me)CO_2CHMe$ (636), $(Me)_2CHCO_2CHMe$ (637).

SCHEME 146

1 h.[199,200,215] Under the same reaction conditions paulomycin A, A_2, B, D and E react with the other above-mentioned mercapto compounds in 1–18 h.[199,200]

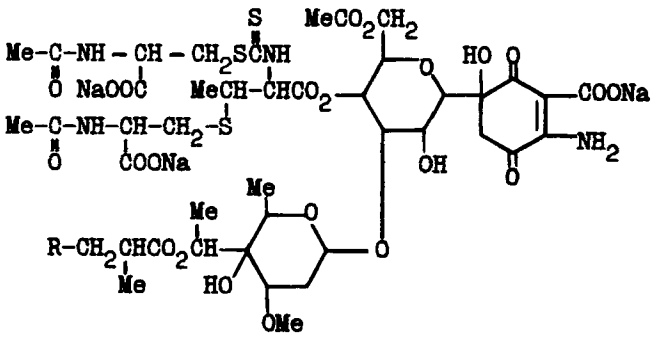
Salts of **695** can also be prepared by reaction with appropriate organic or inorganic bases.[199,200]

Paldimycin is the bis-*N*-acetyl-L-cysteine derivative of paulomycin and is isolated as the trisodium salt **696** (Scheme 147).[214]

The compounds thus prepared are used in the same manner as the paulomycins. They are active against Gram-positive organisms including *Staphylococcus aureus* resistant to methicillin, lincosaminide, and macrolide antibiotics.[199,200,213]

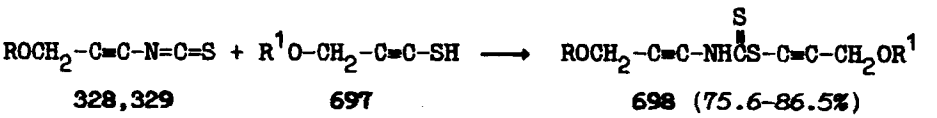
Acetylenic dithiocarbamates of a new type **698** have been claimed by reaction of the 1-isothiocyanatopropargyl ethers **328** and **329** with the 1-mercaptopropargyl ethers **697** in *N,N*-dimethylformamide at 80–90 °C for 5–6 h (Scheme 148).[130]

This work is obviously presented in bad faith since alk-4-yne-4-thiols are known to isomerize spontaneously to the corresponding thioketenes which in turn dimerize to 1,3-dithietanes (desaurines).[130a]



696

SCHEME 147



328,329 **697** **698** (75.6–86.5%)

R = 2,4-$Cl_2C_6H_3$ (**328**), 2,4,6-$Cl_3C_6H_2$ (**329**); R^1 = 2-BrC_6H_4, 2,4,6-$Br_3C_6H_2$.

SCHEME 148

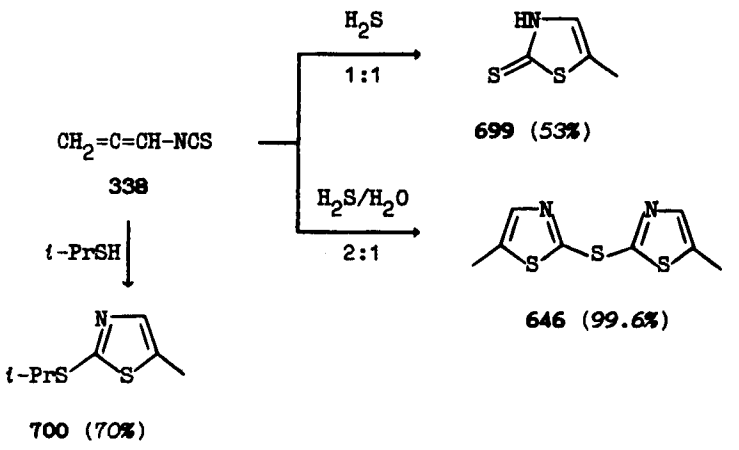
The reaction of allenyl isothiocyanate **338** with hydrogen sulfide leads to the thiazolidinethione **699** or the bis(thiazolyl) sulfide **646** (depending on the ratio of reagents) (Scheme 149).[133,135] With propane-2-thiol the corresponding thiazole **700** was obtained.

3.4. *Reactions with Nitrogen-Containing Compounds*

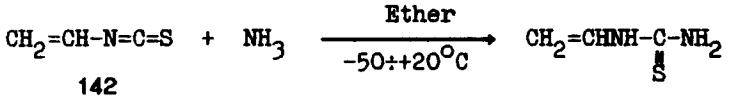
Probably the best documented reactions of isothiocyanates, including α,β-unsaturated isothiocyanates,[59,81] are those with compounds containing a nitrogen-hydrogen bond.[1,2,11–21]

3.4.1. *Reactions with amines and hydrazines* Vinyl isothiocyanate **142** reacts with anhydrous gaseous ammonia in anhydrous ether to give *N*-vinyl thiourea **701** (Scheme 150).[60,64,81]

The highly active allenyl isothiocyanate **338** reacts with ammonia and amines and gives the corresponding thiazoles **647** and **702** in good yields (Scheme 151).[133,135]



SCHEME 149



SCHEME 150

Thus the reaction of **338** with diphenylamine at room temperature leads to the corresponding thiazole **702**. Phenyl isothiocyanate reacts with weak nucleophiles only at 280 °C.[216]

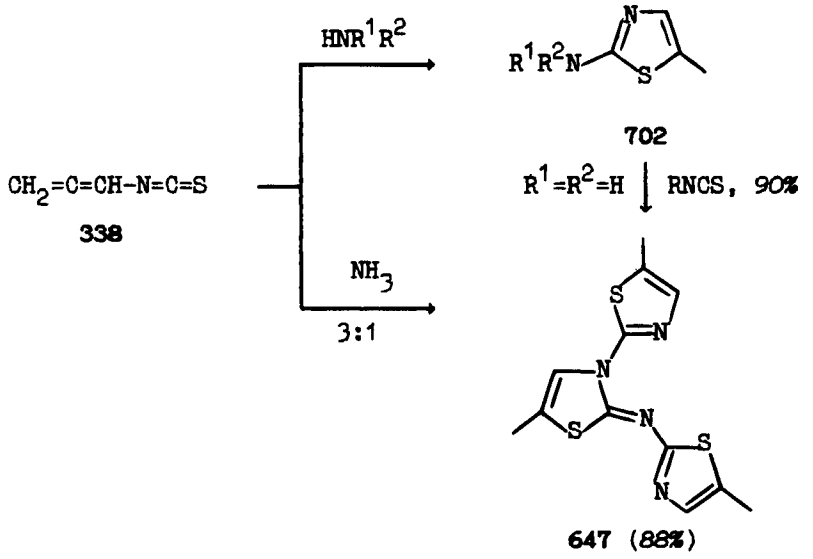
The reaction of 1,3-dimethylbut-1-enyl isothiocyanate **221** with anhydrous ammonia in dry 1,2-dimethoxyethane at elevated temperature affords *N*-(1,3-dimethylbut-1-enyl)thiourea **703** (Scheme 152).[95]

The 3-alkylthio-1-isothiocyanato-2-methylpropenes **605–607** with hydrazine and 4-bromophenylamine give the corresponding thiosemicarbazides **704** and 4-bromophenylthioureas **705**, respectively (Scheme 153).[123]

1-Isothiocyanato-2-methyl-1-phenylprop-1-ene **145** and isothiocyanatotriphenylethene **459** after stirring with methylhydrazine in *absol.* tetrahydrofuran for 0.5–2 h gave the corresponding thiosemicarbazides **706** in 87% and 95% yield, respectively (Scheme 154).[166]

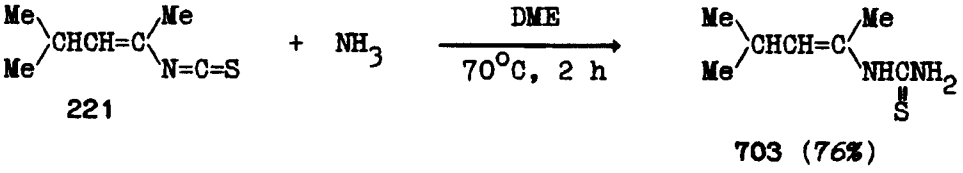
1-Cyclohexenyl isothiocyanate **370** reacts with anhydrous ammonia (in dry THF) and 1,1-dimethylhydrazine (in diethyl ether) at 22 °C to give cyclohex-1-enylthiourea **707** and 4-(cyclohex-1-enyl)-1,1-dimethylthiosemicarbazide **708** in 83% and 70% yield, respectively (Scheme 155).[172]

2-Isothiocyanatovinyl acetate **157** is a valuable synthetic intermediate, combining the chemical properties of an isothiocyanate with the latent functionality of a formyl group.



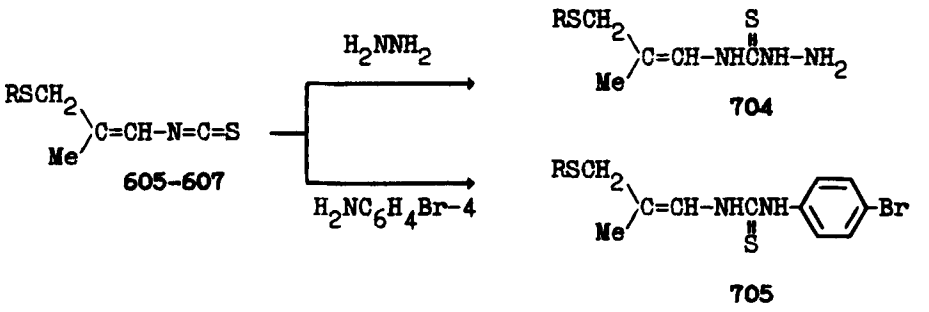
$R^1 = R^2 = H$ (59%); $R^1 = H$, $R^2 = n$-Pr (45%), $R^1 = H$, $R^2 = Ph$ (82%); $R^1 = R^2 = Ph$ (40%); $R = CH_2=C=CH_2$.

SCHEME 151



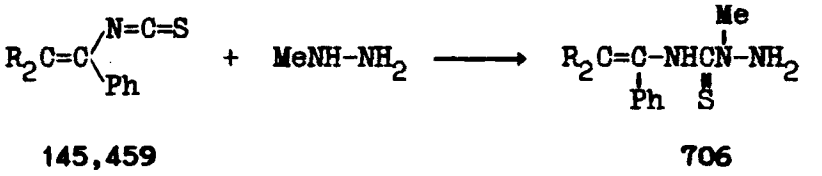
SCHEME 152

Reactions of **157** with retention of the latent formyl functionality are easily carried out with a variety of nitrogen nucleophiles. Thus, 4-chloroaniline, *N*-methylaniline, and cyclohexylamine give the corresponding (acetoxyvinyl)thioureas **709–711** (Scheme 156).[85] Hydrazine gave, at ambient temperature, the expected (acetoxyvinyl)thiosemicarbazide **712** or, when the reaction was conducted under reflux conditions, the triazine **713**, in the formation of which the latent functionality of the formyl group is apparent.[85] *N,N*-Dimethylhydrazine gave 4-(2-acetoxyvinyl)-1,1-dimethylthiosemicarbazide **714**.[85]



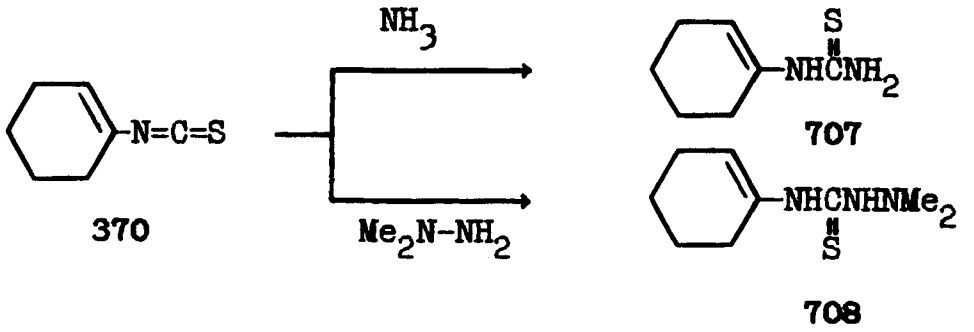
R = *n*-Bu (605), $PhCH_2$ (606), Ph (607).

SCHEME 153



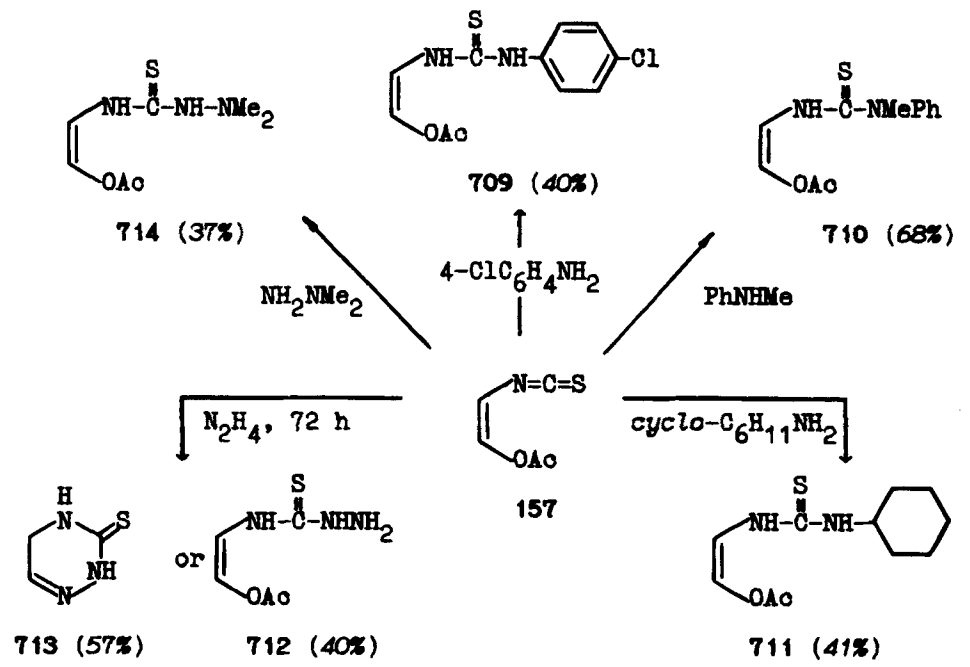
R = Me (145), Ph (459).

SCHEME 154

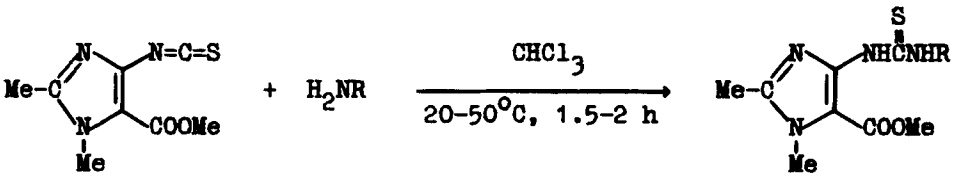


SCHEME 155

Treatment with alkanolamines and alkyleneamines transforms 4-isothiocyanatoimidazole-5-carboxylic acid methyl ester **85** to the expected thiourea derivatives, i.e. the 1,2-dimethyl-4-(*N'*-organyl)thioureidoimidazole-5-carboxylic acid methyl esters **715** (Scheme 157).[71]



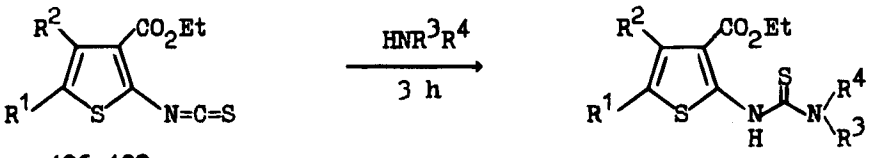
SCHEME 156



R = $(CH_2)_2OH$ (87%), $(CH_2)_3OH$ (83%), $CH_2CH{=}CH_2$ (23%), $CH_2C(Me){=}CH_2$ (38%).

SCHEME 157

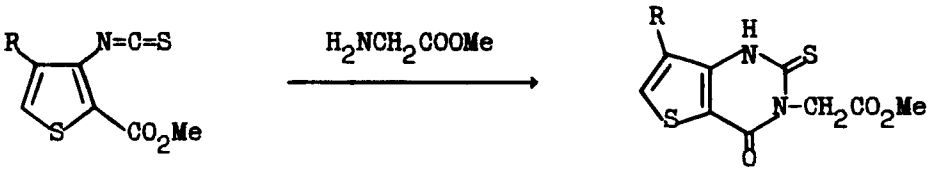
2-Thioureidothiophene-3-carboxylic acid ethyl esters **716** have been prepared[217] in 50–95% yield (mainly 85–87%) by reaction of the ethyl 2-isothiocyanato-3-thiophenecarboxylates **106** and **109** with the appropriate amines in dichloromethane at room temperature (Scheme 158).



106, 109 716

$R^1 = R^2 = Me$ (106), R^3-$R^4 = (CH_2)_2O(CH_2)_2$; R^1-$R^2 = (CH_2)_4$ (109), $R^3 = R^4 = H$; $R^3 = H$, $R^4 = i$-Pr; $R^3 = H$, $R^4 = cyclo$-C_6H_{11}; $R^3 = H$, $R^4 = 4$-$HOOCC_6H_4$; $R^3 = H$, R^4 = pyrid-2-yl; $R^3 = R^4 = Me$; $R^3 = R^4 = Et$; R^3-$R^4 = (CH_2)_2O(CH_2)_2$; R^3 - $R^4 = (CH_2)_2N(Me)(CH_2)_2$; R^3 - $R^4 = (CH_2)_2N(C_2H_4OH)(CH_2)_2$.

SCHEME 158



101, 102 717

R = H (101), Me (102).

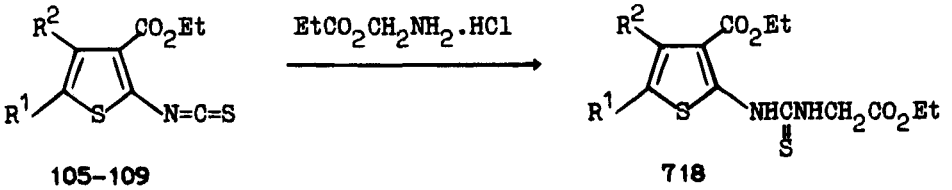
SCHEME 159

Reaction of the methyl 3-isothiocyanato-2-thiophenecarboxylates **101** and **102** with glycine methyl ester in tetrahydrofuran in the presence of triethylamine gave the methyl 1,4-dihydro-4-oxo-2-thioxothieno[3,2-*d*]pyrimidone-3(2*H*)-carboxylates **717** after 20 h at room temperature (Scheme 159).[75]

The ethyl 2-isothiocyanato-3-thiophenecarboxylates **105–109** with glycine ethyl ester hydrochloride and under the same reaction conditions, in *absol.* tetrahydrofuran in the presence of triethylamine at room temperature for 20 h, gave the corresponding thioureas **718** (up to 90% yield) (Scheme 160).[76]

The *N*-(thien-2-yl)-*N'*-(alkoxycarbonylaryl- or alkyl) thioureides **721** have been prepared as pharmaceutical intermediates by reaction of the ethyl 2-isothiocyanato-3-thiophene carboxylates **106**, **109**, **719**, and **720** with amino carboxylic acid esters in benzene at room temperature for 20 h in 61–81% yield (Scheme 161).[218]

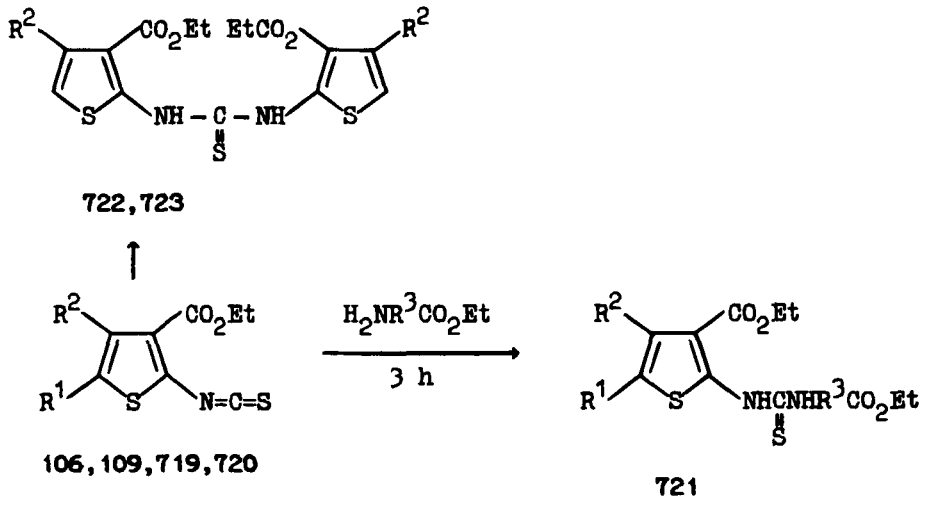
N,N'-Bis-[4-(4-chlorophenyl)-3-ethoxycarbonylthien-2-yl]-thiocarbamide **722** was prepared in 34% yield by treatment of 4-(4-chlorophenyl)-3-ethoxycarbonyl-2-isothio-



105–109 718

$R^1 = R^2 = H$ (105), Me (106); R^1 = Me, R^2 = H (107); R^1 = Ph, R^2 = H (108); R^1–R^2 = $(CH_2)_4$ (109).

SCHEME 160

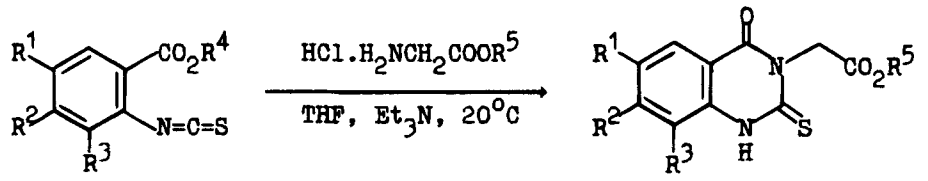


R^1 = H, R^2 = Ph (723), 4-ClC_6H_4 (719,722); R^1 = Et, R^2 = H (720); $R^1 = R^2$ = Me (106); R^1–R^2 = $(CH_2)_4$ (109); R^3 = 1,4-C_6H_4, 1,4-$CH_2C_6H_4$, $(CH_2)_2$, CHMe.

SCHEME 161

cyanatothiophene **719** with 2-amino-4-(4-chlorophenyl)-3-ethoxycarbonylthiophene in refluxing benzene for 6 h (Scheme 161).[218] Similarly was prepared *N*-(3-ethoxycarbonyl-4-phenylthien-2-yl)-*N'*-(3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thiocarbamide **723** (yield 40%).[218]

The 1-isothiocyanato-2-benzenecarboxylates **111**, **112**, **115–117**, **120**, and **121** cyclize directly with methyl (or ethyl) glycinate to give the 1,2,3,4-tetrahydro-2-thioxochinazolin-4-ones **724** (Scheme 162).[76]



111, 112, 115–117, 120, 121

724

R^4 = Me, R^5 = Me, R^1 = R^2 = R^3 = H (111); R^3 = Me, R^1 = R^2 = H (120); R^1 = R^3 = H, R^2 = Cl (117); R^2 = R^3 = H, R^1 = Cl (112); OMe (115); CO_2Me (116); R^4 = R^5 = Et, R^3 = Me, R^2 = Cl, R^1 = H (121).

SCHEME 162

The vinylogous acyl isothiocyanates **382** and **383** react with primary amines to give the 2-thiohydantoins **727** (Scheme 163).[137,219] The structures of **727** were confirmed by X-ray structure analysis.[137]

The reaction of D-8β-aminomethyl-6-methyl-ergoline I with dimethyl isothiocyanatofumarate **382** in ethanol at room temperature for 3 h yielded D-8β-[(4-methoxycarbonylmethylidene-5-oxo-2-thioxoimidazolidin-1-yl)-methyl]-6-methyl-ergoline I **728** (71%) (Scheme 163).[219]

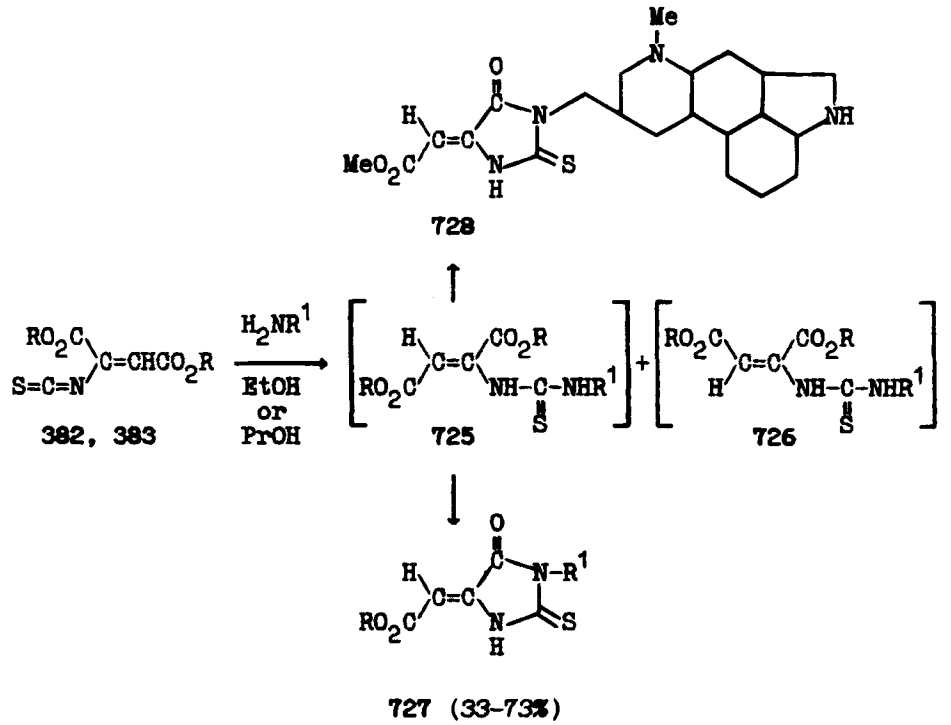
The propargylamines **729** and dimethyl isothiocyanatofumarate **382** in ethanol gave the imidazo[2,1-*b*]thiazoline derivatives **731** *via* intermediates of the 2-thiohydantoin type **730** (Scheme 164).[137]

The reaction of 2-isothiocyanato-3-methylcrotonic acid methyl ester **287** in dioxane with a solution of benzylamine and methylhydrazine in diethyl ether over 12 h at 22 °C leads to 3-benzyl-5-isopropylidene-2-thioxoimidazolidin-4-one **732** and 3-methyl-2-(2-methylthiocarbazoylamino)crotonic acid methyl ester **733**, respectively, in good yields (Scheme 165).[172] With aniline the corresponding reaction in ethanol required heating.[119]

The α-isothiocyanatoacrylates **287**, **557**, **561**, and **562** react with primary amines in an analogous manner (benzene, 60–80 °C, 0.5–3 h) (Scheme 166).[23] With primary amines ring closure of the non-isolable corresponding thioureas **734** as intermediates occurs across the carbonyl group and yields the 3-alkyl- and 3-aryl-5-alkylidene-2-thiohydantoins **735** (75–98%).[23]

Dialkylamines add to the N=C=S group of the α-isothiocyanatoacrylates **287** and **557** in dry benzene at room temperature to yield the thioureas **736** quantitatively (Scheme 166).[23] These cyclize on heating (catalyzed by acid) across the conjugated C=C bond to give the 2-(*N,N*-dialkylamino)-2-thiazoline-4-carboxylates **737**.[23]

(*E/Z*)-2-Isothiocyanato-3-phenylcrotonic acid ethyl ester **561** with diisopropylamine in ethanol gives 2-(*N,N*-diisopropylamino)-4-(1-phenylethylidene)-2-thiazolin-5-one **738** in 40% yield (Scheme 167).[23]



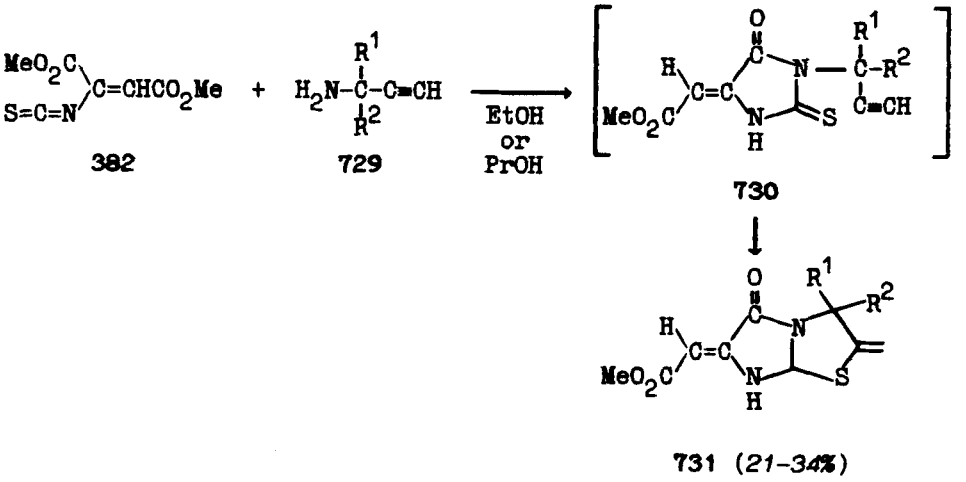
R = Me (**382**), R^1 = Me, *cyclo*-C_6H_{11}, CH(Me)C≡CH, Ph, 4-FC_6H_4, 4-BrC_6H_4; R = Et (**383**), R^1 = *i*-Pr, Ph, 3-$CF_3C_6H_4$.

SCHEME 163

As similar reaction of the 3-indolyl isothiocyanates **201** and **203** with ammonia and aniline in benzene upon heating over 30 min gives the corresponding indolylthioureas **739** in good yields (75–91%) (Scheme 168).[97]

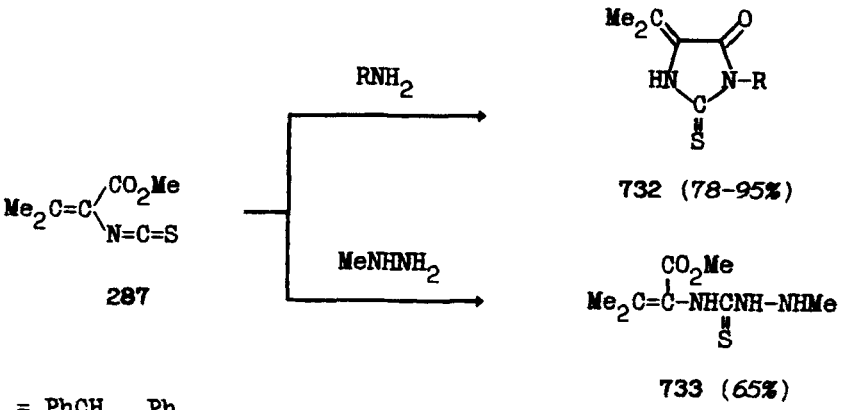
The reactions of 3,4-dioxo-2-phenylcyclobut-1-enyl isothiocyanate **255** with aromatic and heteroaromatic 1,2-diamines have been described in Ref.[106] The corresponding *N*-(3,4-dioxo-2-phenylcyclobut-1-enyl)thicarbamides **740** were obtained in *absol.* acetonitrile for 15–30 min in 54–69% yield (Scheme 169).

3,4-Dioxo-2-phenylcyclobut-1-enyl isothiocyanate **255** with 1,2-benzenediamine **741** (in dry acetonitrile under argon for 10–15 min) and 2,3-pyridinediamine **742** (in dry 1,2-dimethoxyethane at 0 °C for 6–8 h) gave the corresponding imidazoles, 3-(1,3-dihydrobenzimidazol-2-ylidenamino)-4-phenyl-3-cyclobutene-1,2-dione **743** and 3-phenyl-4-(2,3-dihydro-1*H*-imidazo[4,5-*b*]pyridin-2-ylidenamino)-3-cyclobutene-1,2-dione **744** in 32% and 25% yield, respectively (Scheme 169).[106]



$R^1 = R^2$ = Me, Et; R^1-R^2 = $(CH_2)_5$.

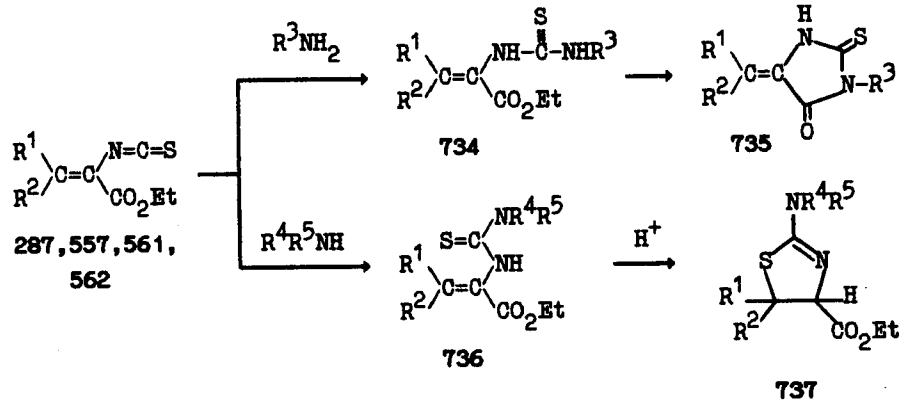
SCHEME 164



R = $PhCH_2$, Ph.

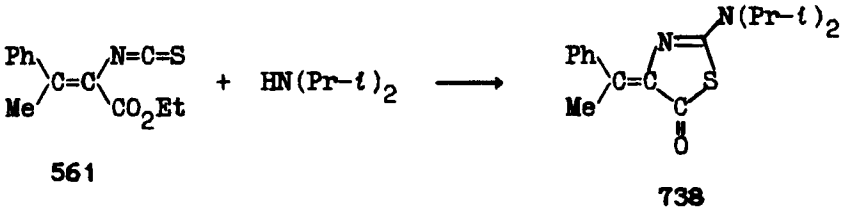
SCHEME 165

4-Methoxybenzyl 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4α-carboxylate **441** reacts with aniline in THF at room temperature for 1.5 h to form 4-methoxybenzyl 7β-phenylacetamido-3-methyl-2-phenylaminothiocarbonylamino-2-cephem-4α-carboxylate **745** in 76.2% yield (Scheme 170).[154]

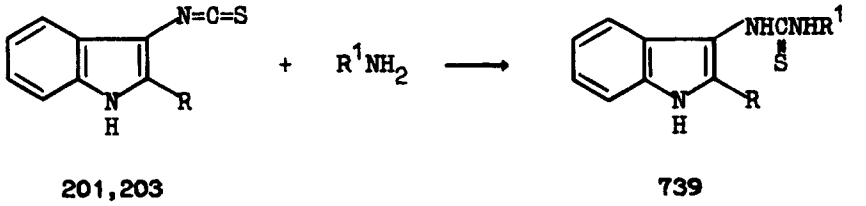


$R^1 = R^2 = Me$ (287), $R^3 = PhCH_2$, $R^4 = R^5 = PhCH_2$; $R^3 = Ph$, $R^4 - R^5 = (CH_2)_5$; $R^1 = Ph$, $R^2 = H$ (557), $R^3 = t\text{-}Bu$, $R^4 = R^5 = PhCH_2$; $R^4 = Me$, $R^5 = Ph$; $R^1 = Ph$, $R^2 = Me$ (561), $R^3 = CH_2CH{=}CH_2$; $R^1 = R^2 = Ph$ (562), $R^3 = t\text{-}Bu$.

SCHEME 166

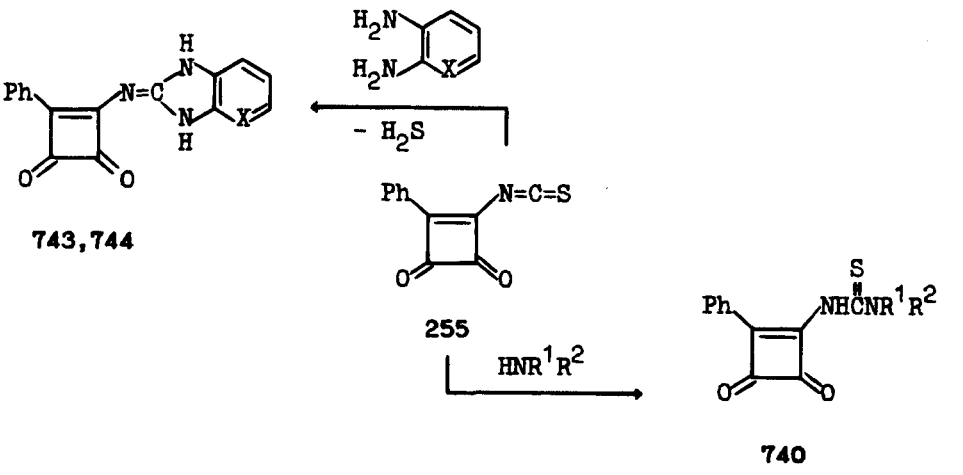


SCHEME 167



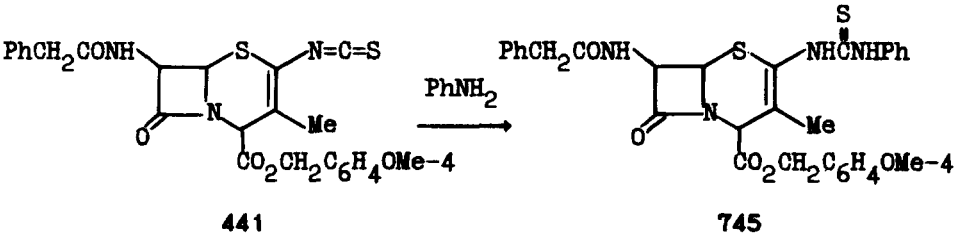
$R = R^1 = H$; $R^1 = Ph$, $R = H$, Me.

SCHEME 168



R^1 = H, R^2 = Ph; R^1-R^2 = $(CH_2)_4$, $(CH_2)_2O(CH_2)_2$; X = CH (**741,743**), N (**742,744**).

SCHEME 169



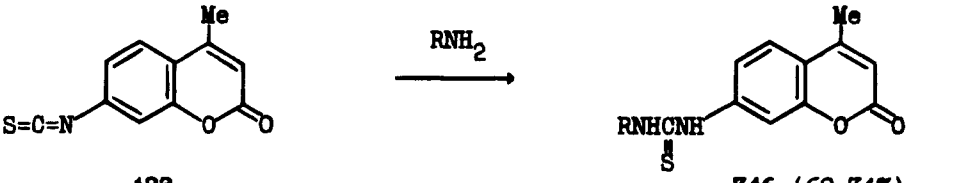
SCHEME 170

4-Methylcoumarin-7-yl isothiocyanate **123** and 7-(*N*,*N*-dimethylamino)-4-methylcoumarin-3-yl isothiocyanate **125** react with amines at 40–50 °C to yield the thioureas **746** and **747**, respectively (Scheme 171).[77]

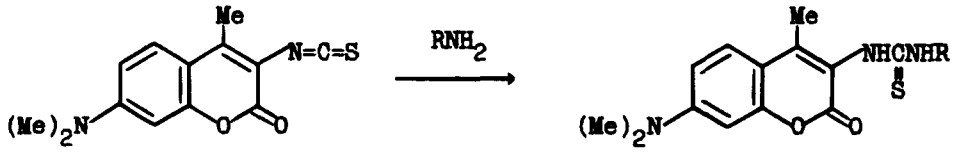
Condensation of various 7-amino-3-heterocyclyl-2*H*-1,4-benzoxazines **748** with aryl **192, 193, 683, 749, 750** and pyridyl **751** isothiocyanates in refluxing benzene furnishes the desired *N'*-substituted *N*-(3-heterocyclyl-2*H*-1,4-benzoxazin-7-yl)thioureas **752** in good yields (Scheme 172).[220]

Cephalexin **753** (ampicillin trihydrate) was treated with phenyl isothiocyanate in *N*,*N*-dimethylformamide in the presence of triethylamine to give 6β-[2-phenyl-2-(phenylthioureido)]acetamidopenicillinic acid triethylammonium salt **754** (Scheme 173).[221]

When cephalexin **753** was treated with 4-methylphenyl isothiocyanate **192** the corresponding thiourea **755** was obtained (Scheme 173).[222]



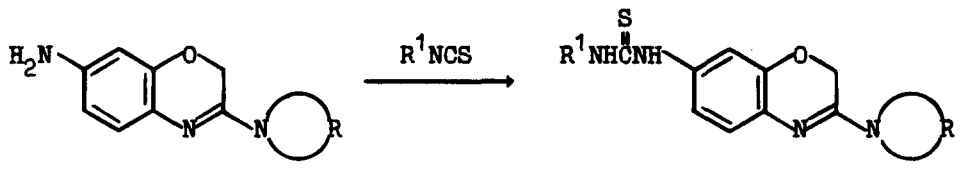
123 746 (63–71%)



125 747 (60–68%)

R = Me, $PhCH_2$.

SCHEME 171



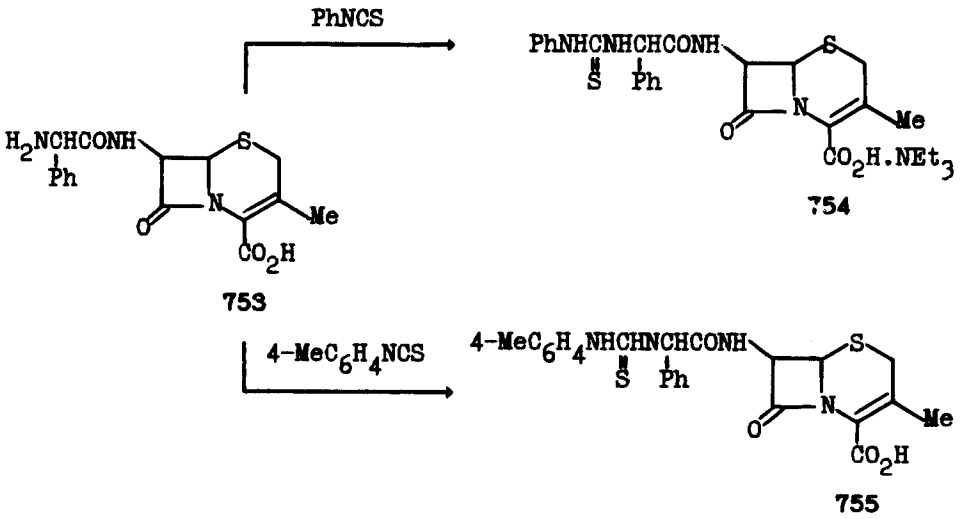
748 752 (44–73%)

R = $MeN[(CH_2)_2]_2$, $PhN[(CH_2)_2]_2$, $(CH_2)_4$, $(CH_2)_5$; R^1 = 4-ClC_6H_4 (193), 2-NO_2-4-MeC_6H_3 (749), 4-$NO_2C_6H_4$ (683), 4-$PhSC_6H_4$ (750), 4-MeC_6H_4 (192), 2-pyridyl (751).

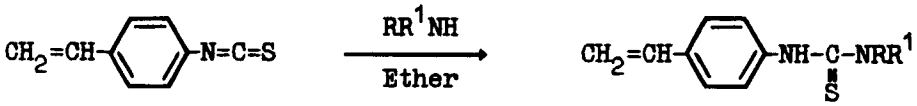
SCHEME 172

From 4-vinylphenyl isothiocyanate **30** and gaseous ammonia and anhydrous liquid dimethylamine in ether have been prepared *N*-(4-vinylphenyl)thiourea **756** and *N*-(4-vinylphenyl)-*N'*,*N'*-dimethylthiourea **757**, respectively (Scheme 174).[64]

A number of benzazolylphenylthiocarbamoylpiperazines **758** have been prepared by reaction of the benzazolylphenyl isothiocyanates **10** and **13–15** with *N*-methyl- and *N*,*N'*-diethylcarbamoylpiperazine in dioxane (under reflux for 3 h) (Scheme 175).[63]



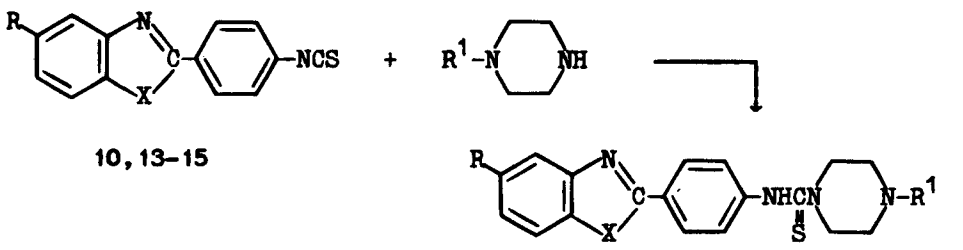
SCHEME 173



30 756,757

R = R^1 = H (756); R = R^1 = Me (757).

SCHEME 174

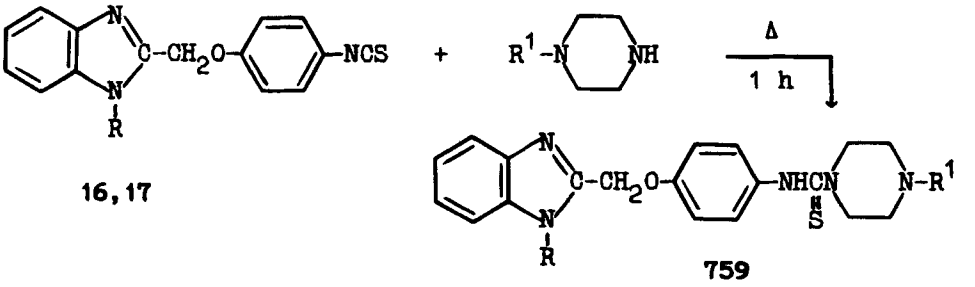


10, 13–15 758 (58–89%)

R = H, X = S (10), NH (13), NMe (15); R = Cl, X = NH (14); R^1 = Me, $CONEt_2$.

SCHEME 175

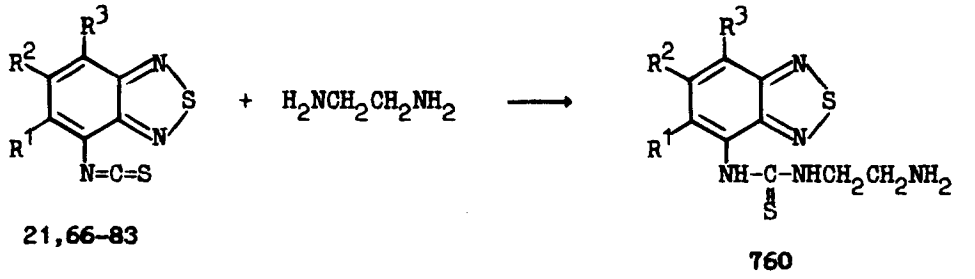
Analogously, 4-(2-benzimidazolyl)methoxyphenyl isothiocyanates **16** and **17** react with *N*-methyl- and *N,N'*-diethylcarbamoylpiperazine in pyridine to form the benzimidazolylmethyloxyphenyl thiocarbamoylpiperazines **759** in 84–98% yield (Scheme 176).[63]



R = H (16), Me (17); R^1 = Me, $CONEt_2$.

SCHEME 176

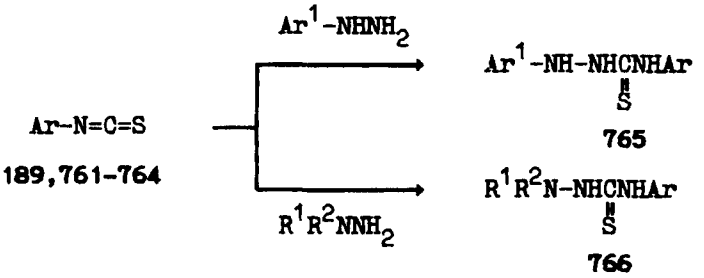
The 4-isothiocyanato-2,1,3-benzothiadiazoles **21**, and **66–83** react with ethylenediamine in chloroform or diethyl ether at room temperature to give the corresponding thioureides **760** (Scheme 177).[70]



R^1 = R^2 = R^3 = H (21); R^1 = R^2 = H, R^3 = Me (66), OMe (67), NO_2 (68), OH (69); R^1 = H, R^2 = R^3 = Cl (70); R^2 = R^3 = H, R^1 = Me (71); R^1 = Me, R^2 = H, R^3 = Cl (72); R^1 = R^2 = Me, R^3 = H (73); R^1 = R^3 = Me, R^2 = H (74); R^2 = R^3 = H, R^1 = Et (75), OMe (76), Cl (77); R^2 = H, R^1 = Cl, R^3 = Me (78); R^1 = Cl, R^3 = Br (79); R^1 = R^2 = Cl, R^3 = H (80); R^1 = R^3 = Cl, R^2 = H (81); R^1 = Br, R^2 = R^3 = H (82), R^1 = Br, R^2 = H, R^3 = Cl (83).

SCHEME 177

The 4-monosubstituted 1-arylthiosemicarbazides **765** have been obtained by action of the aryl isothiocyanates **189**, and **761–764** on arylhydrazines (Scheme 178).[223] It was expected that the attack of the isothiocyanate would occur on the less substituted nitrogen in the case of the arylhydrazines since the other one is less basic. A few selected 4-arylthiosemicarbazides **766** have been obtained from hydrazines and aryl isothiocyanates according to the same Scheme.[223]



Ar = Ph (**189**), 2-PhC_6H_4 (**761**), 2-FC_6H_4 (**762**), 2,5-$Me_2C_6H_3$ (**763**), 3,5-$(CF_3)_2C_6H_3$ (**764**); Ar^1 = 3,5-$(CF_3)_2C_6H_3$; R^1 = R^2 = H, Me.

SCHEME 178

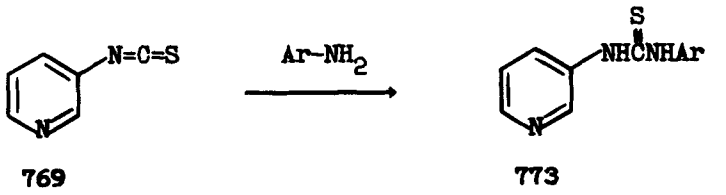
1-(3-Phenoxypropyl)-3-phenyl-2-thiourea **767** and 1-(3-phenoxy-2-hydroxypropyl)-3-phenyl-2-thiourea **768** have been prepared by reaction of phenyl isothiocyanate **189** with, respectively, 3-phenoxypropylamine and 1-phenyl-3-amino-2-propanol in methanol at room temperature for 4 h.[224]

A large number of new *N,N'*-disubstituted thioureas and their heterocyclic analogues **773** and **774** have been obtained,[225] in lower yields than the corresponding ureas, by treatment of the appropriate amine in warm ethanol with an aryl or pyridyl isothiocyanate **769–772** (Scheme 179); in most cases, the product solidified and could be recrystallized from ethanol, benzene, or toluene. The reaction was much slower and required short heating at 60 °C when the amine and/or the isothiocyanate was 2-substituted.[225]

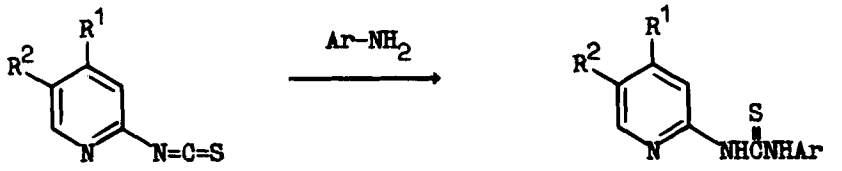
1-Amino-4,6-diphenyl-2-pyridone **775** reacts with phenyl isothiocyanate at room temperature in *N,N*-dimethylformamide for 24 h giving the corresponding thiourea **777** (Scheme 180).[147]

On the other hand, 1-amino-4,6-diphenylpyridine-2-thione **776** reacts with phenyl isothiocyanate at room temperature in dry acetonitrile for 24 h affording 5,7-diphenyl-1,3,4-thiadiazolo[3,2-*a*]pyridinium-2-phenylaminide **778** in 65% yield (Scheme 180).[147] This transformation presumably involves the corresponding thiourea as a highly reactive intermediate which easily undergoes cyclodehydrosulfurization.

Treatment of a solution of 1-amino-2-(hydroxymethyl)pyridinium chloride **779** in H_2O containing potassium carbonate with a solution of phenyl isothiocyanate in dichloromethane



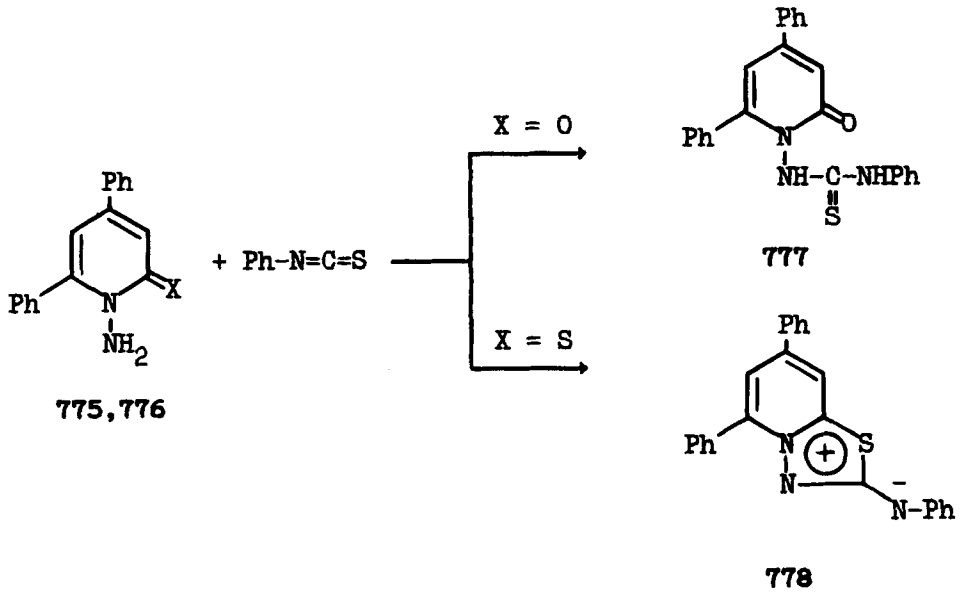
769 773



770–772 774

R^1 = Me, R^2 = H (770); R^1 = H, R^2 = Me (771), Cl (772); Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 4-EtC_6H_4, 4-$MeOC_6H_4$, 4-$EtOC_6H_4$, 4-i-$C_5H_{11}O$, 2,4-$Me_2C_6H_3$.

SCHEME 179

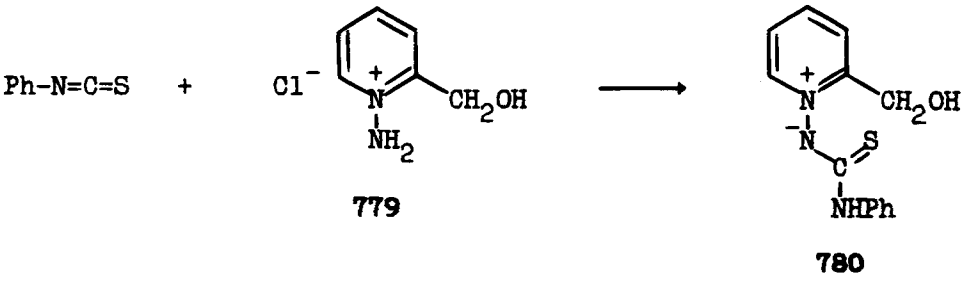


775,776 777 778

X = O (775), S (776).

SCHEME 180

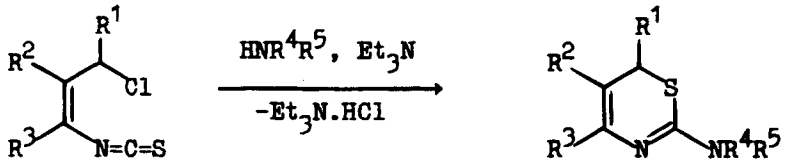
at room temperature for 5 h affords 1-anilinothiocarbonylimino-2-hydroxymethylpyridine **780** in 71.5% yield (Scheme 181).[226]



779 **780**

SCHEME 181

The reaction of the γ-isothiocyanatoallyl chlorides **226**, **306–309**, **314**, **315**, and **320** with secondary amines under catalysis by *tert*-amines in petroleum ether at 5–10 °C gives numerous 2-(*N,N*-dialkylamino)-6*H*-1,3-thiazines **781** (47–85%) (Scheme 182).[124,125,128]



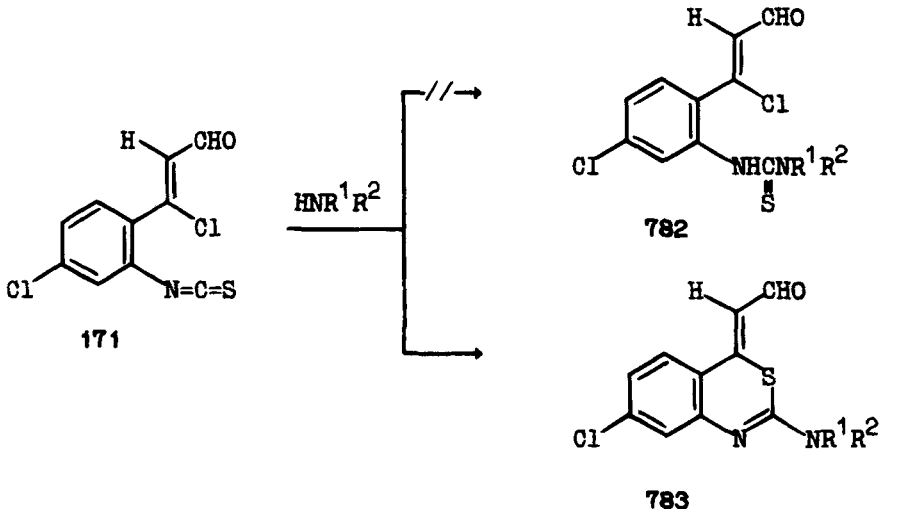
226,306–309,314, 315,320 **781**

$R^1 = R^2 = R^3 = H$ (**306**); $R^1 = R^2 = H$, $R^3 = Me$ (**307**); $R^1 = R^3 = H$, $R^2 = Me$ (**226**); $R^1 = Me$, $R^2 = R^3 = H$ (**308**); $R^1 = H$, $R^2 = R^3 = Me$ (**309**); $R^1 = H$, $R^2 - R^3 = (CH_2)_4$ (**314**), $(CH_2)_5$ (**315**), $(CH_2)_6$ (**320**); $R^4 = R^5 = Me$, Et, *n*-Pr, *n*-Bu; $R^4 = H$, Me, R^5 = *cyclo*-C_6H_{11}, Ph; $R^4 = H$, $R^5 = 4\text{-}HOC_6H_4$, $4\text{-}NO_2C_6H_4NH$; $R^4 - R^5 = (CH_2)_4$, $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$, $(CH_2)_4C{=}O$.

SCHEME 182

The isothiocyanato group of β,4-dichloro-2-isothiocyanatocinnamaldehyde **171** reacted readily with a wide variety of nucleophiles; however, it was not possible in any case to isolate the corresponding thioamide **782**; instead ring closure took place to yield the substi-

tuted benzothiazines **783** (Scheme 183).[91] Primary and secondary amines react with isothiocyanate **171** in ethyl (or methyl) acetate (from 15–30 min to 24 h) to give, in general, 2-R-7-chloro-4-formylmethylene-4*H*-3,1-benzothiazines **783**.[91]



$R^1 = R^2 = H$; $R^1 = H$, $R^2 = (CH_2)_3NMe_2$, 2-$MeCO_2C_6H_4$, 4-ClC_6H_4, 2-pyridyl; $R^1 - R^2 = (CH_2)_4$, $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$.

SCHEME 183

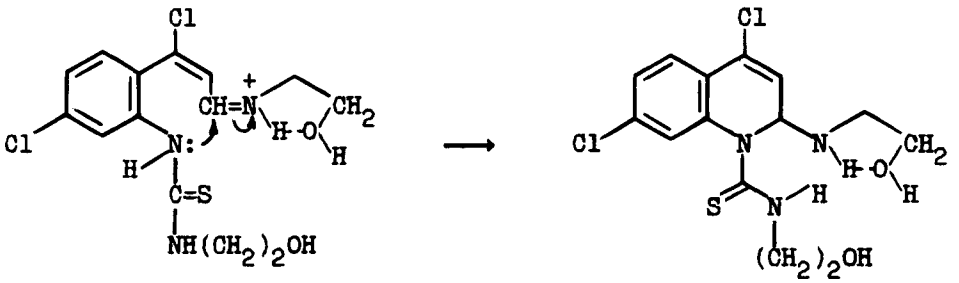
The morpholine derivative, 7-chloro-4-formylmethylene-2-morpholino-4*H*-3,1-benzothiazine [**783**, R^1–$R^2 = (CH_2)_2O(CH_2)_2$], had its stereochemistry disclosed by the nuclear Overhauser effect between the exocyclic vinyl proton and the 5-H.[91]

2-Aminopyridine yields the expected product [7-chloro-4-formylmethylene-2-(2-pyridylamino)-4*H*-3,1-benzothiazine] **783** (R^1 = H, R^2 = 2-pyridyl) together with 4,7-dichloroquinoline **169**.[91]

2-Aminoethanol reacts with isothiocyanate **171** in an anomalous fashion: in this case the only product is 4,7-dichloroquinoline **169**, isolated in 57% yield. Presumably in this reaction some stabilization of the iminium group is provided by the stereochemically favorable position of the oxygen atom of the ethanolamine, as shown in **784** and **785** (Scheme 184).[91]

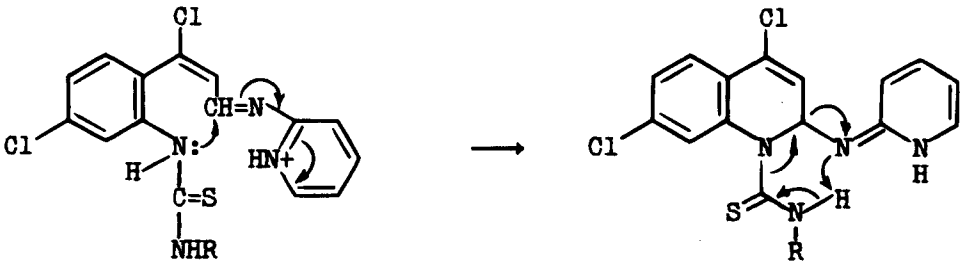
2-Aminopyridine presumably forms, in part, a species of type **786** → **787** to account for the concomitant formation of 4,7-dichloroquinoline **169** (Scheme 185).[91]

2-Isothiocyanato-*trans*-cinnamaldehyde **167**, 2-isothiocyanato-5-methoxy-*trans*-cinnamaldehyde **181** and 3-(2-isothiocyanatophenyl)but-2-enal **182** are converted to the corresponding dihydropyrazoloquinazolinethiones **788** on treatment with hydrazine hydrate (Scheme 186).[89]



784 785

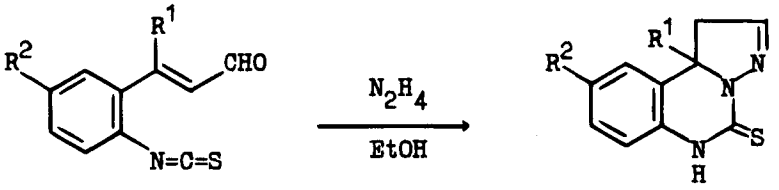
SCHEME 184



786 787

R = 2-pyridyl.

SCHEME 185

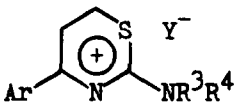


167, 181, 182 788

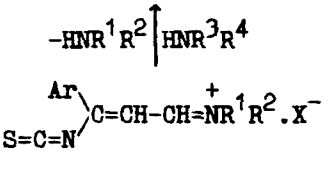
$R^1 = R^2 = H$ (167); $R^1 = H$, $R^2 = OMe$ (181); $R^1 = Me$, $R^2 = H$ (182).

SCHEME 186

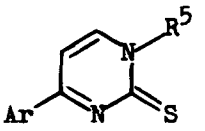
The 1,4-diaryl-2(1*H*)-pyrimidine-2-thiones **792** can be prepared in 39–97% yield by reaction of primary aromatic amines or unsubstituted or substituted hydrazines or hydrazine hydrochlorides (in the latter case in the presence of triethylamine) with the 3-isothiocyanatoprop-2-eneiminium salts **245–248**, **250–252**, **789**, and **791** in ethanol, *n*-propanol, or acetonitrile at room temperature for several min (Scheme 187).[105,227-229]



793 (*27–79%*)



245–248, 250–252, 789–791



792

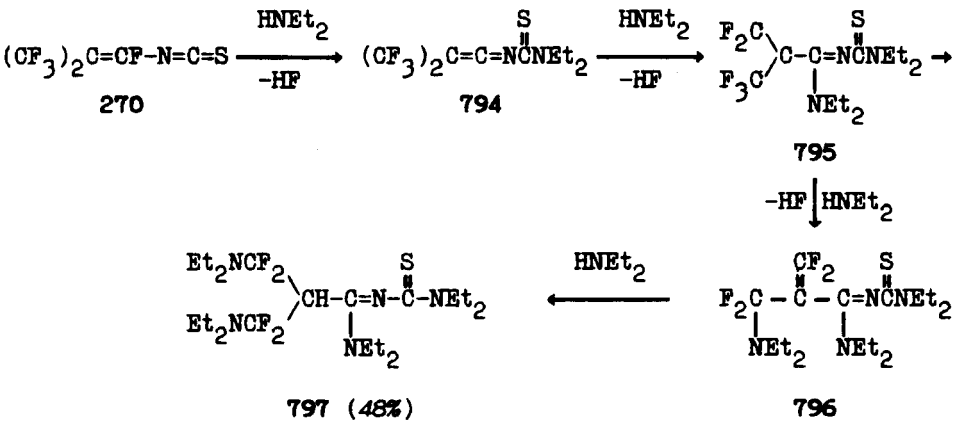
X^- = ClO_4^-, R^1 = R^2 = Me, Ar = Ph (**245**), 4-ClC_6H_4 (**246**), 4-MeC_6H_4 (**247**), 4-$MeOC_6H_4$ (**248**), β-$C_{10}H_7$ (**250**); R^1 – R^2 = $(CH_2)_4$, Ar = 4-$MeOC_6H_4$, (**251**), Ph (**789**); Ar = 4-MeC_6H_4, R^1 – R^2 = $(CH_2)_2O(CH_2)_2$ (**252**), X^- = SCN^-, R^1 = R^2 = Me, Ar = 4-MeC_6H_4 (**790**); X^- = Cl, R^1 = R^2 = Me, Ar = Ph (**791**); R^3 = R^4 = Me, Et; R^3 – R^4 = $(CH_2)_4$, $(CH_2)_4CO$, $(CH_2)_2O(CH_2)_2$; Y^- = ClO_4^-, SCN^-; R^5= Ph, 2-ClC_6H_4, 4-ClC_6H_4, 2-$MeOC_6H_4$, 3-$MeOC_6H_4$, 4-$MeOC_6H_4$, β-$C_{10}H_7$; NH_2, PhNH, 4-$NO_2C_6H_4NH$, 2,4-$(NO_2)_2C_6H_3NH$, 4-$MeC_6H_4SO_2NH$; NHCOMe, NHCOEt, $NHCO_2Et$, NHCOPh, NH_2CO.

SCHEME 187

The same reaction of the isothiocyanates **245**, **247**, **248**, **250**, **251**, and **790** with secondary aliphatic or cycloaliphatic amines in glacial acetic acid or in acetonitrile in the presence of an acid ($HClO_4$) leads to the formation of 2-amino-4-aryl-1,3-thiazinium salts **793** (Scheme 187).[105,230]

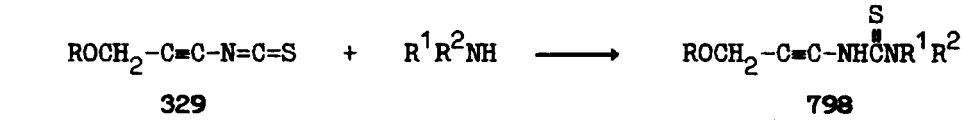
Presumably the reaction proceeds *via* hydrazone formation and conjugate addition to the pyrazoline, followed by cyclization of the isothiocyanate.

Perfluoroisobutenyl isothiocyanate **270** reacts with diethylamine in *absol.* diethyl ether to yield the corresponding thiourea **797**, but accompanied by replacement of one fluorine atom in every trifluoromethyl group by a diethylamino group (apparently, *via* HF elimination and addition of the amine to the double bond) (Scheme 188).[114]



SCHEME 188

1-Isothiocyanato-3-(2,4,6-trichlorophenyloxy)propargyl ether **329** easily reacts with secondary amines at 110–115 °C for 2–2.5 h giving the acetylenic thioureas **797** of a new type in 72–77% yield (Scheme 189).[130]



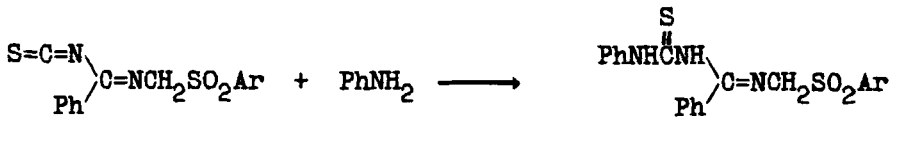
SCHEME 189

The *N*-(arylsulfonylmethyl)benzimidoyl isothiocyanates **279** and **280** react with aniline in acetonitrile at room temperature for 5 h giving the *N*-(arylsulfonylmethylbenzimidoyl)-*N'*-phenyl thioureas **798** (yields 75–77%) (Scheme 190).[117]

4-Isothiocyanato-2-morpholinoquinoline **654** with primary and secondary amines gave the corresponding thioureas **800** and **801** (Scheme 191).[209]

It would be expected that 2-phenylene diisothiocyanate **802** would react with amines to form the bis-substituted thioureas **803**. Actually, 2-phenylene diisothiocyanate **802** reacts with various primary and secondary amines on a 1:1 basis to give the 1-(substituted aminothiocarbonyl)benzimidazoline-2-thiones **804** (yields 14–95%) (Scheme 192).[231]

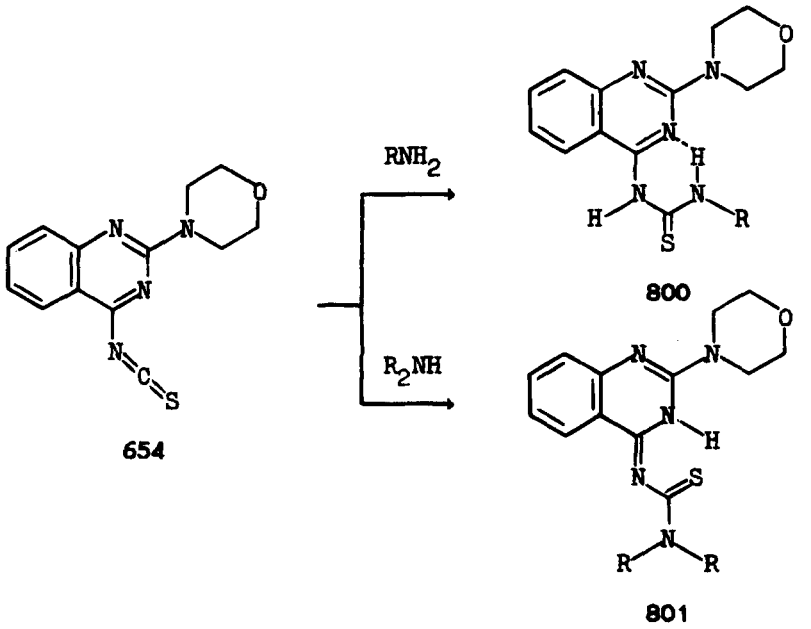
The products obtained with aliphatic primary amines proved to be very unstable and benzimidazoline-2-thione **805** was the main product isolated in the reactions with isopropylamine and *t*-butylamine.[231]



279,280 798

Ar = Ph (279), 4-MeC_6H_4 (280).

SCHEME 190



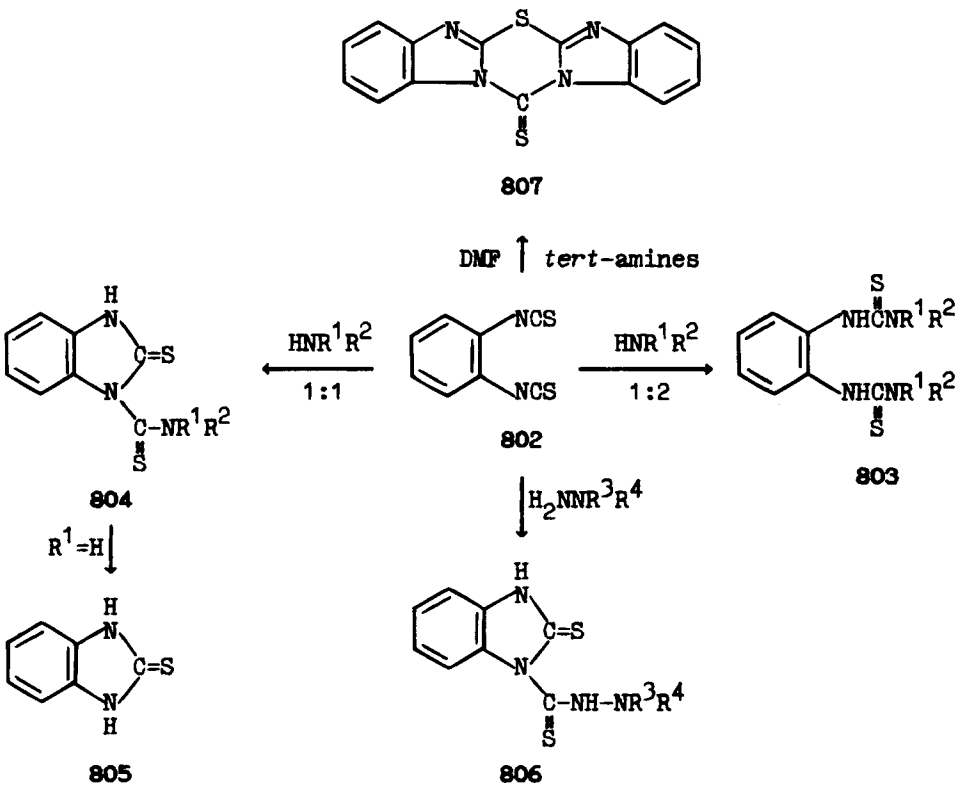
654 800 801

R = H, Me, CH_2=$CHCH_2$, $PhCH_2$, Ph; R_2 = $(CH_2)_2O(CH_2)_2$, $(Me)_2$, $(Et)_2$.

SCHEME 191

Treatment of 2-phenylene diisothiocyanate **802** with substituted hydrazines, *e.g.*, *N,N*-dimethyl-, methoxycarbonyl- and phenylhydrazine, gave the 1-(substituted hydrazinothiocarbonyl)benzimidazoline-2-thiones **806** (yields 37–60%) (Scheme 192).[231]

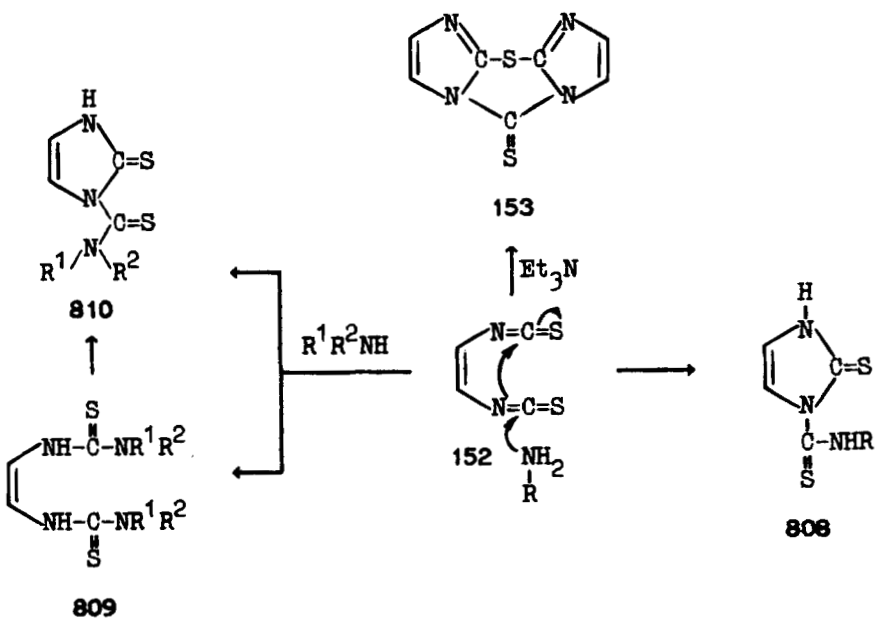
Vinylene diisothiocyanate **152** reacted 1:1 with primary amines (4-chloroaniline and cyclohexylamine) in dichloromethane at room temperature and rapidly formed the substituted thiocarbonylimidazoline-2-thiones **808**[208] of a structure similar to the products formed from 2-phenylene diisothiocyanate **802** (Scheme 193).[231]



SCHEME 192

The reaction of vinylene diisothiocyanate **152** with aniline gave the anticipated 1-(anilinothiocarbonyl)-4-imidazoline-2-thione **808** (R = Ph)[232] which is stable in contrast to the product obtained from diisothiocyanate **152** and 4-chloroaniline.[208]

Secondary amines, exemplified by morpholine and *N*-methylaniline, react in different ways.[208] Morpholine gave the expected 1:1 product, 1-(morpholinothiocarbonyl)-4-imidazoline-2-thione **810** (R^1-R^2 = $(CH_2)_2O(CH_2)_2$) in 75% yield; however, *N*-methylaniline was unusual in that the initial product was a 2:1 adduct, the bis(thiourea) **809**, which lost methylaniline on heating to form 1-[(*N*-methylanilino)thiocarbonyl]-4-imidazoline-2-thione **810**



R = Ph (62%), 4-ClC_6H_4 (63%), *cyclo*-C_6H_{11} (71%); R^1 = Me, R^2 = Ph; R^1 = H, R^2 =NHPh.

SCHEME 193

(*R*¹ = Me, R² = Ph). It is noteworthy that 2-phenylene diisothiocyanate **802** under similar conditions gives only the 1:1 product **804**.[231]

2-Methyl-3-isothiocyanato-4-thiocyanatoheptane **419** reacts with dimethylamine in *absol.* benzene in a glass autoclave at 60 °C for 15 h to give 2-(*N,N*-dimethylamino)-4-propyl-5-isopropylthiazole **811** (yield 60%) (Scheme 194).[145]

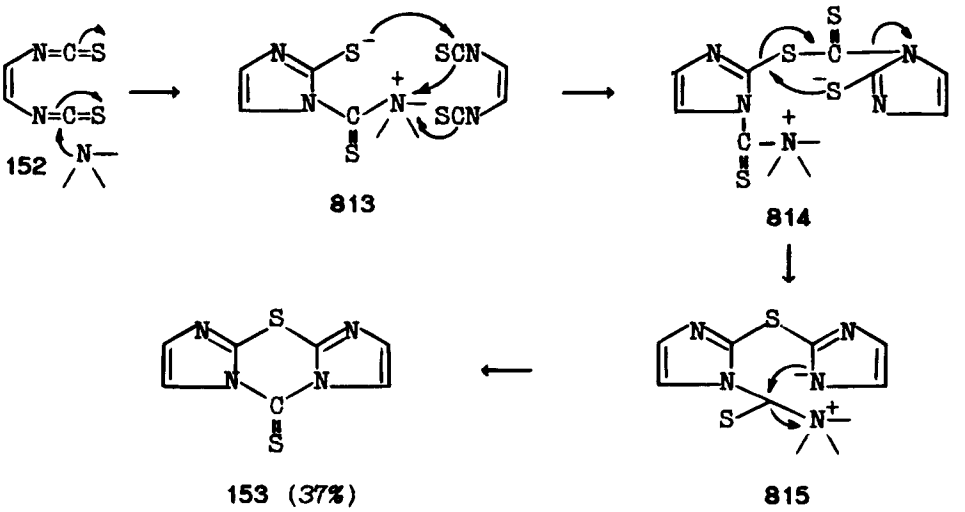
R = R^1 = Me (811); R = H, R^1 = Ph (812).

SCHEME 194

Analogously, the reaction with aniline in *absol.* methanol gives 2-anilino-4-propyl-5-isopropylthiazole **812** (yield 53%).[145]

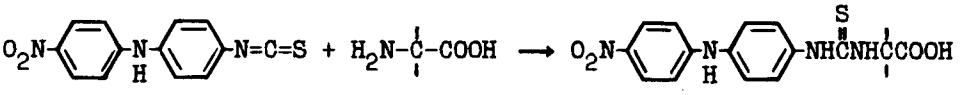
Reaction of tertiary amines, *N,N*-dimethylformamide, and certain other nucleophiles (*e.g.*, nitroaniline) with 2-phenylene diisothiocyanate **802** gave the pentacyclic compound **807** (yield 30%) (Scheme 192).[231]

The tricyclic compound, bisimidazo[2,1-*b*:1′,2′-*e*][1,3,5]thiadiazine-5-thione **153**, has been obtained by attack of a base (*e.g.*, triethylamine) on vinylene diisothiocyanate **152** at room temperature (CH_2Cl_2, 6–8 h), presumably by the following mechanism (Scheme 195):[84,208]



SCHEME 195

Reaction of amoscanate **816** with some amino acids (glycine, L-alanine, L-valine, L-leucine, L-serine, L-glutamine, tryptophane, histamine) in aqueous pyridine in the presence of 1 N aqueous sodium hydroxide at room temperature for 20 min gives the corresponding adducts **817** in 52–78% yield (Scheme 196).[63]



SCHEME 196

The adduct with histamine was prepared in the following way.[63] To a solution of sodium in methanol is added histamine dihydrochloride in methanol. The separated salt is filtered

off and the filtrate evaporated to dryness. To the residue is added amosoanate **816** and pyridine and the mixture heated at 100 °C for 1 h.

The authors of Ref.[193] found an alternative route which allows one to bind a variety of nucleosides and nucleotides to the polymers **818** and **819** with appended amino groups. For this purpose the resulting nucleoside derivatives **590** and **592** with isothiocyanate groups obtained by selective addition of the 5′-hydroxy group of 2′,3′-isopropylideneuridine or 2′,3′-isopropylideneadenosine to the isocyanato groups of ω-isocyanatoalkyl and aryl isothiocyanates were subsequently treated with poly-L-lysine, poly-L-ornithine, isopoly-L-lysine and isopoly-D,L-ornithine (Scheme 197).[193] The IR and 360 MHz ^{1}H NMR spectra allow the conclusion that the reaction of the nucleosidic isothiocyanates **590** and **592** with the basic polypeptides is nearly quantitative.

Rate constants have been tabulated for the addition reactions of heterocyclic isothiocyanates, i.e. 5-isothiocyanato-2-(substituted phenyl)benzotriazoles **31–38**, 5-isothiocyanato-2-(4-substituted phenyl)benzothiazoles **49**, **53**, **54**, **57**, and **58**, 5-isothiocyanato-2-(isothiocyanatophenyl)benzothiazoles **52** and **56** and 5-isothiocyanato-2-(4-isothiocyanatophenyl)benzoxazole (**820**), with glycine and the substituent effects discussed.[233]

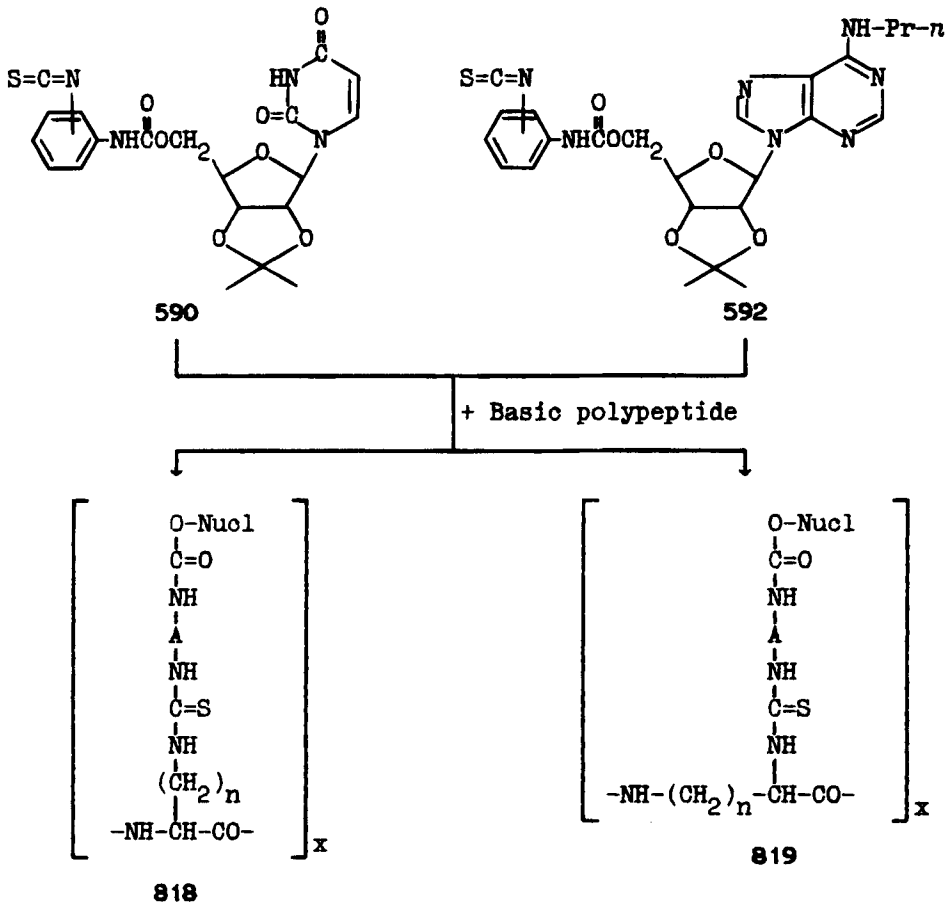
3.4.2. *Reactions with 2-oxoimidazolidine* Several *N*-aryl-2-oxo-1-imidazolidinethiocarboxamides **822** are available by treatment of 2-oxoimidazolidine **821** with aryl isothiocyanates (Scheme 198).[234,235]

3.4.3. *Reactions with 5-oxazolones* The anions of 2-benzyl-5-oxazolone **824** and 2-benzyl-4-methyl-5-oxazolone **825** undergo Michael addition with 2-isothiocyanato-3,3-dimethylacrylate **559** at low temperatures (Scheme 199).[236] The adduct from potassio-2-benzyl-4-oxo-5-oxazolidine **826** and isothiocyanate **559** cyclizes to give 2-benzyl-4,4′-dimethyl-5-oxo-2-thioxospiro[2-oxazoline-4,3′-pyrrolidine]-5-carboxylic acid ethyl ester **828**, whereas the adduct from the reaction of potassio-2-benzyl-4-methyl-5-oxo-4-oxazolidine **827** and isothiocyanate **559** could be trapped as 3-(2-benzyl-4-methyl-5-oxo-2-oxazolin-4-yl)-3,3-dimethyl-2-isothiocyanatobutanoic acid ethyl ester **829**.[236]

3.4.4. *Reactions with imines* *N*-Benzylidenemethylamine **830** (R = Me) and *N*-benzylidenebenzylamine **830** (R = $PhCH_2$) with 2-phenylene diisothiocyanate **802** gave the thiadiazines **832**, presumably via the ionic intermediate **831** (Scheme 200).[231]

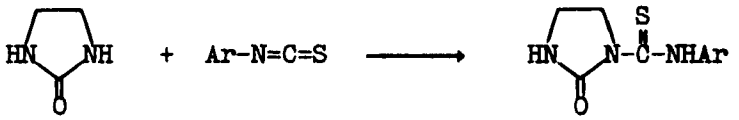
However, Schiff bases from aromatic primary amines [*e.g.*, **830** (R = Ph or 4-HOC_6H_4)] and the diisothiocyanate **802** gave the corresponding substituted benzimidazoline-2-thiones **804**, in which benzaldehyde had been lost during the reaction (Scheme 200).[231]

6,7-Dimethoxy-3,4-dihydroisoquinoline **833**, acting as a cyclic Schiff base, and 2-phenylene diisothiocyanate **802** in acetonitrile gave the pentacyclic compound **834**. Isoquinoline **176** and its 3-bromo derivative **835** both reacted readily with **802** (ether, ambient temperature, 10 min) to give 7,13*b*-dihydroisoquino[2′,1′:5,6][1,3,5]thiadiazino[3,2-*a*]benzimidazole-6-thione **836** and its bromo derivative **837** in good yields (90% and 58%, respectively) (Scheme 200).[231]



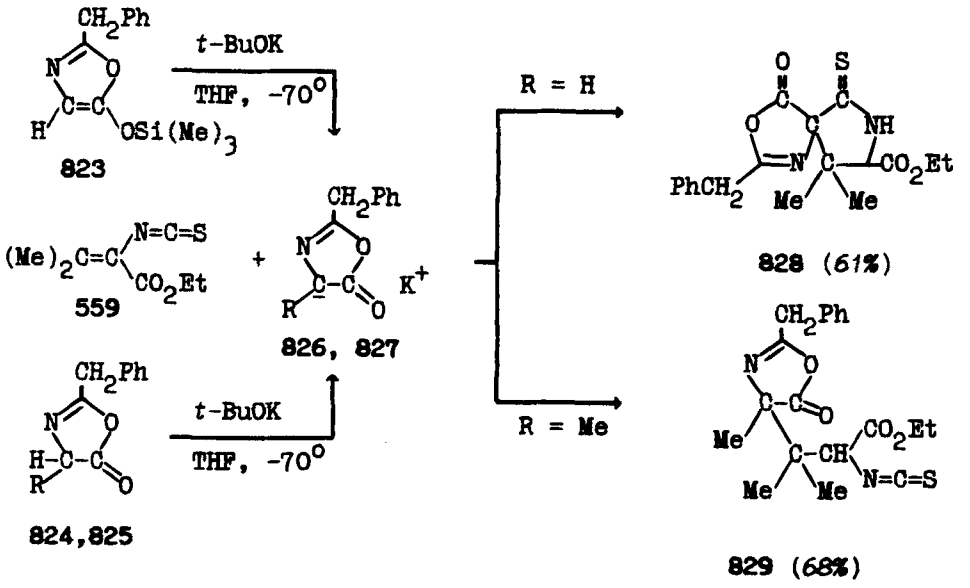
A = $-(CH_2)_m-$ or C_6H_4; Nucl = 2',3'-isopropylidene nucleoside, n = 3, 4.

SCHEME 197



821 822

SCHEME 198



R = H (824), Me (825).

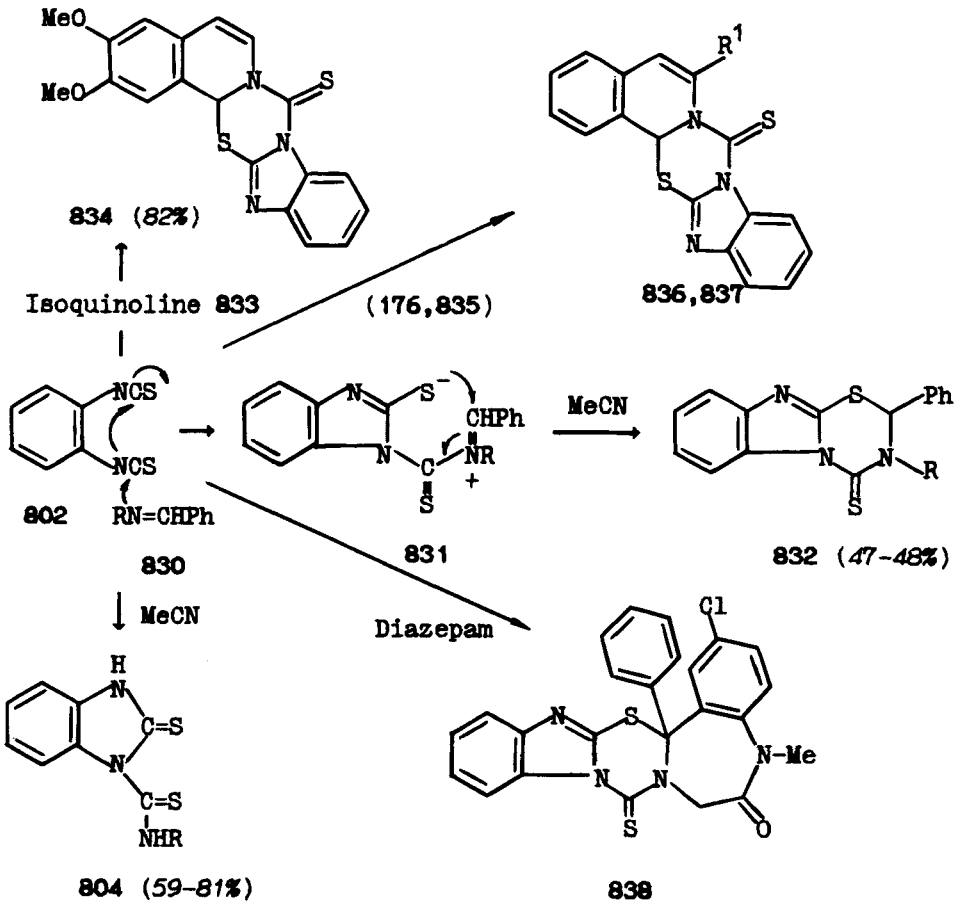
SCHEME 199

It has been found[231] that treatment of 2-phenylene diisothiocyanate **802** with diazepam, a benzodiazepine tranquilizer (acetonitrile, room temperature, 24 h) gives the expected addition across the C=N bond to yield 2-chloro-5-methyl-6-oxo-16*a*-phenyl-6,7-dihydrobenzimidazo[1′,2′:5,6][1,3,5]-thiadiazino[3,2-*d*][1,5]benzodiazepine-5*H*-9-thione **838** (Scheme 200).

6,7-Dimethoxy-3,4-dihydroisoquinoline **833** and isoquinoline **176** both reacted in the same manner with vinylene diisothiocyanate **152** in ether at room temperature for 20–60 min to yield 10,11-dimethoxy-8,12*b*-dihydroimidazo[1,2:3′,2′][1,3,5]thiadiazino[2,3-*a*]isoquinoline-5(6*H*)-thione **839** and imidazo[1,2:3′,2′][1,3,5]thiadiazino[2,3-*a*]isoquinoline-5(12b*H*)-thione **840**, respectively (Scheme 201).[208]

With *N*-benzylidenemethylamine **830** in acetonitrile at room temperature for 4 h vinylene diisothiocyanate **152** gave 2-phenyl-3-methyl-4-thioxoimidazo[1,2-*e*][1,3,5]thiadiazine **842** in 52% yield (Scheme 201).[232] The authors of Ref.[232] suppose that this reaction proceeds *via* the ionic intermediate **841** similarly as with 2-phenylene diisothiocyanate **802**.[231]

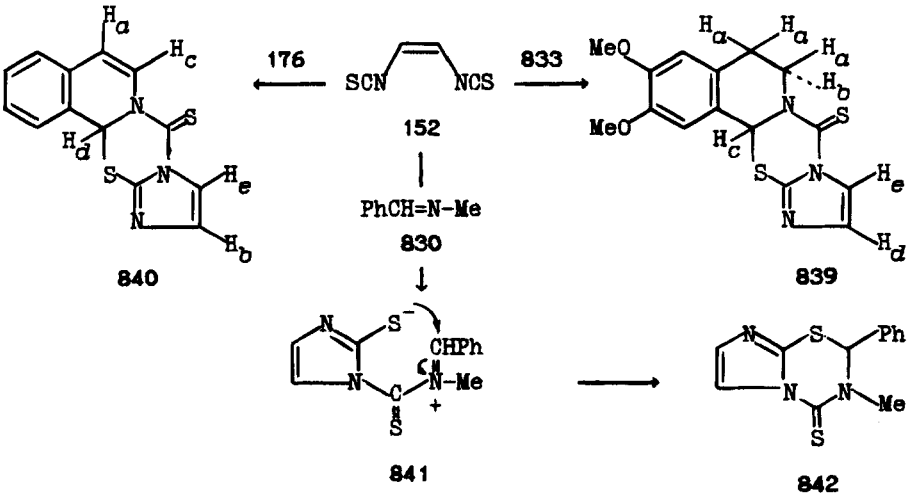
3.4.5. *Reactions with tetraaryl oxamidines* A useful synthetic route to unsymmetric derivatives of imidazolidine (derivatives of parabanic acid), 1,3-diaryl- **846** or 1-phenyl-3-vinyl-4,5-bis(arylimino)-2-thioxoimidazolidines **847**, is demonstrated by the reaction of the tetraaryloxamidines **843** with different aryl substituted isothiocyanates **4**, **193**, **194**, **197**, **199**, **844**, and **845** as well as vinyl isothiocyanate **142** in acetone, acetonitrile or toluene (Scheme 202).[237]



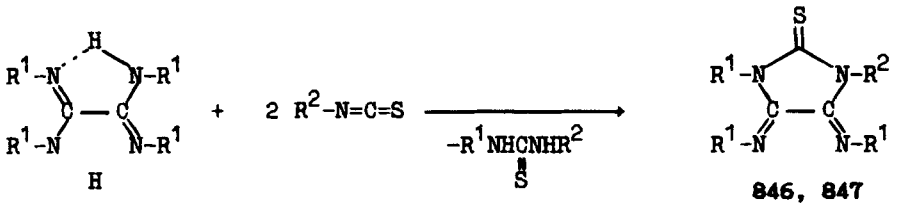
R = Me, $PhCH_2$, Ph, $4\text{-}HOC_6H_4$; R^1 = H, Br.

SCHEME 200

3.4.6. *Reactions with N,O-bis(trimethylsilyl)acetamide* Phenyl isothiocyanate **189** and the commercially available *N,O*-bis(trimethylsilyl)acetamide **852** gave *N*-acetyl-*N'*-phenylthiourea **854** (R = Ph) in quantitative yield after heating of the components at 70–80 °C for 1 h (Scheme 203).[238] The mixture was then methanolysed after standing for 24 h. The same conditions were applied in the preparation of the substituted thioureas **854** in 72–99% yield (Scheme 203).



SCHEME 201



R^1 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$; R^2 = 4-$H_2NSO_2C_6H_4$ (**4**), 4-ClC_6H_4 (**193**), 4-BrC_6H_4 (**194**), 4-$Me_2NC_6H_4$ (**197**), 4-$MeOC_6H_4$ (**199**), 3,5-$Cl_2C_6H_3$ (**844**), 4-FC_6H_4 (**845**), $CH{=}CH_2$ (**142,847**).

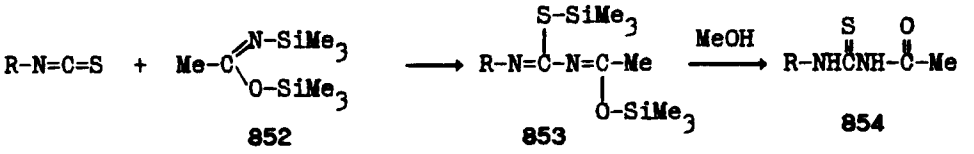
SCHEME 202

3.5. *Reactions with Trialkyl Phosphites*

Perfluoroisobutenyl isothiocyanate **270** adds triethyl phosphite in *absol.* diethyl ether to give the adduct **856** (Scheme 204).[114]

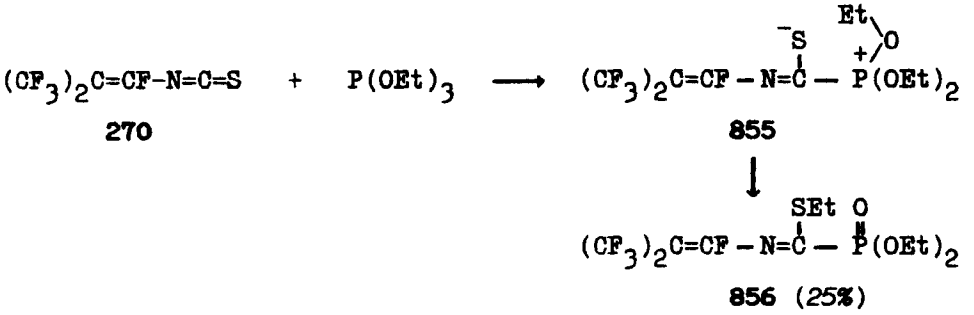
3.6. *Reactions with Tetraisopropyl Methylenebis(phosphonate)*

Tetraisopropyl [*N*-(aryl or 2-benzo[*b*]thienyl)thiocarbamoylmethylene]bis(phosphonates) **870** are prepared by reaction of the corresponding isothiocyanates **189, 192, 193, 195, 212, 845, 848, 851,** and **857–868** with a suspension of sodium hydride (60% oil dispersion) and tetraisopropyl methylenebis(phosphonate) **869** in distilled tetrahydrofuran at ambient temperature for 3 h (Scheme 205).[98]

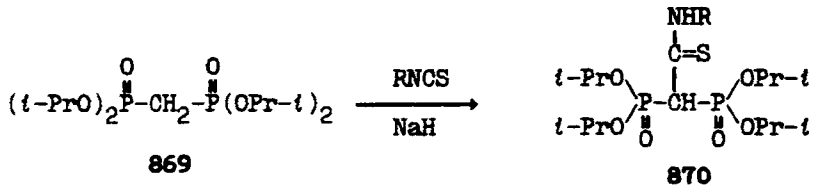


R = Ph (189), 4-FC_6H_4 (845), 4-ClC_6H_4 (193), 4-BrC_6H_4 (194), 4-$NO_2C_6H_4$ (683), 4-MeC_6H_4 (192), 3-ClC_6H_4 (848), 2,4-$Cl_2C_6H_3$ (849), 4-$MeCOC_6H_4$ (682), 3-$Me_2NC_6H_3$ (850), α-naphthyl (851).

SCHEME 203



SCHEME 204

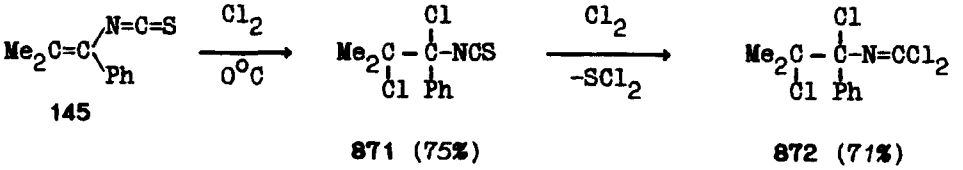


R = Ph (189), 2-ClC_6H_4 (857), 3-ClC_6H_4 (848), 4-ClC_6H_4 (193), 4-FC_6H_4 (845), α-$C_{10}H_7$ (851), 4-MeC_6H_4 (192), 2-$CF_3C_6H_4$ (858), 3-$CF_3C_6H_4$ (859), 4-$CF_3C_6H_4$ (860), 2-$MeOC_6H_4$ (195), 3,4-$Cl_2C_6H_3$ (861), 4-Cl-3-$CF_3C_6H_3$ (862), 4-MeO-3-$CF_3C_6H_3$ (863), 4-$MeSC_6H_4$ (864), 4-$MeSO_2NHC_6H_4$ (865), 3-$MeSO_2NHC_6H_4$ (866), 4-$MeCONHC_6H_4$ (867), 4-$MeCONHC_6H_4$ (868), 2-benzo[b]thienyl (212).

SCHEME 205

3.7. *Reactions with Chlorine*

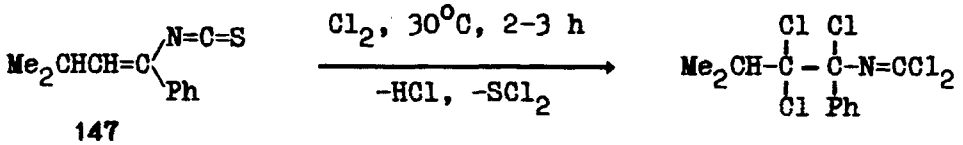
2-Methyl-1-phenylprop-1-enyl isothiocyanate **145** easily adds chlorine to the carbon-carbon double bond in anhydrous carbon tetrachloride at 0 °C to give 2-methyl-1-phenyl-1,2-dichloropropyl isothiocyanate **871** (Scheme 206).[82] Chlorination of the same isothiocyanate **145** with excess chlorine at 30 °C in CCl_4 for 2–3 h gives *N*-(2-methyl-1-phenyl-1,2-dichloropropyl)iminocarbonic acid dichloride **872**.[82]



145 **871** (*75%*) **872** (*71%*)

SCHEME 206

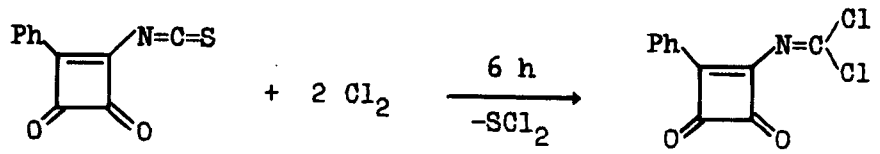
Analogously, *N*-(3-methyl-1-phenyl-1,2,2-trichlorobutyl)iminocarbonic acid dichloride **873** was prepared from chlorine and isothiocyanate **147** (Scheme 207).[82]



147 **873** (*67%*)

SCHEME 207

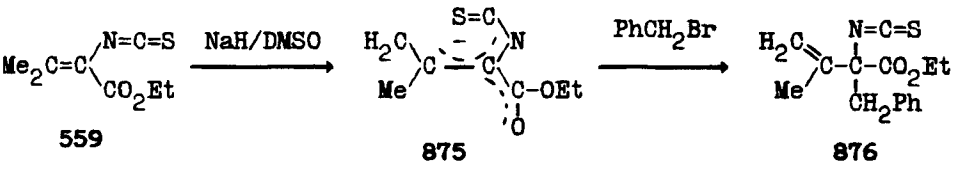
The action of chlorine on 3,4-dioxo-2-phenyl-1-cyclobut-1-enyl isothiocyanate **255** in dry chloroform leads to 3-(dichloromethyleneamino)-4-phenyl-3-cyclobutene-1,2-dione **874** in 39% yield (Scheme 208).[106]



255 **874**

SCHEME 208

3.8. *Reactions with Sodium Hydride and Benzyl Bromide* 2-Isothiocyanato-3,3-dimethylacrylic acid ethyl ester **559** with sodium hydride and benzyl bromide in DMSO/ether gave 60% 2-benzyl-2-isothiocyanato-3-methyl-1-but-3-enoic acid ethyl ester **876** *via* anion **875** (Scheme 209).[239]



559 875 876

SCHEME 209

3.9. *Reactions with Sodium Tetrahydroborate*

Various alkyl 2-isothiocyanatoacrylates, *e.g.*, **559** and **561**, have been converted to unsaturated *S*-methyl-, *S*-trityl-, or *S*-benzylthioformimidates **878** *via* the thioformamide anions **877** by reaction with sodium tetrahydroborate in anhydrous 2-propanol and following interaction with alkyl iodide or bromide and potassium *tert*-butoxide (Scheme 210).[186,240] The thus obtained thioformimidates **878** in dichloromethane/triethylamine with azidoacetyl chloride **879** gave β-lactams, the *trans*-3-azido-4-alkylthio-2-azetidinones **880** (Scheme 210).[186,240]

Analogously, **878** with phthalimidoacetyl chloride **881** gave the *trans*-substituted 3-phthalimido-4-alkylthio-2-azetidinones **882** (Scheme 210).[240]

Treatment of 2-methyl-3-isothiocyanato-4-thiocyanato-hept-3-ene **419**, 1-cyclobutyl-1-isothiocyanato-2-thiocyanato-pent-1-ene **420** and 1-methoxy-1-thiocyanato-2-isothiocyanato-3-methylbut-1-ene **421** with KOH in *absol.* methanol and sodium tetrahydroborate for 16 h leads to 2-mercapto-4-propyl-5-isopropylthiazole **886**, 2-mercapto-4-propyl-5-cyclobutylthiazole **887** and 2-mercapto-4-methoxy-5-isopropylthiazole **888** in 79%, 40% and 60% yield, respectively (Scheme 211).[145]

Analogously, 1-isothiocyanato-2-thiocyanatocyclohept-1-ene **429** can be cyclized to 5,6,7,8-tetrahydro-4*H*-cycloheptathiazole-2-thiol **889** (Scheme 212).[146]

3.10. *Reactions with Sodium Aluminohydrides*

When a solution of 4-isothiocyanato-2-morpholinoquinoline **654** in ether was treated with $NaAlH_2(OCH_2CH_2OMe)_2$ in benzene 2-morpholino-4-(thioformylamino)quinoline **890** was obtained in 60% yield (Scheme 213).[209]

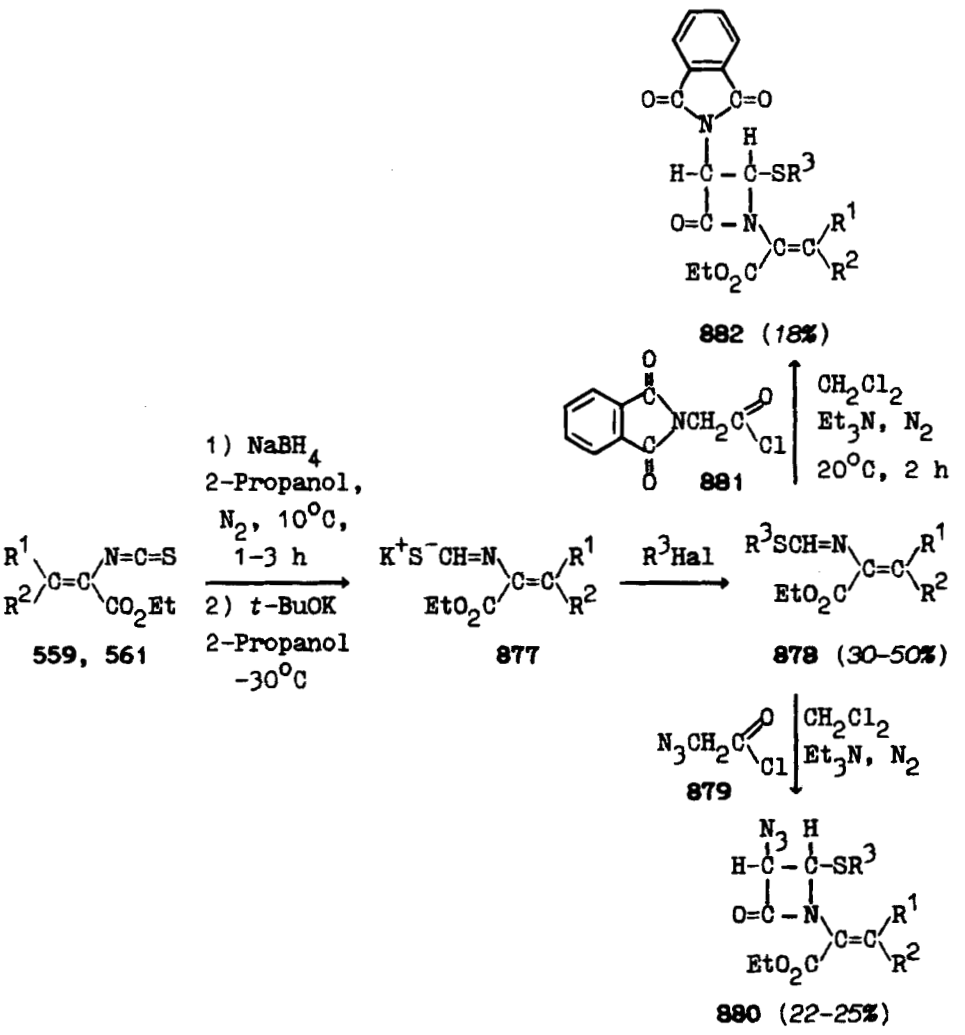
3.11. *Reactions with Alkyl- and Arylmagnesium Bromides*

2-Morpholino-4-(thiobenzoylimino)-3,4-dihydroquinoline **891** has been prepared from 4-isothiocyanato-2-morpholinoquinoline **654** (in 1,2-dimethoxyethane, 2 M) and phenylmagnesium bromide (in THF/1,2-dimethoxyethane, 2:1) in 30–40% yield (Scheme 214).[209]

Allenyl isothiocyanate **338** reacts with isopropylmagnesium bromide to give the corresponding thiazoles **893** and **894** (Scheme 215).[135]

3.12. *Reduction*

The polarographic reduction of the NCS group in a series of substituted 2-(R-phenyl)-5-benzotriazolyl isothiocyanates **31–40**, 1-(R-phenyl)-5-benzotriazolyl isothiocyanates

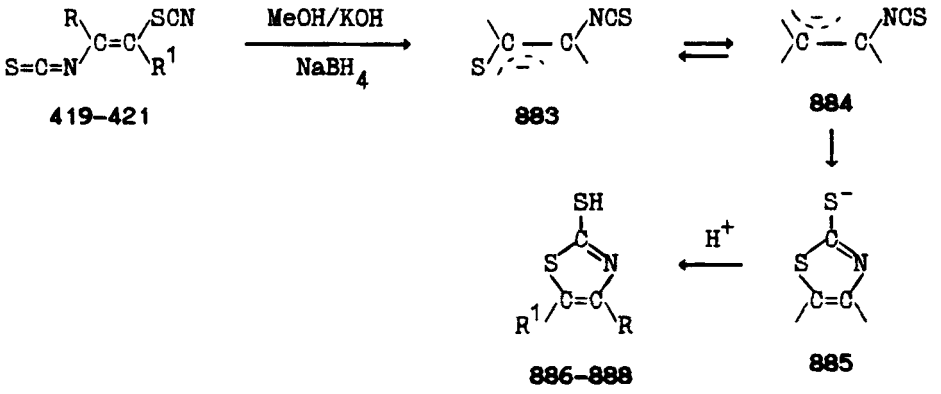


559, 561 **877** **878** (30–50%) **879** **880** (22–25%) **881** **882** (18%)

$R^1 = R^2 = Me$ (**559**), $R^3 = Ph_3C$, $PhCH_2$; $R^1 = Me$, $R^2 = Ph$ (**561**), $R^3 = Me$, Ph_3C; Hal = I, Br.

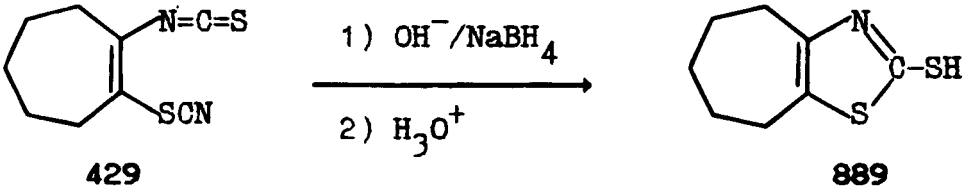
SCHEME 210

41–48, and 2-(R-phenyl)-6-benzothiazolyl isothiocyanates **49–59** has been studied.[68] The rate constants were calculated from the half-wave potentials. From the results of the correlations the transfer coefficients for individual bridge systems were calculated. The results obtained by these authors[68] were compared with those for other conjugated isothiocyanate systems (see Refs. in[68]).

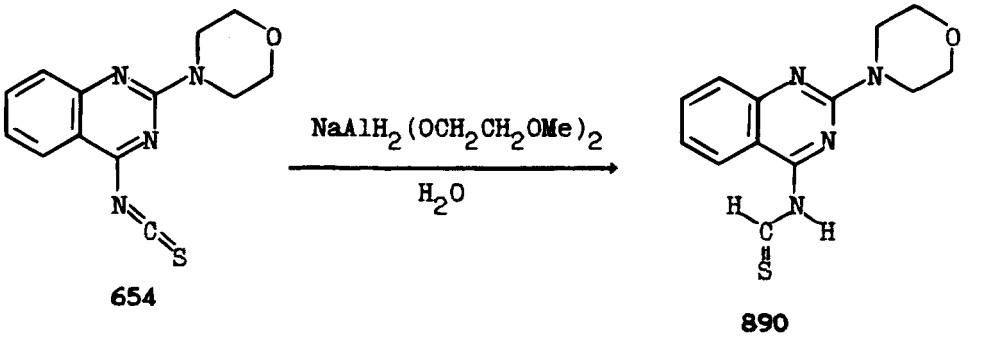


R = *t*-Pr, R^1 = *n*-Pr (**419**); R = *cyclo*-Bu, R^1 = *n*-Pr (**420**); R = *t*-Pr, R^1 = OMe (**421**).

SCHEME 211



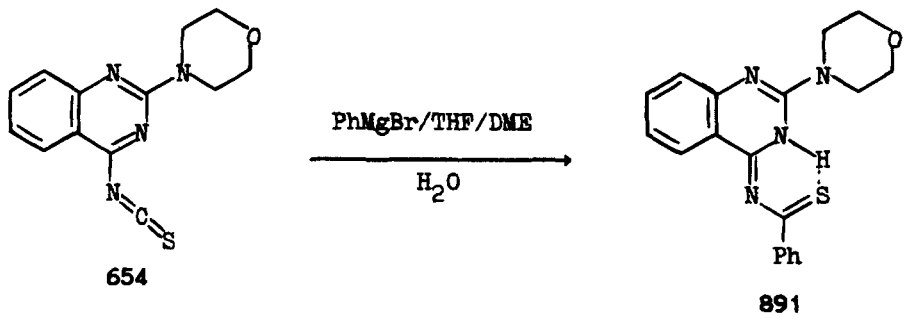
SCHEME 212



SCHEME 213

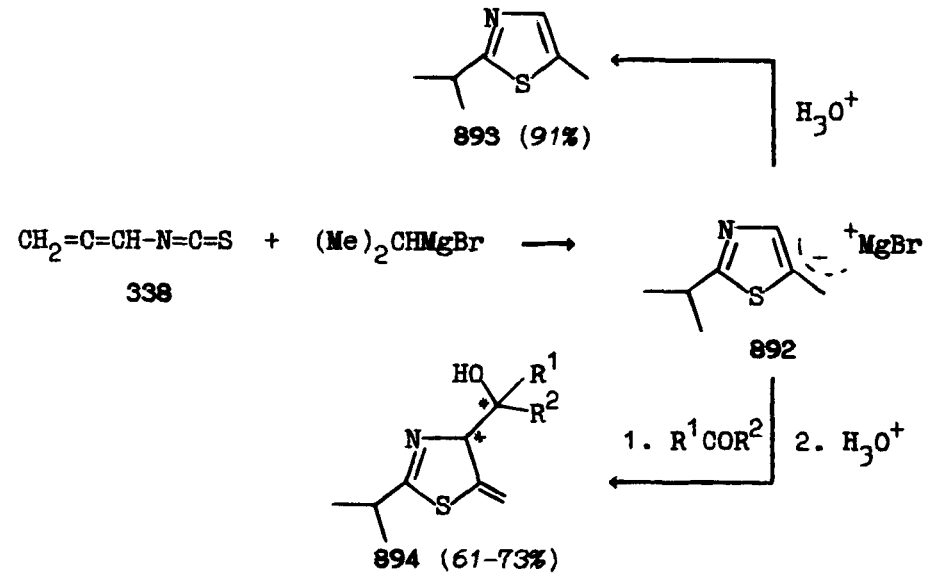
3.13. *Metal Complexes of Isothiocyanates*

In contrast to allyl isothiocyanate **469** no complexes with phenyl isothiocyanate **189** as ligand have been isolated so far, but studies have been made in solution.[241] With appropriate metal chlorides, the Cr/ligand and Co/ligand ratios have been found to be 1/6 and 1/4, respectively. The "first" transition for the chromium complex, in the visible region, is found



654 891

SCHEME 214



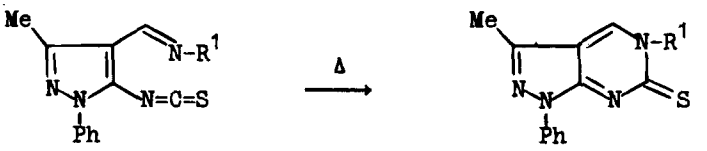
893 (91%) 338 892 894 (61–73%)

SCHEME 215

to be at 1694 cm^{-1}. This may indicate an M–N linkage, taking the spectrochemical series into consideration.[241]

3.14. *Thermal and Photocyclization*

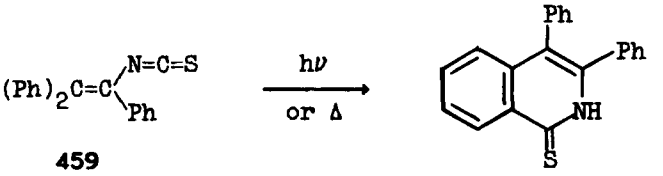
The 4-[*N*-(arylimino)methyl]-3-methyl-1-phenyl-5-isothiocyanato-1*H*-pyrazoles **432** and **433** by heating in dry toluene solution at reflux temperature have been converted to the corresponding fused 5-substituted 3-methyl-1-phenyl-6-thioxo-5,6-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidines **895** in nearly quantitative yields (75–97%) (Scheme 216).[152]



432,433 **895**

R = Ph (**432**), 4-MeC_6H_4 (**433**).

SCHEME 216

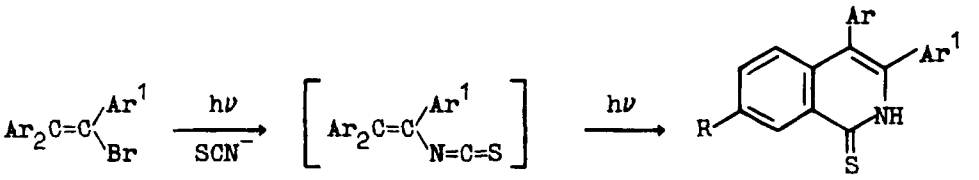


459 **896**

SCHEME 217

Isothiocyanatotriphenylethene **459** upon 30 h refluxing in decaline or 2.5 h UV photolysis in *absol.* cyclohexane rearranged to 75% 3,4-diphenyl-1(2*H*)-isoquinolinethione **896** (Scheme 217).[106]

The isoquinolinethiones **896** and **900** are considered to be formed by photocyclization of the corresponding vinyl isothiocyanates **459** and **897–899** as intermediates upon photolysis of triarylvinyl bromides in the presence of thiocyanate anions (Scheme 218).[102]



459,897-899 **896,900** (*15-34%*)

R = H, Ar = Ar^1 = Ph (**459**); Ar = Ph, Ar^1 = 4-$MeOC_6H_4$ (**897**), 4-MeC_6H_4 (**898**); R = MeO, Ar = Ar^1 = 4-$MeOC_6H_4$ (**899**).

SCHEME 218

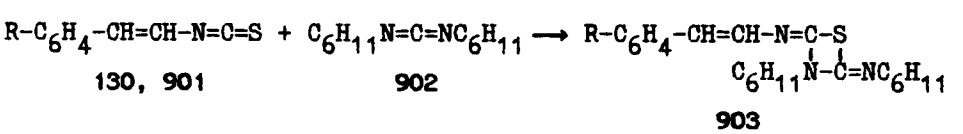
3.15. *Cycloadditions*

Isothiocyanates can be the starting materials for cycloaddition reactions leading to a plethora of heterocyclic compounds.[9,22]

Whereas the heterocumulene grouping in the isothiocyanates –N=C=S can enter cycloaddition reactions either through the C=S or C=N bond, isothiocyanates in which the heterocumulene grouping is conjugated with multiple bond such as C=C, C=O, C=S, C=N, and C=C can react in cyloaddition reactions with double or triple bonds with varying periselectivity: they can act either as a 2π electron component and afford different [2+2] cycloadducts or as a 4π electron component and give [4+2] cycloadducts.[9,22,58,161,242,243] These reactions are interesting both from the mechanistic and the synthetic point of view because they can lead to various four-membered as well as six-membered cycloadducts.[58]

3.15.1. *With carbodiimides* Isothiocyanates having the –NCS group in conjugation with another double bond C=X (X = S, NR_2) can react with the 2π electron system in the already mentioned reactions in four various ways. The cycloaddition can theoretically occur at the C=X, C=N, or C=S bond, the [4+2] cycloaddition at X=C-N=C.[243]

It was of interest which pericyclic process would be involved in the cycloaddition of aliphatic carbodiimides to isothiocyanates with an –NCS group in conjunction with a C=C bond.[243] *N,N*-Dicyclohexylcarbodiimide **902** was, therefore, treated with 2-phenylethenyl isothiocyanate **130**[243] and the cycloaddition was found to proceed as that with phenyl isothiocyanate **189** under the same conditions (Scheme 219).[244] TLC of the reaction mixture showed that the starting 2-phenylethenyl isothiocyanate **130**, a 1:4 mixture of the *cis* and *trans* isomers, afforded two reaction products **903** only. Chromatography through a silica gel column afforded these products in 64% yield; they were the *cis*- and *trans*-isomer of 2-phenylethenylimino-3-cyclohexyl-4-cyclohexylimino-1,3-thiazetidine **903**.[243]



R = H (**130**, *cis/trans* 1:4), 4-NO_2 (**901**, *trans*).

SCHEME 219

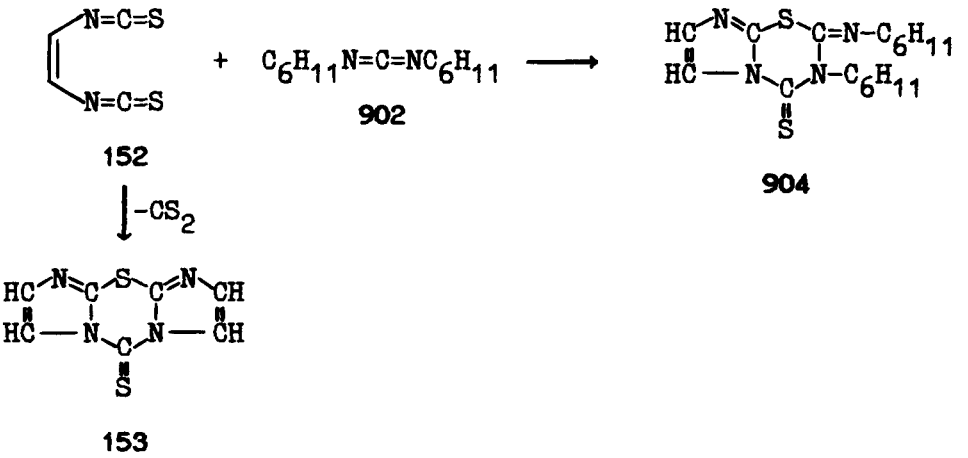
The structure of both cycloadducts, differing in the configuration at the C=C bond, was inferred from IR, ^{1}H NMR and mass spectral data.

trans-2-(4-Nitrophenyl)ethenyl isothiocyanate **901** reacts with *N,N*-dicyclohexylcarbodiimide analogously.[243]

These results allowed the authors of Ref.[243] to conclude that the heterodiene –C=C-N=C=S system reacts with *N,N*-dicyclohexylcarbodiimide selectively through its C=S bond to afford the [2+2] cycloadduct. The alternative [4+2] cycloaddition, also involving the olefinic

C=C bond, remained absent in the reaction of 2-phenylethenyl isothiocyanate **130** and 2-(4-nitrophenyl)ethenyl isothiocyanate **901**.

The reaction of vinylene diisothiocyanate **152** with *N,N'*-dicyclohexylcarbodiimide in ether under nitrogen at ambient temperature afforded 2-cyclohexylimino-3-cyclohexyl-4-thioxoimidazo[1,2-*e*][1,3,5]thiadiazine **904** in 47% yield (Scheme 220).[232] Another crystalline product was obtained from the filtrate. It was identified as bisimidazo[2,1-*b*:1',2'-*e*][1,3,5]thiadiazine-4-thione **153**, formed in 21% yield from two molecules of vinylene diisothiocyanate **152** by loss of CS_2.[232]



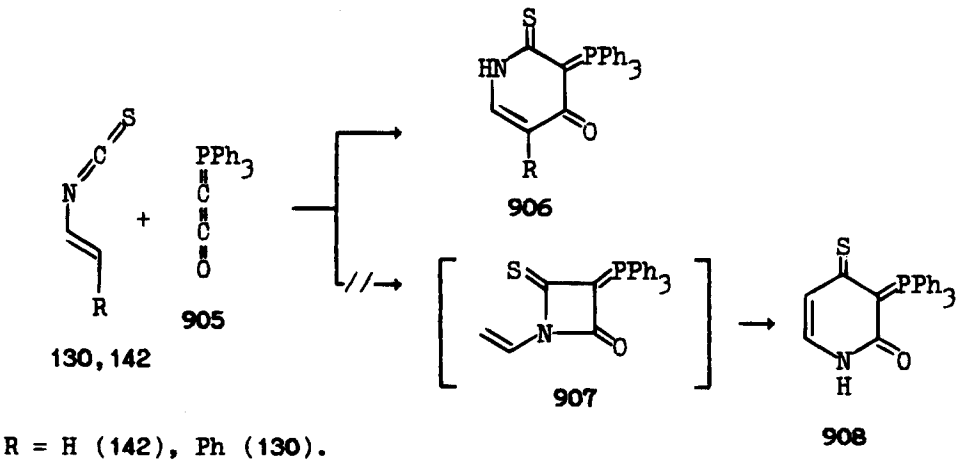
SCHEME 220

3.15.2. *With phosphoranes* Oxovinylidenetriphenylphosphorane **905** and *N*-phenyliminovinylidenetriphenylphosphorane **909** enter cycloaddition reactions with the vinyl isothiocyanates **130** and **142** giving exclusively [4+2] cycloaddition products, i.e. derivatives of 3-(triphenylphosphorano)pyridine-2-thione **906**, **911**, in contrast to alkyl or aryl isothiocyanates.[58] Thus, the reaction of oxovinylidenetriphenylphosphorane **905** with vinyl isothiocyanate **142** in benzene (under nitrogen, at room temperature, 12 h) afforded 4-oxo-3-triphenylphosphorano-2-pyridinethione **906** (R = H) as the sole product in 94% yield (Scheme 221).[58] As shown by the mass spectrum, the reaction product is a 1:1 adduct of the starting compounds.

Styryl isothiocyanate **130** reacts with oxovinylidenetriphenylphosphorane **905** analogously to furnish only one product, 4-oxo-5-phenyl-3-(triphenylphosphorano)pyridine-2-thione **906** (R = Ph) (yield 73%) (Scheme 221).[58]

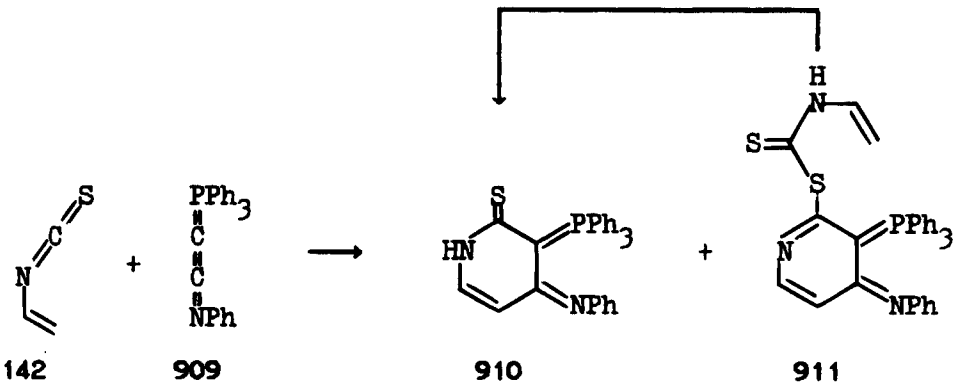
As follows from experience with the reaction of vinyl isothiocyanate **142** with an ynamine,[242] the reaction of **142** with **905** could be a [2+2] cycloaddition to the N=C bond of the –N=C=S group.

Equimolar amounts of vinyl isothiocyanate **142** and *N*-phenyliminovinylidenetriphenylphosphorane **909** afforded a mixture of two products with identical mass spectra, 4-



SCHEME 221

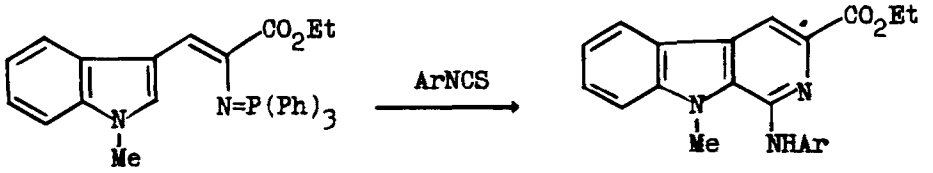
phenylimino-3-(triphenylphosphorano)pyridine-2-thione **910** (yield 31%) and 2-(*N*-ethenyldithiocarbamoyl)-4-phenylimino-3-(triphenylphosphorano)-pyridine **911** (yield 29%) (Scheme 222).[58] The second product **911** formed from 4-phenylimino-3-(triphenylphosphorano)pyridine-2-thione **910** by reaction with a further molecule of vinyl isothiocyanate **142**.



SCHEME 222

Upon standing in chloroform solution or during mass spectral measurements, 2-(*N*-ethenyldithiocarbamoyl)-4-phenylimino-3-(triphenylphosphorano)pyridine **911** loses vinyl isothiocyanate under formation of 4-phenylimino-3-(triphenylphosphorano)pyridine-2-thione **910** whose structure was confirmed by X-ray diffraction.

Ethyl 3-(1-methylindol-3-yl)-2-(triphenylphosphoranylideneamino)prop-2-enoate **437** reacts with the aromatic isothiocyanates **189**, **192**, **193**, and **199** in dry toluene at 0 °C under nitrogen and subsequent heating under reflux for 12 h to yield the corresponding 1-arylamino-3-ethoxycarbonyl-9-methylpyrido[3,4-*b*]indoles **912** (Scheme 223).[153]

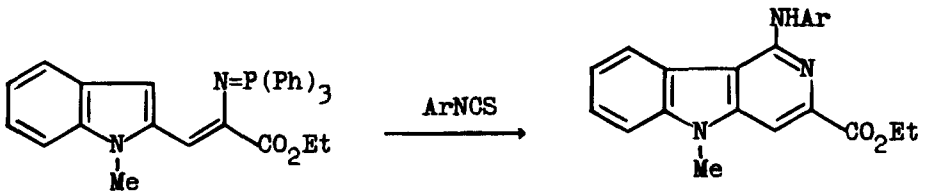


437 **912** (*70–84%*)

Ar = Ph (**189**), 4-MeC_6H_4 (**192**), 4-ClC_6H_4 (**193**), 4-$MeOC_6H_4$ (**199**).

SCHEME 223

Ethyl 3-(1-methylindol-2-yl)-2-(triphenylphosphoranylideneamino)prop-2-enoate **913** under similar conditions yields the 1-arylamino-3-ethoxycarbonyl-5-methylpyrido[4,3-*b*]indoles **914** (Scheme 224).[153]



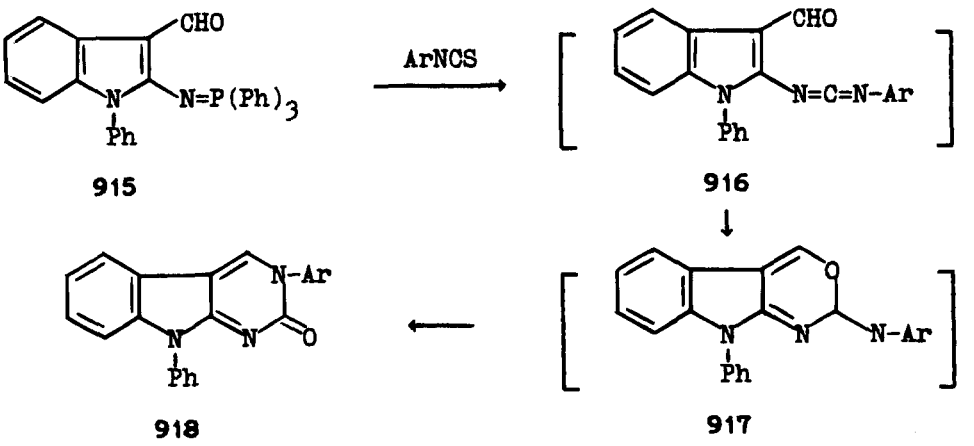
913 **914** (*81–94%*)

Ar = Ph (**189**), 4-MeC_6H_4 (**192**), 4-ClC_6H_4 (**193**), 4-$MeOC_6H_4$ (**199**).

SCHEME 224

The reaction of 3-formyl-1-phenyl-2-(triphenylphosphoranylideneamino)indole **915** with the isothiocyanates **189**, **193**, and **199** at room temperature in dry dichloromethane leads directly to the 3-aryl-2,3-dihydro-2-oxo-9-phenylpyrimido[4,5-*b*]indoles **918** in good yields (82–76%) (Scheme 225).[153]

Presumably, the conversion of 3-formyl-1-phenyl-2-(triphenylphosphoranylideneamino)indole **915** to 3-aryl-2,3-dihydro-2-oxo-9-phenylpyrimido[4,5-*b*]indoles **918** in-

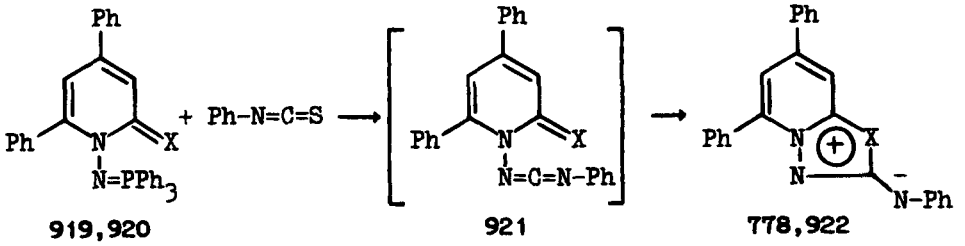


Ar = Ph (189), 4-ClC_6H_4 (193), 4-$MeOC_6H_4$ (199).

SCHEME 225

volves an initial aza-Wittig reaction between the iminophosphorane **915** and the isothiocyanate to give the carbodiimide **916**, which undergoes electrocyclic ring closure to an unstable 1,3-oxazine-2-imine **917** which, by a typical Dimroth rearrangement, undergoes ring opening and closure to furnish the 2-oxopyrimido[4,5-*b*]indole **918** (Scheme 225).[153]

1-(Triphenylphosphoranylideneamino)-4,6-diphenyl-2(1*H*)-pyridone **919** reacts with phenyl isothiocyanate at room temperature in dry benzene for 15 h to give 5,7-diphenyl-1,3,4-oxadiazolo[3,2-*a*]pyridinium-2-aminide **922** (X = O) in high yield (86%) (Scheme 226).[147]

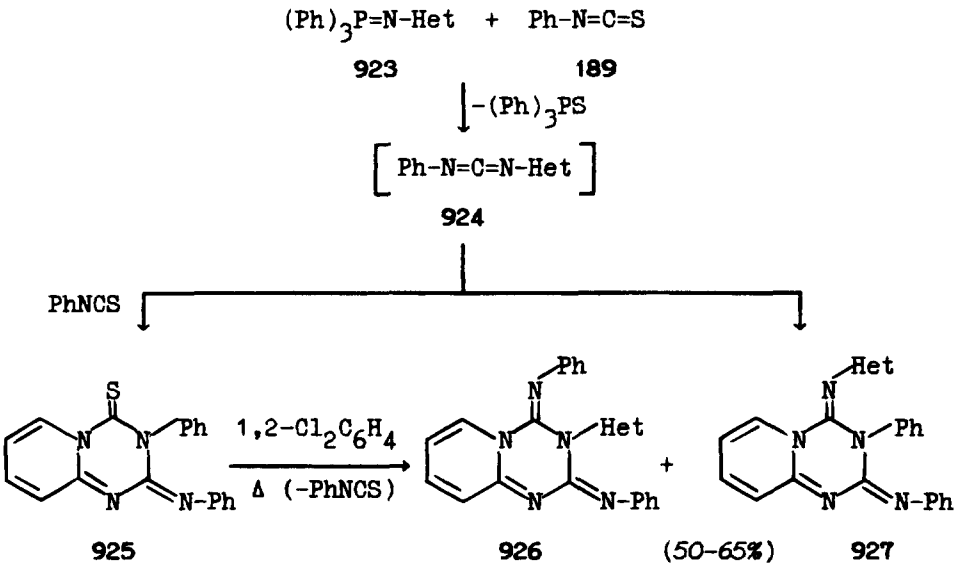


X = O (919,922), S (920,778).

SCHEME 226

In the same way 1-(triphenylphosphoranylideneamino)-4,6-diphenylpyridine-2(1*H*)-thione **920** leads to 5,7-diphenyl-1,3,4-thiadiazolo[3,2-*a*]pyridinium-2-aminide **922** (X = S) in 80% yield (Scheme 226).[147]

The α-*N*-heteroaryliminotriphenylphosphoranes **923** react with phenyl isothiocyanate to form symmetrical and unsymmetrical carbodiimides **924** (Scheme 227).[245] These cannot be isolated as monomers because they behave predominantly as 1,3-diazabutadienes and form [4+2] cycloadducts. The monomeric intermediates **924** cyclodimerize in dry benzene for 20 h to the 3-(heteroaryl)-2,4-di(phenylimino)pyrido[1,2-*a*]-1,3,5-triazines **926** and the 3-phenyl-2-phenylimino-4-heteroaryliminopyrido[1,2-*a*]-1,3,5-triazines 927 (regioisomers). Concurrent interaction of the intermediate **924** with the isothiocyanate **189** leads to a mixture of 3-(pyrid-2-yl)-2,4-di(phenylimino)pyrido[1,2-*a*]-1,3,5-triazine **926** (Het = pyrid-2-yl) and 3-phenyl-2-phenyliminopyrido[1,2-*a*]-1,3,5-triazine-4-thione **925**, for example, in 48% and 37% yield, respectively (in refluxing dry benzene for 23 h) (Scheme 227).[245]

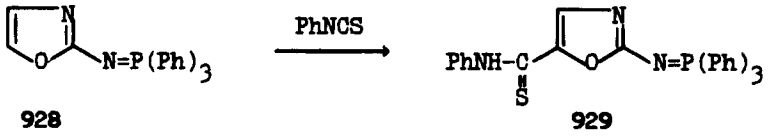


Het = pyrid-2-yl, pyrimidin-2-yl, thiazol-2-yl.

SCHEME 227

3-Phenyl-2-phenylimino-pyrido[1,2-*a*]-1,3,5-triazine-4-thione **925** has also been prepared by cycloaddition of *N*-pyrid-2-yl-*N*-phenylcarbodiimide **924**, Het = pyrid-2-yl, with phenyl isothiocyanate.[245]

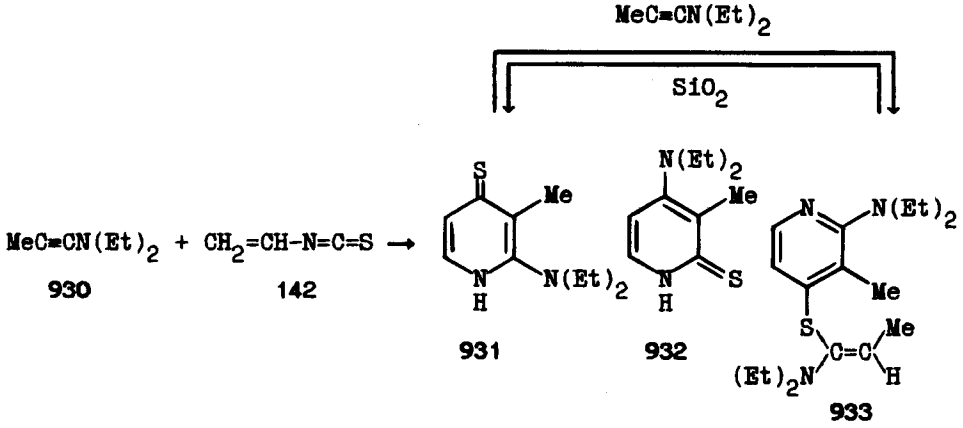
N-Oxazol-2-yliminotriphenylphosphorane **928** with phenyl isothiocyanate at room temperature for 200 h yields 68% 5-(*N*-phenylthiocarbamoyl)-2-(triphenylphosphoranylideneamino)oxazole **929** (Scheme 228).[245]



928 **929**

SCHEME 228

3.15.3. *With 1-(N,N-diethylamino)propyne* The reaction[174] between equimolar quantities of vinyl isothiocyanate **142** and 1-(*N,N*-diethylamino)propyne **930**, a typical electron-rich dienophile, in refluxing ethyl ether gave, after chromatography over silica gel, the two 1:1 adducts, the γ-pyridinethione **931** (20%) and the pyridine-2-thione **932** (ca. 3%) (Scheme 229).

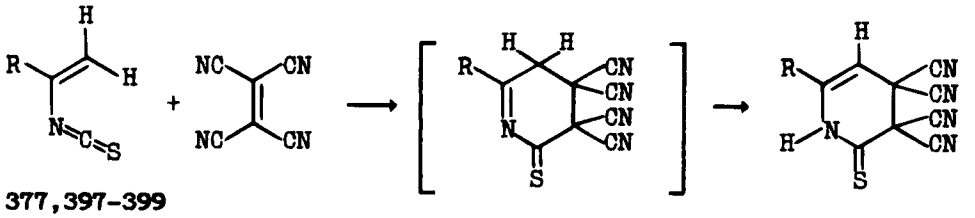


SCHEME 229

In a subsequent experiment, the NMR spectrum of the reaction mixture resulting from a 0.5 molar equivalent of vinyl isothiocyanate **142** and ynamine **930** indicated the presence of two 2:1 adducts in a 7.5:1 ratio, which were formulated as the (*E*)- and (*Z*)-vinyl sulfides **933**, without detectable amounts of 2-(*N,N*-diethylamino)-3-methylpyridine-4-thione **931** and 4-(*N,N*-diethylamino)-3-methylpyridine-2-thione **932**.[174]

The mixture of vinyl sulfides **933**, isolated as an uncrystallizable oil, gave on chromatography over silica gel the pyridine-4-thione **931** (87%) and traces of the 2-isomer **932**. A mixture of the (*E*)- and (*Z*)-vinyl sulfides **933** in a 7.7:1 ratio was also obtained by treatment in an NMR tube of the pyridine-4-thione **831** with 1 equivalent of ynamine **930** (Scheme 229).[174]

3.15.4. *With tetracyanoethylene* The [4+2] cycloaddition of some vinylic isothiocyanates (*e.g.*, **377**, **397–399**) to the electron-poor tetracyanoethylene (TCNE) affords 6-substituted 1,2,3,4-tetrahydro-2-thioxopyridine-3,3,4,4-tetracarbonitriles **935** through the mechanism shown in Scheme 230.[246]



377, 397–399 934 935 (> 80%)

R = *n*-Bu (**397**), n-C_7H_{15} (**398**), *t*-Bu (**399**), Ph (**377**).

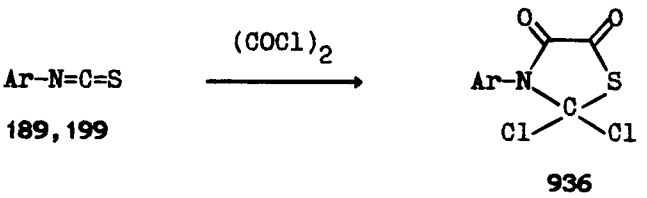
SCHEME 230

The intermediate adducts **934** are not observed and the reaction spontaneously leads to the cycloadducts **935** which corresponds to the prototropic migration of one hydrogen atom of the ring in intermediate **934** to the heterocyclic nitrogen atom.

The reaction was generally performed in acetonitrile, and took 2–3 days at 50 °C for the isothiocyanates with **397–399** but was much more rapid for the isothiocyanate **377** (*ca.* 1 h at 20 °C); the starting concentrations of both reactants were 1 M. The process was monitored by ^{1}H NMR, no other compound than the expected adducts being detected.

The reaction between 2-isothiocyanatonon-1-ene **398** and TCNE was followed (NMR, GLC) in different solvents (acetonitrile, 1,4-dioxane, and benzene) but no appreciable effect of the solvent on the reaction rate was detected. No change in the course of the reaction between isothiocyanate **398** and TCNE in acetonitrile was observed in the dark. Experiments carried out with other dienophiles [maleic anhydride, 1,4-benzoquinone, MeO_2C-C≡C-CO_2Me, EtO-CH=C(CO_2Et)$_2$] showed no reaction to occur with isothiocyanate 398 or with 1-isothiocyanato-1-phenylethene **377**.[246]

3.15.5. *With oxalyl chloride* The aryl isothiocyanates **189** and **199** react with oxalyl chloride at both double bonds of the heterocumulene to yield the 3-aryl-2,2-dichlorothiazolidine-4,5-diones **936** (Scheme 231).[24]



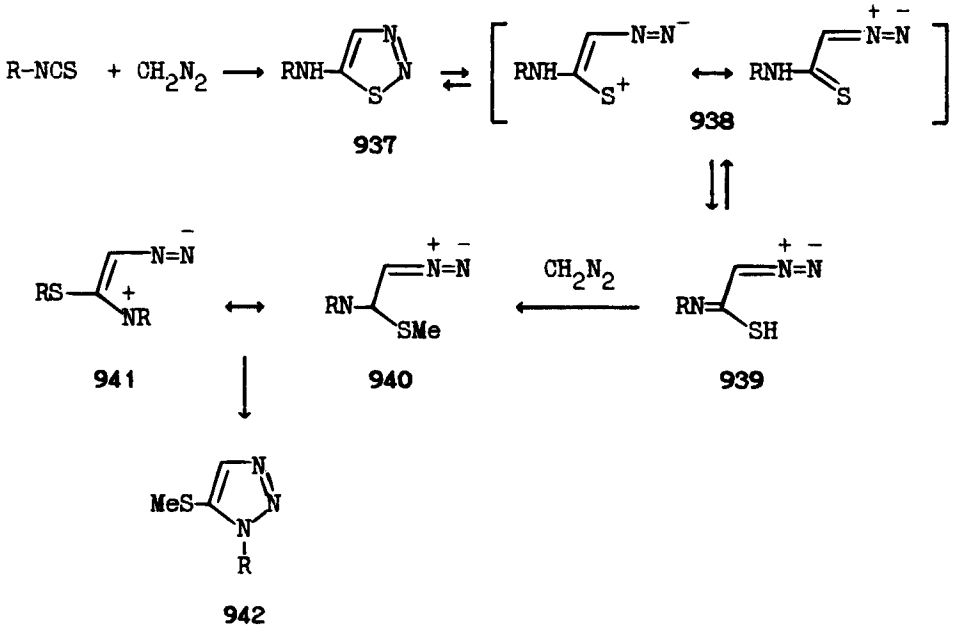
189, 199 936

Ar = Ph (**189**), 4-$MeOC_6H_4$ (**199**).

SCHEME 231

In contrast to aliphatic isothiocyanates, the reactions between phenyl isothiocyanate **189** or 4-methoxyphenyl isothiocyanate **199** with oxalyl chloride under similar conditions (equivalent amounts of reagents, at room temperature) were found to require extremely long reaction times (25 and 40 days) for the conversion to reach 25% and 23%, respectively.[24] The progress of the reactions was monitored by IR spectroscopy following the disappearance of the N=C=S bands (between 2100–2200 cm^{-1}) and the carbonyl bands of oxalyl chloride (at 1750–1800 cm^{-1}); the new adducts show one characteristic intense carbonyl band at 1745–1750 cm^{-1} in the double-bond region.

3.15.6. *With diazomethane* The 1-alkenyl isothiocyanates **189**, **218**, and **221** can react with diazomethane at room temperature in dry acetonitrile to give the corresponding 5-(substituted amino)-1,2,3-thiadiazoles **937** (Scheme 232).[247] In the presence of an excess of diazomethane these thiadiazoles **937** rearrange to 1-substituted 5-(methylthio)-1*H*-1,2,3-triazoles **942**.[247]



R = *t*-PrCH=CMe (**221**, *Z*-isomer), EtCH=CH (**218**, *cis*-isomer), Ph (**189**).

SCHEME 232

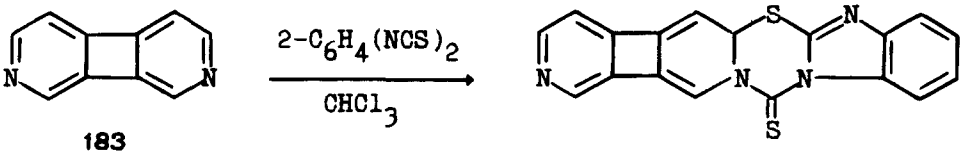
This 1,3-cycloaddition takes place across the C=S bond which is the known mode of addition for aryl and alkyl isothiocyanates to afford the thiadiazole **937**, which then under-

goes heterolytic cleavage to yield **938**. The positive charge prefers to reside on sulfur rather than on nitrogen because of the higher electronegativity of nitrogen. The tautomeric diazothioamide **939** is subsequently methylated at the sulfur atom by diazomethane to yield **940**, whose mesomeric structure **941** has exactly the right charge distribution for the formation of the 1-substituted 5-(methylthio)-1*H*-1,2,3-triazole **942** (Scheme 232).[247]

When the addition reaction was carried out in the presence of excess isothiocyanate the final reaction mixture consisted of starting material, triazole **942** and the thiadiazole **937**, the latter of which could be isolated and characterized. Furthermore, treatment of **937** with diazomethane in acetonitrile afforded the triazole **942**.[247]

In the case of isothiocyanate **189** a 1:1 mixture of 1,2-dimethoxyethane and acetonitrile was employed as reaction medium.

3.15.7. *With 2,7-diazabiphenylene* The reaction and the formation of the unusual bismethylenecyclobutapyridine **943** obtained by reaction of 2,7-diazabiphenylene **183** with 1,2-phenylene diisothiocyanate **802** can be explained if an initial electrophilic quaternization of the ring nitrogen is followed by nucleophilic addition to C-3 (Scheme 233).[94]



183 **943**

SCHEME 233

3.15.8. *With hydrazoic acid* The reaction of 1,3-dimethylbut-1-enyl isothiocyanate **221** with hydrazoic acid in benzene/acetonitrile afforded the expected 5-[(1,3-dimethyl-1-butenyl)amino]-1,2,3,4-thiatriazole **944** in 77% yield (room temperature, 3 days) (Scheme 234).[247]

221 **944** **945**

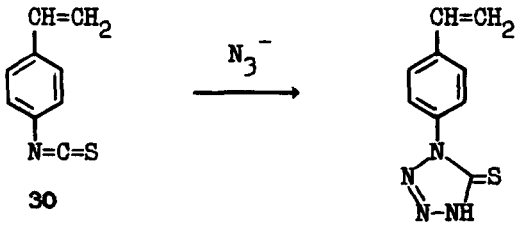
R = *t*-PrCH=CMe.

SCHEME 234

Subsequent treatment of the thiatriazole **944** with diazomethane in dry acetonitrile after standing overnight gave the *N*-methylated thiatriazole, 5-[methyl-(1,3-dimethylbut-1-enyl)-

amino]-1,2,3-thiatriazole **945** (identified by HNMR, mass and UV spectra). In this case no thiatriazole-tetrazole rearrangement occurs.[247]

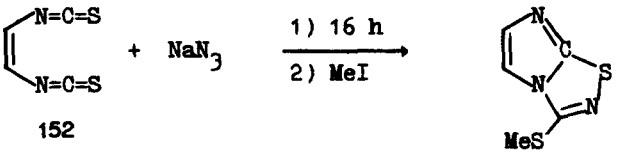
3.15.9. *With sodium azide* From 4-vinylphenyl isothiocyanate **30** and sodium azide in distilled water (N_2, 70–75 °C, 2 h) was obtained the desired 1-(4-vinylphenyl)-2-tetrazoline-5-thione **946** (Scheme 235).[248]



30 **946** (*70%*)

SCHEME 235

Loss of nitrogen occurred when sodium azide and vinylene diisothiocyanate **152** were allowed to react at room temperature in aqueous 1,2-dimethoxyethane leading, after methylation, to 3-methylthioimidazo[1,2-*d*][1,2,4]thiadiazole **947** (Scheme 236).[208]

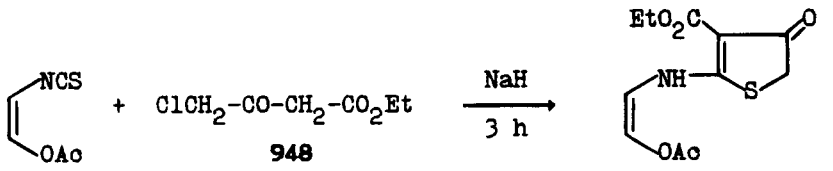


152 **947**

SCHEME 236

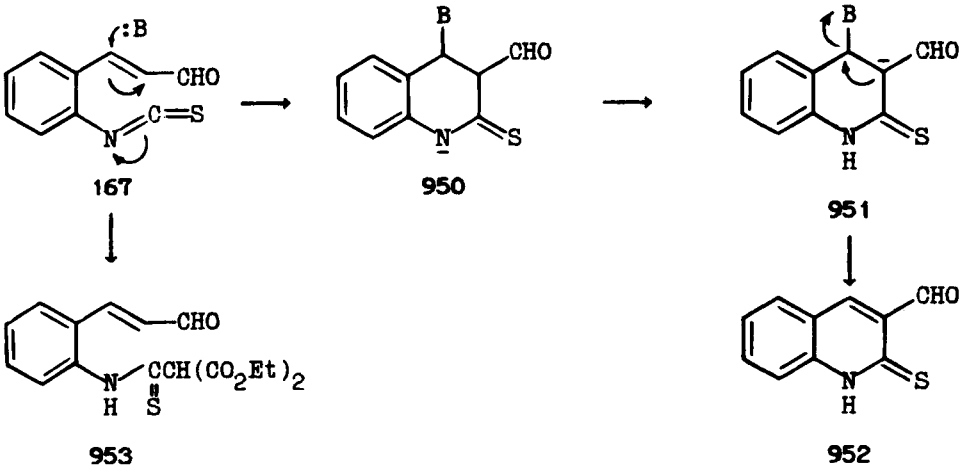
A similar reaction has been found to take place with 1,2-phenylene diisothiocyanate **802**.[249]

3.15.10. *With γ-chloroacetoacetic acid ethyl ester* When the carbanion of γ-chloroacetoacetic acid ethyl ester **948** was treated with 2-isothiocyanatovinyl acetate **157** in 1,2-dimethoxyethane, ethyl 2-(2-acetoxyvinylamino)-4,5-dihydro-4-oxothiophen-3-carboxylate **949** was obtained (Scheme 237).[85]



SCHEME 237

3.15.11. *With dialkyl sodio- or potassiomalonates* The action of a variety of nucleophiles towards 2-isothiocyanato-*trans*-cinnamaldehyde **167** was first examined by *Hull*.[93] Dilute alkali, in aqueous or alcoholic solution, alkoxides or tertiary bases gave 3-formylquinoline-2(1*H*)-thione **952** (Scheme 238). Serendipity played a role in the achievement of the best yields (92%).

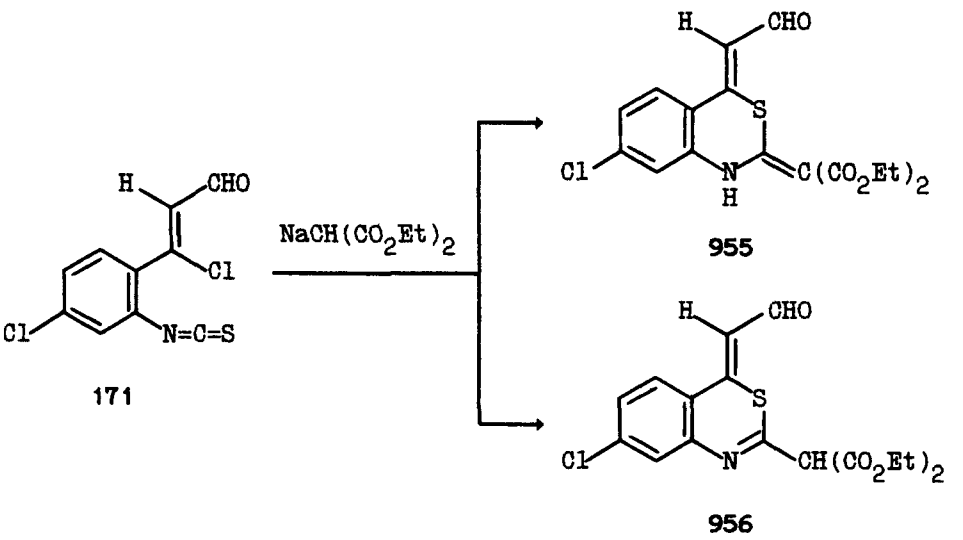


SCHEME 238

An attempt to obtain the thioamide **953** by conventional attack on the isothiocyanate group of **167** by malonate ion failed; instead 3-formylquinoline-2-(1*H*)-thione **952** was obtained (in dry benzene, room temperature, overnight) (Scheme 238).[93] To account for these results one could envisage an initial attack of the base at the β-carbon atom of the unsaturated aldehyde **167**, resulting in the tetrahydroquinoline **950** (a Michael type condensation) which, by charge transfer and elimination of base, yields the quinolinethione **952**.[93]

The reaction of diethyl sodiomalonate **954** with β,4-dichloro-2-isothiocyanatocinnamaldehyde **171** in *N,N*-dimethylformamide gave an ester which the authors of Ref.[91] regard as possessing the exomethylene structure **955**, 2-[bis(ethoxycarbonyl)methylene]-

7-chloro-4-(formylmethylene)-1,2-dihydro-4*H*-3,1-benzothiazine, rather than the tautomeric structure **956** (Scheme 239).



171 **955** **956**

SCHEME 239

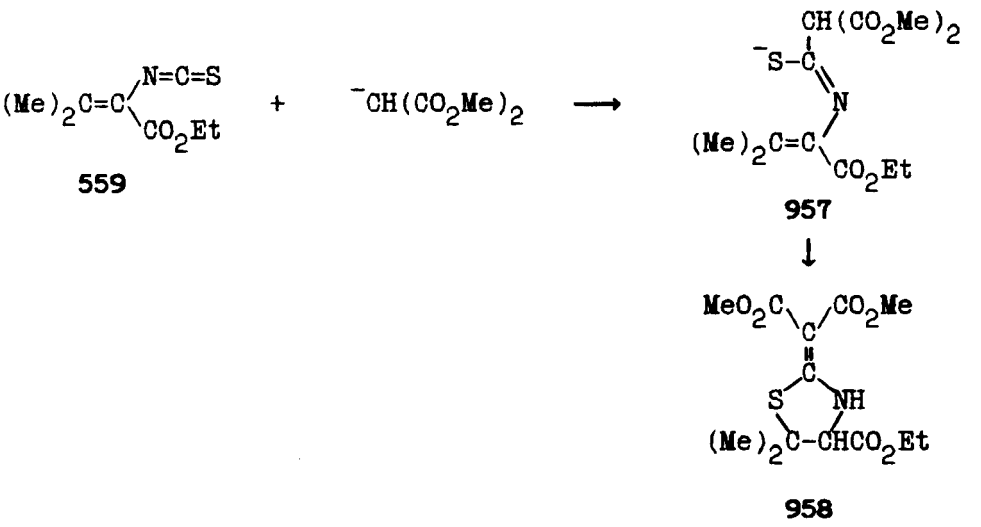
Dimethyl potassiomalonate adds to the N=C=S group of ethyl 2-isothiocyanato-3,3-dimethylacrylate **559** in THF under N_2 in the presence of potassium *tert*-butoxide at –70 °C (Scheme 240).[236] The resulting thioamide anion **957** yields, after cyclization (at 20 °C for 10 h), α-(4-ethoxycarbonyl-5,5-dimethyl-2-thiazolidinylidene)malonic acid dimethyl ester **958** (yield 82%).

Allenyl isothiocyanate **338** with diethyl sodiomalonate gave the corresponding thiazolidine derivative **959** (Scheme 241).[135]

3.15.12. *With malononitrile* Phenyl **189** and prop-1-enyl **960** isothiocyanate react with malonitriles **961** in *absol.* ethanol in the presence of sodium at room temperature for 0.5 h to give the α-cyanothioamides **962** as intermediates the subsequent treatment of which with chloroacetonitrile leads to the 4-amino-2-cyanomethylene-Δ^4-thiazolines **963** in 60–80% yield (Scheme 242).[250]

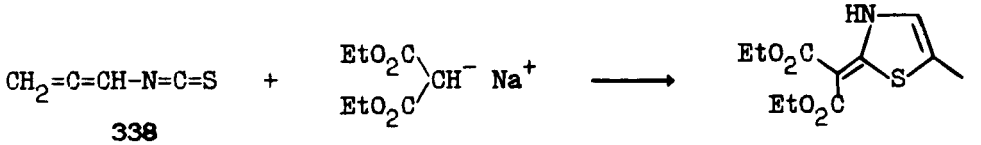
Allenyl isothiocyanate **338** with sodiomalononitrile gave the corresponding thiazolidine derivative **964** (Scheme 243).[135]

3.15.13. *With γ-haloacetoacetic acid p-toluidides* The γ-haloacetoacetic acid *p*-toluidides **965** react with an equimolar amount of phenyl isothiocyanate in dry dioxane at room temperature in the presence of sodium hydride for 5 h to yield the enaminothiophene de-



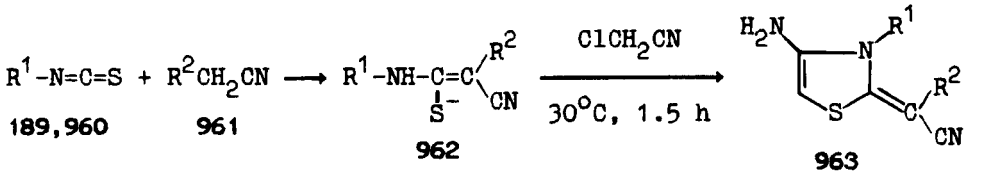
559 957 958

SCHEME 240



338 954 959 (82%)

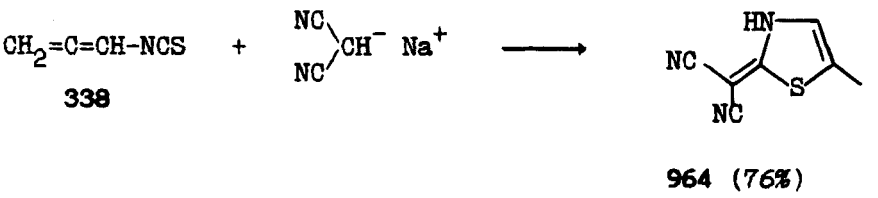
SCHEME 241



189, 960 961 962 963

R^1 = Ph (189), R^2 = CO_2Et; CN; R^1 = MeCH=CH (960), R^2 = CO_2Et.

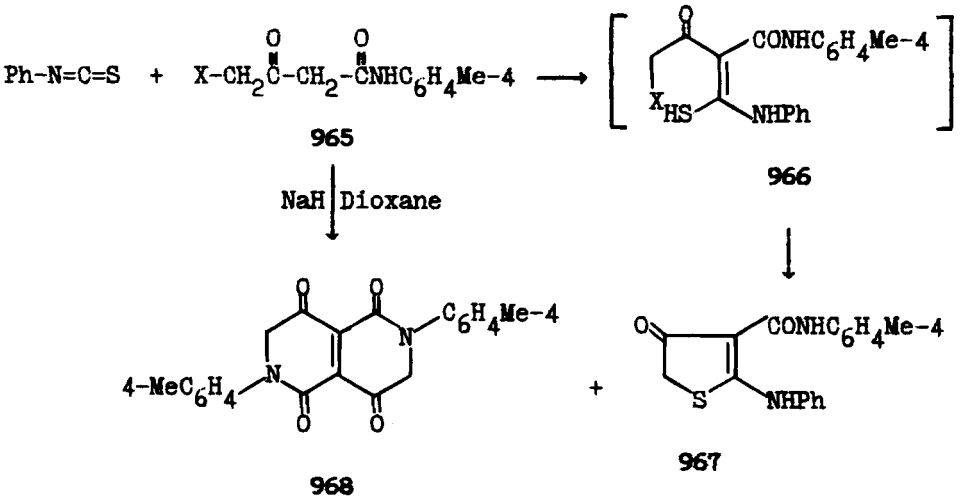
SCHEME 242



338 **964** (76%)

SCHEME 243

rivative **967** (65%) and **968**, the product of self-condensation of two molecules of γ-haloacetoacetic acid *p*-toluidide (< 10%) (Scheme 244).[251]



X = Br, I.

SCHEME 244

3.16. *Polymers and Their Applications*

Copolymers with good heat resistance can be prepared by copolymerization of monomers (and/or oligomers) including various polyfunctional aryl **969**, **971**, **974–982**, **984–994**, heteroaryl **970**, **983**, furyl **972** and thienyl **973** isothiocyanates.[252–254] Thermostable compositions which containing various polyfunctional monomeric and oligomeric aryl, heteroaryl, thienyl, cycloalkenyl isothiocyanates as components have been described in a patent.[255] Such compositions are useful as binders and adhesives.

An expanded listing of revised *Q* and *e* values for a variety of monomers, including vinyl isothiocyanate **142**, has been presented.[256]

The structural formulas, methods of synthesis and physico-chemical properties of α,β-unsaturated isothiocyanates are summarized in Table 5.

TABLE 5 α,β-Unsaturated Isothiocyanates

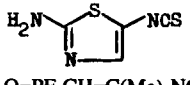
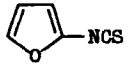
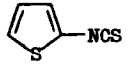
Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
1	—	$C_3H_2F_2NOPS$	$O{=}PF_2CH{=}CH{-}NCS$	$Cl_2P(O)CH{=}CHN{=}CCl_2$, NaF, hexamethyldisilthiane				263
2	**142**	C_3H_3NS	$CH_2{=}CH{-}NCS$	1) Thermal decomposition of 2-(*S*-phenyloxycarbonylthio)-ethyl isothiocyanate (1,2-dichlorobenzene, reflux under N_2, 2 h)	12	51–62/15 kPa or 24/13 kPa		167
				2) Addition of thiocyanic acid to acetylene in the presence of Hg(II) salts				143
				3) Dehydrohalogenation of 2-bromoethyl isothiocyanate with Et_3N	61	48/100 torr	1.5175	237
				4) From colza oil				197
				5) From vegetable oils				196
				Reactions, spectra				143,174,256, 261, 264–266
3	**152**	$C_4H_2N_2S_2$	SCN-CH=CH-NCS (*E*:*Z*)	Reaction of imidazole with $CSCl_2$ (CH_2Cl_2/H_2/H_2O, $CaCO_3$)	46	Oil (IR, ^{1}H NMR, MS)		84
				Reactions				208,232
4	**338**	C_4H_3NS	$CH_2{=}C{=}CH{-}NCS$	Gas-phase thermolysis of propargyl thiocyanate	95–100			133–135
5	—	$C_4H_3N_3S_2$						267
6	—	$C_4H_4F_2NOPS$	$O{=}PF_2CH{=}C(Me){-}NCS$	$Cl_2P(O)CH{-}CMeN{=}CCl_2$, NaF, hexamethyldisilthiane				263
7	**306**	C_4H_4ClNS	$ClCH_2CH{=}CH{-}NCS$	3-Chloro-1-chloropropene, KSCN (DMSO, room temp.); rearrangement (dioxane, reflux, 6 h)	74	40–41/0.25 (IR, ^{1}H NMR, Anal.)	1.5930	123
				Reactions				128

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
8	**507**	C_4H_4BrNS	$BrCH_2CH{=}CH\text{-}NCS$ (*cis/trans* = 3:1)	Radical bromination of allyl isothiocyanate by NBS (dibenzoyl peroxide, dry CBr_4, reflux, 1 h)	54.2	98–100/13.3 kPa (IR, ^{13}C NMR, MS, Anal.)		169
			(2:*E*)	Crystallized from the mixture on standing at –30 °C for several h		(24–28) (IR, ^{1} NMR, Anal.)		169
			(2:*Z*)	After separation of the, crystalline *trans*-3-bromo-1-propenyl isothiocyanate, the mixture contained 81% of *cis*-isomer and 19% of *trans*-isomer		(IR, ^{1}H NMR, Anal.)		169
9	**960**	C_4H_5NS	$MeCH{=}CH\text{-}NCS$	Reactions				250
10	**514**	C_4H_5NS	$CH_2{=}C(Me)\text{-}NCS$	1) α-Bromoisopropyl isothiocyanate, Et_3N, *absol.* pentane, autoclave, 100 °C, 2 h	63	(133–136) (IR, ^{1}H NMR, MS, Anal.)		172
				2) Isopropyl isothiocyanate, NBS (hν, pentane, 4 h); Et_3N (autoclave, 100 °C, 3 h)	65	(132–134)		172
11	—	C_5H_3NOS						268
12	**452**	$C_5H_3NS_2$		Pyrolysis of *S*-[*N*-(2-thenyl) carbamoyl]-*O,O'*-diethyl dithiophosphate (150 °C)	11	44/0.4 torr (yellow oil) (^{1}H NMR, Anal.)		62 220 269
				Reactions				62,220,269

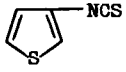
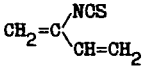
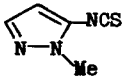
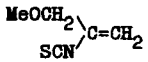
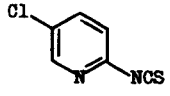
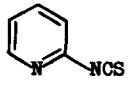
13	**453**	$C_5H_3NS_2$		Pyrolysis OF *S*-[*N*-(3-thenyl) carbamoyl]-*O,O'*-diethyl dithiophosphate (135–140 °C/18 torr)	34	(98–99) (Oil) (^{1}H NMR, Anal.	1.6771[25]	62
14	**602**	$C_5H_4N_2S_2$	SCN-CH_2CH=CH-NCS (2:Z)	3-Bromo-1-propenyl isothiocyanate, KSCN (dry acetone, 1 h)	44	(31–34) (IR, ^{1}H NMR, Anal.)		169
15	—	$C_5H_5NO_2S$	MeCH=C(NCS)COOH					202
16	**157**	$C_5H_5NO_2S$	$MeCO_2$CH=CH-NCS	2-Methyloxazole, $CSCl_2$ ($CaCO_3$, CH_2Cl_2/H_2O, ~20 °C, 16 h)	66	70–71/0.3 torr (^{1}H NMR, Anal.)		85
17	**340**	C_5H_5NS	MeCH=C=CH-NCS	[3,3]-Sigmatropic isomerization of the acetylenic thiocyanate				133–135
18	**341**	C_5H_5NS	CH_2=C=C(Me)-NCS	[3,3]-Sigmatropic isomerization of the acetylenic thiocyanate				133–135
19	**344**	C_5H_5NS		[3,3]-Sigmatropic isomerization of allenyl-methyl thiocyanate				133
20	—	$C_5H_5N_3S$						270
21	**387**	$C_5H_6ClHgNS$	ClHg(Me)C=C(Me)-NCS (2:*E*)	MeC≡CMe, $HgCl_2$, *aq.* HSCN (~3 M), ~25 °C	<5	Decomp. (IR, ^{1}H NMR)		140
22	**226**	C_5H_6ClNS	$ClCH_2$C(Me)=CH-NCS	1) 1-Methylcyclopropene, ClSCN ($CHCl_3$, −15 °C, in the dark)		1.5562 (IR, ^{1}H NMR, Anal.)		100
				2) ClCH=C(Me)CH_2SCN (dioxane, reflux, 6 h)	50	72–74/1.2 torr (IR, ^{1}H, ^{13}C NMR, MS)	1.5998	121–125, 128
23	**307**	C_5H_6ClNS	$ClCH_2$CH=C(Me)-NCS	1,3-Dichloro-2-methyl-1-propene, NH_4SCN (DMSO, 3 h); rearrangement (dioxane, reflux, 6 h)	29–50	90–92/12 torr (IR, ^{1}H NMR, Anal.)	1.5872	122, 123 128
24	**308**	C_5H_6ClNS	ClCH(Me)CH=CH-NCS	3-Chloro-1-chloro-1-butene, KSCN: rearrangement (dioxane, reflux, 6 h)	20	100–102/20 torr (IR, ^{1}H NMR, Anal.)	1.5882	122,123, 125,128

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
25	**599**	C_5H_6INS	$ICH_2C(Me)=CH\text{-}NCS$	1-Isothiocyanato-3-chloro-2-methyl-1-propene, NaI (acetone, ~ 20 °C, 10 h)		108–112/2.5 torr		121,122
26	**400**	C_5H_7NOS		$MeOCH_2C{\equiv}CH$, $HBF_4.Et_2O$, $n\text{-}Bu_4N^+SCN^-$, $Hg(SCN)_2$ (40 °C, 168 h)	10.5	(IR, ^1H NMR)		141
27	**219**	C_5H_7NS	$MeCH=C(Me)\text{-}NCS$ (2:*Z*)	1) Protodemercuration of $ClHg(Me)C=C(Me)\text{-}SCN$	30			140
			(*Z*)	2) $MeC=CMe$, $Hg(SCN)_2$, H_2SO_4, $n\text{-}Bu_4N^+SCN^-$ (20 °C, 240 h)	9.9	(IR, ^1H NMR)		142
				3) $MeCH=C(Me)NHC(S)SNa$, isopropyl chloroformate (H_2O, O °C, 45 min; Et_3N, 50 °C, 30 min)	54	78/60 torr (IR, ^1H NMR)		95
28	**218**	C_5H_7NS	$EtCH=CH\text{-}NCS$ (2:*Z*) (2:*E*)	$EtCH=CHNHC(S)SNa$, isopropyl chloroformate (H_2O, O °C, 45 min; Et_3N, 50 °C, 30 min)	65	77–78/50 torr (IR, ^1H NMR)		95
29	**270**	C_5F_7NS	$(CF_3)_2C=CF\text{-}NCS$	Reactions				247
				1) $(CF_3)_2C=CF_2$, KSCN (*absol.* PhCN, –78 °C)	66	(108) (IR, ^{19}F NMR, Anal.)	1.4222	114
				2) $(CF_3)_2C=CF_2$, KSCN (sulfolane, autoclave, 100°C, 20 h)	6			113
30	**772**	$C_6H_3ClN_2S$		Reactions				225
31	**751**	$C_6H_4N_2S$		Reactions				98,220

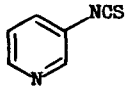
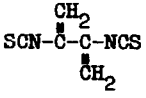
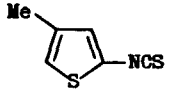
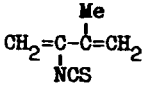
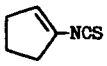
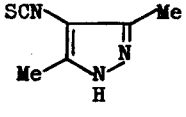
32	769	$C_6H_4N_2S$		Reactions				225
33	**347**	$C_6H_4N_2S_2$		3,3-Sigmatropic isomerization of 1,4-dithiocyanato-2-butyne				133,135
34	—	C_6H_5NOS	O=CHCH=CHCH=CH-NCS	1) Pyridine, $CSCl_2$ (CH_2Cl_2/H_2O, $BaCO_3$)				
	162		(*E,E*)	a) 0 °C, 25 min		(84.5–85.5) (Anal.)		88
	161		(*E,Z*)			(52–55) (Anal.)		88
			(*E,E*)	b) 5–10 °C, 1 h and 15 ° C,	6	(84–85)		87
			(2:*Z,E*) 1.5 h		8	(59–61) (Anal.)		87
35	—	$C_6H_5NS_2$						98
36	**601**	$C_6H_6N_2S_2$	$SCNCH_2C(Me)=CH$- NCS	1-Isothiocyanato-2-methyl-3-chloro-1-propene, NH_4SCN (DMSO, ~20 °C, 5 h); rearrangement (dioxane, Δ, 6 h)		120–122/0.5 torr	1.6420	121,122
37	**600**	$C_6H_6N_2S_2$	$NCS\text{-}CH_2C(Me)=CH\text{-}NCS$	1-Isothiocyanato-2-methyl-3-chloro-1-propene, NH_4SCN, DMSO				121,122
38	**345**	C_6H_7NS		[3,3]-Sigmatropic isomerization of the corresponding allenylmethyl thiocyanate				133,135
39	**369**	C_6H_7NS		2) *trans*-1-Isothiocyanato-2-(phenylseleno)cyclopentane, O_3 (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, Δ, 0.5 h)	43.5	(IR, ^1H NMR, Anal.)		136

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
				2) Cyclopentanone, $Si(NCS)_4$, $Zn(NCS)_2$, DME	52	52–58/14 torr (IR, (IR, ^{1}H NMR, Anal.)		184
40	**580**	$C_6H_7N_3S$		Reactions				189
41	**309**	C_6H_8ClNS	$ClCH_2C(Me)=C(Me)$-NCS	1-Chloro-3-chloro-2-methyl-2-butene, KSCN; rearrangement (dioxane, Δ, 6 h)	19	105–110/30 torr (IR, ^{1}H NMR, Anal.)	1.5405	122,123 125,128
42	**222**	C_6H_9NS	$Me_2C=C(Me)$-NCS	$(Me)_2C=C(Me)NHC(S)SNa$, isopropyl chloroformate (0 °C, 45 min; Et_3N, 50 °C, 0.5 h)	88	86–87/28 torr (IR)		95
43	**396**	C_6H_9NS	$CH_2=C$ (*n*-Pr)-NCS	1) *n*-PrC≡CH, Hg $(SCN)_2$, H_2SO_4, *n*-$Bu_4N^+SCN^-$ (35 °C, 10 h)	3.3	(^{1}H NMR		142,143
				2) *n*-PrC≡CH, $Hg(SCN)_2$, HBF_4 (~54% sol. in Et_2O), *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 48 h)	37.8	69/26 torr (IR, ^{1}H NMR, Anal.)		141
44	**532**	C_6H_9NS	$CH_2=C$(*i*-Pr)-NCS	1) 1-Bromo-3-methyl-2-butene, Me_3SiNCS (HMPA, ~20 °C)		(IR, ^{1}H NMR)		179
				24 h	37			
				48 h	27			
				72 h	23			
				120 h	15			

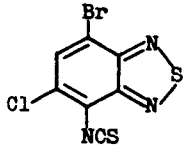
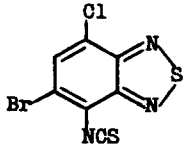
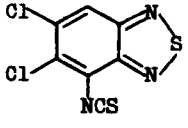
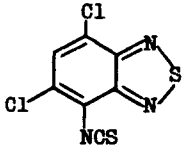
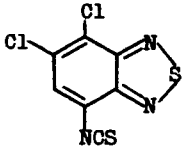
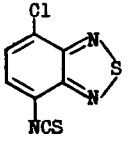
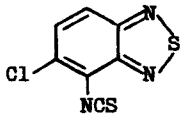
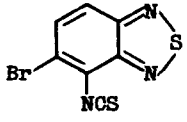
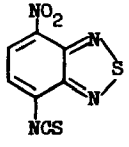
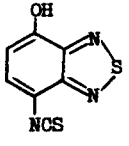
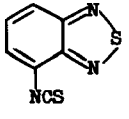
45	**79**	$C_7HClBrN_3S$		Amine, $CSCl_2$ (H_2O/HCl, ~20 °C)		70
46	**83**	$C_7HClBrN_3S$		Amine, $CSCl_2$ (H_2O/HCl, ~20 °C)		70
47	**80**	$C_7HCl_2N_3S$		Amine, $CSCl_2$ $CSCl_2$ (H_2O/HCl, ~20 °C)		70
48	**81**	$C_7CHl_2N_3S$		Amine, $CSCl_2$ (H_2O/HCl, ~20 °C)		70
49	**70**	$C_7HCl_2N_3S$		Amine, $CSCl_2$ (H_2O/HCl, ~20 °C)		70
50	—	$C_7H_2ClN_3S_2$		4-Amino-7-chloro-2,1,3-benzothiadiazole, $CSCl_2$ (HCl, 24 h)	(134–136)	70 271

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
51	**77**	$C_7H_2ClN_3S_2$		4-Amino-5-chloro-2,1,3-benzothiadiazole, $CSCl_2$ (HCl, 24 h)				70
52	**82**	$C_7H_2BrN_3S_2$		4-Amino-5-bromo-2,1,3-benzothiadiazole, $CSCl_2$ (HCl, 24 h)				70
53	**68**	$C_7H_2N_4O_2S_2$		4-Amino-7-nitro-2,1,3-benzothiadiazole, $CSCl_2$ (HCl, 24 h)				70
54	**849**	$C_7H_3Cl_2NS$	2,4-$Cl_2C_6H_3$-NCS	Reactions				238
55	**861**	$C_7H_3Cl_2NS$	3,4-$Cl_2C_6H_3$-NCS	Reactions				98
56	**844**	$C_7H_3Cl_2NS$	3,5-$Cl_2C_6H_3$-NCS	Reactions				237
57	**69**	$C_7H_3N_3OS_2$		4-Amino-7-hydroxy-2,1,3-benzothiadiazole, $CSCl_2$ (HCl, 24 h)				70
58	**21**	$C_7H_3N_3S_2$		4-Amino-2,1,3-benzothiadiazole, $CSCl_2$ (HCl/H_2O, ~20 °C)	32	(68–69)		63

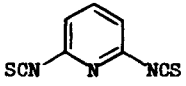
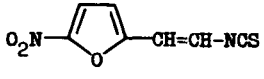
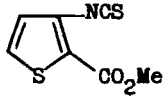
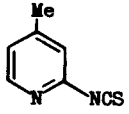
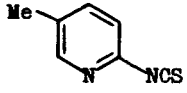
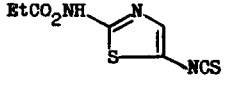
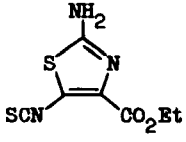
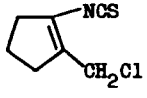
59	**28**	$C_7H_3N_3S_2$		1,6-Diaminopyridine, $CSCl_2$		(54–55)	63
60	**762**	C_7H_4FNS	2-FC_6H_4NCS	Reactions			223
61	**845**	C_7H_4FNS	4-FC_6H_4-NCS	Reactions			98,237,238
62	**857**	C_7H_4ClNS	2-ClC_6H_4-NCS	Reactions			98
63	**848**	C_7H_4ClNS	3-ClC_6H_4-NCS	Reactions			98,238
64	**193**	$C_{74}ClNS$	4-ClC_6H_4-NCS	Modified Kaluza synthesis, 72 h	70		96,220, 237,238
65	**194**	C_7H_4BrNS	4-BrC_6H_4-NCS	Modified Kaluza synthesis, 3–4 d	73		96,212, 237,238
66	**999**	C_7H_4INS	4-IC_6H_4-NCS				63,247
67	**683**	$C_7H_4N_2O_2S$	4-$NO_2C_6H_4$-NCS	Reactions			10,238
68	**444**	$C_7H_4N_2O_3S$		5-Nitro-2-furylvinylene-*N*-iminotriphenylphosphorane, CS_2 (Ar, 100 °C)		(87–91) (IR, ^1H NMR, MS, Anal.)	155
				a) autoclave, 6 h	80		
				b) toluene, 50 h	60	(87–92)	
				c) 100 h	45	(87–90)	
69	**101**	$C_7H_5NO_2S_2$		3-Amino-2-thiophenecarboxylic acid methyl ester hydrochloride, $CSCl_2$ ($CCl_4/H_2O/Na_2CO_3$, –20 °C, 1.5 h		(60–61)	75
70	**189**	C_7H_5NS	Ph-NCS	Modified Kaluza synthesis, 24 h			96
				Reactions			10,147,212, 224,238,245
71	**4**	$C_7H_6N_2O_2S_2$	4-$H_2NSO_2C_6H_4$-NCS	Amine, $CSCl_2$		(215–216)	63,237
72	**770**	$C_7H_6N_2S$		Reactions			225
73	**771**	$C_7H_6N_2S$		Reactions			225

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
74	**382**	$C_7H_7NO_4S$	$MeCO_2$–C(NCS)=$CHCO_2Me$ (*Z*/*E* = 97:3)	$MeCO_2C{\equiv}CCO_2Me$, KSCN, H_2SO_4/H_2O (benzene, ~20 °C, 24 h); (MeCN, KSCN, Δ, 6 h)	58	119/0.4 torr (IR, ^{1}H NMR,Anal.)		137,142
				Reactions				137,142,219
75	—	$C_7H_7N_3O_2S_2$						267
76	**265**	$C_7H_7N_3O_2S_2$		Ethyl 2-amino-4-thiazole-carboxylate, KSCN (*absol.* MeOH, N_2, –5 °C; Br_2/MeOH/NaBr, –5–10 °C)	98	(178)		110
77	**313**	C_7H_8ClNS		2-Chloromethyl-1-chloro-cyclopentene, KSCN	55	95–97/1 torr (IR, ^{1}H-NMR, Anal.)	1.5860	123 128
78	**287**	$C_7H_9NO_2S$	Me_2C(NCS)–CO_2Me	1) 1-Bromo-1-isothiocyanato-isopropylmethyl methyl ester (*absol.* CCl_4, Et_3N, 3 h)	83	56–58/0.1 torr (^{1}H NMR)		172
				2) Isothiocyanatoacetic acid methyl ester, acetone, NaH or *t*-BuOK, N_2; THF, diphenyl chlorophosphate, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, THF, 20 °C, 15 min	41 51[a]	(17) (IR, ^{1}H NMR, Anal.)		187
			(*E*)	3) $MeCO_2CH$=C(Me)CH_2Br, KSCN, EtOH: distillation (143–153 °C/50 torr)	33[b]			119

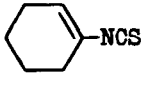
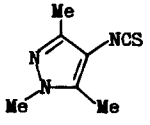
79	**286**	$C_7H_9NO_2S$	$MeCH(NCS)CO_2Et$	1) Isothiocyanatoacetic acid ethyl ester, acetaldehyde, NaH or *t*-BuOK, N_2; THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 1 h	29	60/0.2 torr (IR, ^1H NMR, Anal.)	187
			(*Z*/*E* = 95/ < 5)				
			(*E*)	2) $EtCO_2CH{=}CHCH_2Br$, KSCN, EtOH; distillation (128–134 °C/24 *mm*)	76	(IR, ^1H NMR)	119
80	**370**	C_7H_9NS		1) α-Bromocyclohexyl isothiocyanate, ET_3N (CCl_4, 2 h)	79	92–94/13 torr (IR, ^1H NMR, MS, Anal.)	172 184
				2) Cyclohexyl isothiocyanate, NBS (hν, CCl_4, N_2, 3 h; CCl_4, *absol.* Et_3N, 1.5 h)	92	92–94/13 torr	172
				3) *trans*-1-Isothiocyanato-2-(phenylseleno)cyclohexane, O_3 (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.16 h)		(IR, ^1H NMR, Anal.)	136
				4) Cyclohexanone, $Si(NCS)_4$ (25 °C, THF)			184
				a) $(Me_3SiO)_2SO_2$-*n*-Bu_3SnF	98		
				b) $Zn(NCS)_2$	80		
				c) $ZnBr_2$	30		184
				d) $EtAlCl_2$	40		184
81	—	$C_7H_9N_3S$					272
82	**311**	$C_7H_{10}ClNS$	$ClCH_2CH{=}C(i\text{-}Pr)\text{-}NCS$	1-Chloro-1-isopropyl-3-thiocyanato-1-propene (dioxane, Δ, 6 h)			122,217
83	**310**	$C_7H_{10}ClNS$	$ClCH(Me)C(Me){=}CH\text{-}NCS$ (Me on C)	1-Chloro-1,2,3-trimethyl-3-thiocyanato-1-propene (dioxane, Δ, 6 h)			122

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
84	**388**	$C_7H_{10}ClHgNS$	EtC=C(Et)HgCl ↓ NCS	EtC≡CEt, $HgCl_2$, NH_4SCN, H_2SO_4, ~20 °C, 120 h	27	(95) (IR, ^1H NMR)		139,140
			(*Z*/*E* = ≥ 90/10)					
			(2:*E*)					141
85	---	$C_7H_{11}NOS$	$EtOCH_2C(Me)$=CH-NCS	SCN-CH=C(Me)CH_2Cl, EtOH				124
86	**378**	$C_7H_{11}NS$	*t*-BuCH=CH-NCS	Ozonization of *trans*-1-isothiocyanato-2-(phenylseleno)-heptane (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.16 h)	67	(IR, ^1H NMR, Anal.)		136
87	**391**	$C_7H_{11}NS$	EtCH=C(Et)-NCS	1) *erythro*-3-Iodo-4-isothiocyanatohexane, Adogen 464, $Na_2S·9H_2O$ ($CHCl_3$/H_2O, 20 °C, 0.5 h)	trace			175
			(2:*E*) (2:*Z*) (*Z*/*E* = ~90/10)	48 h	100	82/13 torr		
				2) ClHg (Et)C=C(Et)-NCS, Ph_3P, $HBF_4·Et_2O$ (CH_2Cl_2, 40 °C, 15 min)				140
			(*Z*/*E* = 88/12)	3) EtC≡CEt, $Hg(SCN)_2$, H_2SO_4, *n*-$Bu_4N^+SCN^-$ (40 °C, 46 h)	49.8	84/25 torr (IR, ^1H NMR)		142
			(*Z*/*E* = ~90/10)	4) EtC≡CEt, $Hg(SCN)_2$, HBF_4 (~54% sol. in Et_2O), *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 48 h)	60	82/13 torr (IR, ^1H NMR, Anal.)		141
88	**397**	$C_7H_{11}NS$	CH_2=C(*n*-Bu)-NCS	1) *n*-BuC≡CH, $Hg(SCN)_2$, H_2SO_4, *n*-$Bu_4N^+SCN^-$ (40 °C, 4 h)	3.5	(IR, ^1H NMR)		142 246
				2) *n*-BuC≡CH, $Hg(SCN)_2$, HBF_4 (~54% sol. in Et_2O), *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 42 h)	51.2	82/25 torr (IR, ^1H NMR, Anal.)		141
89	**399**	$C_7H_{11}NS$	CH_2=C(*t*-Bu)-NCS	1) *t*-BuC≡CH, $Hg(SCN)_2$, H_2SO_4, *n*-$Bu_4N^+SCN^-$ (40 °C, 30 h)	18.9	78–84/31 torr (IR, ^1H NMR)		142
				2) *t*-BuC≡CH, $Hg(SCN)_2$,	42	70/25 torr		141

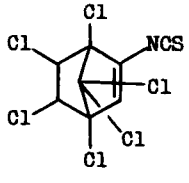
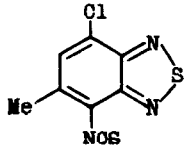
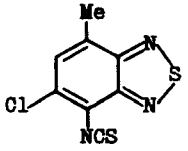
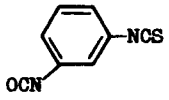
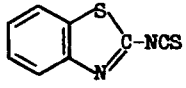
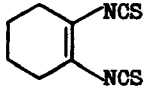
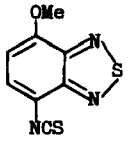
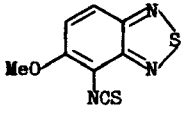
				HBF_4 (~54% sol. in Et_2O), n-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 30 h)		(IR, ^1H NMR, Anal.)		143,246
90	**402**	$C_7H_{11}NS$	n-PrCH=C(Me)-NCS (Z/E = 85/15)	MeC≡CPr-n, $Hg(SCN)_2$, H_2SO_4, n-$Bu_4N^+SCN^-$ (40 °C, 65 h)	14.8	(^1H NMR)		142
91	**401**	$C_7H_{11}NS$	MeCH=C(n-Pr)-NCS (Z/E = ~85/15)	MeC≡CPr-n, $Hg(SCN)_2$, H_2SO_4, n-$Bu_4N^+SCN^-$ (40 °C, 65 h)	15.4	(^1H NMR)		142,
92	**221**	$C_7H_{11}NS$	i-PrCH=C(Me)-NCS (2:Z)	i-PrCH=C(Me)NHC(S)SNa, isopropyl chloroformate, (0 °C, 45 min; Et_3N, 50 °C, 30 min)	76	66/12 torr (IR, ^1H NMR)		95,247
93	**223**	$C_7H_{11}NS$	EtC(Me)=C(Me)-NCS (2:Z)	Etc (Me)=C(Me)NHC(S)SNa, isopropyl chloroformate (0 °C, 45 min; Et_3N, 50 °C, 30 min)	82	86–87/18 torr (IR)		95
94	**604**	$C_7H_{11}NS_2$	$EtSCH_2C(Me)$=CH-NCS	1-Isothiocyanato-3-chloro-2-methyl-1-propene, toluene, EtSNa in EtOH, 5 h	40	60–62/0.1 torr (IR, ^1H NMR, MS, Anal.)	1.5938	121,123
95	**540**	$C_7H_{13}NO_2SSi$	$Me_3SiOC(OMe)$=CH-NCS (2:Z)	$MeCO_2CH_2NCS$, $CF_3SO_3SiMe_3$ (Et_3N, 0–20 °C, 6 h)	71	56–57/0.01 torr (^1H NMR, Anal.)		183
96	**862**	$C_8H_3F_3ClNS$	3-CF_3-4-Cl-C_6H_3-NCS	Reactions				98
97	**1000**	$C_8H_3Cl_6NS$						262
98	**858**	$C_8H_4F_3NS$	2-CF_3-C_6H_4-NCS	Reactions				98,223
99	**859**	$C_8H_4F_3NS$	3-CF_3-C_6H_4-NCS	Reactions				98
100	**860**	$C_8H_4F_3NS$	4-CF_3-C_6H_4-NCS	Reactions				98
101	**72**	$C_8H_4ClN_3S_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C				70,271

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
102	**78**	$C_8H_4ClN_3S_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C)				70
103	—	$C_8H_4CN_2OS$		Reactions				193
104	**20**	$C_8H_4N_2S_2$		Amine, $CSCl_2$	92	(93–94)		63
105	**802**	$C_8H_4N_2S_2$		Reactions				232
106	**67**	$C_8H_5N_3OS_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20°C)				70
107	**76**	$C_8H_5N_3OS_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C)				70

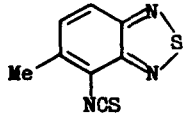
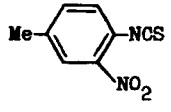
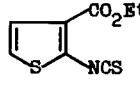
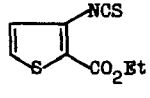
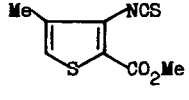
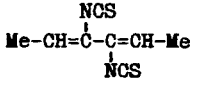
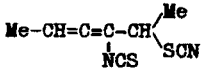
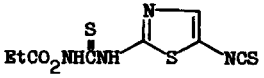
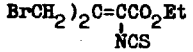
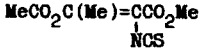
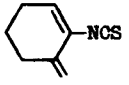
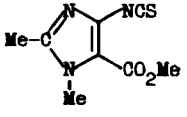
108	**66**	$C_8H_5N_3S_2$		Amine, $CSCl_2$ (HCl/H_2O ~20 °C)			70
109	**71**	$C_8H_5N_3S_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C)			70
110	**749**	$C_8H_6N_2O_2S$		Reactions			220
111	**195**	C_8H_7NOS	2-$MeOC_6H_4$-NCS	Modified Kaluza synthesis	82		98,273
112	**199**	C_8H_7NOS	4-$MeOC_6H_4$-NCS	Modified Kaluza synthesis	92		10,237
113	**105**	$C_8H_7NO_2S_2$		2-Amino-3-thiophenecarboxylic acid ethyl ester, $CSCl_2$ ($CHCl_3/H_2O/NaHCO_3$)		(43–44)	76
114	**103**	$C_8H_7NO_2S_2$		3-Amino-2-thiophenecarboxylic acid ethyl ester, $CSCl_2$ ($CHCl_3/H_2O/NaHCO_3$)		(60–61)	76
115	**102**	$C_8H_7NO_2S_2$		3-Amino-4-methyl-2-thiophenecarboxylic acid methyl ester hydrochloride, $CSCl_2$, ($CHCl_3/H_2O/NaCO_3$, 1.5 h)		(227–228)	75
116	**190**	C_8H_7NS	2-MeC_6H_4-NCS	Modified Kaluza synthesis, 24 h	81		96
117	**191**	C_8H_7NS	3-MeC_6H_4-NCS	Modified Kaluza synthesis, 24 h	80		96
118	**192**	C_8H_7NS	4-MeC_6H_4-NCS	Modified Kaluza synthesis, 24 h			98
119	**864**	$C_8H_7NS_2$	4-$MeSC_6H_4$-NCS	Reactions			98
120	**866**	$C_8H_8N_2O_2S_2$	3-$MeSO_2NHC_6H_4$-NCS	Reactions			98
121	**865**	$C_8H_8N_2O_2S_2$	4-$MeSO_2NHC_6H_4$-NCS	Reactions			98

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
122	**350–352**	$C_8H_8N_2S_2$		[3,3]-Sigmatropic isomerization of 2,5-di thiocyanatohex-3-yne				133,135
123	**349**	$C_8H_8N_2S_2$		[3,3]-Sigmatropic isomerization of 2,5-di thiocyanatohex-3-yne				133,135
124	—	$C_8H_8N_4O_2S_3$		Ethoxycarbonyl isothiocyanate, 4,5-substituted 2-aminothiazole				267
125	**572**	$C_8H_9Br_2NO_2S$		$Me_2C{=}C(NCS)CO_2Et$ in CCl_4, NBS, dibenzoyl peroxide, reflux, 2.5 h	95	(IR, ^{1}H NMR, Anal.)		188
126	**288**	$C_8H_9NO_4S$	 (2:*E*) (2:*Z*)	$MeCO_2CH{=}C(CO_2Me)CH_2Br$, KSCN, EtOH; distillation (200 °C/35 torr)	10			119
127	**317**	C_8H_9NS		1-Chloro-2-(chloromethyl)-cyclohexene, KSCN (DMSO, 50 °C)	42	76–80/1 torr (IR, ^{1}H NMR, UV, MS)	1.5662	126,127
128	**85**	$C_8H_9N_3O_2S$		4-Amino-1,2-dimethylimidazole-5-carboxylic acid methyl ester in HCl, $CSCl_2$, ($H_2O/CH_2Cl_2/CaCO_3$, 2 h)	70	(82–84) (IR, ^{1}H NMR, Anal.)		71

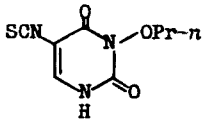
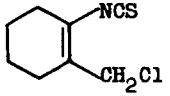
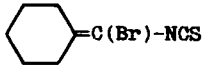
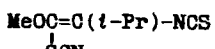
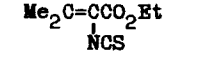
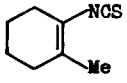
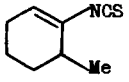
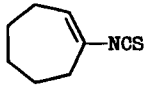
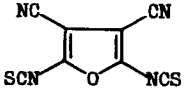
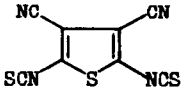
129	**995**	$C_8H_9N_3O_3S$		Reactions				259
130	**408**	$C_8H_{10}HgN_2S_2$	NCS-HgCH=C(*n*-Bu)-NCS	*n*-Bu-C≡CH, $Hg(SCN)_2$, *n*-$Bu_4N^+SCN^-$, CH_2Cl_2	46			141
131	**409**	$C_8H_{10}HgN_2S_2$	NCS-HgCH=C(*t*-Bu)-NCS	*t*-Bu-C≡CH, $Hg(SCN)_2$, *n*-$Bu_4N^+SCN^-$, CH_2Cl_2				141
132	**314**	$C_8H_{10}ClNS$		1-Chloro-2-chloromethyl-cyclohexene, KSCN (DMSO, ~20 °C)	55	85–90/0.7 torr (IR, ^1H NMR, Anal.)	1.5885	123 128,210
133	**505**	$C_8H_{10}BrNS$		Cyclohexylmethyl isothiocyanate, NBS (CCl_4, hν, 22 °C)				168
134	**421**	$C_8H_{10}N_2OS_2$		Ph_3P=C (OMe)C(O)Pr-*i*, $(SCN)_2$	50	65–70/0.05 torr (IR, ^1H NMR, Anal.)		145
135	**410**	$C_8H_{10}N_2S_2$ (2:*E*)	NCS-CH=C(*t*-Bu)-NC) 2 isomers (60/40 (2:*Z*)	1) *t*-Bu-C≡CH, 2 $Hg(SCN)_2$, *n*-$Bu_{44}N^+SCN^-$ (CH_2Cl_2, 40 °C, 40 h)	36	102/1 torr (IR, ^1H, ^{13}C, NMR, MS)		141
				2) *t*-BuC(NCS)=CH-HgSCN, $(SCN)_2$ (C_6H_6, ~20 °C, 4 h)				140
136	**559**	$C_8H_{11}NO_2S$		1) 5,5-Dimethyl-2-thioxo-1,3-oxazolidine-4-carboxylic acid ethyl ester, THF, NaH, 20–30 °C, 0.5 h; $(PhO)_2P(O)Cl$; –60 °C, *t*-BuOK, 20 °C, 15 min	67	(34–35)		185,186, 188
				2) Isothiocyanatoacetic acid or ethyl ester, acetone, NaH or *t*-BuOK, N_2;THF, diphenyl chlorophosphate, 20–30 °C, 0.5 h; –60 °C, Reactions	67	(34-35) (IR, ^1H NMR, Anal.)		187 23,236, 239,240

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
137	**546**	$C_8H_{11}NS$		2-Methylcyclohexanone, $Si(NCS)_4$, THF, $(Me_3SiO)_2SO_2$, *n*-Bu_3SnF	96	Oil		184
138	**547**	$C_8H_{11}NS$						184
139	**371**	$C_8H_{11}NS$		1) Ozonization of *trans*-1-isothiocyanato-2-(phenylseleno)cycloheptane (CH_2Cl_2, −78 °C, 0.5 h; CCl_4, reflux, 0.16 h)	47.2	(IR, ^{1}H NMR, Anal.)		136
				2) Cycloheptanone, $Si(NCS)_4$ $(Me_3SiO)_2SO_2$, *n*-Bu_3SnF, 25 °C, in:		87–93/12 torr (IR, ^{1}H NMR, MS, Anal.)		184
				THF	49			
				DME	80			
				Dioxane	76			
				CH_2Cl_2	25			
				$CHCl_3$	12			
140	**972**	$C_8N_4OS_2$		Polymers				253,254
141	**973**	$C_8N_4S_3$		Polymers				253,254
142	**764**	$C_9H_3F_6NS$	3,5-$(CF_3)_2C_6H_3$-NCS	Reactions				223

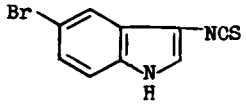
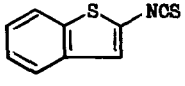
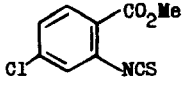
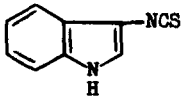
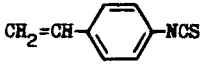
143	**202**	$C_9H_5BrN_2S$		5-Bromo-3-aminoindole, EtONa, *absol.* EtOH, CS_2, (~20 °C, 1 h)	64	(MS, Anal.)		97
144	**500**	$C_9H_5Br_2NS$	Br_2C=C(Ph)-NCS`	Bromination of 1-phenyl-1-isothiocyanato-2-bromo-ethene with following dehydrobromination				168
145	**415**	$C_9H_5I_2NS$	I_2C=C(Ph)-NCS	1-Iodo-2-phenylacetylene, bis(pyridine)iodine tetrafluoroborate, NCS (H_2O/ dioxane,~20 °C, 60 h)	75			144
146	**212**	$C_9H_5NS_2$		2-Amino-benzo[*b*]thiophene, *absol.* toluene, CS_2, Et_3N, 0–5 °C, 3 d, N_2; $CHCl_3$, Et_3N, 0 °C, $ClCO_2Et$, ~20 °C, 1 h		Oil	98 (IR, ^{1}H.NMR)	
147	**863**		3-CF_3-4-MeO-C_6H_3-NCS	Reactions				98
148	**117**	$C_9H_6ClNO_2S$		Appropriate amine and $CSCl_2$				76
149	**112**	$C_9H_6ClNO_2S$		Appropriate amine and $CSCl_2$				76
150	**138**	C_9H_6ClNS (2:*E*)	4-ClC_6H_4CH=CH-NCS (*E*/*Z* = 3.4)	2-Chloro-2-(4-chloro-phenyl)ethyl isothiocyanate, Et_3N, (dioxane, 100°C, 24 h)	76.2	105/18.7 Pa (67–74) (IR, ^{1}H NMR, UV, Anal.) (104–106)		80 80
151	**498**	C_9H_6BrNS (2:*E*)	BrCH=C(Ph)-NCS	Bromination of 1-phenyl-1-isothiocyanatoethene with following dehydrobromination		(IR, ^{1}H NMR, MS)		168
152	**139**	$C_9H_6N_2O_2S$	4-$NO_2C_6H_4CH$=CH-NCS (2:*E*)	2-Chloro-2-(4-nitrophenyl)-ethyl isothiocyanate, Et_3N (dioxane, 100 °C, 8 h)	6.12	(160–162) (IR, ^{1}H NMR, UV, Anal.)		80
				Reactions				243
153	**201**	$C_9H_6N_2S$		3-Aminoindole, CS_2, *absol.* EtOH, ~20 °C:		(80–81 (IR, MS, Anal.)		97
				EtONa, 1 h	60			97
				KOH/H_2O, 2 h	3			

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
				Ac_2O, 1 h	6			
154	**682**	C_9H_7NOS	4-$MeC(O)C_6H_4$-NCS	Reactions				10,238
155	**111**	$C_9H_7NO_2S$	2-$MeCO_2C_6H_4$-NCS	Appropriate amine and $CSCl_2$				76
156	**130**	C_9H_7NS	PhCH=CH-NCS	1) 1-Phenyl-1-chloroethyl ammonium chloride, $CSCl_2$ ($CHCl_3/H_2O$/NaOH); (N_2, Et_3N, dioxane, 100 °C, 36 h)	67	83–86/0.25 (IR, ^{1}H NMR, UV, Anal.)101–102/ 130 Pa)		79 178 243
			E/*Z* = 4) (*E*/*Z* = 56:44)	2) $(Me_3Si)_2CHNCS$, PhCHO, *n*-Bu_4NF, THF,.N_2, ~20 °C, 8 h)	31	(IR, ^{1}H NMR, MS)		177,178
				3) $(Me_3Si)_3CNCS$,.PhCHO, *n*-Bu_4NF, THF, N_2, ~20 °C, 24 h)	6			178
				Reactions				79, 212,243
157	**30**	C_9H_7NS		4) Vinylphenylamine, $CSCl_2(CH_2Cl_2/H_2O/CaCO_3)$	37.3	129–130/12 77/0.25 IR, UV, ^{1}H NMR, Anal.)	1.6792	64
158	**377**	C_9H_7NS	CH_2=C(Ph)-NCS	1) Me(Ph)CHNCS, NBS (hv, 22 °C, CCl_4); (-HBr, 40 h)		(^{1}H NMR)		168
				2) Ozonization of *trans*-1-iso thiocyanato-1-phenyl-2-(phenylseleno)ethane (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.16 h)	27	(^{1}H NMR)		136 143
				3) PhC≡CH, $Hg(SCN)_2$, HBF_4 (~54% sol. in Et_2O), *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 40 h)	24.3	(IR, H NMR)		141 246
				4) Dehydroiodination of 1-iodo-2-phenyl-2-isothi ocyanato-ethane (*t*-BuOK, *absol.* ether, 20 °C, 2 h)	54	Orange oil (IR, ^{1}H NMR, MS)		176 141

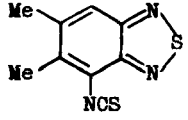
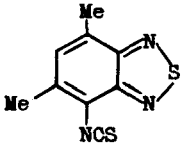
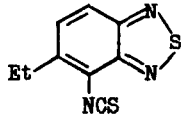
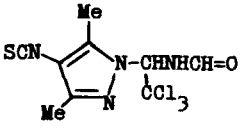
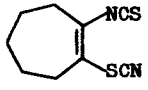
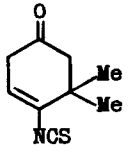
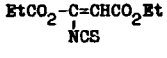
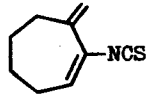
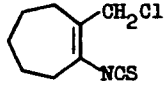
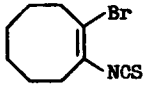
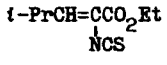
159	**901**	$C_9H_7N_2O_2S$	4-$NO_2C_6H_4$-CH=CH-NCS	Reactions				243
160	**73**	$C_9H_7N_3S_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C)				70
161	**74**	$C_9H_7N_3S_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C)				70
162	**75**	$C_9H_7N_3S_2$		Amine, $CSCl_2$ (HCl/H_2O, ~20 °C)				70
163	**868**	$C_9H_8N_2OS$	3-$MeCONHC_6H_4$-NCS	Reactions				98
164	**867**	$C_9H_8N_2OS$	4-$MeCONHC_6H_4$-NCS	Reactions				98
165	**582**	$C_9H_9Cl_3N_4OS$		Condensation of 3,5-dimethyl-4-isothiocyanatopyrazole and *N*-(1-chloro-2,2,2-trichloroethyl)-formamide, Et_3N, acetone, ~20 °C, 1 h				189
166	**196**	C_9H_9NOS	4-$EtOC_6H_4$-NCS	Modified Kaluza synthesis	88			96
167	**107**	$C_9H_9NO_2S_2$		2-Amino-5-methyl-3-thiophenecarboxylic acid ethyl ester, $CSCl_2$ ($CHCl_3/H_2O$/$NaHCO_3$)		(45–46)		76
168	**763**	C_9H_9NS	2,5-$Me_2C_6H_3$-NCS	Reactions				223
169	**997**	C_9H_9NS	2-EtC_6H_4-NCS		64.6	124/24 torr	1.6212	260
170	**998**	C_9H_9NS	4-EtC_6H_4-NCS		45.4	143–144/24 torr	1.6220	260
171	**850**	$C_9H_{10}N_2S$	3-$Me_2NC_6H_4$-NCS	Reactions				238
172	**197**	$C_9H_{10}N_2S$	4-$Me_2NC_6H_4$-NCS	Modified Kaluza synthesis	60			96

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
173	**429**	$C_9H_{10}N_2S_2$		2-(Triphenylphosphoranylidene)cycloheptanone, $(SCN)_2$	60	Oil (IR, ^1H, ^{13}C NMR, MS, Anal.)		146
174	**292**	$C_9H_{11}NOS$		4-Bromo-5,5-dimethyl-2-cyclohexen-1-one, KSCN, (acetonitrile, dibenzo-18-crown-6, reflux)	43	(IR, ^1H NMR)		119
175	**383**	$C_9H_{11}NO_4S$		$EtCO_2C{\equiv}CCO_2Et$, KSCN, H_2SO_4, (benzene, ~20 °C, 24 h; *absol.* MeCN, KSCN, reflux, 6 h)	68	108/0.2 torr (IR, ^1H NMR, Anal.)		137
176	**318**	$C_9H_{11}NS$		1-Chloro-2-(chloromethyl)-cyclopentene, KSCN	35	94/0.6 torr (IR, ^1H NMR, UV, MS)	1.5660	126
177	**315**	$C_9H_{12}ClNS$		2-(Chloromethyl)-1-chloro-cycloheptene, KSCN	71	100-104/0.2 torr (IR, ^1H NMR, Anal.)	1.6000	123 128
178	**496**	$C_9H_{12}BrNS$		Cyclooctenyl isothiocyanate, Br_2	78	(98–100) (IR, ^1H NMR, MS, Anal.)		168
179	**556**	$C_9H_{13}NO_2S$		Isothiocyanatoacetic acid ethyl ester, isobutyraldehyde, NaH or *t*-BuOK, N_2;	60	60/0.2 torr (IR, ^1H NMR, UV, Anal.)		185 187

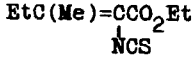
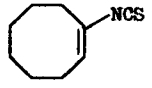
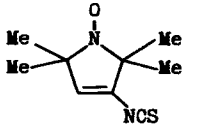
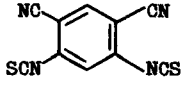
			(2:*Z*) (*Z*/*E* = 95 < 5)	THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min; –60 °C, $MeCO_2H$; NaH, CS_2, 30 °C, 1 h			
180	**560**	$C_9H_{13}NO_2S$ (*Z*/*e* = 55/45) (2:*Z*) (2:*E*)		Isothiocyanatoacetic acid ethyl ester, butan-2-one, NaH or *t*-BuOK, N_2; THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min	51 75[a]	Oil (IR, ^{1}H NMR, Anal.)	187
181	**372**	$C_9H_{13}NS$		1) Cyclooctanone, $Si(NCS)_4$, $Zn(NCS)_2$, DME	66	75-83/3 torr (IR, ^{1}H NMR, Anal.)	184
				2) *trans*-1-Isothiocyanato-2-(phenylseleno)cyclooctane, O_3 (CH_2Cl_2, -78 °C, 0.5 h; CCl_4, reflux, 0.5 h)	71.4	(IR, ^{1}H NMR, Anal.)	136
				3) Cyclooctyl isothiocyanate, NBS (*absol.* CCl_4, N_2, hν, 22 °C, 4 h)			168
182	—	$C_9H_{13}N_{2.z}OS$					274
183	**374**	$C_9H_{15}NS$	*n*-PrCH=C(*n*-Pr)-NCS (*Z*/*E* = >99:<1) (*Z*/*E* = 11:89) (2:*E*) (2:*Z*)	1) *erythro*-1-Isothiocyanato-2-(phenylseleno)octane, O_3 (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.16 h)	71.4	(IR, ^{1}H NMR, Anal.)	136
				2) *threo*-1-Isothiocyanato-2-(phenylseleno)-4-octane, O_3 (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.16 h)	35.4	(IR, ^{1}H NMR, Anal.)	136
				3) *erythro*-4-Iodo-5-isothiocyanatooctane, Adogen 464, $Na_2S·9H_2O$ ($CHCl_3/H_2O$, ~20 °C, 1 h)	15	67/2 torr (IR, ^{1}H NMR, MS, Anal.)	175 140

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
184	**376**	$C_9H_{15}NS$	CH_2=C(*n*-C_6H_{13})-NCS	1) *trans*-1-Isothiocyanato-2-(phenylseleno)octane, O_3 (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.5 h)	50	(IR, ^{1}H NMR, Anal.)		136
				2) *n*-$C_6H_{13}C{\equiv}CH$, $Hg(SCN)_2$, HBF_4 (~54% sol. in Et_2O), *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 24 h)	56.4	112/23 torr (IR, ^{1}H NMR, UV, Anal.)		141 143
185	**605**	$C_9H_{15}NS_2$	*n*-$BuSCH_2C(Me)$=CH-NCS	3-Chloro-1-isothiocyanato-2-methyl-1-propene, EtOH, *n*-BuSNa, *n*-BuSH	28	97-100/2 torr (IR, ^{1}H NMR, MS, Anal.	1.5635	123
186	**405**	$C_9H_{15}NS_2$	*n*-$C_5H_{11}CH$=C(SMe)-NCS	$MeSC{\equiv}CC_5H_{11}$-*n*, $Hg(SCN)_2$, $HBF_4{\cdot}OEt_2$, *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C, 24 h)	54[c]	114/2 torr (IR, ^{1} NMR)		141 143
			2 stereoisomers (~70/30)	16 h	26			142
			(~75/25)	Spectra				143
187	**969**	$C_{10}H_2N_4S_2$		Application				253
188	**329**	$C_{10}H_4Cl_3NOS$	2,4,6-$Cl_3C_6H_2OCH_2C{\equiv}C$-NCS	2,4,6-Trichlorophenyl 1-halopropargyl ether, K(Na)SCN, ethanol/acetone, 55–60 °C, 2–3 h				130,131
189	**330**	$C_{10}H_4Cl_3NOS$	3,4,6-$Cl_3C_6H_2OCH_2C{\equiv}C$-NCS	3,4,6-Trichlorophenyl 1-halopropargyl ether, K(Na)SCN, ethanol/acetone, 55–60 °C, 2–3 h				130,131
190	**334**	$C_{10}H_4Br_3NOS$	2,4,6-$Br_3C_6H_2OCH_2C{\equiv}C$-NCS	2,4,6-Tribromophenyl 1-halopropargyl ether, K(Na)SCN, ethanol/acetone, 55–60 °C, 2–3 h				130,131

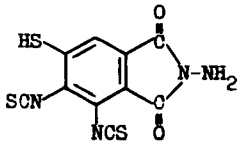
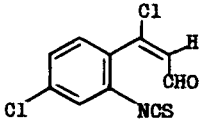
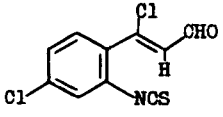
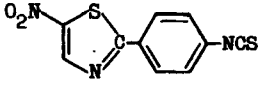
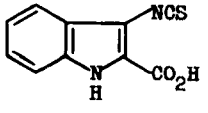
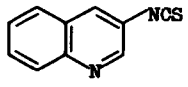
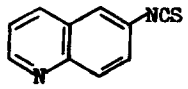
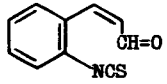
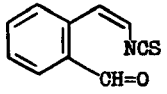
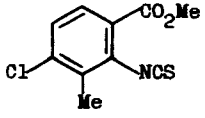
191	**982**	$C_{10}H_4N_4O_2S_3$		Application		253
192	**170**	$C_{10}H_5Cl_2NOS$		4,7-Dichloroquinoline, $CSCl_2$ (CH_2Cl_2/H_2O/ $BaCO_3$, 0 °C, 4 h)	58	91
193	**171**	$C_{10}H_5Cl_2NOS$		4,7-Dichloroquinoline, $CSCl_2$ (CH_2Cl_2/H_2O/ $BaCO_3$, 0 °C, 4 h)		91
194	**328**	$C_{10}H_5Cl_2NOS$	2,4-$Cl_2C_6H_3OCH_2C{\equiv}C$-NCS	2,4-Dichlorophenyl 1-halopropargyl ether, K(Na)SCN, ethanol/ acetone, 55–60 °C, 2–3 h		130,131
195	**333**	$C_{10}H_5Br_2NOS$	2,4-$Br_2C_6H_3OCH_2C{\equiv}C$-NCS	2,4-Dibromophenyl 1-halopropargyl ether, K(Na)SCN, ethanol/ acetone, 55–60 °C, 2–3 h		130,131
196	**9**	$C_{10}H_5N_3O_2S_3$		Amine, $CSCl_2$	(104–105)	63
197	**7**	$C_{10}H_6ClNOS$	2-$ClC_6H_4OCH_2C{\equiv}C$-NCS	2-Chlorophenyl 1-halopropargyl ether, K(Na)SCN, ethanol/ acetone, 55–60°C, 2–3 h		130,131
198	**2**	$C_{10}H_6BrNOS$	2-$BrC_6H_4OCH_2C{\equiv}C$-NCS	2-Bromophenyl 1-halo-propargyl ether, K(Na)SCN, ethanol/ acetone, 55–60°C, 2–3 h		130,131
199	**2**	$C_{10}H_6N_2O_2S$		Reactions		110

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
200	**2**	$C_{10}H_6N_2S$		Amine, $CSCl_2$	34	(65–67)		63
201	**19**	$C_{10}H_6N_2S$		Amine, $CSCl_2$	64	(87–91)		63
202	—	$C_{10}H_7NOS$		Quinoline, $CSCl_2$, CH_2Cl_2/H_2O				
	167		*trans*	a) KCN, 5–10 °C, 8 h; 20 °C, 2 d	4.3	(78.5) (IR, NMR, Anal.)		88
	166		*cis*	b) 2 N NaOh, <10 °C, 1.5 h	36	(78)		88
				c) $BaCO_3$, 0 °C, 1 h	78.8	Oil		88,92
203	**177**	$C_{10}H_7NOS$		Isoquinoline, $CSCl_2$, CH_2Cl_2/H_2O,	42	Yellow oil (IR, NMR		88
			(2:*Z*)					
			(2:*Z*)	a) NaOH, 5–10 °C, 105 min				
				b) $BaCO_3$				92
204	**119**	$C_{10}H_8ClNO_2S$		Amine, $CSCl_2$ ($CHCl_3$/ H_2O/$NaHCO_3$, ~20 °C)				76

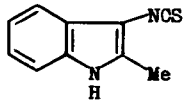
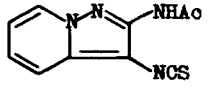
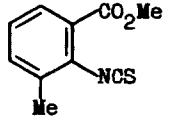
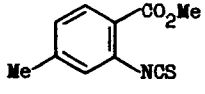
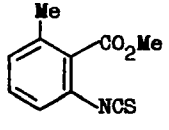
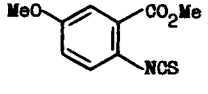
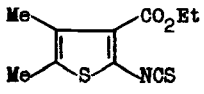
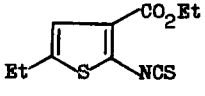
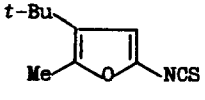
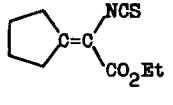
205	**203**	$C_{10}H_8N_2S$		2-Methyl-3-aminoindole, EtONa, *absol.* EtOH, CS_2 ~20 °C, 2 h	40	Oil (IR)	97
206	—	$C_{10}H_8N_4OS$					226
207	**120**	$C_{10}H_9NO_2S$		Amine, $CSCl_2$ ($CHCl_3$/ H_2O/$NaHCO_3$, ~20 °C)			76
208	**118**	$C_{10}H_9NO_2S$		Amine, $CSCl_2$ ($CHCl_3$/ H_2O/$NaHCO_3$, ~20 °C)			76
209	**113**	$C_{10}H_9NO_2S$		Amine, $CSCl_2$ ($CHCl_3$/ H_2O/$NaHCO_3$, ~20 °C)			76
210	**115**	$C_{10}H_9NO_3S$		Amine, $CSCl_2$ ($CHCl_3$/ H_2O/$NaHCO_3$, ~20 °C)			76
211	—	$C_{10}H_9NS$	$PhCH_2CH{=}CH\text{-}NCS$	Reactions			273
212	**137**	$C_{10}H_9NS$	$4\text{-}MeC_6H_4CH{=}CH\text{-}NCS$ (E/Z = 4.5)	2-Chloro-2-(4-methylphenyl)-ethyl isothiocyanate, Et_3N, (dioxane, N_2, 100 °C, 50 h)	63.6	96–98/28 Pa (42–47) (IR, ^1H NMR, UV, Anal.)	80
213	**403**	$C_{10}H_9NS$ ~80% (*Z*)	PhCH=C (Me)-NCS	MeC=CPh, $Hg(SCN)_2$, $n\text{-}Bu_4N^+SCN^-$, 40 °C,			
	404	~20% (*Z*) (*Z*)	MeCH=C(Ph)-NCS	a) HBF_4, 168 h	17	100/1 (IR, ^1H NMR)	141
				b) H_2SO_4, 408 h	4.3		142
				Spectra		(^1H NMR)	143

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
214	**404**	$C_{10}H_9NS$	MeCH=C(Ph)-NCS	1) MeC≡CPh, $Hg(SCN)_2$, H_2SO_4, n-$Bu_4N^+SCN^-$, 40 °C, 408 h	1.7			142
			(2:*Z*)			(^{1}H NMR)		141
			(*E*/*Z* = 1/1)	2) 1-Isothiocyanato-1-phenyl-2-iodopropane, *t*-BuOK, *absol.* ether, 20 °C, 2 h	66	Oil (IR, ^{1}H NMR, MS)		176
			(2:*E*)	3) Isomerization of *E*-1-isothiocyanato-1-phenylpropene (20 °C, 1 d)	>90			176
215	**106**	$C_{10}H_{11}NO_2S_2$		2-Amino-4,5-dimethylthiophenecarboxylic acid ethyl ester, $CSCl_2$, $CHCl_3/H_2O/NaHCO_3$		(69–71)		76 218
216	**720**	$C_{10}H_{11}NO_2S_2$		Reactions				218
217	**325**	$C_{10}H_{13}NOS$		4-*tert*-Butyl-2-(chloromethyl)furan, *aq.* KSCN, ~20 °C, 24 h	65.9[a]	70–72/0.6 torr (IR, ^{1}H NMR, Anal.)		129
				37 °C	14			
218	**564**	$C_{10}H_{13}NO_2S$		1) 5-(Cyclopentyl)-2-thioxo-1,3-oxazolidine-4-carboxylic acid ethyl ester, $(PhO)_2P(O)Cl$, NaH, THF, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, THF; 20 °C, 15 min	63	(32–33)		185
				2) Isothiocyanatoacetic acid ethyl ester, cyclopentanone, NaH or *t*-BuOK, N_2; THF, $(PhO)_2P(O)Cl$, 20–30 °C,	63 72[a]	(32–33) (IR, ^{1}H NMR, UV, Anal.)		187

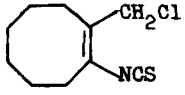
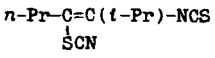
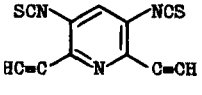
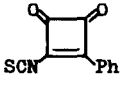
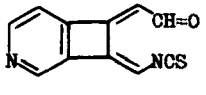
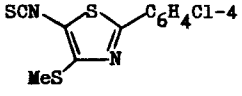
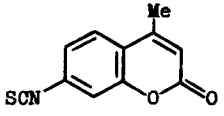
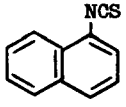
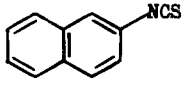
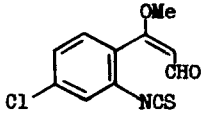
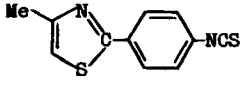
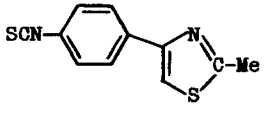
				0.5 h; –60 °C, *t*-BuOK, THF, 20 °C, 15 min				
219	**320**	$C_{10}H_{14}ClNS$		1-Chloro-2-(chloromethyl)-cyclooctene, KSCN (DMSO, ~20 °C, 3 h)	64	131–134/200 Pa (IR, ^{1}H NMR, MS)	1.5952	128
220	**419**	$C_{10}H_{14}N_2S_2$		Ph_3P=C(*n*-Pr)C(O)Pr-*i*, $(SCN)_2$	86	95–105/0.005 torr (IR, ^{1}H NMR, Anal.)		145
221	**398**	$C_{10}H_{17}NS$	CH_2=C(*n*-C_7H_{15})-NCS	*n*-$C_7H_{15}C{\equiv}CH$, $Hg(SCN)_2$, *n*-$Bu_4N^+SCN^-$, 40 °C,				
				a) H_2SO_4, 3 h	2.2			142,246
				b) HBF_4 (~54% sol. in Et_2O), 24 h	59.2	105/3 torr (IR, ^{1}H NMR, Anal.)		141
				c) CH_2Cl_2, 40 °C, 8 h,				
				CF_3COOH	17.8			141
				$Cl_2CHCOOH$	13.5			141
				$ClCH_2COOH$	11.3			141
				HCOOH	12.0			141
				CH_3COOH	~4			141
				2,4,6-$(NO_2)_3$-C_6H_2OH	24.3			141
				2,4-$(NO_2)_2$-C_6H_3OH	9.0			141
				Reactions				246
222	**331**	$C_{10}Cl_5NOS$	$C_6Cl_5OCH_2C{\equiv}C$-NCS	Pentachlorophenyl 1-halo-propargyl ether, K(Na)SCN, ethanol/acetone, 55–60 °C, 2-3 h				130,131
223	**970**	$C_{11}H_3N_3S_2$		Application				253
224	**255**	$C_{11}H_5NO_2S$		3-Bromo-(or 3-chloro)-4-phenyl-3-cyclobutene-1, 2-dione, KSCN, MeCN, 35–40 °C)-	28	(105) (IR, Anal.)		106
225	**185** **186**	$C_{11}H_6N_2OS$		2,7-Diazabiphenylene, $CSCl_2$ (CH_2Cl_2/H_2O/$BaCO_3$, 0 °C)	60	(157–158) (IR, ^{1}H NMR, UV, MS, Anal.)		92,94

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
226	**89**	$C_{11}H_7ClN_2S_3$		5-Amino-4-methylthio-2-(4-chlorophenyl)thiazole, $CSCl_2$ ($CHCl_3/H_2O$, 15 °C, 0.5 h)				72
227	**123**	$C_{11}H_7NO_2S$		7-Amino-4-methylcoumarin, $CSCl_2$ (40–55 °C, 8 h)		(185–187) (IR, ^{1}H NMR, Anal.)		77
228	**851**	$C_{11}H_7NS$		Reactions				44,238
229	**198**	$C_{11}H_7NS$		Modified Kaluza synthesis, 7 d	73			44,96,238
230	**174**	$C_{11}H_8ClNO_2S$		7-Chloro-4-methoxy quinoline, $CSCl_2$ ($CH_2Cl_2/H_2O/BaCO_3$, 0 °C, 2 h)				90
231	**7**	$C_{11}H_8N_2S_2$		Amine, $CSCl_2$ ($CHCl_3$/ $H_2O/NaHCO_3$)	(133–135)			63
232	**8**	$C_{11}H_8N_2S_2$		Amine, $CSCl_2$ ($CHCl_3$/ $H_2O/NaHCO_3$)	(115-117)			63

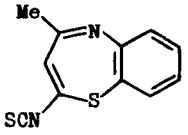
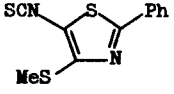
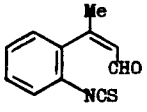
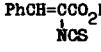
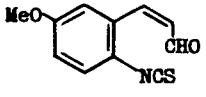
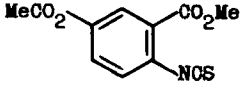
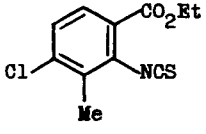
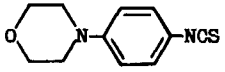
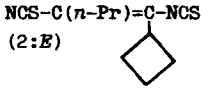
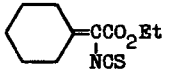
233	—	$C_{11}H_8N_2S_2$					275
234	**87**	$C_{11}H_8N_2S_3$		Amine, $CSCl_2$ (H_2O, 15 °C, 0.5 h)			72
235	**182**	$C_{11}H_9NOS$		4-Methylquinoline, $CSCl_2$ ($CH_2Cl_2/H_2O/CaCO_3$, 4 h)			89
236	**555**	$C_{11}H_9NO_2S$	 (Z/E = 95/<5)	Isothiocyanatoacetic acid methyl ester, benzaldehyde, NaH or *t*-BuOK, N_2 THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 1 h	48	(56) (IR, ^{1}H NMR, Anal.)	23,187
237	**181**	$C_{11}H_9NO_2S$		6-Methoxyquinoline, $CSCl_2$ ($CH_2Cl_2/H_2O/CaCO_3$, 4 h)	62		89
238	**116**	$C_{11}H_9NO_4S$		Amine, $CSCl_2$ ($CHCl_3$/ $H_2O/NaHCO_3$, ~20 °C)			76
239	**312**	$C_{11}H_{10}ClNS$	$ClCH_2C(Me)=C(Ph)$-NCS	1-Chloro-1-phenyl-2-methyl-3-thiocyanato-1-propene (dioxane, Δ, 6 h)			122,125
240	**121**	$C_{11}H_{10}ClNO_2S$		Amine, $CSCl_2$ ($CHCl_3$/ $H_2O/NaHCO_3$, ~20 °C)			76

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
241	**145**	$C_{11}H_{11}NS$	$Me_2C{=}C(Ph)\text{-}NCS$	1) $Me_2CHC(Ph){=}NH$, $CSCl_2$, toluene, 2–3 h	73	65/0.1 torr	1.6120	82,83
				2) 5,5-Dimethyl-4-phenyl-Δ^3-1,3-thiazoline-2-thione (*absol.* benzene, Ar, UV, 7 h)	68	74–76/0.03 torr (Oil) (IR, ^{1}H NMR, UV, Anal.)		166
				3) Photolysis of 1-phenyl-2,2-dimethylvinyl bromide in the presence of SCN, 3 h	29	Oil (IR, ^{1}H NMR)		102
242	**220**	$C_{11}H_{11}NS$	$PhCH_2CH{=}C(Me)\text{-}NCS$ (2:*Z*) (2:*E*)	$PhCH_2CH{=}C(Me)NHC(S)SNa$, isopropyl chloroformate, (0 °C, 45 min; Et_3N, 50 °C, 30 min)	81	104–106/12 torr (IR, ^{1}H NMR)		95
243	**607**	$C_{11}H_{11}NS_2$	$PhSCH_2C(Me){=}CH\text{-}NCS$	3-Chloro-1-isothiocyanato-2-methyl-1-propene, PhSNa, PhSH, EtOH	56	(128–130) (IR, ^{1}H NMR, MS, Anal.)	1.6548	123
244	**1**	$C_{11}H_{12}N_2OS$		Amine, $CSCl_2$		(87–88)		63
245	**420**	$C_{11}H_{14}N_2S_2$	 (2:*E*)	$(Ph)_3P{=}C(n\text{-}Pr)C(O)CH(CH_2)_3$, $(SCN)_2$	60	75–85/0.01 torr (Anal.)		145
246	**565**	$C_{11}H_{15}NO_2S$		1) 5-(Cyclohexyl)-2-thioxo-1,3-oxazolidine-4-carboxylic acid ethyl ester, $(PhO)_2P(O)Cl$, NaH, THF, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min	65			185
				2) Isothiocyanatoacetic acid ethyl ester, cyclohexanone, NaH or *t*-BuOK, N_2;	44 62[a]	60/0.05 torr (IR, ^{1}H NMR, Anal.)		187

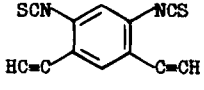
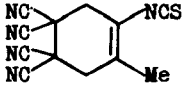
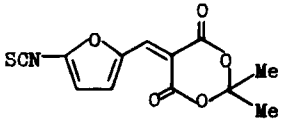
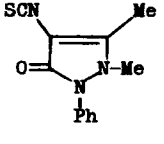
				THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min			
247	**384**	$C_{11}H_{15}NO_4S$	*t*-$PrCO_2CH{=}C(NCS)CO_2Pr$-*t*	1) *i*-$PrCO_2CH{=}C(SCN)100Pr$-*i*, KSCN *aq.* H_2SO_4, benzene, ~20 °C, 24 h)	27	112/0.1 torr (IR, ^1H NMR, Anal.)	137
			(*Z*/*E* = 69:31) (2:*Z*) (2:*E*)	2) (*Z*,*E*)-*i*-$PrCO_2CH{=}C(SCN)CO_2Pr$-*i*, KSCN, *absol.* MeCN, reflux, 6 h			
248	**389**	$C_{11}H_{18}ClHgNS$	$ClHgC(n\text{-}Bu){=}C(n\text{-}Bu)(NCS)$	*n*-BuC≡CBu-*n*, $HgCl_2$, HSCN, 120 h	12	(60) (IR, ^1H NMR)	140
			(*Z*/*E* = > 90:10)				
249	**392**	$C_{11}H_{19}NS$	*n*-BuCH=C(*n*-Bu)-NCS (*Z*/*E* ≈ 90/10)	*n*-BuC≡CBu-*n*, $Hg(SCN)_2$, *n*-$Bu_4N^+SCN^-$, CH_2Cl_2, 40 °C, a) HBF_4 (54% sol. in Et_2O), 48 h	65	133/16 torr	141
			(*Z*/*E* = 85/15)	b) H_2SO_4, 144 h	66.2	133/16 torr (IR, ^1H NMR)	142
250	**977**	$C_7H_4N_2S_2$		Application			253
251	**597**	$C_{19}H_7N_5S$		Condensation of isothiocyanato-1,3-butadiene and tetracyanoethylene			133
252	**575**	$C_{12}H_9ClN_2S$	4-$ClC_6H_4N{=}CHCH{=}CHCH{=}CH$-NCS	Condensation of 4-$ClC_6H_4NH_2$ and SCNCH=CHCH=CHCHO			87
253	**261**	$C_{12}H_9NO_5S$		2,2-Dimethyl-5-(halofurfurylidene-2)-1,3-dioxane-4,6-diones, thiourea, KSCN			108
254	**573**	$C_{12}H_{10}BrNO_2S$	$BrCH_2C(Ph){=}CCO_2Me(NCS)$	PhC(Me)=C(NCS)CO_2Me (*E*/*Z* = 30/70), NBS (dibenzoyl peroxide, CCl_4, 80 °C, 2.5 h)	89	(^1H NMR)	188
			(*E*/*Z* = 70/30)				

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
255	**289**	$C_{12}H_{11}NO_2S$	PhC(Me)=C(NCS)CO_2Me (2:*Z*) (2:*E*)	$MeCO_2CH$=C(Ph)CH_2Br, KSCN, EtOH; distillation (190 °C/ 20 torr)	28			119 188
256	**557**	$C_{12}H_{11}NO_2S$	PhCH=C(NCS)CO_2Et (2:*Z*)	1) 5-Phenyl-2-thioxo-1,3-oxazolidine-4-carboxylic acid ethyl ester, THF, $(PhO)_2P(O)Cl$, NaH, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK; –60 °C, $MeCO_2H$; CS_2, NaH, 30–40 °C, 3 h	51	(30–31)		187
			(*Z*/*E* = 95/< 5)	2) Isothiocyanatoacetic acid ethyl ester, benzaldehyde, NaH or *t*-BuOK, N_2; THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 1 h	51	(IR, ^{1}H NMR, UV, Anal.)		23,187
				Reactions				23
257	**456**	$C_{12}H_{11}N_3OS$		Thermal decomposition of poly[*N*-(2,3-dimethyl-1-phenyl-5-oxo-3-pyrazolin-4-yl)-*N'*-acrylolylthiourea]				164
258	**246**	$C_{12}H_{12}ClN_2S.ClO_4$	4-ClC_6H_4C(NCS)=CHCH=NMe_2ClO_4	$ClC(_4$-ClPh)=CH=NMe_2ClO_4, KSCN, *n*-$Bu_4N^+I^-$, MeCN	56	(204–206) (UV)		103–105
				Reactions				103,227 –229

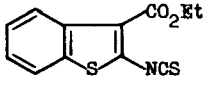
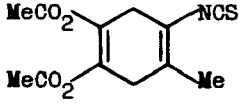
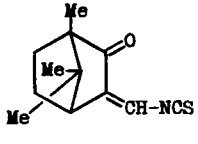
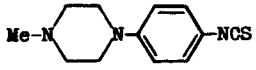
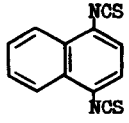
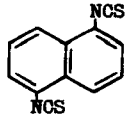
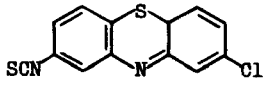
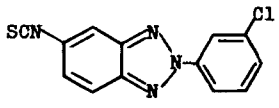
259	**240**	$C_{12}H_{13}NOS$	4-MeOC$_6$H$_4$C(NCS)=CMe$_2$	Photolysis of 1-(4-methoxyphenyl)-2,2-dimethylvinyl bromide in the presence of SCN^-, 1.5 h		27 Oil (IR, ^{1}H NMR)		102
260	**109**	$C_{12}H_{13}NO_2S_2$		2-Amino-4,5,6,7-tetrahydrobenzo[*b*]thiophenecarboxylic acid ethyl ester, $CSCl_2$, $CHCl_3/H_2O/NaHCO_3$		(46–47)		76 217,218
261	**598**	$C_{12}H_{13}NO_4S$		Condensation of isothiocyanato-1,3-butadiene and 1,2-butynedioic acid dimethyl ester				133
262	**147**	$C_{12}H_{13}NS$	*i*-PrCH=C(Ph)-NCS	*i*-PrCH$_2$C(Ph)=NH, $CSCl_2$, toluene, 2–3 h	77	85/0.1 torr	1.6018	82,83
				Reactions				82
263	**146**	$C_{12}H_{13}NS$	*n*-PrCH=C(Ph)-NCS	*n*-PrCH$_2$C(Ph)=NH, $CSCl_2$, toluene, 2–3 h	62	92/0.1 torr	1.6000	83
264	**606**	$C_{12}H_{13}NS_2$	PhCH$_2$SCH$_2$C(Me)=CH-NCS	3-Chloro-1-isothiocyanato-2-methyl-1-propene, PhSNa, PhSH, EtOH	53	135–138/0.2 torr (IR, ^{1}H NMR, MS, Anal.)	1.6410	123
265	**791**	$C_{12}H_{13}N_2S.Cl$	PhC(NCS)=CHCH=$^+$NMe$_2$ Cl^-	Reactions				229
266	**245**	$C_{12}H_{13}N_2S.ClO$	PhC(NCS)=CHCH=$^+$NMe$_2$ ClO_4^-	ClC(Ph)=CHCH=$^+$NMe$_2$ ClO_4^- KSCN, *n*-Bu$_4$N$^+$I$^-$, MeCN	72	(150–152) (UV)		103–105 227
				Reactions				103,228–230
267	**127**	$C_{12}H_{15}NOS$		From 3-aminomethylene-DL-camphor and $CSCL_2$	45	(37–40) (Anal.)		78
268	**537**	$C_{12}H_{15}NSSi$	PhCH=C(NCS)SiMe$_3$	$(Me_3Si)_3C$-NCS, PhCHO, *n*-Bu$_4$NF (THF, N_2, 20 °C, 24 h)	26	(IR, ^{1}H NMR, MS)		178

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
269	**2**	$C_{12}H_{15}N_3S$		Amine, $CSCl_2$		(120–122)		63
270	**26**	$C_{12}H_{16}N_2S_2$		Amine, $CSCl_2$		(126–127)		63
271	**27**	$C_{12}H_{16}N_2S_2$		Amine, $CSCl_2$		(176–177)		63
272	—	$C_{12}HX_{18}HgN_2S_2$	NCS-HgC(*n*-Bu)=C(*n*-Bu) NCS	Dec-5-yne, $Hg(SCN)_2$, *n*-$Bu_4N^+SCN^-$, CH_2Cl_2, 40 °C, 25 d	46	(60) (IR, ^1H NMR)		141
273	**568**	$C_{13}H_6ClN_3S$	4-ClC_6H_4C=CHCH=C(CN)$_2$ NCS	4-$ClC_6H_4C(NCS)$=CHCH= $NMe_2.ClO_4^-$, $CH_2(CN)_2$	73	(208–210)		103
274	**22**	$C_{13}H_7ClN_2S_2$		Amine, $CSCl_2$	91	(195–197)		63
275	**32**	$C_{13}H_7ClN_4S$		Amine, $CSCl_2$ Reactions Spectra				68 233 257,258

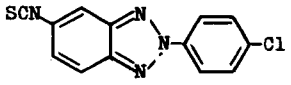
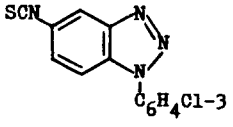
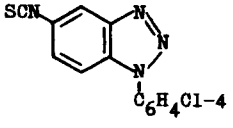
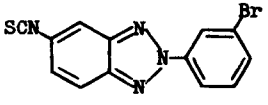
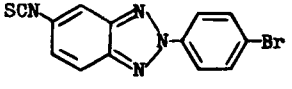
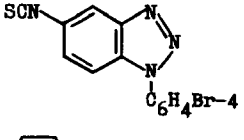
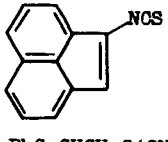
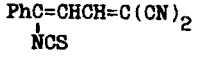
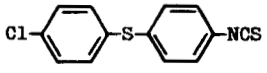
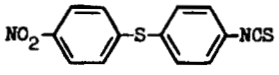
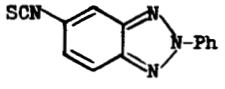
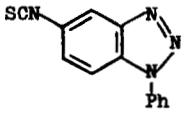
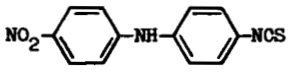
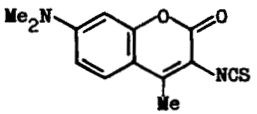
276	**36**	$C_{13}H_7ClN_4S$		5-Amino-2-(4-chlorophenyl)-benzotriazole, $CSCl_2$ $CHCl_3$ /H_2O/K_2CO_3 Reactions Spectra			68,69 233 257,258
277	**42**	$C_{13}H_7ClN_4S$		Amine, $CSCl_2$			68
278	**44**	$C_{13}H_7ClN_4S$		Amine, $CSCl_2$			68
279	**33**	$C_{13}H_7BrN_4S$		Amine, $CSCl_2$ Reactions Spectra			68 233 258
280	**37**	$C_{13}H_7BrN_4S$		Amine, $CSCl_2$ Reactions Spectra			68 233 257,258
281	**45**	$C_{13}H_7BrN_4S$		Amine, $CSCl_2$			68
282	**235**	$C_{13}H_7NS$		Elimination of HSCN from *cis*-1-isothiocyanato-2-thiocyanatoacenaphthene			101
283	**567**	$C_{13}H_7N_3S$		1) PhC(NCS)=CH–Cu=N$^+$Me$_2$·ClO_4^- $CH_2(CN)_2$, Et_3N 2) PhC(NCS)=CH–Cu=N$^+$Me$_2$·ClO_4^- $CH_2(CN)_2$, Et_3N	59 62	(160–161)	103 103

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
284	**5**	$C_{13}H_8ClNS_2$		Amine, $CSCl_2$	32	(48–50)		63
285	**6**	$C_{13}H_8N_2O_2S_2$		Amine, $CSCl_2$		(124–125)		63
286	**31**	$C_{13}H_8N_4S$		5-Amino-2-(phenyl)benzotriazole, $CSCl_2$ ($CHCl_3$/H_2O/K_2CO_3, 2 h)	67			68,69,233, 257,258
287	**41**	$C_{13}H_8N_4S$		Amine, $CSCl_2$				68
288	**761**	$C_{13}H_9NS_2$	2-$PhSC_6H_4$-NCS	Reactions				223
289	**750**	$C_{13}H_9NS_2$	4-$PhSC_6H_4$-NCS	Reactions				220
290	**816**	$C_{13}H_9N_3O_2S$		Reactions				63
291	**574**	$C_{13}H_{12}BrNO_2S$	$BrCH_2C(Ph)=CCO_2Et$ (NCS) (E/Z = 65/35) (2:*Z*), (2:*E*)	PhC(Me)=C(NCS)CO_2Et (E/Z = 40/60, NBS, dibenzoyl peroxide (CCl_4, 80 °C, 2.5 h)	92	(^{1}H NMR)		188
292	**125**	$C_{13}H_{12}N_2O_2S$		3-Amino-7-methylamino-4-methylcoumarin, $CSCl_2$		(200–201) (IR, ^{1}H NMR, Anal.)		77

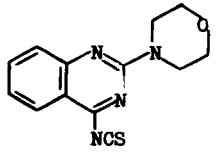
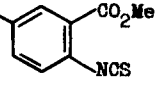
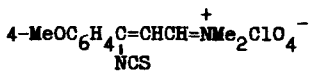
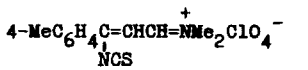
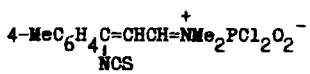
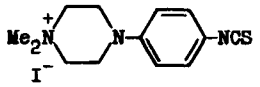
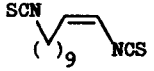
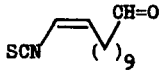
293	**576**	$C_{13}H_{12}N_2S$	SCN-CH=CH-CH=CH-CH=NC$_6$H$_4$Me-4	Condensation of *trans,cis*-1-formyl-4-isothiocyanato-buta-1,3-diene and 4-methyl-aniline			87
294	**654**	$C_{13}H_{12}N_4OS$		Reactions			209
295	**561**	$C_{13}H_{13}NO_2S$	PhC(Me)=C(NCS)CO$_2$Et				185,186,240
			(*Z*/*E* = 1.5) (2:*E*) (2:*Z*)	1) 5-Methyl-5-phenyl-2-thioxo-1,3-oxazolidine-4-carboxylic acid ethyl ester, THF, $(PhO)_2P(O)Cl$, NaH, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK; –60 °C, $MeCO_2H$; NaH, CS_2, 30–40 °C, 3 h	56		23,187,188
			(*Z*/*E* = 57/43)	2) Isothiocyanatoacetic acid ethyl ester, acetophenone, NaH or *t*-BuOK, N_2; THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 3 h	61	(IR, ^{1}H NMR, Anal.)	187
			(*Z*/*E* = 35/65)	30 °C, 1 h 3) $BrCH_2C(Ph)=C(NCS)CO_2Et$, potassium hydridotetracarbonylferrate, DME, 30 °C, 3 h	69		23,187
				Reactions			23,188
296	**114**	$C_{13}H_{15}NO_2S$		Amine, $CSCl_2$			76

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
297	**248**	$C_{13}H_{15}N_2$ OS·ClO_4		4-MeOPhC(Cl)=CHCH=$^+NMe_2ClO_4^-$, KSCN	61	(199–202)		104,
				Reactions				227–230
298	**247**	$C_{13}H_{15}N_2S·ClO_4$ CHCH=$^{+N}$ Me_2ClO_4		4-MePhC(Cl)=CHCH= $^+NMe_2ClO_4^-$, KSCN, MeCN in the	97	(193-195)		104,105
				presence of *n*-Bu_4NI, KCl	78	(UV)		
				n-Bu_4NI, NaCl	76			
				Et_4NI, KCl	97			
				n-Bu_4NI, KCl	44			
				n-Bu_4NI, KCl in DMF	90			
				Reactions				103,227–230
299	—	$C_{13}H_{15}N_2S·Cl_2O_2P$		Reactions				103
300	**790**	$C_{13}H_{15}N_2S·CNS$		Reactions				228,230
301	**3**	$C_{13}H_{18}IN_3S$		Amine, $CSCl_2$		(270–272)		63
302	**617**	$C_{13}H_{20}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
303	**627**	$C_{13}H_{21}NOS$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194

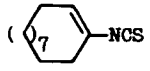
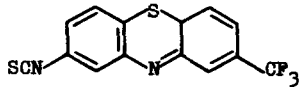
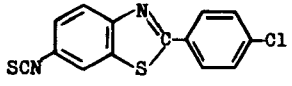
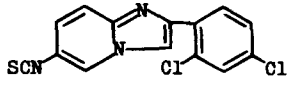
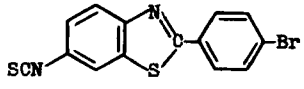
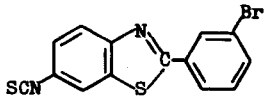
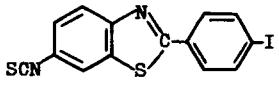
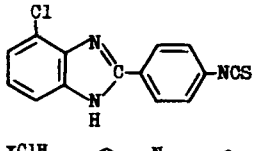
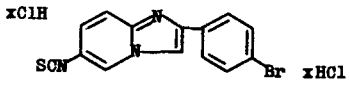
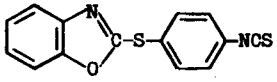
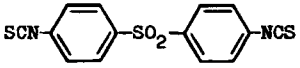
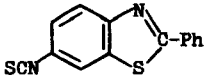
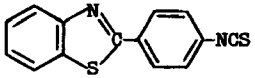
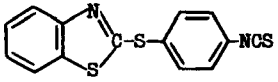
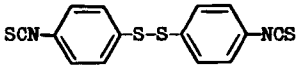
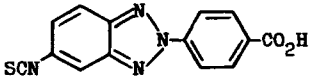
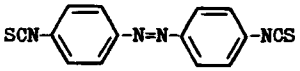
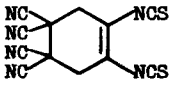
304	**373**	$C_{13}H_{21}NS$	 Z/E = >99:<1	1) *trans*-1-Isothiocyanato-2-(phenylseleno)cyclododecane, O_3 (CH_2Cl_2, –78 °C, 0.5 h; CCl_4, reflux, 0.5 h)	54.4		136
				2) Cyclododecanone, $Si(NCS)_4$, $Zn(NCS)_2$, DME	77	61–67/0.2 torr (IR, ^1H NMR, Anal.)	184
305	**23**	$C_{14}H_7F_3N_3S$		Amine, $CSCl_2$	38	(116–118)	63
306	**53**	$C_{14}H_7ClN_2S_2$		Amine, $CSCl_2$			68
307	—	$C_{14}H_7Cl_2N_3S$					276
308	**54**	$C_{14}H_7BrN_2S_2$		Amine, $CSCl_2$			68
309	**50**	$C_{14}H_7BrN_2S_2$		Amine, $CSCl_2$			68
310	**55**	$C_{14}H_7IN_2S_2$		Amine, $CSCl_2$			68
311	**14**	$C_{14}H_8ClN_3S$		Amine, $CSCl_2$		(294–295)	63
312	–	$C_{14}H_8BrN_3S \cdot xClH$					276

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
313	**12**	$C_{14}H_8N_2OS_2$		Amine, $CSCl_2$		(79–82)		63
314	**24**	$C_{14}H_8N_2O_2S_3$		Amine, $CSCl_2$		(182–183)		63
315	**49**	$C_{14}H_8N_2S_2$		Amine, $CSCl_2$				68
316	**10**	$C_{14}H_8N_2S_2$		Amine, $CSCl_2$		(82–84)		63
317	**11**	$C_{14}H_8N_2S_3$		Amine, $CSCl_2$				63
318	**25**	$C_{14}H_8N_2S_4$		Amine, $CSCl_2$		(87–98)		63
319	—	$C_{14}H_8N_4O_2S$		Fluorescence spectrum				257
320	**976**	$C_{14}H_8N_4S_2$		Application				253
321	**595** **596**	$C_{14}H_8N_6S_2$		Condensation of isothiocyanate **350** and TCNE				133

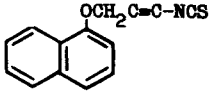
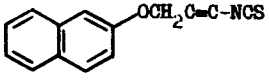
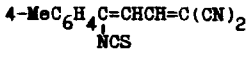
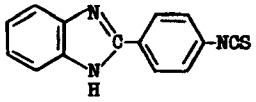
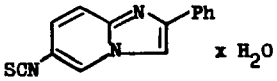
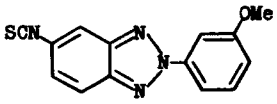
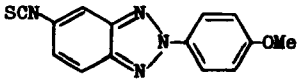
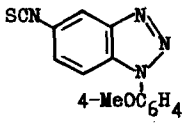
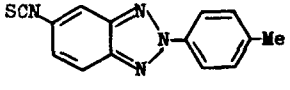
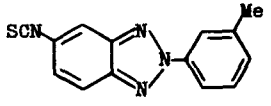
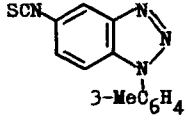
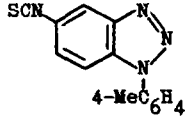
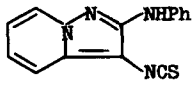
322	**335**	$C_{14}H_9NOS$		α-Naphthyl 1-halopropargyl ether, K(Na)SCN, ethanol/ acetone, 55–60 °C, 2–3 h			130, 131
323	**336**	$C_{14}H_9NOS$		β-Naphthyl 1-halopropargyl ether, K(Na)SCN, ethanol/ acetone, 55–60 °C, 2–3 h			130, 131
324	**243**	$C_{14}H_9N_3S$		1) a) 4-$MeC_6H_4C(NCS)$=CHCH=$^+NME_2.ClO_4^-$,$CH_2(CN)_2$	66		103
				b) in the presence of Et_3N	48	(174–176)	103
				c) 4-$MeC_6H_4C(NCS)$=CHCH=$^+NMe_2 \cdot PO_2Cl_2^-$,$CH_2(CN)_2$, Et_3N	12		103
				2) 4-$MeC_6H_4C(Cl)$=CHCH=$C(CN)_2$, *n*-Bu_4NI, MeCN			103
				a) KSCN	52		
				b) NaSCN	43		
325	**13**	$C_{14}H_9N_3S$		Amine, $CSCl_2$	21	(250–252)	63
326	—	$C_{14}H_9N_3S \cdot H_2O$					276
327	**719**	$C_{14}H_{10}ClNO_2S_2$		Reactions			218
328	**35**	$C_{14}H_{10}N_4OS$		Amine, $CSCl_2$			68
				Reactions			233
				Spectra			257,258
329	**39**	$C_{14}H_{10}N_4OS$		5-Amino-2-(4-methoxyphenyl)-benzotriazole, $CSCl_2$, $CHCl_3$/ H_2O/K_2CO_3			68,69
				Spectra			257,258

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
330	**47**	$C_{14}H_{10}N_4OS$		Amine, $CSCl_2$				68
331	**38**	$C_{14}H_{10}N_4S$		5-Amino-2-(4-methylphenyl)-benzotriazole, $CSCl_2$, $CHCl_3/H_2O/K_2CO_3$ Reactions Spectra				68,69 233 257,258
332	**34**	$C_{14}H_{10}N_4S$		5-Amino-2-(3-methylphenyl)-benzotriazole, $CSCl_2$, $CHCl_3$ $/H_2O/K_2CO_3$ Reactions Spectra				68,69 233 258
333	**43**	$C_{14}H_{10}N_4S$		Amine, $CSCl_2$				68
334	**46**	$C_{14}H_{10}N_4S$		Amine, $CSCl_2$				68
335	—	$C_{14}H_{10}N_4S$						226

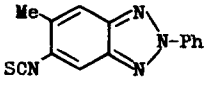
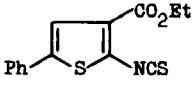
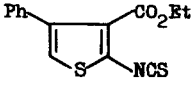
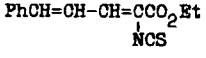
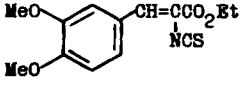
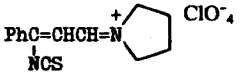
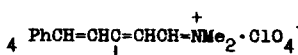
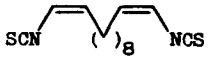
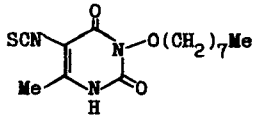
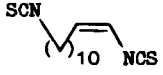
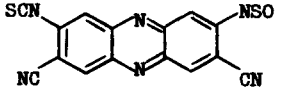
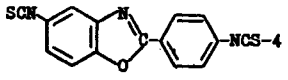
336	—	$C_{14}H_{10}N_4S$		Spectra			257,258
337	**108**	$C_{14}H_{11}NO_2S_2$		2-Amino-5-phenyl-3-thiophenecarboxylic acid ethyl ester, $CSCl_2$, $CHCl_3/H_2O/NaHCO_3$		(99–101)	76
338	—	$C_{14}H_{11}NO_2S_2$		Reactions			217,218
339	**447**	$C_{14}H_{13}N_2S$		1) 5-(β-Styryl)-2-thioxo-1,3-oxazolidine-4-carboxylic acid ethyl ester, THF, $(PhO)_2P(O)Cl$, NaH, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK; –60 °C, $MeCO_2H$; NaH, CS_2, 30–40 °C, 3 h	54	(75–83)	185
			(2:*Z*,*E*)				
			(*Z*/*E*=75/25)	2) Isothiocyanatoacetic acid ethyl ester, cinnamaldehyde, NaH (*t*-BuOK), N_2; $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, THF, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30°C, 2 h	54	(80–83) (IR, ^{1}H NMR, UV, Anal.)	187
				3) PhCH=CHCH=C(CO_2Et)N=PPh_3,CS_2	73		156
340	**558**	$C_{14}H_{15}NO_4S$		Isothiocyanatoacetic acid ethyl ester, 3,4-dimethoxybenzaldehyde, NaH (*t*-BuOK), N_2; $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, THF, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 3 h	55	(104–106) (IR, ^{1}H NMR, Anal.)	187
			(*Z*/*E* = 95/<5)				
341	**789**	$C_{14}H_{15}N_2S \cdot$		Reactions			103

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
342	**249**	$C_{14}H_{15}N_2SClO_4$		PhCH=CHC(Cl)=CHCH=$^+$NMe$_2$ ClO_4^-, KSCN, in the presence of KCl and *n*-Bu_4NI, MeCN	70	(198–199)		104
343	**411**	$C_{14}H_{20}HgN_2S_2$	[EtC(NCS)=C(Et)]$_2$Hg	1) EtC≡CEt, $HgCl_2$, HSCN, CH_2Cl_2				140
				2) EtC≡CEt, *n*-$Bu_4N^+SCN^-$ $Hg(SCN)_2$, CH_2Cl_2, 40 °C, 48h				141
344	**609**	$C_{14}H_{20}N_2S_2$	 (2:*Z*,*Z*)	From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
345	**996**	$C_{14}H_{21}N_3O_3S$		Reactions				259
346	**618**	$C_{14}H_{22}N_2S_2$	 (2:*Z*)	From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
347	**983**	$C_{15}H_4N_6OS_2$		Application				253
348	**820**	$C_{15}H_7N_3OS_2$		Reactions				233

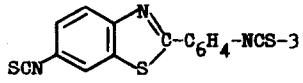
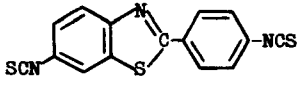
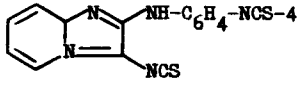
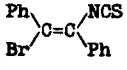
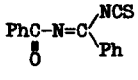
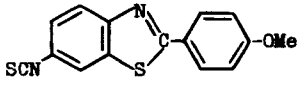
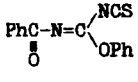
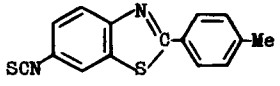
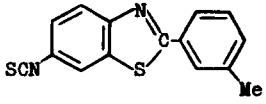
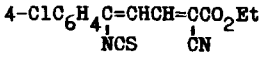
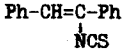
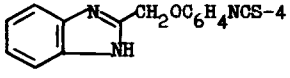
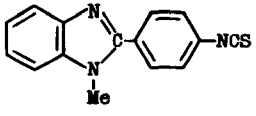
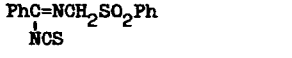
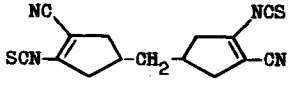
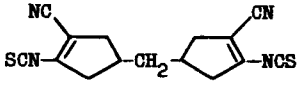
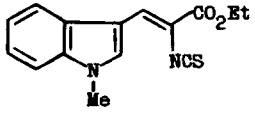
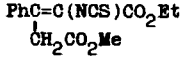
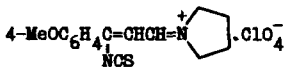
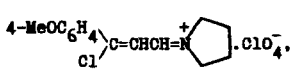
349	**52**	$C_{15}H_7N_3S_3$		Amine, $CSCl_2$			68
350	**56**	$C_{15}H_7N_3S_3$		Amine, $CSCl_2$			68
351	—	$C_{15}H_9N_5S_2$					226
352	**503**	$C_{15}H_{10}BrNS$		1,2-Diphenylvinyl isothiocyanate, Br_2	60	(90–91) (IR, MS, Anal.)	168
353	**274**	$C_{15}H_{10}N_2OS$		Corresponding benzimidoyl chloride, NaSCN, acetone			115
354	**58**	$C_{15}H_{10}N_2OS_2$		Amine, $CSCl_2$			68
355	**275**	$C_{15}H_{10}N_2O_2S$		*N*-Benzoylimidoyl chloride, NaSCN, acetone			115
356	**57**	$C_{15}H_{10}N_2S_2$		Amine, $CSCl_2$			68
357	**51**	$C_{15}H_{10}N_2S_2$		Amine, $CSCl_2$			68
358	**570**	$C_{15}H_{11}ClN_2O_2S$		4-$ClC_6H_4C(NCS)$=CHCH=$^+NMe_2$ ClO_4^-, $EtCO_2CH_2CH_2CN$, Et_3N	21	(128–129)	103
359	**501**	$C_{15}H_{11}NS$		$PhCH_2CH(Ph)NCS$, NBS ($h\nu$, 22°C, 3 h, CCl_4, N_2)		(^{1}H NMR)	168

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
360	**16**	$C_{15}H_{11}N_3OS$		Amine, $CSCl_2$, $CHCl_3$/ H_2O/$NaHCO_3$		(174–175)		63
361	**15**	$C_{15}H_{11}N_3S$		Amine, $CSCl_2$, $CHCl_3$/H_2O/ $NaHCO_3$		(148–150)		63
362	**279**	$C_{15}H_{12}N_2O_2S_2$		*N*-(Phenylsulfonyl)benz-imidoyl chloride, NaSCN (MeCN, ~20 °C, 24 h)				117
363	**991**	$C_{15}H_{12}N_4S_2$		Application				252,255
364	–	$C_{15}H_{12}N_4S_2$		Application				255
365	**438**	$C_{15}H_{14}N_2O_2S$		Ethyl-3-(1-methylindol-3-yl)-2-(triphenylphosphoranylidene-amino)prop-2-enoate, CS_2, dry toluene, reflux, 12 h	89	(IR, ^{1}H NMR, MS, Anal.)		153
366	**603**	$C_{15}H_{15}NO_4S$ CH_2CO_2Me	 (2:*E*) (2:*Z*)	4-Bromo-2-isothiocyanato-3-phenylbut-2-enoic acid ethyl ester (*E*/*Z* = 65/35), dicyclo-hexylammonium acetate (acetone, 25 °C, 2 h)	61	(^{1}H NMR)		188
367	**251**	$C_{15}H_{17}N_2$ $OS{\cdot}ClO_4$			71	(216–220) (UV)		104,105

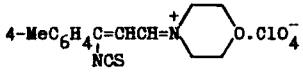
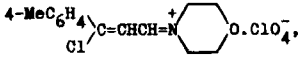
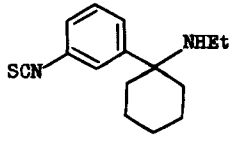
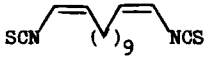
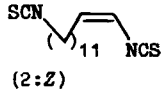
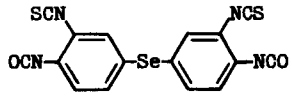
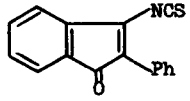
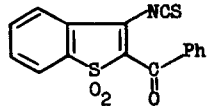
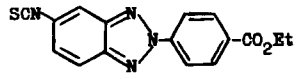
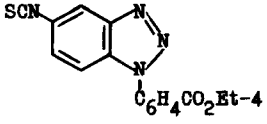
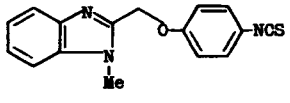
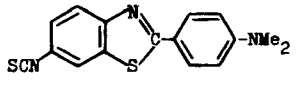
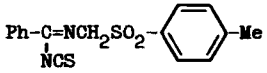
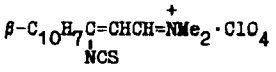
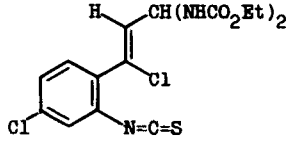
				KSCN, *n*-Bu_4NI,KCl, MeCN Reactions			228–230
368	**252**	$C_{15}H_{17}N_2OS{\cdot}ClO_4$			89	(164–167)	104
				KSCN, *n*-Bu_4NI, KCl, MeCN Reactions			228,229
369	**94**	$C_{15}H_{20}N_2S$		Amine, $CSCl_2$, $CHCl_3/H_2O$/ $NaHCO_3$			74
370	**610**	$C_{15}H_{22}N_2S_2$		From a Fijian sponge, *Pseudoxinyssa sp.*			28,194
371	**619**	$C_{15}H_{24}N_2S_2$	 (2:*Z*)	From a *Fijian* sponge, *Pseudaxinyssa sp.*			28,194
372	**985**	$C_{16}H_6N_4O_2S_2Se$		Application			255
373	**258**	$C_{16}H_9NOS$		3-Thiocyanato-2-phenyl-1-indenone, *absol.* DMF, 60 °C, 4 h	99	(58–60) (IR, MS, Anal.)	107
374	**263**	$C_{16}H_9NO_3S_2$		2-Benzoyl-3-chlorobenzo[*b*]-thiophene 1,1-dioxide, KSCN, DME	80	(147) (Anal.)	109
375	**40**	$C_{16}H_{12}N_4O_2S$		Amine, $CSCl_2$ UV Spectrum			68 258

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
376	**48**	$C_{16}H_{12}N_4O_2S$		Amine, $CSCl_2$				68
377	**17**	$C_{16}H_{13}N_3OS$		Amine, $CSCl_2$, $CHCl_3$/ H_2O/$NaHCO_3$	31	(149–150)		63
378	**59**	$C_{16}H_{13}N_3S_2$		Amine, $CSCl_2$				68
379	**280**	$C_{16}H_{14}N_2O_2S_2$		*N*-(4-Methylphenyl-sulfonylmethyl)benz-imidoyl chloride, NaSCN, MeCN, ~20 °C, 24 h				117
380	**250**	$C_{16}H_{15}N_2$ $S{\cdot}ClO_4$		β-$C_{10}H_7C(Cl)$=CHCH= NMe_2ClO_4, KSCN, *n*-Bu_4NI, KCl, MeCN	93	(225–227)		103–105
				Reactions				227–230
381	**579**	$C_{16}H_{17}Cl_2N_3O_4S$		β-4-Dichloro-2-isothio-cyanatocinnamaldehyde, ethyl carbamate				91

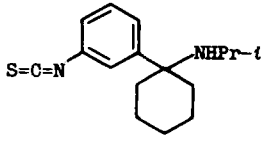
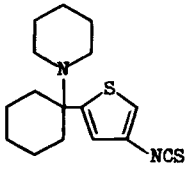
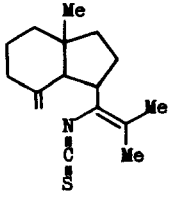
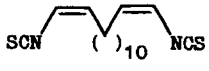
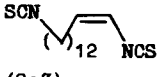
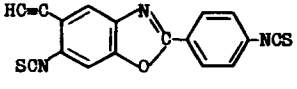
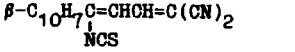
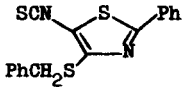
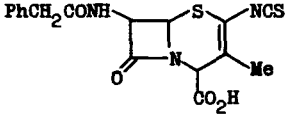
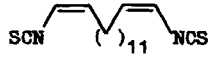
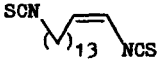
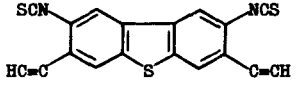
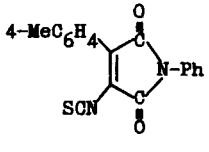
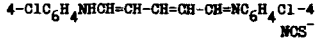
382	**95**	$C_{16}H_{22}N_2S$		Amine, $CSCl_2$, $CHCl_3$/ H_2O/$NaHCO_3$			74
383	**97**	$C_{16}H_{22}N_2S_2$		1-[1-(4-Aminothiophen-2-yl)cyclohexyl]piperidine, $CSCl_2$, $CHCl_3/H_2O/NaHCO_3$			73,74
384	**630**	$_{16}H_{23}NS$		From the marine sponge, *Axinella cannabina*	$[\alpha]_D$ –35.9° (IR, ^{1}H NMR, MS)	1.5493	33,195
385	**611**	$C_{16}H_{24}N_2S_2$	 (2:Z,Z)	From a Fijian sponge, *Pseudaxinyssa sp.*			28,194
386	**620**	$C_{16}H_{26}N_2S_2$	 (2:Z)	From a Fijian sponge, *Pseudaxinyssa sp.*			28,194
387	**981**	$C_{17}H_7N_3S_2$		Application			253
388	**569**	$C_{17}H_9N_3S$		β-$C_{10}H_7C$(NCS)=CHCH=N·Me_2· ClO_4^-, $CH_2(CN)_2$, Et_3N	96	(195–196)	103

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
389	**88**	$C_{17}H_{12}N_2S_3$		5-Amino-4-(benzylthio)-2-phenylthiazole, $CSCl_2$, $CHCl_3/H_2O$, 15 °C, 0.5 h				72
390	**593**	$C_{17}H_{15}N_3O_4S_2$		4-Methoxybenzyl 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4α-carboxylate, anisole, CF_3CO_2H, 0.5 h	51.9	(164) (IR, ^{1}H NMR, Anal.)		154
391	**612**	$C_{17}H_{26}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
392	**621**	$C_{17}H_{28}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
393	**992**	$C_{18}H_6N_2S_3$		Application				255
394	**268**	$C_{18}H_{12}N_2O_2S$		2-(4-Methylphenyl)-3-thiocyanato-*N*-phenylmaleimide, KSCN (catalyst), CH_3CN, Δ, 10 h	42	(175–176) (IR, MS, Anal.)		111,112
395	**577**	$C_{18}H_{14}Cl_2N_2 \cdot NCS$		*trans,cis*-1-Formyl-4-isothiocyanatobuta-1,3-diene, $4\text{-}ClC_6H_4NH_2$				87

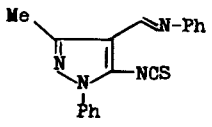
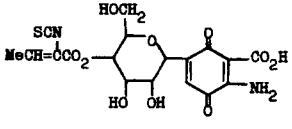
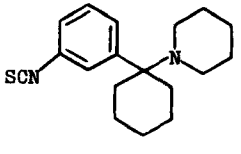
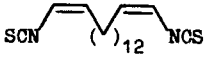
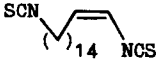
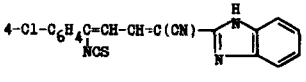
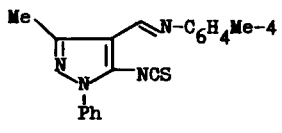
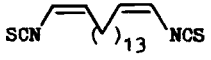
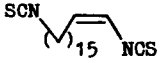
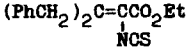
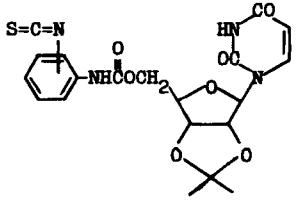
396	**432**	$C_{18}H_{14}N_4S$		4-[(*N*-Phenylimino)methyl]-3-methyl-1-phenyl-5-[(triphenylphosphoranylidene)-amino]-1*H*-pyrazole, CS_2, dry CH_2Cl_2, N_2, ~20 °C, 2 h			152
397	**562**	$C_{18}H_{15}NO_2S$	$(Ph)_2C{=}CCO_2Et$ NCS	Isothiocyanatoacetic acid ethyl ester, benzophenone, NaH or *t*-BuOK, N_2; THF, $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 2 h	32	(128–129) (IR, ^{1}H NMR, UV, Anal.)	23,187
398	**608**	$C_{18}H_{15}NO_2S_2$	$PhSCH_2C(Ph){=}CCO_2Me$ NCS (2:*E*) (2:*Z*)	4-Bromo-2-isothiocyanato-3-phenylbut-2-enoic acid methyl ester, PhSNa, (1,2-DME, 10 °C, 30 min)	63	(^{1}H NMR)	188
399	**587**	$C_{18}H_{18}N_2O_{10}S$		A mixture of paulomycin A and B, 1 N HCl in MeOH, room temp., 3 h		(157–160), $[\alpha]^{25}_D$ +108° (IR, ^{1}H, ^{13}C NMR, UV, MS, Anal.	190,191
400	**93**	$C_{18}H_{24}N_2S$		1-[1-(3-Aminophenyl)cyclohexyl]piperidine, $CSCl_2$, $CHCl_3/H_2O/NaHCO_3$; $MeSO_3H$ or HCl			73
401	**613**	$C_{18}H_{28}N_2S_2$		From a Fijiam sponge, *Pseudaxinyssa sp.*			28,194
402	**622**	$C_{18}H_{30}N_2S_2$		From a Fijiam sponge, *Pseudaxinyssa sp.*			28,194
403	**571**	$C_{19}H_{11}ClN_4S$		4-$ClC_6H_4C(NCS){=}CH{-}CH{=}$ $^+NMe_2{\cdot}ClO_4^-$, benzimidazol-2-ylacetonitrile, Et_3N	89	(218–219)	103

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
404	**433**	$C_{19}H_{16}N_4S$		4-[(*N*-*p*-Tolylimino)methyl]-3-methyl-1-phenyl-5-[(triphenylphosphoranylidene)-amino]-1*H*-pyrazole, CS_2, dry CH_2Cl_2, N_2, ~20 °C, 2 h				152
405	**614**	$C_{19}H_{30}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
406	**623**	$C_{19}H_{32}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
407	**628**	$C_{19}H_{33}NOS$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
408	**563**	$C_{20}H_{19}NO_2S$		Isothiocyanatoacetic acid ethyl ester, 1,3-diphenylacetone, NaH or *t*-BuOK, N_2; $(PhO)_2P(O)Cl$, 20–30 °C, 0.5 h; –60 °C, *t*-BuOK, THF, 20 °C, 15 min; –60 °C, $MeCO_2H$; CS_2, NaH, 30 °C, 2 h	35	(33–35) (IR, ^{1}H NMR, Anal.)		187
409	**590**	$C_{20}H_{20}N_4O_7S$		2′,3′-Isopropylidene-uridine, isocyanatophenyl isothiocyanate				193

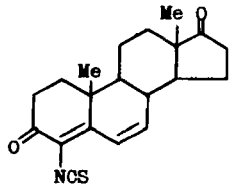
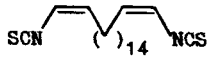
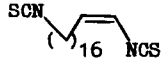
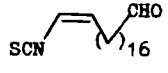
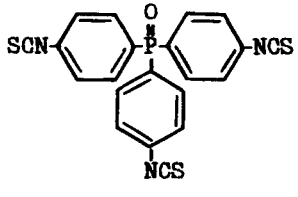
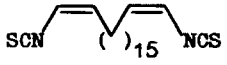
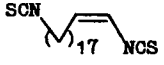
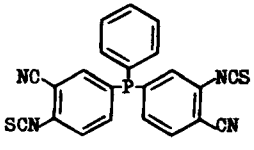
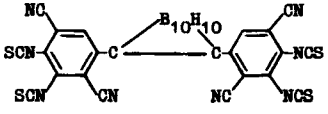
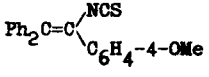
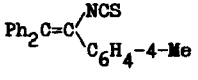
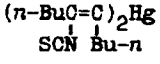
410	**296**	$C_{20}H_{23}NO_2S$		Allylic rearrangement of the corresponding 6β-thiocyanate in DMF, benzene, or toluene			120
411	**578**	$C_{20}H_{23}N_3S$	$4\text{-}MeC_6H_4NHCH{=}CH{-}CH{=}CH{-}CH{=}\overset{+}{N}HC_6H_4Me\text{-}4$ (NCS$^-$)	*trans,cis*-1-Formyl-4-iso-thiocyanatobuta-1,3-diene, $4\text{-}MeC_6H_4NH_2$			87
412	**615**	$C_{20}H_{32}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*			28,194
413	**624**	$C_{20}H_{34}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*			28,194
414	**629**	$C_{20}H_{35}NOS$		From a Fijian sponge, *Pseudaxinyssa sp.*			28,194
415	**989**	$C_{21}H_{12}N_3OPS_3$		Application			255
416	**459**	$C_{21}H_{15}NS$	$Ph_2C{=}CPhNCS$	Sulfur elimination from 4,5,5-triphenyl- Δ^3-1,3-thiazoline-2-thione			
				a) *absol.* xylene, reflux, 55 h	72	(153–154) (IR, Anal.)	166
				b) *absol.* benzene, trimethyl phosphite, light, reflux, 7 h	92		166

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
417	**616**	$C_{21}H_{34}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
418	**625**	$C_{21}H_{36}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*				28,194
419	**986**	$C_{22}H_{11}N_4PS_2$		Application				255
420	**978**	$C_{22}H_{12}B_{10}N_8S_4$		Application				253
421	**897**	$C_{22}H_{17}NOS$		Photolysis of 2,2-diphenyl-1-4-methoxyphenyl)vinyl bromide in the presence of SCN^-				102
422	**898**	$C_{22}H_{17}NS$		Photolysis of 2,2-diphenyl-1-4-methylphenyl)vinyl bromide in the presence of SCN^-				102
423	**412**	$C_{22}H_{36}HgN_2S_2$		*n*-BuC≡CH, 2 $Hg(SCN)_2$, *n*-$Bu_4N^+SCN^-$ (CH_2Cl_2, 40 °C)	15			141

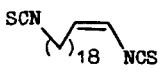
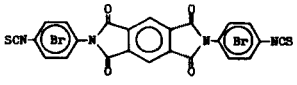
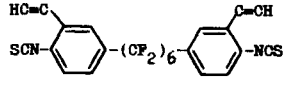
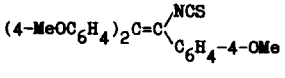
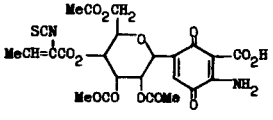
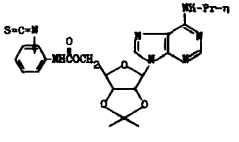
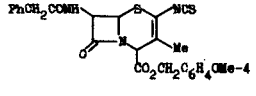
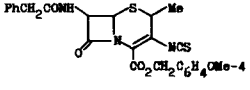
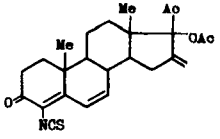
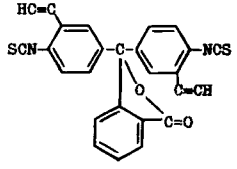
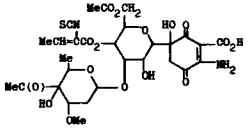
424	**626**	$C_{22}H_{38}N_2S_2$		From a Fijian sponge, *Pseudaxinyssa sp.*			28,194
425	**974**	$C_{24}H_2Br_8N_4O_4S_2$		Application			253
426	**980**	$C_{24}H_8F_{12}N_2S_2$		Application			253
427	**899**	$C_{24}H_{21}NO_3S$		Photolysis of tris-4-methoxyphenyl)vinyl bromide in the presence of SCN^-			102
428	**594**	$C_{24}H_{24}N_2O_{13}S$		11-*O*-Pauloylpaulinone, AcOH, $(Ac)_2O$, 4-MeC_6H_4-$SO_3H{\cdot}H_2O$, ~20 °C, 18 h		(IR, ^1H, ^{13}C NMR, UV, MS, Anal.)	192
429	**592**	$C_{24}H_{27}N_7O_5S$		2′,3′-Isopropylidene-adenosine, isocyanato phenyl isothiocyanate			193
430	**441**	$C_{25}H_{23}N_3O_5S_2$		a) 4-Methoxybenzyl 7β-phenylacetamido-2-azido-2-cephem-4α-carboxylate, Ph_3P, CH_2Cl_2, 1 h; 4-methoxybenzyl 7β-phenylacetamido-3-methyl-2-(triphenylphosphinimino)--2-cephem-4α-carboxylate, CS_2, Δ, 1.5 h	64.1	(173–175.5) (IR, ^1H NMR, UV, Anal.)	154
				b) 4-Methoxybenzyl 7β-phenylacetamido-	60.9	(173–175.5), $[\alpha]^{20}_D$ + 275.5°	154

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
431	**442**	$C_{25}H_{23}N_3O_5S_2$		2-azido-2-cephem-4α-carboxylate, Ph_3P, CS_2, Δ, 2 h a) 4-Methoxybenzyl 7β-phenylacetamido-3-methyl-2β-(triphenylphosphinimino)-3-cephem-4-carboxylate, CS_2, Δ, 1.5 h b) 4-Methoxybenzyl 7β-phenylacetamido-2β-azido-3-cephem-4-carboxylate, Ph_3P, CH_2Cl_2, 4 h; CS_2, 2–4 h (or Ph_3N, CS_2, 60 °C, 3 h)		(IR)		154
432	**298**	$C_{25}H_{29}NO_4S$		Allylic rearrangement of the corresponding 6β-thiocyanate in DMF, benzene, or toluene				120
433	**988**	$C_{26}H_{12}N_2O_2S_2$				255		
434	**634**	$C_{29}H_{36}N_2O_{16}S$		Biosynthesis				200,201

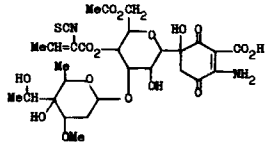
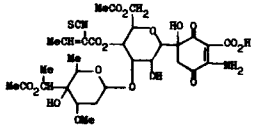
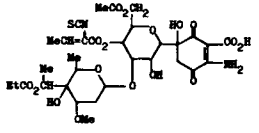
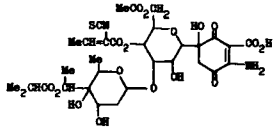
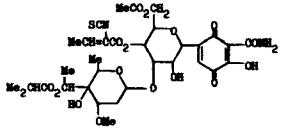
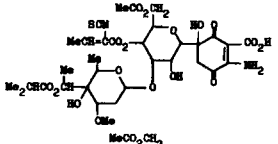
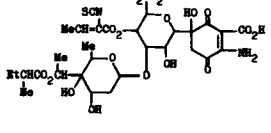
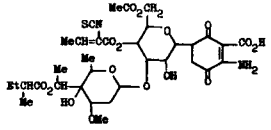
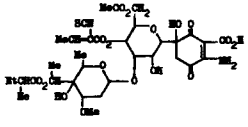
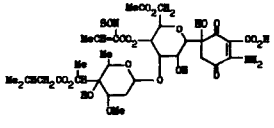
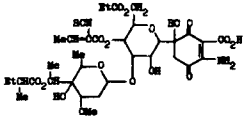
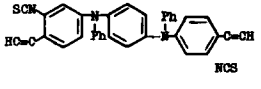
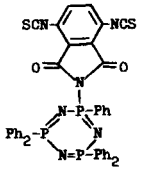
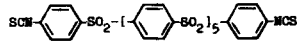
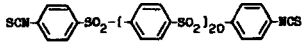
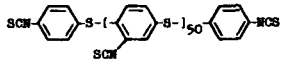
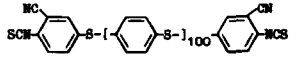
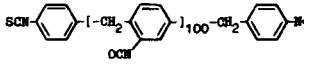
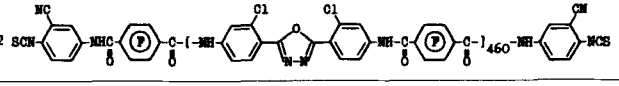
435	**635**	$C_{29}H_{38}N_2O_{16}S$		Biosynthesis	201
436	**633**	$C_{31}H_{40}N_2O_{17}S$		Biosynthesis	200,201
437	**632**	$C_{32}H_{42}N_2O_{17}S$		Biosynthesis	199,201,203
438	**637**	$C_{32}H_{42}N_2O_{17}S$		Biosynthesis	199
439	**586**	$C_{33}H_{42}N_2O_{16}S$		Paulomycin B, MeOH, room temp.	190
440	**584**	$C_{33}H_{44}N_2O_{17}S$		Biosynthesis	190–192,199–203, 205,206,213–215
441	**636**	$C_{33}H_{44}N_2O_{17}S$		Biosynthesis	199

TABLE 5 α,β-Unsaturated Isothiocyanates *(Continued)*

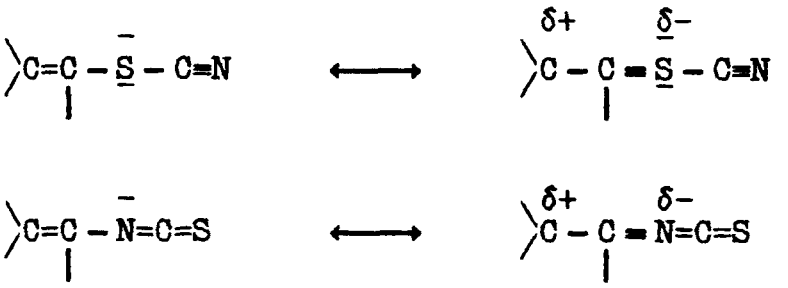
Entry No.	Cpd. No.	Formula	Isothiocyanate	Method	Yield, %	Bp/Pressure (mp), °C	n_D^{20}	Ref.
1	2	3	4	5	6	7	8	9
442	**585**	$C_{34}H_{44}N_2O_{16}S$		Paulomycin A, MeOH, room temp., 5d		(57–73), $[\alpha]^{25}_D$ +2° (IR, ^1H, ^{13}C NMR, UV, MS, Anal.)		190–192
443	**583**	$C_{34}H_{46}N_2O_{17}S$		Biosynthesis				190-192,199–203, 205–207,213–215
444 199–201	**631**	$C_{34}H_{46}N_2O_{17}S$		Biosynthesis				
445	**638**	$C_{35}H_{48}N_2O_{17}S$		Biosynthesis				207
446	**987**	$C_{36}H_{22}N_4S_2$		Application				255

447	**971**	$C_{40}H_{27}N_6O_2S_2P_3$		Application	253
448	**990**	$C_{44}H_{28}N_2O_{12}S_8$		Application	255
449	**993**	$C_{134}H_{88}N_2O_{42}S_{23}$		Application	255
450	**975**	$C_{364}H_{158}N_{52}S_{103}$		Application	253
451	**994**	$C_{616}H_{406}N_4S_{103}$		Application	255
452	**979**	$C_{815}H_{508}N_{102}O_{100}S_2$		Application	253
453	**984**	$C_{10144}H_{3688}F_{1844}$ $Cl_{920}N_{1846}O_{1382}S_2$			253

[a]Crude product. [b]A mixture of α,β- and β,γ-unsaturated isothiocyanates. [c]Ratio of isothiocyanate/thiocyanate = 5/5. [d]Total.

4. PHYSICO-CHEMICAL PROPERTIES

^1H, ^{13}C, and ^{15}N NMR spectra of thiocyanato (RSCN) and isothiocyanato (RNCS) compounds, especially for the vinylic series $R^1C(SCN)=CHR^2$ and $R^1(NCS)=CHR^2$ (**142**, **376**, **377**, **396**, **391**, **399**, **403**, **404**), have been reported.[143] The ^{13}C chemical shifts of thiocyanates (δ *ca.* 100 ppm) and of isothiocyanates (δ, *ca.* 275 ppm) are very different, the value for the thiocyanate ion $(SCN)^-$ being intermediate (δ, 165 ppm). A comparison of the spectra of vinyl thiocyanates and isothiocyanates with those of the corresponding saturated compounds suggests that the SCN group exerts both attractive σ and π effects on the C=C bond, mainly through the intervention of the *d* orbitals of the sulfur atom. The NCS group appears to be slightly electron donating towards the double bond (Scheme 245).[143]



SCHEME 239

Solvent effects on the ^{15}N chemical shift of *n*-BuSCN and *n*-BuNCS have been discussed in terms of Taft's linear solvation energy relationship.[143]

Fluorescence spectra of 21 5-isothiocyanato-2-(substituted phenyl)benzothiazoles, 5-isothiocyanato-2-phenylbenzoxazole, 2-(4-isothiocyanatophenyl)benzothiazole, benzothiazole and benzoxazole, in $CHCl_3$ solution, have been given.[257] The fluorescence intensity is affected by the substituents, maximum intensity was exhibited by the compounds having N=C=S bonded to a benzene ring.

Ultraviolet spectra (in dioxane) have been given for 5-isothiocyanato-2-phenylbenzotriazole **31–40**, 5-isothiocyanato-1-phenylbenzotriazole **41**, **44**, **46**, **47**, and 2-phenylbenzotriazole.[258]

5. BIOLOGICAL PROPERTIES

In Ref. [259] a quantitative structure-activity relationship (QSAR) has been formulated for the inhibition of the Hill reaction by 3-alkoxyuracils, including 3-propoxy-5-isothiocyanatouracil **995** and 3-octyloxy-5-isothiocyanato-6-methyluracil **996**. Topological indices were used as quantitative descriptors of the molecular structures. A detailed analysis shows that the molecular connectivity model performs best in all cases except 3-propoxy-5-isothiocyanatouracil **995** and 1-methyl-3-propoxy-5-bromo-6-methyluracil.[259]

It has been found[130,131] that 1-isothiocyanatopropargyl ethers **327–334** possess strong biocidal properties against fungi of epidermophytons, penicillus and aspergillus.

Twenty-one substituted, including benzyl, benzoyl and phenyl isothiocyanates*, have been tested for fungistatic and bacteriostatic properties.[260] The substances were particularly active against fungi and less active against bacteria. In both cases benzyl isothiocyanates were the most active; 3-ethyl-4-fluorobenzyl isothiocyanate showed the highest fungistatic activity and 3,4-dichlorobenzyl isothiocyanate the highest bacteriostatic activity.[260]

Paulomycin A **583** and B **584** belong to a class of novel antibiotics, produced by *Streptomyces paulus* UC 8560, which are equally active against a variety of pathogenic bacteria[205,213] (and references therein). An antibiotic complex containing an isothiocyanato group and active against multiply resistant strains of staphylococci and other Gram-positive bacteria has been isolated from cultures of *Streptomyces albus* G.

N-(1,2,2,2-Tetrachloroethyl)formamido-3,5-dimethyl-4-isothiocyanatopyrazole **582** has fungicidal activity against *Xanthomonas campestris pv. oryzae* and *Pyricularia oryzae*.[189]

3-Isothiocyanatomethylene-DL-camphor **127** showed higher antiparasitic activity than the corresponding terpene alcohols.[78]

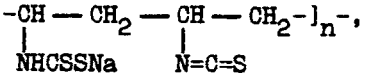
4-Substituted phenyl isothiocyanates **1–17**, heterocyclyl isothiocyanates **18–23** and bisisothiocyanates **24–28** and their adducts with various amino compounds have been tested for antihookworm activity in the *N. americanus* infested hamster.[63] Fairly good activity was exhibited by 4-(4-chlorophenylthio)phenyl isothiocyanate **5**, 4-(2-methyl-4-thiazolyl) phenyl isothiocyanate **8**, 4-(2-benzothiazolyl)phenyl isothiocyanate **10** and 4-(2-benzimidazoyl)phenyl isothiocyanate **13**, among which 4-(2-benzthiazolyl)phenyl isothiocyanate **10** was the most active.[63]

α-Naphthyl **851** and phenyl isothiocyanate **189** are effective ovicides when applied to ascarid eggs during short exposure. α-Naphthyl isothiocyanate **851** is most effective.[44]

The bacteriostatic activity of 4-methoxybenzyl 7β-phenylacetamido-2-isothiocyanato-3-methyl-2-cephem-4α-carboxylate **491** has been investigated.[154]

In vitro tests against *Micrococcus pyogenes* var. *aureus* showed several polyhalogenated carbanilides and thiocarbanilides **773** and **774** prepared by reaction of aryl isocyanates and aryl isothiocyanates with amines, to be active in a concentration range $1:10^{-5}$–10^{-6}; notable activity *in vitro* and *in vivo* against *Mycobacterium tuberculosis* (strain H37 Rv), as well as *in vivo* against *Mycobacterium leprae*, was shown by 4-(*N,N*-diethylamino)-4′-isopentyloxythiocarbanilide.[225]

Copoly(sodium vinyl dithiocarbamate-vinyl isothiocyanate), obtained by the dithiocarbamoylation of poly(vinylamine) had an inhibitory effect on the mycelial growth of *Aspergillus niger* and *Trichoderma viride*.[261]



SCHEME 246

*Z-ethyl- (**997**) 3-ethylphenyl isothiocyanate

The 5-isothiocyanato-2-phenylbenzotriazoles **31**, **34**, **36**, **38**, and **39** are useful as biocidal agents, especially against yeasts, dermatophytes, and HeLa cells.[69]

The effectiveness of 1-[1-(3-isothiocyanatophenyl)cyclohexyl]piperidine **93** as acylating agent for the [^{3}H]phencyclidine (PCP) receptors has been demonstrated in rats.[73] 1-[1-(3-Isothiocyanatophenyl)cyclohexyl]ethylamine **94** and -isopropylamine **95** and 1-[1-(4-isothiocyanatothiophen-2-yl)cyclohexyl]piperidine **97** are effective irreversible inhibitors of the PCP receptor.[74]

β-Lactam derivatives and penicillin analogs obtained by reaction of cephalexin **753** with various aryl isothiocyanates and pharmaceutical compositions containing them have been described.[222] It was found that cephalexin **753** after treatment with 4-methylphenyl isothiocyanate **192** as its triethylamine salt gave 50% inhibition of *Escherichia coli* β-lactamase at 43.19 mmol.[222]

4-Iodophenyl isothiocyanate **999** and 1,2,3,4,7,7-hexachloro-5-isothiocyanatobicyclo[2,2,1]hept-5-ene **1000** have been tested against one susceptible and five resistant strains of *Musca domestica* (housefly) for cross resistance.[262]

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