Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

β-Heterosubstituted α,β-Unsaturated Thioketones. Some Problems of Synthesis and Structure

Vladimir A. Usov[a]; Mikhail G. Voronkov[a]
[a] Institute of Organic Chemistry, Siberian Division of the USSR Academy of Sciences, Irkutsk, USSR

To cite this Article Usov, Vladimir A. and Voronkov, Mikhail G.(1982) 'β-Heterosubstituted α,β-Unsaturated Thioketones. Some Problems of Synthesis and Structure', Journal of Sulfur Chemistry, 2: 2, 39 — 75
To link to this Article: DOI: 10.1080/01961778208082426
URL: http://dx.doi.org/10.1080/01961778208082426

Sulfur Reports
Volume 2 (2), March 1982, pp. 39–85

Printed in the United States of America

β-HETEROSUBSTITUTED α,β-UNSATURATED THIOKETONES. SOME PROBLEMS OF SYNTHESIS AND STRUCTURE

VLADIMIR A. USOV and MIKHAIL G. VORONKOV
Institute of Organic Chemistry, Siberian Division of the USSR Academy of Sciences, 664033 Irkutsk, USSR

A review of synthetic routes to aliphatic, alicyclic, and heterocyclic thioketones having an X—C=C—C=S group (X = NR^1R^2, OR, SH, SR, Cl, CN) is given. Enamino thioketones have been most thoroughly studied synthetically. The preparation of these compounds involves processes of building up of the thioketone group, on one hand, and insertion of the amino function into sulfur organic compounds, on the other hand. The synthesis of β-alkoxy, β-alkylthio and β-chloro substituted vinylene thioketones is based on sulfhydrolysis of immonium salts of the type X—C=C—C=$\overset{\oplus}{N}<$ (X = OR, SR, Cl) at the C=$\overset{\oplus}{N}$ bond as described in papers from the latest three years. The sulfhydrolysis of β-alkoxy (or alkylthio) vinylene thioketones has provided a convenient synthetic approach to some β-mercaptovinylene thioketones (β-dithiodiketones). The synthesis of the first β-cyanovinylene thioketone stabilized as a trimer is described involving the cyanolysis of β-alkoxy and β-chlorovinylene thioketone. The main synthetic routes to enamino thiocarboxamides, enamino dithiocarboxylic acids and their derivatives are also considered. Tautomerism, cis-trans-isomers and rotamers of enamino thioketones and β-dithiodiketones are discussed in terms of ^1H NMR, ^{13}C NMR, IR, and UV spectroscopic data and quantum-chemical calculations.

Contents

I. INTRODUCTION

The chemistry of thioketones possessing an X—C═C—C═S group (X = H, RO, R_2N, SH, RS, Hal, CN, NO_2, etc.) has not been studied much. This is due to difficulties encountered in the preparation and purification of many compounds of this class. During the latest two decades, enolthiones (monothio-β-diketones; X = HO) the chemistry of which is considered in several reviews, for example,[1,2] have been studied in detail.

At the beginning of our investigation[3,4] some data on the synthesis of enamino thioketones (X = R_2N) had been reported from time to time. The monography by Freimanis[5] contains only 30 references on enamino thioketones and their functional analogs. At present, on the other hand, enaminothionic fragments can be found in aliphatic, alicyclic, and heterocyclic compounds. The synthetic routes to these com-

pounds are very numerous since the preparation of each type of enamino thioketone requires the development of a specific method. Reports of syntheses and properties of other β-hetero substituted α,β-unsaturated thioketones (X = RO, SH, SR, Cl, CN, etc.) have appeared only recently. The high and multifaceted reactivity of conjugated thioketones makes these compounds of special interest as far as the problems of synthesis and structure of new types of sulfur organic compounds and the search for their practical application are concerned.

II. SYNTHESIS OF ENAMINO THIOKETONES (VINYLOGOUS THIOCARBOXAMIDES)

II.1. Synthesis by sulfurization reactions (thiolation)

II.1.1. Reaction of enamino ketones with tetraphosphorus decasulfide Tetraphosphorus decasulfide is widely used in the synthesis of thioamides from amides.[6] One knowledge of the reactions of enamino ketones (vinylogous amides) with P_4S_{10} is rather limited.

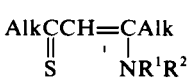
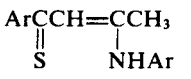
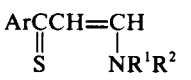
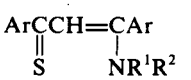
The reaction of aliphatic enamino ketones with tetraphosphorus decasulfide depends on the substitution at C^1 and C^3, and at the N atom. The yield of enamino thioketones is usually not high since the reaction is accompanied by poorly understood processes and leads to a complex mixture in most cases.[7-16]

$$R^1-C(=O)-CH=C(R^2)-NR^3R^4 \xrightarrow{P_4S_{10}} R^1-C(=S)-CH=C(R^2)-NR^3R^4 + \text{other compounds}$$

Depending on the type of substitution, the enamino thioketones prepared by the above reaction can reasonably be divided into four groups (Table I). Some features of this reaction should be noted. 2-(2-Thioxopropylidene)-4-methyl-6-aryl-2H-thiopyranes (*1*), for example, were obtained as by-products under the conditions of the syn-

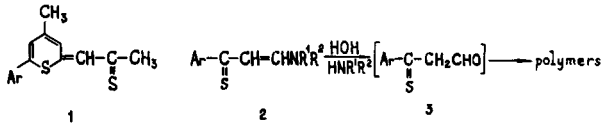
TABLE I

The Main Types of Aliphatic Enamino Thioketones Prepared by the Reaction of Enamino Ketones with Tetraphosphorus Decasulfide

Group	Compound	Formula	Solvent	Yield, %	References
1	1,3-Dialkyl-3-[alkyl(dialkyl)amino]-2-propene-1-thiones		benzene	10–23	7
2	1-Aryl-3-(arylamino)-2-butene-1-thiones		carbon disulfide	20	8, 9
3	1-Aryl-3-[dialkyl(aryl)amino]-2-propene-1-thiones		benzene carbon disulfide	5–18 50	10–14
4	1,3-Diaryl-3-[dialkyl(aryl)amino]-2-propene-1-thiones		carbon disulfide	30–75	15, 16

thesis of Group 2 enamino thioketones. Consequently, when preparing aliphatic enamino thioketones one should bear in mind the possibility of heterocyclization.

During the synthesis of Group 3 enamino thioketones *2* the reaction mixture is occasionally treated with aqueous sodium bicarbonate solution. It turned out that Group 3 N,N-dialkyl derivatives (R^1, R^2 = Alk) are prone to hydrolysis to form polymerizable 2-thioxo-2-arylpropanals.

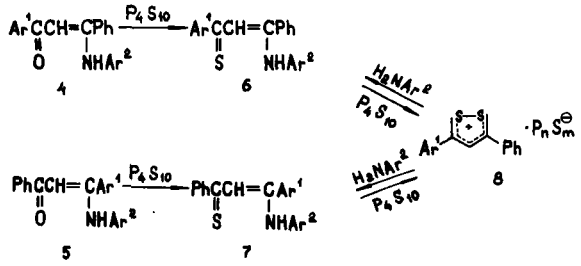


Use of an appropriate dialkylamine (instead of $NaHCO_3$) increases the yield of the main products to 50 %. However, the authors[13,14] do not give any explanation for this observation.

A reversible substitution of an amino group by a sulfur nucleophile and the corresponding esters of the type ArC(=S)—CH=CH—S—P< can occur under the conditions of the synthesis of Group 3 enamino thioketones *2* where the C^3 atom is sterically less hindered than in Group 1, 2, and 4 compounds (Table I). The reaction of these compounds with the secondary aliphatic amines used in the work-up of the reaction mixture should give, under mild conditions, enamino thioketones *2*. When N-aryl substituted analogs of *2* (R^1 = H, R^2 = Ar) were to be isolated, treatment of the reaction mixture with a corresponding arylamine failed to increase the yield of enamino thioketone.[13,14] This may be explained by the fact that aminolysis by aromatic amines usually requires more drastic conditions.

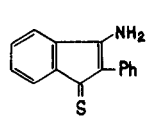
The effect of steric factors on the reaction of enamino ketones with P_4S_{10} has been reported.[12] Enamino thioketones *2* were obtained only from the cis-isomers of the starting ketones, the trans-isomers affording intractable resins.

The yields of 1,3-diaryl substituted enamino thioketones *6* and *7* (Group 4) are comparatively high. If the starting enamino ketones contain different aryl substituents at C^1 and C^3 the reaction with tetraphosphorus decasulfide leads to a mixture of two enamino thioketone isomers. Substituted aminopropenones *4* and *5*, for example, give a mixture of 1-(4-methoxyphenyl)-3-phenyl-3-(4-methylphenylamino)-2-propene-1-thione (*6*) with 1-phenyl-3-(4-methoxyphenyl)-3-(4-methylphenylamino)-2-propene-1-thione (*7*). No thermal isomerization *6* ⇄ *7* occurs. However, the reaction of aliphatic enamino thioketones with tetraphosphorus decasulfide has been shown to yield 3,5-diaryl-1,2-dithiolium salts (*8*) which are able to react further with amines[10,12,15] (see Section II.2.4). Therefore, the following scheme:

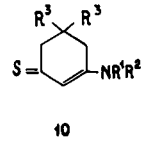


$Ar^1 = 4\text{-}CH_3OC_6H_4$; $Ar^2 = 4\text{-}CH_3C_6H_4$

has been proposed for the explanation of the *6* ⇌ *7* conversion. The reactions of cyclic enamino ketones with tetraphosphorus decasulfide have been less extensively studied. According to Ref. 17, 3-amino-2-phenyl-1-indenethione (*9*) is formed upon refluxing the initial amino ketone with P_4S_{10} in carbon disulfide, however, no data concerning the yield and purity of the thioketone were reported. Recently a method for the preparation of substituted 3-amino-2-cyclohexene-1-thiones (*10*) by the reaction of the corresponding enamino ketones with P_4S_{10} in hot pyridine or dioxane has been developed.[18,19] This method makes it possible to obtain compounds *10* with different types of substitution at the nitrogen atom. The yield of thio derivatives amounts to 25–78 %.



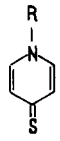
9



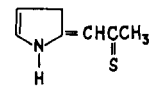
10

R^1=H; R^2=H, Alk, Ar-Alk, Ar; R^1=R^2=Alk, cyclo-Alk } R^3=H, Me

The corresponding ketone, when refluxed with tetraphosphorus decasulfide in the absence of solvent, forms 4-thioxo-1,4-dihydropyridine (*11*) in 86 % yield.[20] For the synthesis of 1-(4-pyridyl)-4-thioxo-1,4-dihydropyridine (*12*), the initial ketone was refluxed with P_4S_{10} in toluene and the resultant product of unidentified structure decomposed with ammonium sulfide.[21] The yield was 50 %. The author assumed the intermediate to be a molecular compound composed of *12* and P_4S_{10}. As it has become known later,[22] pyridine readily forms with tetraphosphorus decasulfide a crystalline compound, $P_4S_{10} \cdot C_5H_5N$ which releases pyridine when treated with bases. A method for the synthesis of 2-(2-thioxopropylidene)-2,3-dihydropyrrole (*13*) is worth of notice.[23] The reaction of the starting ketone with P_4S_{10} in an inert atmosphere was carried out first in refluxing carbon disulfide and then in a 2-methyl-pyridine–xylene mixture (1:20) at 130 °C. The yield of thioketone *13* is 73 %. No explanation is given for this experiment.



11, R=H; 12, R = 

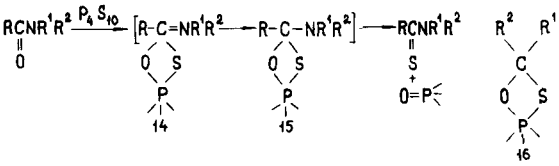


13

II.1.2. Some features of the application of tetraphosphorus decasulfide for the sulfurization of the carbonyl group Numerous examples show that a successful synthesis of thiocarbonyl compounds by means of tetraphosphorus decasulfide depends, to a large extent, on the appropriate choice of solvent and reaction temperature, the treatment of the reaction mixture and the stability of the thio compound. P_4S_{10} is hardly soluble in refluxing aromatic hydrocarbons.[24] In some cases, however, thermal activation and vigorous stirring of the reaction mixture increases the yield of thiocarboxamides to 80 %.[25-29] For the nucleophilic activation of P_4S_{10} molecules in the synthesis of aromatic thiocarboxamides Kindler[30] used potassium sulfide additives. As it has been found later, this approach is inefficient in those cases where the thiocarboxamide is able to react with alkali metal sulfides.[31]

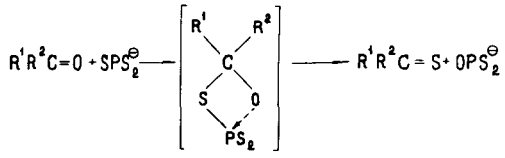
The yield of thioketones and thiocarboxamides frequently reaches 95 % when dry pyridine[26,32-34] (which dissolves phosphorus decasulfide upon heating[22]) or dioxane[35] is used. Acetonitrile,[36-38] diglyme, and diethyl ether[36] with an activating sodium bicarbonate additive are also very efficient agents.

Several schemes accounting for sulfurization with tetraphosphorus decasulfide under various conditions have been proposed. It is believed[39] that in the case of amides electrophilic attack of a thermally activated P_4S_{10} molecule at the oxygen atom is the first step affording the intermediate zwitterion *14*. The latter undergoes cyclization to a 1,3,2-oxathiaphosphetane derivative *15* which is later cleaved to give the thiocarboxamide according to the scheme:

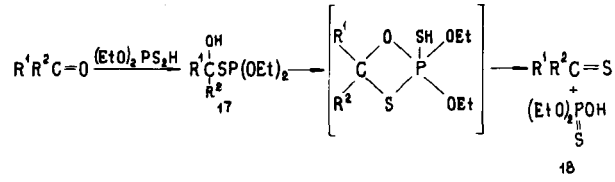


The sulfurization of alicyclic[34] and aromatic[36,40,41] ketones seems to occur in a similar way since an intermediate *16* can be formed in this case.

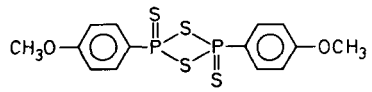
A catalytically initiated reaction, for example that of benzamide with P_4S_{10} in the presence of potassium sulfide in xylene, is thought to involve the formation of the RC=O . . . $(S)_2P—S—P(S)_2$ . . . O=CR complex.[30] Upon heating the latter is converted to thiobenzamide and, possibly, to P_4O_{10}. It is also assumed[36] that tetraphosphorus decasulfide when reacting with sodium bicarbonate or potassium sulfide in acetonitrile first forms salts of the type $SPS_2^{\ominus}\cdot Na^{\oplus}(K^{\oplus})$ or $OPS_2^{\ominus}\cdot Na^{\oplus}(K^{\oplus})$. Then the $SPS_2^{\ominus}$anion attacks the C=O group in a nucleophilic substitution leading to the following thiocarbonyl compound:



It is possible that the reaction of O,O′-diethyl dithiophosphoric acid with ketones and aldehydes could explain some stages of the sulfurization of carbonyl compounds by tetraphosphorus decasulfide.[42] The intermediate adducts *17* and O,O′-diethyl thiophosphoric acid (*18*) which could be isolated lead credence to the proposed scheme.

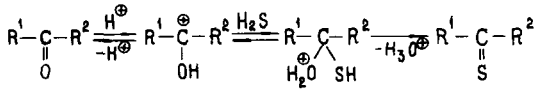


II.1.3. Reaction of enamino ketones with 2,4-bis-[4-methoxyphenyl]-2,4-dithioxo-P^V,P^V-1,3,2,4-dithiadiphosphetane The reaction[43] of the appropriate enamino ketones with a dithiophosphetane derivative of the following formula

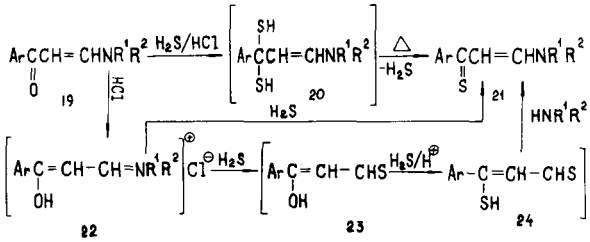


has been suggested for the preparation of aliphatic enamino thioketones of Group 1 (See Table I) and their cyclic analogs of type *10* having an N—H bond. Sulfurization with the above agent at 20 °C in 1,2-dimethoxyethane leads to enamino thioketones in high yield (60–80 %).

II.1.4. Reaction with hydrogen sulfide Many aldehydes and ketones are readily converted to their thio analogs by reaction with hydrogen sulfide in the presence of HCl, HF or H_2SO_4:[20,44–50] The reaction is usually carried out in alcohols the acidity of the medium being sufficiently high to favor the optimal ratio of protonated carbonyl compound to unprotonated hydrogen sulfide (*cf.* Refs. 51 and 52).

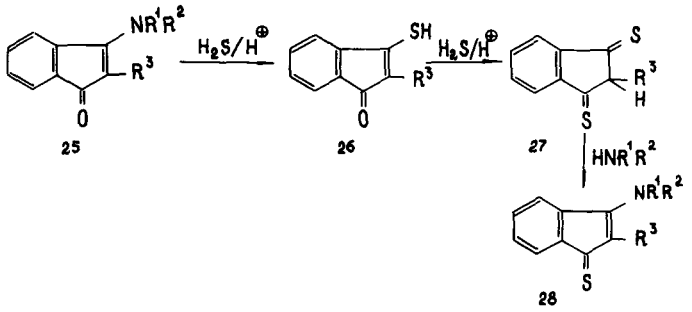


The synthesis of thioamides from amides fails when carried out in this way.[53] This is explained by the fact that the protonation of amides gives cations of low electrophilicity: $[R^1C(OH)NR^2R^3]^{\oplus}$. However some amide vinylogs convert to enamino thioketones even under these conditions. Thus, 1-aryl-3-(N,N-dialkylamino)-1-propenones (*19*) react with hydrogen sulfide in alcoholic HCl solution to form thio analogs *21* in 3–10 % yield.[10–13] An intermediate formation of the corresponding gem-dithiols *20* or immonium salts *22*[54] is also assumed.[13]



Taking into account that various enamino ketones form immonium salts with Brønsted acids[55–57] the assumption of intermediate *22* seems more attractive. The direct *22* → *21* conversion is subject to some doubt, however, since 3-(N,N-dialkylamino)-2-aryl-1-indenones (*25*) when treated with hydrogen sulfide in the presence of alcoholic HCl are readily converted to mercaptoindenones *26* in high yield.[58] Under the same conditions, compounds *26* form β-dithiodiketones *27*[59] which readily react with highly basic amines to give the enamino thioketones *28*.[60] For this reason, a more complicated *19* → *22* → *23* → *24* → *21* conversion which also accounts for the low yield of enamino thioketones *21*, may be assumed (*cf.* Refs. 8, and 61–63). And it becomes clear why N-aryl substituted analogs of compound *19* cannot undergo any conversion of this type.[13]

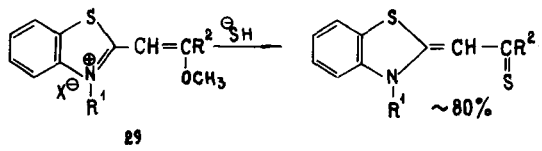
In the presence of bases the carbonyl group in amides and their vinylogs fails to react with hydrogen sulfide



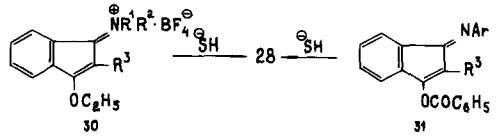
II.1.5. The effect of sulfur nucleophiles on compounds containing the groups

$$-N{=}C{-}C{=}C{-}Z \text{ or } \overset{\oplus}{>}N{=}C{-}C{=}C{-}Z \; (Z = NR_2, OR, SR, Cl)$$

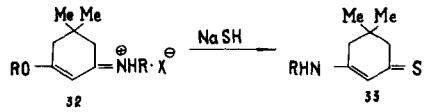
II.1.5.1. Reaction of β-organyloxyvinylene methinimmonium salts with sodium sulfide or sodium hydrosulfide The synthetic value of this route to enamino thioketones was demonstrated for the first time in the case of the sulfurization of 1,3-benzothiazolium salts *29*:[64,65]



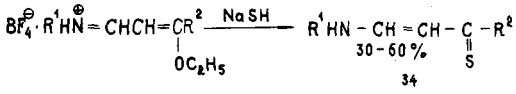
The first two representatives of enamino thioketones of the indene series *28* were prepared by refluxing N-(3-ethoxy-2-phenylindene-1-ylidene)-immonium tetrafluoroborate (*30*) or its N-phenyl substituted analog with sodium sulfide in methanol.[17] Later it was found that the use of sodium hydrosulfide enables the reaction to be carried out without heating and a large number of enamino thioketones *28* with different substituents at C^2 and N were obtained in high yields.[19,66,67] 1-(Arylimino)-2-aryl-3-benzoyloxyindenes (*31*) are appropriate starting materials for the preparation of N-(monoaryl) substituted analogs of *28*.[66,68]



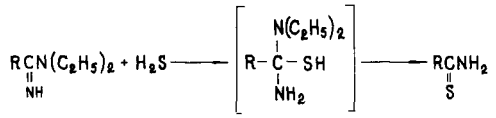
The reaction of N-monosubstituted N-(3-ethoxy-5,5-dimethyl-2-cyclohexene-1-ylidene)-immonium salts (*32*) or the corresponding bases with sodium hydrosulfide in alcohol at 20 °C leads to a complicated mixture of sulfur compounds, the corresponding enamino thioketones *33* being obtained in low yield.[18,66]



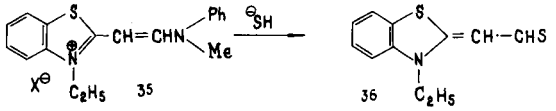
Aliphatic enamino thioketones (*34*) were prepared in an analogous way:[69]



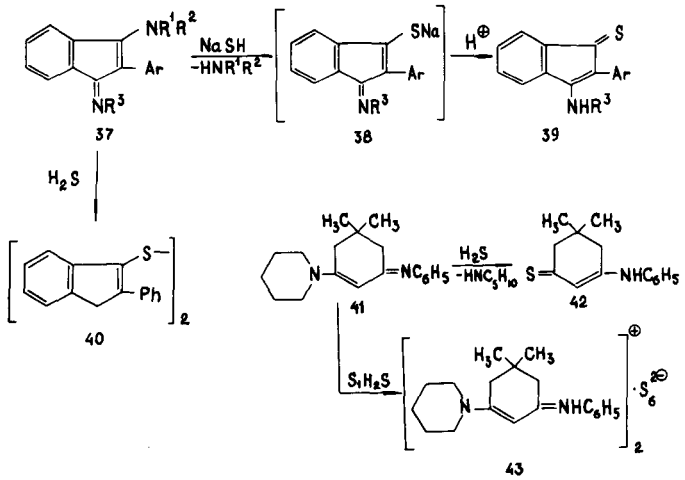
II.1.5.2. Sulfhydrolysis and sulfurization of enamino imines Enamines react with hydrogen sulfide in the presence of organic bases[70,71] or acids[55,72,73] to form the corresponding thioketones: $RC{=}CN\lessdot + H_2S \rightarrow HN\lessdot + RC{=}C{-}SH \rightleftharpoons RCHC{=}S$. Imines and anils[74-76] when treated with hydrogen sulfide in alcohol are readily converted to thioketones according to the scheme: $R^1C{=}NR^2 + H_2S \rightarrow R^1C{=}S + H_2NR^2$. The sulfhydrolysis of amidines with hydrogen sulfide in pyridine affords thiocarboxamides.[77,78]



The sulfhydrolysis of enamino imines (amidine vinylogs) was first encountered in the reaction of the 3-ethyl-2-(2-N-methyl-N-phenylaminoethyl)-1,3-benzothiazolium salt (*35*) with sodium hydrosulfide in methanol which leads to the enamino thioaldehyde *36* in good yield:[65]



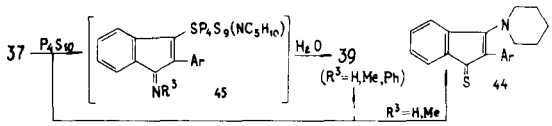
N-Unsubstituted 1-imino-2-aryl-3-aminoindenes (*37*) react with sodium hydrosulfide in refluxing dry alcohol to form solutions of the sodium salts of the corresponding 1-imino-2-aryl-3-indenethiols (*38*) which upon neutralization give 3-amino-2-aryl-1-indenethiones (*39*).[79,80] When the above reaction is carried out in 96 % alcohol, the yield of these compounds decreases due to their ready hydrolysis in aqueous-alcoholic base.[59]



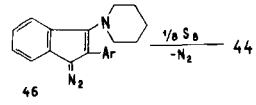
Compounds with both a non-tautomerizable enamine group and imine groups with different N-substituents (R^1, $R^2 = (CH_2)_5$; R^3 = H, Me, Ph) have been used for the determination of the reaction center (C^1 or C^3) of the indene enamines *37* during sulfurization with sodium hydrosulfide. The thiolation of the enamino group is observed in all cases, the end products being N-unsubstituted, N-methyl and N-phenyl substituted enamino thioketones *39*, respectively. No thiolation of enamino imines *37* with sodium sulfide occurs under these conditions. When treated with hydrogen sulfide in alcohol, enamino imines *37* eliminate the corresponding amines to form a mixture of sulfur-containing compounds from which the bisindenyldisulfide *40* has been isolated.

Unlike the indene enamino imines, 1-piperidino-3-(phenylimino)-5,5-dimethyl-1-cyclohexene (*41*) with hydrogen sulfide readily affords the anilino substituted thioketone *42*. The joint effect of sulfur and hydrogen sulfide on compound *41* leads to the enamino thioketone *42* and the hexasulfide of the starting base *43*.[18,81] The reactions of ketimines and enamines with tetraphosphorus decasulfide are little known. The ketimino group may be assumed to undergo sulfurization similarly to the carbonyl group (see II.1.2.). Besides, thiolysis of the amino group has been observed upon the action of P_4S_{10} on some amides.[82] Indene enamino imines react with P_4S_{10},[79] the reaction course being dependent on the type of substitution at the nitrogen atom. Upon heating of N-unsubstituted ($R^1 = R^2 = R^3$ = H) or N,N'-diphenyl substituted (R^1 = H; $R^2 = R^3$ = Ph) compounds *37* in pyridine or dioxane, the corresponding enamino thioketones *39* were obtained in approximately 50 % yield. The orientation of the reaction (C^1 or C^3) has been determined using enamino imines *37* with a tertiary amino group (R^1, $R^2 = (CH_2)_5$; R^3 = Me or Ph). The reaction of the compound containing a phenylimino group (R^3 = Ph) with P_4S_{10} does not involve the sterically inaccessible C^1-phenylimino carbon atom and, consequently, no 3-piperidino-2-phenyl-1-indenethione (*44*) is formed. Only after treatment of the reaction mixture with water 3-phenylamino-2-phenyl-1-indenethione (*39*, Ar = R^3 = Ph) was isolated as the sole product.

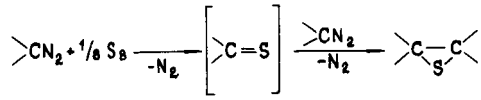
In this case, P_4S_{10} is assumed to attack C^3 of the enamine to form thiolates *45* which can be decomposed by water to form the enamino thioketone *39* and the compound $HOP_4S_9 \cdot (NC_5H_{10})$. In the case of enaminoimines *37* with R^3 = H or Me the thiolysis proceeds in both the C^1 and C^3 direction and the treatment of the reaction mixture with water leads to N-unsubstituted (*39*, R^3 = H) or N-methyl substituted (39, R^3 = Me) enamino thioketones, respectively, along with the piperidino analog *44*.



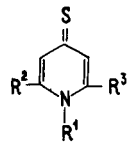
II.1.5.3. Sulfurization of diazo compounds The reaction of the enamino diazoindenes *46* with elemental sulfur[83] or the hexasulfides *43*[81] gives the corresponding enamino thioketones *44* in low yield which, probably due to a significant influence of steric factors on the thiocarbonyl group, fail to react further with the diazo compounds *46*.



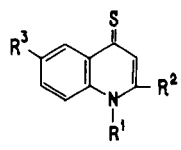
This reaction is the first to support the reaction scheme of the conversion of diazo compounds to thiiranes through thioketones, previously suggested by several authors.[84]



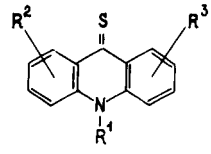
II.1.5.4. Reaction of β-chlorovinylene methinimmonium salts with sulfur nucleophiles The salts of nitrogen-containing heterocyclic compounds containing a $Cl—C=C—C=\overset{\oplus}{N}< \cdot X^{\ominus}$ group have been long known and are comparatively readily available. The reaction of these salts with sodium sulfide or hydrosulfide proceeds at the C—Cl bond leading to the corresponding enamino thioketones. For the thiolysis of salts of the above type one can use thiosulfate or sodium N,N-dimethyldithiocarbamate[85] as well as thiourea.[86] In this way the following heterocyclic enamino thioketones have been prepared.



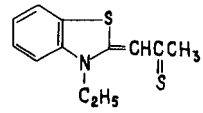
Ref.[86,87]



Ref.[86,88]

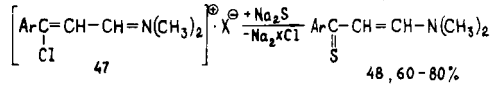


Ref.[89,90]



Ref.[91]

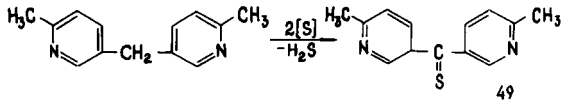
Recently a synthetic route to aliphatic enamino thioketones *48*, based on the reaction of β-chlorovinylene methinimmonium salts *47* with sodium sulfide in a dimethylformamide-ethylene glycol medium has been proposed:[92,93]



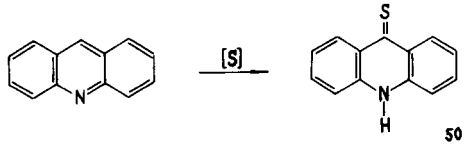
47 48, 60–80%

The reaction of analogous salts derived from cyclohexene has been shown[18] to proceed through the $C=\overset{\oplus}{N}$ bond involving both elimination of amine and retention of the C—Cl bond (see Section VI).

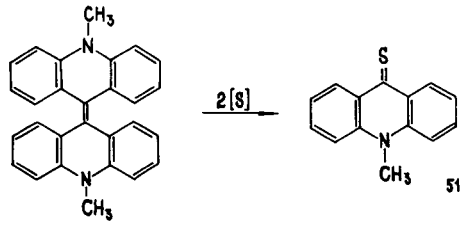
II.1.5.5. Reaction of nitrogen-containing heterocyclic compounds with elemental sulfur Thermally activated elemental sulfur is able to dehydrogenate organic molecules with liberation of hydrogen sulfide, to attack C—H and C=C bonds which ultimately leads to thioketones.[94] On fusion of bis-(6-methyl-3-pyridyl)-methane,[95] acridine, or its derivatives,[96–98] for example, with sulfur at 190–200 °C the thermally stable heterocyclic enamino thioketones *49*, *50* and *51* respectively are formed.



49



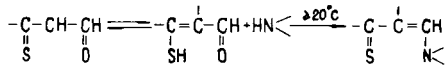
50



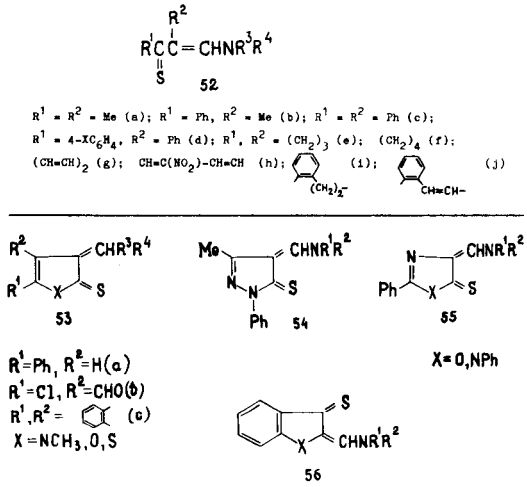
51

II.2. Synthesis of enamino thioketones by aminolysis of organosulfur compounds

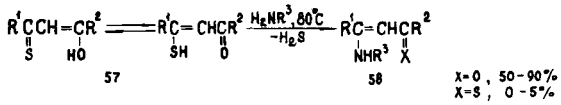
II.2.1. Aminolysis of monothio-β-dicarbonyl compounds (vinylogous thiocarboxylic acids) Compounds containing a β-mercaptovinylene aldehyde group readily react with various amines through the aldehyde group to form enamino thioketones according to the following scheme:



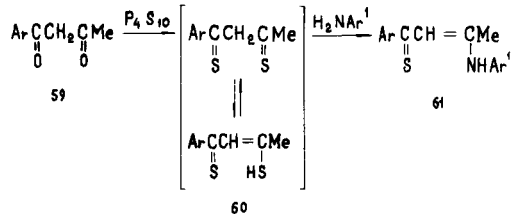
In this way, aliphatic *52a–c,*[99–102] carbocyclic *52c–j*[101,103,104] and heterocyclic *53, 54, 55, 56*[105–111] enaminothioketones have been prepared using ammonia, primary and secondary aliphatic amines, and aniline and its derivatives.



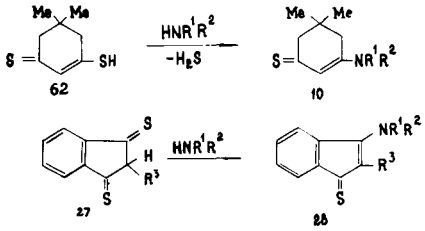
Unlike β-mercapto aldehydes, monothio-β-diketones *57* react with amines upon heating to liberate hydrogen sulfide thus yielding mainly enamino ketones *58.*[112,113]



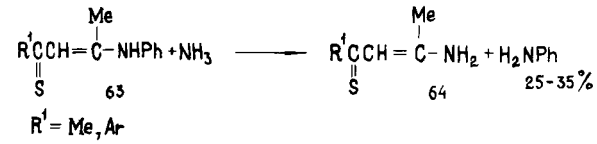
II.2.2 Aminolysis of β-dithiodiketones (vinylogous dithiocarboxylic acids) Until 1975, only one case of aminolysis of β-dithiodiketones had been reported.[8] The reaction of the aliphatic β-diketones *59* with tetraphosphorus decasulfide was believed to give the unstable β-dithiodiketones *60.* Treatment of the reaction mixture with aromatic amines readily led, in that particular case, to the enamino thioketones *61* with an aryl substituent attached to the thiocarbonyl group.



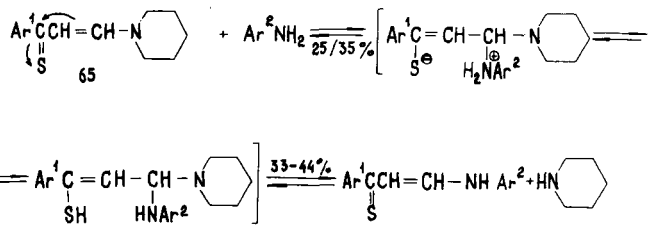
It has been found later that the readily available compounds *62*[114] as well as the 2-aryl-1,3-indanedithiones *27*[60] with secondary amines give the corresponding enamino thioketones *10* and *28*.



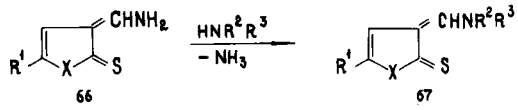
II.2.3. Transamination of enamino thioketones Amine exchange can sometimes constitute a simple preparative procedure for the synthesis of enamino thioketones with an appropriate amino group. The reaction is usually carried out in alcohol with heating or in benzene at 20 °C with excess amine. This treatment causes, to some extent, concomitant aminolysis of the thiocarbonyl group. For aliphatic enamino thioketones one may expect the heterocyclization reaction to take place as well. It should be noted that a series of N-unsubstituted aliphatic amino thioketones *64* can efficiently be prepared by ammonolysis of their N-phenyl substituted analogs *63*.[115,116]



The reaction of piperidino thioketones *65* with aromatic amines is a reversible one and may be interpreted as a 1,4-addition-elimination.[12,13]



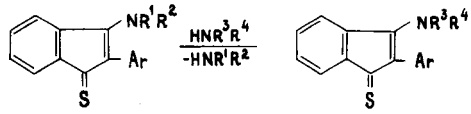
2-Thioxo-2,3-dihydrofuran (*67a*) and its thiophene analog (*67b*) 3-aminomethylenic derivatives were prepared by the reaction of their N-unsubstituted analogs *66a,b* with aliphatic,[117,118] alicyclic,[118] araliphatic,[117,119] aromatic,[117,119] and heterocyclic[120] amines:



66 67

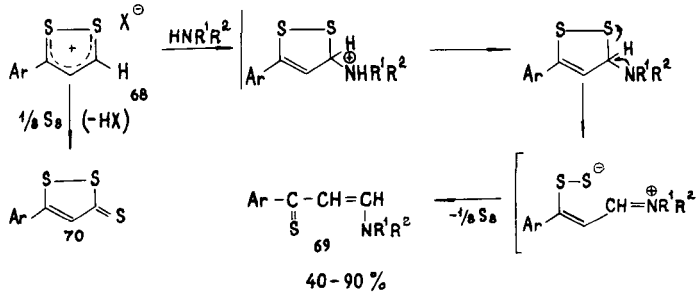
X = O.(a), S(b); R¹ = H, Alk

Some cases of successful transamination of indene enamino thioketones are known.[3,17]



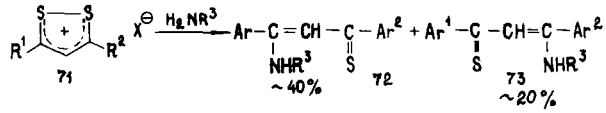
II.2.4. Aminolysis of 1,2-dithiolium salts The possibilities of the synthesis of aliphatic enamino thioketones by reaction of 1,2-dithiolium salts with primary and secondary amines are well recognized and widely used. Since the result of this reaction depends on the substituents in positions 3 and 5 of the heterocycle, the literature data are most conveniently considered in the following order.

II.2.4.1. 3-aryl-1,2-dithiolium salts 3-Aryl-1,2-dithiolium salts readily react with primary aliphatic[69] and aromatic amines,[11,15,121,122] dialkylamines,[10,12,123] and N-methylaniline.[12,15] In all cases the nucleophilic attack is believed to take place at the sterically accessible C^5 atom of the heterocycle *68*. The sulfur eliminated at the stage of formation of the enamino thioketones *69* is able to react with the starting dithiolium salts which gives rise to concomitant formation of 5-aryl-1,2-dithiole-3-thiones *70*.[10] With excess dimethylamine aminolysis of the compounds *69* the thiocarbonyl group is also observed.[10]



40-90 %

II.2.4.2. 3,5-diaryl-1,2-dithiolium salts In the case of the salts *71a* the reaction is performed as described in Section II.2.4.1. leading to 1,3-diaryl substituted enaminothioketones of type *72* in 40–70 % yield.[15,16,124–126] The aminolysis of the salts *71b* involves the C^3 and C^5 atoms resulting in a mixture of the isomers *72* and *73* (*cf.* II.1.1.).

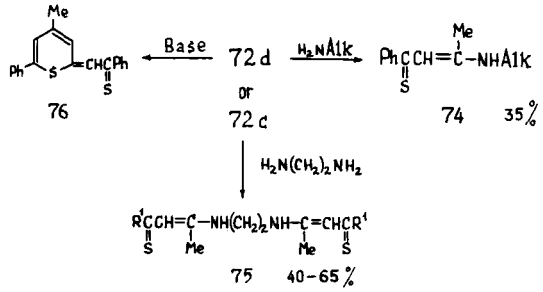


71 ~40% 72 73 ~20%

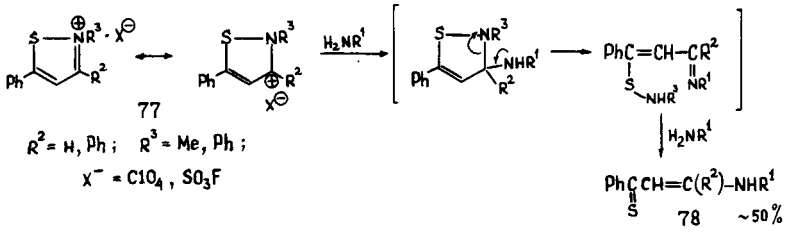
$R^1 = R^2 = Ar$ (a) $R^1 = Ar^1$, $R^2 = Ar^2$ (b)

$R^1 = R^2 = Me$ (c) $R^1 = Ph$, $R^2 = Me$ (d)

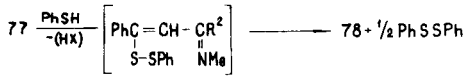
II.2.4.3. 3,5-dimethyl- and 3-methyl-5-phenyl-1,2-dithiolium salts The salts *71c,d* are very sensitive to the action of bases and air oxygen. The compounds *71d* form enamino thioketones *74* with primary aliphatic amines only. The reaction of the salts *71c,d* with ethylenediamine allows to obtain the corresponding bis-(enamino thioketones) *75*. Aromatic amines and other bases mainly favor self-condensation of the compounds *71d* leading to 2-(2-thioxo-2-phenylethylidene)-4-methyl-6-phenyl-thiopyrane *76*.[8,124]



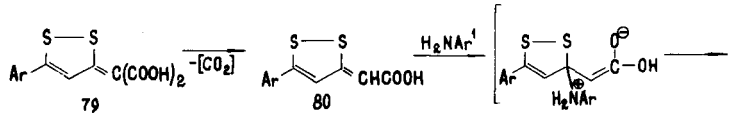
II.2.5. Reaction of 1,2-isothiazolium salts with amines and benzenethiol The 1,2-isothiazolium salts *77* readily react with N- and S-nucleophiles.[127,128] They are decomposed by secondary amines with elimination of sulfur. Benzylamine, aniline, and 2-aminoethanethiol when treated with the 5-mono- and 3,5-disubstituted salts *77* in alcohol at 20 °C or with heating attack the ring atom C^3. The corresponding enamino thioketones *78* have been suggested[127] to be formed according to the following scheme:

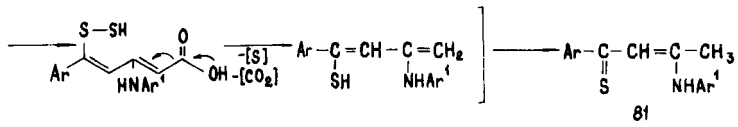


The reaction of some salts *77* with benzenethiol unexpectedly yields the enamino thioketones *78*. The authors[128] explain this conversion as follows:



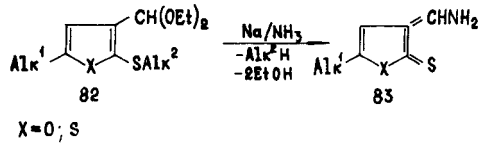
II.2.6. Aminolysis of (5-aryl-1,2-dithiol-3-ylidene)-malonic acids In the reaction of the malonic acid derivatives *79* with aromatic amines, decarboxylation occurs first followed by formation of the (5-aryl-1,2-dithiol-3-ylidene)-acetic acids *80*[129] which are further attacked by the amine at the ring atom C^3 and cleaved to eliminate sulfur and CO_2. N-Aryl substituted aminobutenethioketones *81* are obtained in 60 % yield:[10,11]





81

II.2.7. Aminolysis of some heterocyclic aldehyde acetals When treated with a mixture of sodium and liquid ammonia 2-alkylthio-5-alkyl-3-thiophene (or furan)aldehyde acetals and some of their analogs are converted to the enamino thioketones *83* in high yield:[105]

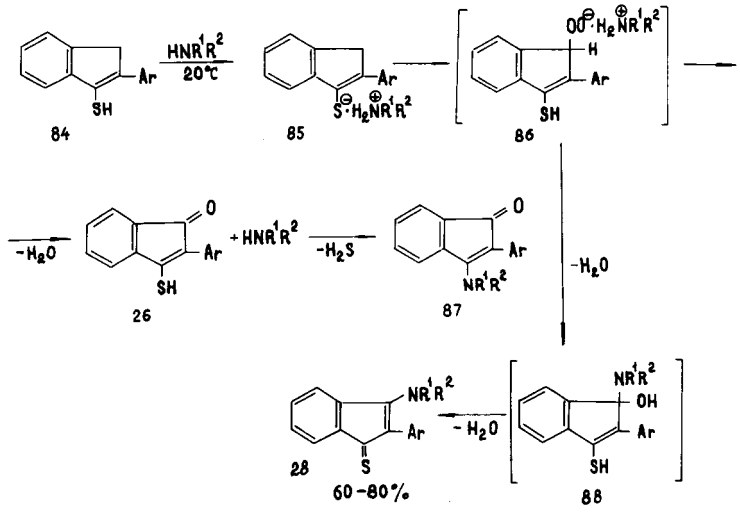


82 83

X=O; S

II.2.8. Synthesis of 3-amino-2-aryl-1-indenethiones by concomitant action of amines and air oxygen or amines and sulfur on 2-aryl-3-indenethiols The ability of 2-aryl-3-indenethiols (*84*) to form 3-amino-2-aryl-1-indenethiones (*28*) by reaction with amines in the presence of air oxygen[130] or sulfur[60] seems unexpected at first sight.

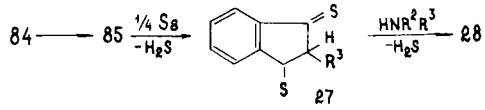
The indenethiols *84* readily react with secondary aliphatic and heterocyclic amines (dialkylamines, piperidine, morpholine) and somewhat less readily with ammonia and alkylamines. The reaction proceeds at approximately the same rate in methanol, acetone, N,N-dimethylformamide, acetonitrile, dioxane, and tetrahydrofuran at 20 °C. The yield of enamino thioketones *28* ranges from 75 to 85 %. The optimal *84*: HNR^1R^2 ratio is 1:1.4, the reaction time being 6–10 hours. Less basic aromatic amines (aniline and its derivatives) react with indenethiols in the above media only slowly. The reaction can be accelerated with triethylamine as a catalyst. The first stage of the process in question rapidly leads to the corresponding ammonium thiolates *85*. In some cases the salts *85* were isolated and characterized as crystalline solids.[131] Further conversion of *85* depends on autoxidation in the presence of bases by an ionic mecha-



nism (*cf.* Ref. 132). Cleavage of the hydroperoxide salts *86* affords the corresponding oxothiols *26* in insignificant yields (5–10 %). In a special test it has been shown that the compounds *26* in the presence of the amine involved eliminate slowly hydrogen sulfide to form exclusively the enamino thioketones *87*.

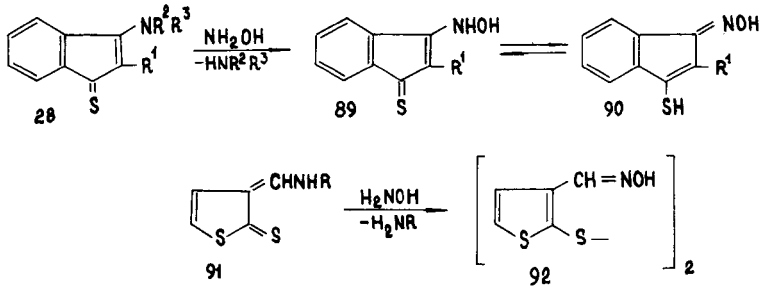
The formation of the (indene)C^1-NR^1R^2 bond by cleavage of the hydroperoxide salts *86* and the subsequent conversion to enamino thioketones *28* may be interpreted as a concerted process of oxidation of the amine with hydroperoxide (loss of $HONR^1R^2$) and direct amination at the C^1-H bond by the $HONR^1R^2$ molecule involving H_2O elimination. The resultant geminal amino alcohols *88* can be readily dehydrated which leads, in the present case, to the amino thioketones *28*.

The combined effect of sulfur and highly basic amines on the indenethiols *84* may be explained in an analogous way.[60] However, 2-aryl-1,3-indenedithiones (*27*) may be intermediates in this reaction since the aminolysis of authentic *27* samples proceeds just as rapidly[60] as the *84* → *28* conversion.



III. SYNTHESIS OF N-HYDROXYENAMINO THIOKETONES (VINYLOGOUS N-HYDROXY THIOCARBOXAMIDES) AND N-AMINOENAMINO THIOKETONES (VINYLOGOUS THIOHYDRAZIDES)

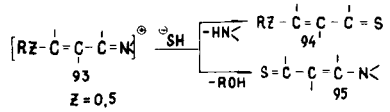
The hydroxyaminolysis and hydrazinolysis of enamino thioketones are considered to be the most convenient synthetic routes to compounds with a Z—C=C—C=S group (Z = NHOH, $NHNH_2$). It was possible, however, to choose the conditions for the substitution of the enamine group by a hydroxyamino group without affecting the thioketone only in the case of the indene (*28*)[133] and the dihydrothiophene (*91*)[117] enamino thioketones. In the first case, a mixture of thione-thiol tautomers *80* and *90* with predominance of the latter was obtained.



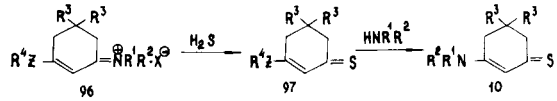
In the second case only the disulfide *92* was isolated. A majority of the reactions of aliphatic[10–12] and cyclic[83] enamino thioketones with hydroxylamines and hydrazines occur at the thiocarbonyl group with elimination of hydrogen sulfide.

IV. β-ALKOXYVINYLENE THIOKETONES (VINYLOGOUS O-ALKYL THIOCARBOXYLATES) AND β-ALKYLTHIOVINYLENE THIOKETONES (VINYLOGOUS ALKYL DITHIOCARBOXYLATES)

A general consideration of the synthetic routes to thioketones allows to draw the conclusion that the β-alkoxy(alkylthio)vinylene methinimmonium salts *93* are the most suitable starting materials for the preparation of compounds containing a β-alkoxy (alkylthio)vinylene thioketonic group, *i.e., 94.* As shown in Section II.1.4.1., however, the oxygen analogs of such salts react with sulfur nucleophiles at the RO—C group to form the enamino thioketones *95.*

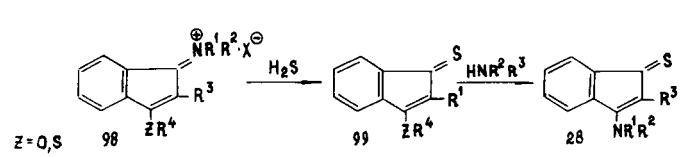


It has been found[18,134,135] that the N,N-disubstituted N-[3-alkoxy(alkylthio)-2-cyclohexene-1-ylidene] immonium salts (*96*) react with hydrogen sulfide or sodium hydrosulfide in DMF at −60 to −40 °C to form the corresponding 3-alkoxy(alkylthio)-2-cyclohexene-1-thiones (*97*) containing the rare RZ—C=C—C=S (Z = O or S) group. The conditions of the thiolation of the salts *96* seem to shift the electrophilic center to the C^1 atom. The presence of triethylamine, piperidine, or morpholine accelerates the *96* → *97* conversion, thus increasing the yields of the thioketones *97.* Other solvents such as HMPTA, DMSO, and pyridine, which can enhance the nucleophilicity of the $HS^{\ominus}$ anion may well be used in the above reaction.



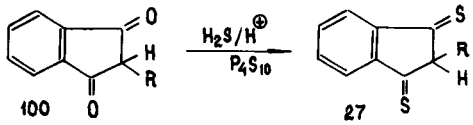
Z = O,S; R^1R^2 = $-(CH_2)_3-$, $-(CH_2)_2O(CH_2)_2-$; R^3 = H, CH_3; R^4 = CH_3, C_2H_5; X = BF_4, I

The compounds *97* readily react with ammonia and primary and secondary amines at 20 °C in alcohol. The aminolysis proceeds, in this case, at the C^3 atom of an enol ester group, leading to the corresponding enamino thioketones *10* in good yield. The *97* → *10* conversion rate increases with increasing nucleophilicity of the amine. This is also true of the N,N-disubstituted and N-substituted 3-alkoxy(alkylthio)-2-arylindene-1-ylideneimmonium salts (*98*). It is more difficult, however, to prepare the corresponding 3-alkoxy(alkylthio)-2-aryl-1-indenethiones (*99*) analytically pure, but this does not impede their use in the synthesis of enamino thioketones of the indene series *28.*[136,137]

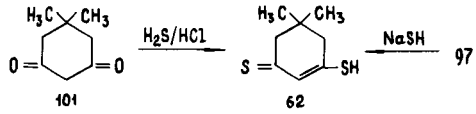


V. β-DITHIODIKETONES (VINYLOGOUS DITHIOCARBOXYLIC ACIDS)

The chemistry of β-dithiodiketones has not been studied much since attempts to synthesize these compounds from β-diketones mainly lead to the monothio analogs. The reaction of some aliphatic β-diketones with hydrogen sulfide in the presence of HCl allows unstable β-dithiodiketones to be prepared in the form of enethiolo thioketones identified only as metal complexes.[61,62,138] Treatment of the 2-substituted 1,3-indanediones (*100*) in a similar manner or with tetraphosphorus decasulfide has led, for the first time, to the relatively stable β-dithiodiketones *27* in good yield.[59] Also the sulfhydrolysis of the compounds *99* gives the dithiodiketones *27*.[136,137]

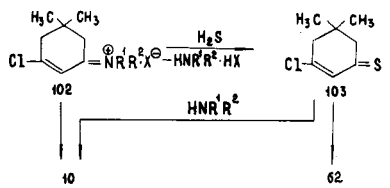


Dimedone (*101*) reacts with hydrogen sulfide in the presence of HCl at −50 °C to form its dithio analog in 35 % yield, predominantly as its enethiolo thioketone, 3-mercapto-5,5-dimethyl-2-cyclohexene-1-thione (*62*).[114,139] The reaction of the 3-alkoxy (alkylthio)-5,5-dimethyl-2-cyclohexene-1-thiones (*97*) with sodium hydrosulfide in an inert atmosphere at 20 °C gives the enethiolothione *62* in quantitative yield.[139]



VI. β-HALOVINYLENE THIOKETONES (VINYLOGOUS THIOCARBOXYL HALIDES)

It should be noted that substitution of the chlorine atom is considered a usual course of the reaction of β-chlorovinylene methinimmonium salts with different nucleophiles which results in the corresponding β-aminovinylene thioketones (see Section II.1.4.4.). However, N,N-disubstituted N-(3-chloro-5,5-dimethyl-2-cylcohexene-1-ylidene)-immonium perchlorates (*102*) react with hydrogen sulfide in polar aprotic solvents at −60 °C in the presence of triethylamine to form compound *103* containing the unusual Cl—C=C—C=S group.[140] The β-chlorovinylene thioketone *103* may be considered as a stable intermediate of the thiolation of the salts *102* since it reacts immediately at 20 °C with amines or sodium hydrosulfide to form the previously described enamino thioketones *10* and the enthiolothione *62*, respectively. It is not possible to prepare the

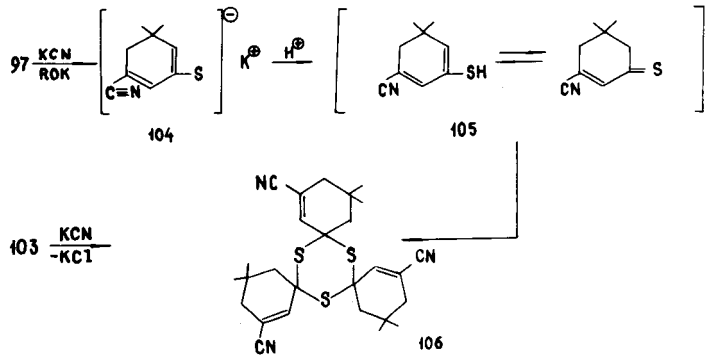


chlorovinylene thioketone *103* in the usual manner, *i.e.*, by reaction of its oxygen analog with hydrogen sulfide in the presence of HCl.[140]

VII. β-CYANOVINYLENE THIOKETONES (VINYLOGOUS THIOCARBOXYL CYANIDES) AND THEIR ANALOGS CONTAINING A π-ELECTRON-WITHDRAWING β-SUBSTITUENT

β-Heterosubstituents in the α,β-unsaturated thioketones described in Sections II–VI exhibit +M and +E effects. Mesomeric stabilization of the type X—C=C—C=S ↔ $^{\oplus}$X=C—C=C—S$^{\ominus}$ is likely to favor the stability of the thioketone form. In what way do the properties of both the thiocarbonyl group and the molecule as a whole change if the β-substituent X of these conjugated systems displays −M and −E effects? Two ways seem possible. First, the electron density distribution in a β-cyanovinylene thioketone moiety could be affected by the two competing electron-withdrawing C≡N and C=S groups, *i.e.*, $\overset{\ominus}{N}\equiv C-C\overset{2\oplus}{=}C-C=\overset{\ominus}{S}$. Second, the bipolar $^{\ominus}$N=C=C—C=C—S$^{\oplus}$ form could contribute to the electronic structure of β-cyanovinylene thioketones due to the repolarizability of the thiocarbonyl group under the effect of stronger electron-withdrawing substituents.[141]

It is evident that the synthesis of thioketones with a X—C=C—C=S group where X = C≡N, NO_2, SO_2R, etc., from their oxo analogs or by other conventional methods is not possible, and hence no compounds of this type are available up to now. The β-alkoxyvinylenethiones of the cyclohexene series *97* readily react with potassium cyanide in methanol at 20 °C to form a solution of potassium 3-cyano-5,5-dimethyl-2,4-cyclohexadiene-1-thiolate (*104*).[142] After treatment of this solution with carbon dioxide instead of the expected 3-cyano-5,5-dimethyl-2-cyclohexene-1-thione (*105*) its trimer *106* is formed in high yield. The latter is formed directly from the β-chlorovinylenethione *103* and potassium cyanide.[142]



The C≡N group in the cyanothione *105* destabilizes the thiocarbonyl group thus facilitating enethiolization under basic and trimerization under neutral conditions.

The use of synthons such as *97* and *103* is likely to permit other α,β-unsaturated thioketones having π-withdrawing substituents in the β-position to be synthesized in the future.

VIII. SYNTHESIS OF SOME FUNCTIONAL ANALOGS OF ENAMINO THIOKETONES

The most abundant functional analogs of enamino thioketones are enamino thiocarboxamides ($>N-\underset{|}{C}=\underset{|}{C}-C(=S)-N<$), enamino derivatives of thio- and dithiocarboxylic acids, their salts and esters. The synthetic routes to these compounds have some special features as compared with the methods for the synthesis of enamino thioketones and it is necessary, therefore, to consider some general examples.

VIII.1. Synthesis of enamino thiocarboxamides (thiourea vinylogs)

The preparation of enamino thiocarboxamides is carried out first of all, using the reaction of enamines and their derivatives with alkyl or aryl isothiocyanates[143–156] according to the following general scheme:

$$R^1R^2N-C(R^3)=CHR^4 + R^5NCS \longrightarrow R^1R^2N-C(R^3)=C(R^4)-\underset{\underset{S}{\|}}{C}-NHR^5$$

Aliphatic,[143–145] alicyclic,[145–150] and heterocyclic[151] enamines; aliphatic[152–154] and cyclic [145] enamino ketones; alkyl aryl ketone anils,[155] and β-aminocrotonic acid esters and their derivatives[152,153,156] readily lend themselves as starting materials. Each of these reactions requires special conditions.

The second route to enamino thiocarboxamides is based on the aminolysis of functionally substituted organosulfur compounds. In this way, methyl esters of N-substituted 3-amino-2-propene-dithiocarboxylic acid react with amines under mild conditions to form the thiourea vinylogs *108*:[122]

$$R^1R^2NCH=CH-\underset{\underset{S}{\|}}{C}-SMe + R^1R^2NH \xrightarrow[-MeSH]{20^\circ C} R^1R^2NCH=CH-\underset{\underset{S}{\|}}{C}-NR^1R^2$$

107 108

$R^1 = H,\ R^2 = Ar;\quad R^1,R^2 = (CH_2)_4;\quad (CH_2OCH_2)_2$

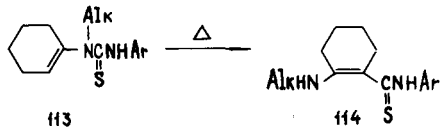
The acyl substituted thiocarboxamides *109* and the dithiocarboxylates *110* react with primary amines in an analogous way. The aminolysis of the C=O and SMe groups leads to the enamino derivatives *111* and *112*, respectively, in 25–50 % yield.[150,157]

$$R^1\underset{\underset{O}{\|}}{C}CH(R^2)-\underset{\underset{S}{\|}}{C}-Z + H_2NR^4 \xrightarrow{20-80^\circ C} R^1\underset{\underset{NHR^4}{|}}{C}=C(R^2)-\underset{\underset{S}{\|}}{C}-Z$$

109 Z = NHR^3 111 Z = NHR^3

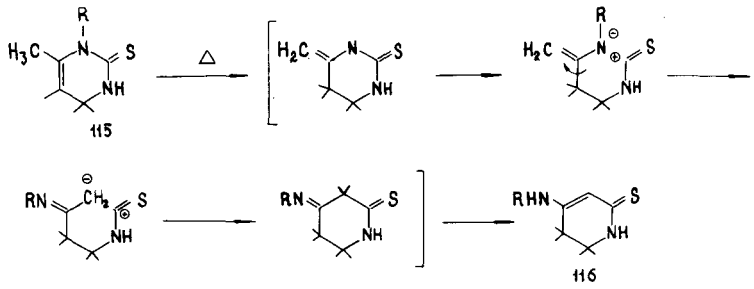
110 Z = SMe 112 Z = NHR^4

The alicyclic enamino thiocarboxamides *114* can be prepared by thermal rearrangement of the corresponding thiourea derivatives *113*:[158]



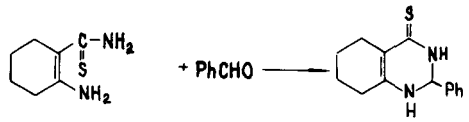
113 114

Thermolysis of the 2-thioxo-1,2,3,4-tetrahydropyrimidine derivatives *115* in an inert solvent leads to the 4-alkyl(aryl)amino-5,6-dihydro-2(1H)-pyridinethiones *116* formed according to the following scheme:[159]

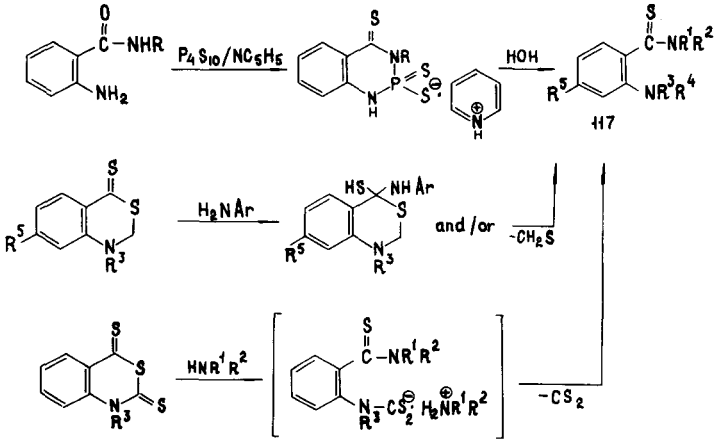


115 116

Heterocyclic enamino thiocarboxamide analogs are also formed by condensation of aldehydes with N-unsubstituted enamino thiocarboxamides,[149,158,160–163] for example:



The following three processes can be used for the preparation of "aromatic" enamino thiocarboxamides, *i.e.*, 2-aminothiobenzamides and their substituted derivatives *117*:[160,164–167]

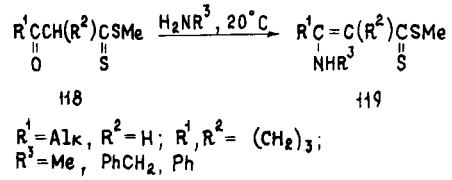


117

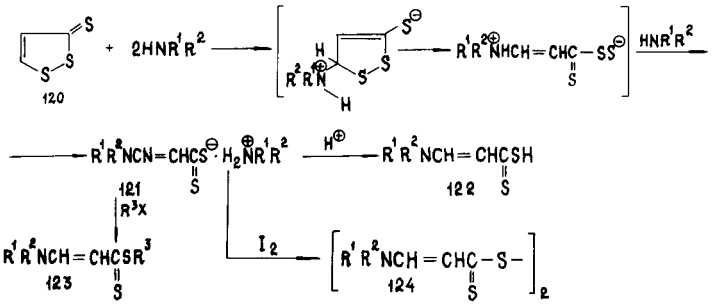
VIII.2. Synthesis of enamino dithiocarboxylic acids and their derivatives

VIII.2.1. Aminolysis of functionally substituted organosulfur compounds The aminolysis of the acyl substituted dithiocarboxylates *118* at 20 °C occurs, in general, only at the carbonyl group leading to the corresponding enamino derivatives *119*.[157,168,169] This

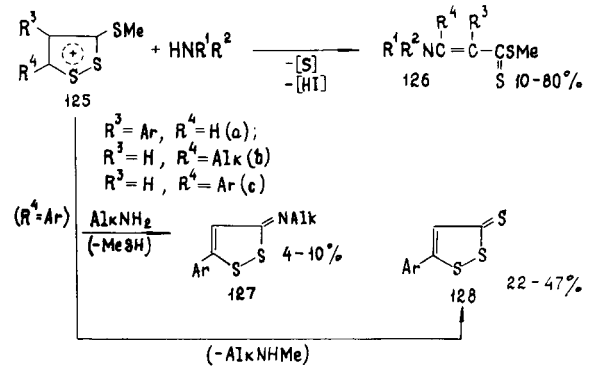
reaction course is sterically hindered at the carbonyl carbon atom and this facilitates the aminolysis of the methylthio group.[157]



The reaction of 1,2-dithiol-3-thione *120* with amines readily affords the ammonium salts *121* which can be converted to 2-aminodithioacrylic acids *122,* their S-alkyl derivatives *123* or the disulfides *124.*[122]

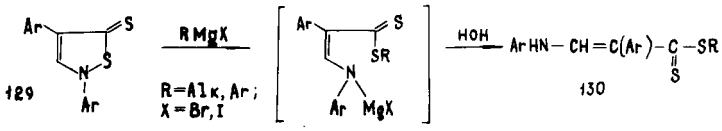


The 4-aryl and 5-alkyl substituted 3-methylthio-1,2-dithiolium salts *125a,b* react with primary and secondary amines in a similar manner to form the enamino dithiocarboxylates *126.*[122,157,169,170,171] The 5-aryl-3-methylthio-1,2-dithiolium salts *125c,* however, react with alkylamines in three directions: through the C^5 atom to give the enamino thioketone analogs *126* (i), by aminolysis at the C^3 atom to form the 1,2-dithiolium-3-imines *127* (ii), and by reaction at the methyl group to give the 5-aryl-1,2-dithiol-3-thiones *128* (iii).[171–174] The salts *125c* react with aromatic amines unequivocally with elimination of the methylthio groups to form the corresponding 1,2-dithiol-3-imines *127* in high yield.[169,173]



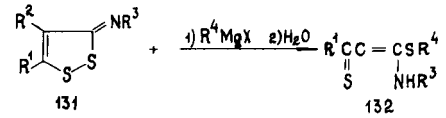
VIII.2.2. Reactions of sulfur-containing heterocyclic compounds with Grignard reagents
Enamino dithiocarboxylates can be prepared by cleavage of appropriate heterocyclic compounds with a Grignard reagent. 1,4-Diaryl-5-thioxo-2,5-dihydro-1,2-thiazoles

(*129*), for example, containing all necessary fragments of the $>N-C=C-C(=S)-S-$ group react with alkyl- and arylmagnesium halides through the S—N bond to form the 3-arylamino-2-aryl-1-alkylthio(arylthio)-1-propenethiones (*130*).[170]



129 130

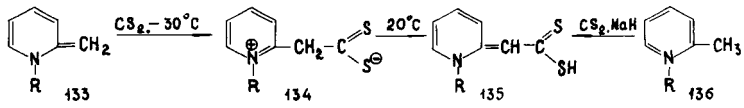
The cleavage of the S—S bond in the 5-alkylthio-1,2-dithiol-3-imines (*131*) proceeds analogously. The yield of alkylthio and arylthio substituted enamino thioketones *132* ranges from 60–90 %.[173,174]



131 132

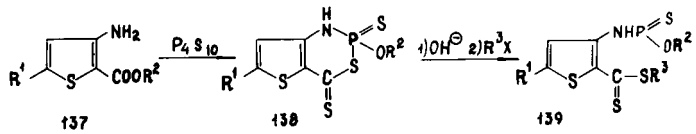
R^1=Ar,(a), MeS(b); R^2=Alk; R^3=Alk, Ar; R^4=Me, i-C_3H_7, Ph; X=Br, I

VIII.2.3. Some reactions with carbon disulfide and tetraphosphorus decasulfide Carbon disulfide is a fairly convenient reagent for the insertion of a —C(=S)—S— unit into molecules.[175] Carbon disulfide reacts readily with N-substituted 2-methylene-1,2-dihydropyridines (*133*) to form the corresponding dithioacetic acid betaines *134* which undergo rearrangement to the enamino thioketone analog *135* at 20 °C. The reaction of N-substituted 2-methylpyridinium salts (*136*) with carbon disulfide in the presence of sodium hydride affords the compounds *135*.[176] This approach to enamino dithiocarboxylic acids is also valid for other heterocyclic analogs of the compounds *133* and *136*.[175,176]



133 134 135 136

Of interest is the preparation of complex enamino dithiocarboxylate analogs, the 2-alkoxy-1,2-dihydrothieno [2,3-e]-3,1,2P-thiazophosphorine-2,4-dithiones (*138*) by action of tetraphosphorus decasulfide in xylene upon the 3-amino-5-alkyl-2-thiophenecarboxylates (*137*). Compounds *138*, with alkali and an alkyl halide or dimethyl sulfate, give the N-substituted enamino dithiocarboxylates *139*.[162]



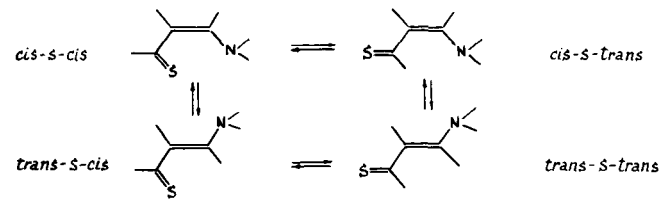
137 138 139

IX. SOME PROBLEMS CONCERNING THE STRUCTURES OF ENAMINO THIOKETONES AND THEIR FUNCTIONAL ANALOGS

The first attempt to summarize the scarce data concerning the structures of enamino thioketones was made by Freimanis[5] in 1974. The framework of the RHN—C=C—C=S group suggested the possibility of three tautomers: enamino thioketone (A) ⇄ imino thioketone (B) ⇄ imino enethiol (C).

$$\underset{(A)}{RHN{-}C{=}C{-}C{=}S} \rightleftharpoons \underset{(B)}{RN{=}C{-}CH{-}C{=}S} \rightleftharpoons \underset{(C)}{RN{=}C{-}C{=}C{-}SH}$$

Besides, in aliphatic enamino thioketones or their cyclic analogs with an exocyclic $R_2N{-}C{=}C$ group geometric isomerism may be caused by cis- and trans-orientation of the R_2N— and C=S fragments relative to the $C^2{=}C^3$ bond. Aliphatic enamino thioketones also occur as S-cis and S-trans rotamers due to hindered rotation around the $C^1{-}C^2$ bond:



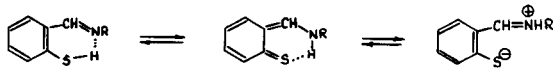
Most enamino thioketones possess an exocyclic amino group and this allows the hindered rotation around the C—N bond to be recorded on a certain time scale. Investigation of this dynamic process provides valuable information on electronic and steric interactions in enamino thioketones.

IX.1. Tautomerism of enamino thioketones

Attempts have been made to demonstrate tautomerism of the type (A) ⇄ (B) ⇄ (C) in various enamino thioketones by physico-chemical methods.[5,10,12,13,92,93,100–102,104–106,108–110, 115,116,120,177–192] This postulated equilibrium was studied within a wide temperature range and in a number of organic solvents. As a result, the rather general conclusion may be drawn that most enamino thioketones either neat or in solution state in fact do not contain the iminothionic (B) nor the iminoenethiolic (C) form. This conclusion is confirmed by NMR, IR and UV data and should be considered as highly reliable since the corresponding model enamino thioketones with N—D and ^{15}N—H labels as well as the N,N-disubstituted $R_2N{-}C{=}C{-}C{=}S$ compounds where no prototropy is possible, and the S-alkyl substituted iminoenethiols $RN{=}C{-}C{=}C{-}SR$[5,10,100,105] were included in the spectral studies. This allowed one of us to rule out, already by examination of the IR and UV spectra, the presence of tautomers (B) and (C) in the enamino thioketones examined. The presence of δNH, μNH, and μC=C vibration bands and the absence of μSH absorption, for example, permit a reliable IR identification of the form (A). It was not possible, however, to determine clearly the position of the μC=S

bands. Quantum-chemical calculation using a Hückel approximation MO method for hypothetic moieties of the type (A), (B) and (C)[5] and a Pariser-Parr-Pople method for 1-arylamino-3-propenethiones $ArNHCH{=}C(R^1){-}C(R^2){=}S$[100] and their cyclic analogs[110,192] confirmed the energetic advantage of the enamino thioketonic form (A).

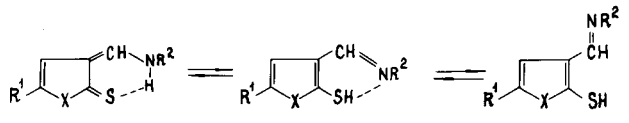
The iminoenethiol form (C) is observed on comparatively rare occasions. Thus, the tautomer conversions of N-substituted 1-aminomethylene-2-thioxo-1,2-dihydrobenzenes *52*[104] have been studied by comparison of their UV spectra in solvents of low polarity with those of the sodium salts of the corresponding enethiols *52B* and their S—Me derivatives. The IR spectra of *52* in dichloroethane display the $\mu C{=}N$ (1625 cm^{-1}) and $\mu SH\ldots N$ (2400 cm^{-1}) bands. A close agreement of the calculated and measured values of the electron transfer energies in the excited state has been established for *52B*. All this indicates that the above compounds in solvents of low polarity exist mainly in the enethiol benzenoid form *52B* stabilized by the intramolecular hydrogen bond.



52B 52A 52C

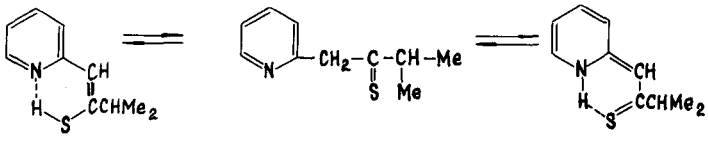
The IR spectra of *52* in the aggregate ground state exhibit no absorption in the μSH and μNH regions, the $\mu C{=}C{-}N$ band being observed at 1644-1656 cm^{-1}. The calculated electron spectra of *52A* are in good agreement with the experimental ones in DMSO, the electron transfer energies for the long-wave band being indicative of a certain contribution from the bipolar structure *52C*. It is, therefore, believed that it is the enamino thioketonic quinonoid form *52A* with an intramolecular hydrogen bond that predominates in the aggregate ground state and in polar solvents. The iminoenethiol form *52B* is stabilized by electron-withdrawing C- or N-substituents and destabilized by electron-donating ones which increase the basicity of the amino group. Similar results have been obtained with naphthalene analogs of *52*.[103]

Interesting results have been obtained with enamino thioketones containing five-membered heteroaromatic rings, such as thiophene,[105,117] pyrrole,[106] furan,[178] etc.[110,177] As judged by their IR spectra ($\mu C{=}N$ 1637-1640 cm^{-1}), the thiophene derivatives *53* (X = S) were originally thought to exist in the form *53B*.[117] Further examination[105] of the ^1H NMR spectra of different S-substituted compounds and their ^{15}N-analogs (X = O,S,NR^3) led to the conclusion that the species present in the crystalline state and in solution were the cis-enamino thioketones *53A*. [^1H NMR spectra: NH = 12-15 ppm, $^2J\ ^{15}N,H$ = 85-87 Hz, ^3J NH,CH = 13-15 Hz; IR spectra: 1570 cm^{-1} (δNH), 1645 cm^{-1} ($\mu C{=}C$), 2600-3200 cm^{-1} (μNH_{ass})]. In DMSO as well as in going from thiophene to furan derivatives of *53*, some weakening of the intramolecular hydrogen bond takes place. In melts or upon heating in solvents, some N-substituted enamino thioketones *53A* are partially converted to the iminoenethiols *53B* and *53C*.[105,120,178,179,191]



53A 53B 53C

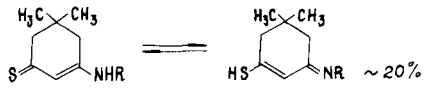
According to their ^{1}H NMR and UV spectra, 2-(2-methyl-3-thioxobutyl)pyridine (*140A*) in solution is in equilibrium with its enethiol tautomer *140B* which dominates in the aggregate ground state.[193,194] However, a very high value of the proton chemical shift in the chelate-bound SH group (δ 18.60 ppm) has been reported for *140B*.[193] A comparison of the chemical shifts of the labile proton in six-membered chelates with NH...S=,[105,173,195] OH...S=,[193] and SH...N=[173] suggests that the thioketone *140A* in solution converts to the chelated enamino thioketone form *140C* rather than to the enethiol form *140B*. The spectrum of a model enamino thioketone *132*, for example, displays a signal at 16.10 ppm (NH) whereas in the enethiol *141* a signal is observed at 6.28 ppm (SH).[173] Similar conclusions could be drawn by examination of structural analogs of the thioketones *140A*.[194]



140 B 140 A 140 C

132 141

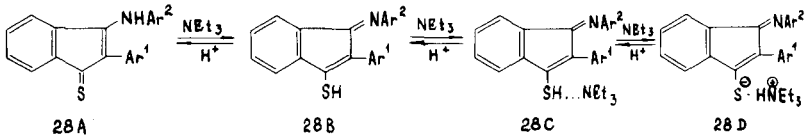
The ^{1}H NMR data show that 3-amino-5,5-dimethyl-2-cyclohexene-1-thiones (*33A*) containing a N—H bond are able to convert in chloroform to the corresponding tautomers, 1-imino-5,5-dimethyl-2-cyclohexene-3-thiols (*33B*).[196] In bipolar aprotic solvents, this tautomeric equilibrium is completely shifted toward the enamino thioketone form *33A*.



33 A 33 B

R = H, Alk, Ar

3-Amino-2-alkyl(aryl)-1-indenethiones and their N-substituted derivatives *28A*, both in the crystalline state and in solution, exist exclusively in the enamino thioketone form.[17,66,67] 3-Arylamino-2-aryl-1-indenethiones (*28A*), however, with pKa ⩽ 19.94 (in acetonitrile), readily react with triethylamine in acetonitrile or dichloroethane. This is accompanied by the formation of an equilibrium mixture of the corresponding 1-arylamino-2-aryl-3-indenethiols (*28B*) with their H-complexes *28C* and their salts *28D* with triethylamine.[67] The S—H, S—H...NEt_3 and $-S^{\ominus}\cdot H\overset{\oplus}{N}Et_3$ bonds were in this case detected by IR spectroscopy.

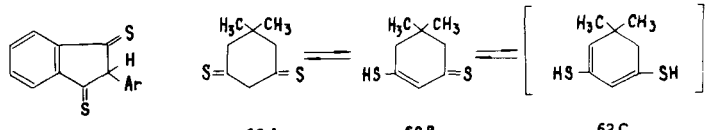


28A 28B 28C 28D

All this shows the necessity of a more thorough and detailed investigation of the tautomerism of various enamino thioketones involving kinetic and thermodynamic parameters to be undertaken in the future.

IX.2. Tautomerism of β-dithiodiketones

The synthesis of β-dithiodiketones able to undergo prototropic conversions has been successful only in a few cases.[59,114] No enethiol form of 2-aryl-1,3-indanedithiones (*27*) has been found in either the crystalline state or in solution.[59] The dimedone dithio analog *62A*, however, exists as 3-mercapto-5,5-dimethyl-2-cyclohexene-1-thione (*62B*).[114,139] The ^{1}H NMR spectrum of the latter at −70 °C displays two signals due to the 4-CH_2 and 6-CH_2 groups (δ 2.27 and 2.66 ppm, respectively) and a signal due to the SH-group (δ 3.97 ppm). An increase in the solvent temperature shifts the S—H signal upfield (to δ 3.32 ppm at 20 °C) and causes coalescence of the 4- and 6-CH_2 signals (T_c = −14 °C) and narrowing of the averaged signal (2.49 ppm at 20 °C). The above spectral changes are most likely due to an intramolecular proton exchange of the type —C=S + HS—C ⇄ =C—SH + S=C— the rate of which depends on the solvent and the temperature. The activation enthalpy $\Delta G^{\neq}_{T_c}$ of this process found using spectral parameters is significantly higher than that of the proton exchange in dimedone (13.1 and < 8kcal/mole, respectively).[197] The action of triethylamine on enethiolthione *62B* is assumed to involve enethiolization of the thioketonic group to form the dienedithiol *62C* which upon oxidation affords linear and macrocyclic oligodisulfides.[198]



27 62A 62B 62C

IX.3. Cis-trans-isomers and rotamers of enamino thioketones and their functional analogs

Enamino thioketones and their functional analogs with no ring C^2=C^3 bond can exist as both cis- and trans-isomers. Most aliphatic,[7,8,10,69,100,180,199] carbocyclic[100,103,104,] and heterocyclic[105,108-110,177,183-189,200,201] enamino thioketones with an N—H group display cis-orientation (*142*) of the RHN— and C=S groups, as well as a strong intramolecular N—H...S=C hydrogen bond. NMR, IR, and UV spectral data confirm that both the hydrogen bond strength and the C—N bond multiplicity in heteroatomic analogs of *142* increase in the order X = O < X = S < X = Se. N,N-Disubstituted enamino thioketones unable to form an intramolecular hydrogen bond assume the trans-configuration *143*.[7,10,14,108,118,185,190,199]

142 143

X=O, S, Se

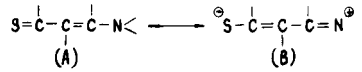
The ^{1}H NMR spectra of the N-phenylsubstituted enamino thioketones *144a* suggest[199] that these compounds in chloroform display both cis- and trans-configuration (appr. 10 %). For the N-picolyl substituted analogs *144b* comparable concentrations of the two analogs are observed. The barrier to rotation around the C^2—C^3 bond in this compound (at 145 °C) is about 23 Kcal/mole.[199]

144

a) R= 

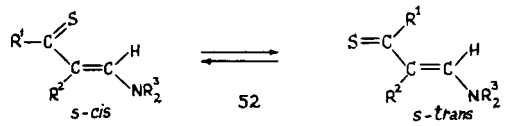
b) R= 

A general and important feature of enamino thioketones is hindered rotation around the C^3—N and C^1—C^2 bonds (for aliphatic analogs) due to a certain contribution of resonance structure (B) to the ground state of the molecules (A). These dynamic processes are revealed by NMR spectroscopy.[14,56,80,108,118,185,199,202-208] They mainly depend on steric and electronic effects of the C- and N-substituents affecting the degree of p,π-conjugation.



(A) (B)

The equilibrium concentration of rotamer *52a,* for example, is dependent, to a large extent, on the effective bulk of R^1. An increase in the latter disfavors the s-trans-form.[202,204,205] In the case of the 1,2-diphenyl-substituted enamino thioketones *52b,* on the contrary, the steric hindrance in both rotamers is approximately equal and their equilibrium concentrations are comparable.[203,204] In the enamino thioketones *52* the barrier of the hindered rotation around the C^1—C^2 bond is lower than that around the C—N bond and increases with the amino group basicity[203,205] (Table II).



s-cis 52 s-trans

a R^1 = H, Alk, Ar; R^2 = H; R^3 = Me

b R^1 = R^2 = Ph; R^3 = Me, Et, CH_2Ph etc.

c R^1 = (X = OMe, Me, H, Cl, Br); R^2 = H; R^3 = Me, Et etc.

The barrier to rotation around the C—N bond is higher in enamino thioketones than in the corresponding ketones[14,56,80,108,118,185,204] (Table III). A similar conclusion has been drawn in a comparison of thiocarboxamides and amides.[212,213]

TABLE II

Barriers to Rotation Around the C^3—N and C^1—C^2 Bonds in Enamino Thioketones $PhC(=S)—C(Ph)=CH—R$[203]

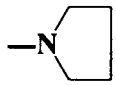
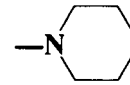
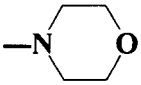
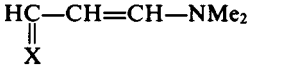
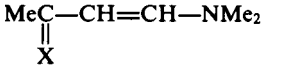
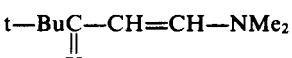
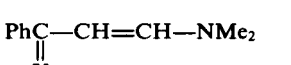
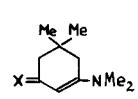
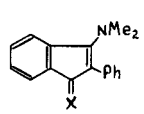
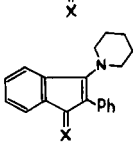
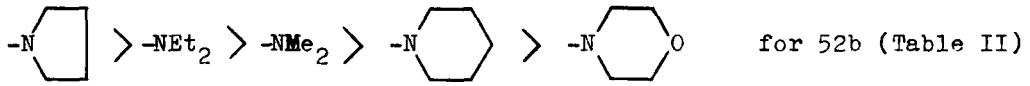
ΔG_{Tc} Kcal/mole / R		—NEt_2	—NMe_2	—$N(CH_2Ph)_2$		
C^3—N	14.7	14.1	13.7	13.4	13.4	11.7
C^1—C^2	13.0	13.3	12.8	11.5	12.8	10

TABLE III

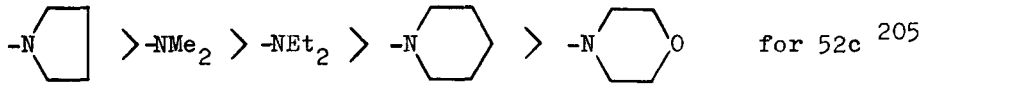
Barriers to Rotation Around the C—N Bond in Some Enamino Thioketones and Their Oxygen Analogs

No.	Compound	X	$\Delta G^{\neq}_{Tc}$ Kcal/mole	Solvent	Reference
1		S	17.1	$CDCl_3$	202
		O	14.6	CH_2CCl_2	209
2		S	16.4	$CDCl_3$	202
		O	13.4	CH_2CCl_2	209
3		S	15.8	$CDCl_3$	202
		O	13.1	CH_2CCl_2	209
4		S	16.5	CH_2Br_2	14
			16.7	$CDCl_3$	203, 204
		O	14.4	CH_2Br_2	14
			15.1	$CDCl_3$	210
5		S	14.5	CD_3COCD_3	56
		O	12.3	CD_3COCD_3	211
6		S	11.6	CH_2Cl_2	80
		O	9.5	CH_2Cl_2	80
7		S	11.0	CH_2Cl_2	80
		O	9.3	CH_2Cl_2	80

In the isostructural N,N-disubstituted compounds *52* the rotation barrier around the C—N bond decreases with decreasing C—N bond order in the following order:

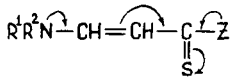


for 52b (Table II)



for 52c [205]

The regularity found is due to several factors.[205] These are the extent of delocalization of the lone electron pair at the nitrogen atom, the basicity of the amine moiety, and variations of the Pitzer strain. Besides, the value of the rotation barrier around the C—N bond in enamino thioketones *52* is also affected by steric interaction of the substituents at the N and C^2 atoms which disturbs the p,π-conjugation. This leads to lower $\Delta G^{\neq}_{Tc}$ values than in the corresponding C^2-unsubstituted analogs.[203] For the isostructural series of compounds *52c* a linear correlation between the Hammett constants, σ_p and $\sigma_p^{\oplus}$ of the substituents X and the $\Delta G^{\neq}_{Tc}$ values has been found. The rotation barrier is the higher the stronger the electron-withdrawing properties of the substituent X.[204] The $\Delta G^{\neq}_{Tc}$ value with respect to the C—N bond rotation in 3-(N,N-dimethylamino)-1-phenyl-2-propene-1-thione (*52a*) (R^1 = Ph) depends on the polarity of the solvent[204] (Table IV). Upon increase of the polarity, the ground state of the enamino thioketone seems to be characterized by a greater contribution from the bipolar structure $^{\ominus}S—C(Ph)=CH—CH=\overset{\oplus}{N}Me$[204] (*cf.* Ref. 108). Numerous linear correlations between $\Delta G^{\neq}_{Tc}$ with respect to the C—N bond rotation and parameters of the corresponding molecular diagrams as well as ^{13}C NMR spectra have been found for a number of enamino thioketones *52c* during the latest time.[199] This is also true of the structures of the functional analogs of enamino thioketones with the same carbon skeleton, the enamino thiocarboxamides *145a*[122,152,153,160,214] and the enamino dithiocarboxylates *145b*.[122,162,170,171,173,174,195,215-219] The conjugation in the $R^1R^2N—C=C—C=S$ moiety is weakened due to a competing Z-thiocarbonyl group conjugation in *145*. The ^1H NMR spectra of these compounds display, therefore, the proton signals of the vinylene and amino groups, shifted upfield compared to the corresponding enamino thioketones. In the IR spectra, the μC=C bands and μNH_{ass} are observed at a higher frequency.



145

Z = NR^3R^4 (a), SR (b)

TABLE IV

The Solvent Effect on the Barrier to Rotation Around the C—N Bond in Ph—C(=S)—CH=CH—NMe_2[203]

Solvent	CD_3OD	DMSO-d_6	DMF-d_7	Acetone-d_6	CH_2Cl_2	Nitrobenzene	Pyridine-d_5	$CDCl_3$	CS_2
E_T, Kcal/mole	55.5	46.0	43.8	42.9	42.2	42.0	40.2	39.1	32.5
$\Delta G^{\neq}_{Tc}$ Kcal/mole	16.9	18.0	17.5	16.9	16.8	17.1	17.0	16.7	15.55

REFERENCES

1. E. Uhlemann, H. Müller and P. Thomas, *Z. Chem.*, **11,** 401 (1971).
2. E. Uhlemann and R. Morgenstern, *Z. Chem.*, **17,** 405 (1977).
3. V. A. Usov, Ya. S. Tsetlin and M. G. Voronkov, *Int. J. Sulfur Chem.*, **A2,** 216 (1972).
4. V. A. Usov, N. A. Korchevin, Ya. S. Tsetlin and M. G. Voronkov, *Zh. Org. Khim.*, **9,** 2149 (1973).
5. Ya. F. Freimanis, "Khimiya enaminoketonov, enaminoiminov, enaminotionov," Zinatne, Riga, 1974.
6. W. Walter and J. Voss in "The Chemistry of Amides" edited by J. Zabitzki, Interscience Publishers, London, 1970, p. 383.
7. K. Kamienska-Trela, U. Dabrowska and J. Dabrowski, *Bull. Polon. Acad. Sci., Ser. Sci. Chim.*, **19,** 549 (1971).
8. G. Duguay, H. Quiniou and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 4485 (1967).
9. G. Duguay and H. Quiniou, *Bull. Soc. Chim. Fr.*, 2146 (1966).
10. J. Bignebat, H. Quiniou and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 1699 (1966).
11. J. Bignebat and H. Quiniou, *Bull. Soc. Chim. Fr.*, 1180 (1966).
12. J. Bignebat, H. Quiniou and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 127 (1969).
13. F. Clesse and H. Quiniou, *Bull. Soc. Chim. Fr.*, 1940 (1969).
14. M.-L. Filleux-Blanchard, F. Clesse, J. Bignebat and G. J. Martin, *Tetrahedron Lett.*, 981 (1969).
15. D. Leaver, D. M. McKinnon and W. A. Robertson, *J. Chem. Soc.*, 32 (1965).
16. G. Duguay and H. Quiniou, *Bull. Soc. Chim. Fr.*, 1918 (1970).
17. D. Ya. Murniece and Ya. F. Freimanis, *Zh. Org. Khim.*, **5,** 1482 (1969).
18. L. V. Timokhina, V. A. Usov, Ya. S. Tsetlin, E. O. Tsetlina and M. G. Voronkov, *Zh. Org. Khim.*, **15,** 82 (1979).
19. L. I. Lavlinskaya, E. O. Tsetlina, V. A. Pestunovich, V. A. Usov, Ya. S. Tsetlin and M. G. Voronkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2108 (1975).
20. H. King and L. L. Ware, *J. Chem. Soc.*, 873 (1939).
21. F. Arndt, Ber. **65,** 92 (1932).
22. M. Meisel and H. Grunze, *Z. Anorg. Allg. Chem.*, **360,** 277 (1968).
23. W. Fuhrer, R. Hobi, A. Pflanz and P. Schneider, *Helv. Chim. Acta.*, **57,** 1498 (1974).
24. *Gmelins Handbuch der anorganischen Chemie,* **Band 16,** Phosphor, Teil C, Verlag Chemie, GmbH, Weinheim, 1965, p. 580.
25. A Gutbier, *Ber.*, **33,** 3358 (1900).
26. T. Y. Sen, G. Walford and B. Witzel, Ger. Patent 2,059,355 (1971); C. A. **75,** 63630 (1971).
27. A. S. Sarenko, L. N. Poznyakova, I. Ya. Kvitko and L. S. Efros, *Khim. Geterotsikl. Soedin.*, 805 (1972).
28. T. Hino, K. Tsuneoka, M. Nakagawa and S. Akabochi, *Chem. Pharm. Bull.*, **17,** 550 (1969).
29. A. Sammour, T. Zimaity and S. Kamel, *J. Prakt. Chem.*, **314,** 271 (1972).
30. K. Kindler, *Ann.*, **431,** 187 (1923).
31. L. Ruzička, *Helv. Chim. Acta.*, **16,** 1323 (1933).
32. V. P. Khilya and G. I. Galadan, *Khim. Geterotsikl. Soedin.*, 1282 (1973).
33. V. N. Konyukhov, T. G. Koksharova, K. V. Agmetskaya and Z. V. Pushkareva, *Khim. Geterotsikl. Soedin.*, 426 (1971).
34. J. W. Greidanus and W. J. Schwalm, *Can. J. Chem.*, **47,** 3715 (1969).
35. L. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, John Wiley, New York, 1968, p. 377.
36. J. W. Scheeren, P. H. J. Ooms and R. J. F. Nivard, *Synthesis,* 149 (1973).
37. J. Daunis, J. Guindo and P. Viallefont, *Bull. Soc. Chim. Fr.*,1975 (1972).
38. J. Daunis, M. Guerret-Rigail and R. Jaguier, *Bull. Soc. Chim. Fr.*, 3198 (1972).
39. Reference 6, p. 420.
40. L. Gattermann and H. Schulze, *Ber.*, **29,** 2944 (1896).
41. C. Andrieu, Y. Mollier and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 2457 (1965).
42. S. Oae, A. Nakanishi and N. Tsujimoto, *Chem. Ind.* (*London*), 575 (1972).
43. W. Walter and T. Proll, *Synthesis,* 941 (1979).
44. E. E. Reid, *Organic Chemistry of Bivalent Sulfur,* Vol. 3, Chemical Publ., New York, 1960, p. 159.
45. A. Schönberg and A. Wagner, in "Methoden der organischen Chemie", **Band 9,** Houben-Weyl, Stuttgart, 1955, p. 694.
46. E. Campaigne and B. E. Edwards, *J. Org. Chem.*, **27,** 3760 (1962).
47. H. Staudinger and H. Freudenberger, *Ber.*, **61,** 1576 (1928).

48. R. W. Bost and B. Q. Cosby, *J. Amer. Chem. Soc.*, **57**, 1404 (1935).
49. J. Ashoby and H. Suschitzky, *Tetrahedron Lett.*, 1315 (1971).
50. R. M. Elofson, L. A. Baker, F. F. Gadallach and R. A. Sikstrom, *J. Org. Chem.*, **29**, 1355 (1964).
51. D. Cook, *Can. J. Chem.*, **39**, 1184 (1961).
52. S. H. H. Chaston and S. E. Livingstone, *Aust. J. Chem.*, **18**, 673 (1965).
53. Reference 6, p. 419.
54. Reference 5, p. 233.
55. Reference 5, p. 187.
56. L. I. Lavlinskaya, V. A. Pestunovich, Ya. S. Tsetlin, V. A. Usov and M. G. Voronkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2091 (1976).
57. L. Kozerski and J. Dabrowski, *Org. Magn. Reson.*, **4**, 253 (1972).
58. K. Buggle, D. O'Sullivan and N. D. Ryan, *Chem. Ind. (London)*, 164 (1974).
59. V. A. Usov, N. A. Korchevin, Ya. S. Tsetlin and M. G. Voronkov, *Zh. Org. Khim.*, **11**, 410 (1975).
60. V. A. Usov, K. A. Petriashvili and M. G. Voronkov, *Zh. Org. Khim.*, **16**, 1550 (1980).
61. R. L. Martin and J. M. Stewart, *Nature*, **210**, 522 (1966).
62. G. Schrauzer, *Accounts Chem. Res.*, **2**, 72 (1969).
63. Ya. S. Tsetlin, Dissertation, Institute of Organic Chemistry, Moscow, 1976.
64. N. N. Sveshnikov, I. I. Levkoev, A. F. Vompe and B. S. Portnaya, *Dokl. Akad. Nauk SSSR*, **88**, 281 (1953).
65. Reference 5, p. 27.
66. V. A. Usov, Ya. S. Tsetlin and M. G. Voronkov, *Izv. Sib. Otdel. Akad. Nauk SSSR, Ser. Khim. Nauk*, No. 4, 159 (1975).
67. Ya. S. Tsetlin, V. A. Usov, T. V. Kashik, S. M. Ponomareva and M. G. Voronkov, *Zh. Org. Khim.*, **15**, 1680 (1979).
68. V. A. Usov, Ya. S. Tsetlin, N. A. Korchevin and M. G. Voronkov, *Izv. Sib. Otdel. Akad. Nauk SSSR, Ser. Khim. Nauk*, No. 12, 99 (1974).
69. D. N. Gerlach and R. H. Holm, *J. Amer. Chem. Soc.*, **91**, 3457 (1969).
70. Y. Nomura and Y. Takeuchi, *Bull. Chem. Soc. Japan*, **33**, 1743 (1960).
71. R. S. Asquith, D. L. Hammik and P. L. Williams, *J. Chem. Soc.*, 1181 (1948).
72. S. Bleisch and R. Mayer, *Z. Chem.*, **4**, 146 (1964).
73. Z. Yoshida, H. Konishi, Y. Tawara and K. Nishikawa, *Tetrahedron Lett.*, 2619 (1973).
74. C. Reddelien and H. Danilof, *Ber.*, **54**, 3135 (1921).
75. W. Backer, J. B. Harborne and W. D. Ollis, *J. Chem. Soc.*, 1294 (1952).
76. W. Fehrmann, *Ber.*, **20**, 2844 (1887).
77. P. Reinaud, R. C. Moreau and P. Foder, *C. R. Hebd. Seances Acad. Sci.*, C **264**, 1414 (1967).
78. P. Reinaud, R. C. Moreau and J. P. Samama, *Bull. Soc. Chim. Fr.*, 3623 (1965).
79. Ya. S. Tsetlin, V. A. Usov and M. G. Voronkov, *Zh. Org. Khim.*, **11**, 1945 (1975).
80. L. I. Lavlinskaya, V. A. Pestunovich, V. A. Usov, N. A. Korchevin, Ya. S. Tsetlin and M. G. Voronkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2630 (1978).
81. V. A. Usov, L. V. Timokhina and M. G. Voronkov, *Zh. Org. Khim.*, **13**, 2324 (1977).
82. B. J. Haske, M. E. Matthews, J. A. Conkling and H. P. Perzanowski, *J. Org. Chem.*, **32**, 1579 (1967).
83. N. A. Korchevin, V. A. Usov and M. G. Voronkov, *Zh. Org. Khim.*, **12**, 2412 (1976).
84. A. V. Fokin and A. F. Kolomiets, *Usp. Khim.*, **44**, 306 (1975).
85. O. M. Cherntsov, *Zh. Obshch. Khim.*, **17**, 186 (1944).
86. E. Campaigne, R. E. Cline and C. E. Kaslow, *J. Org. Chem.*, **15**, 600 (1950).
87. A. Michaelis and A. Hölken, *Ann.*, **331**, 245 (1904).
88. D. I. Biskunskaya and A. V. Voropaeva, *Khim. Geterotsikl. Soedin.*, 1688 (1971).
89. K. Gleu and R. Schaarschmidt, *Ber.*, **72**, 1246 (1939).
90. M. Jonesen and M. Vlassa, *Rev. Roum. Chim.*, **16**, 743 (1971); C. A. **75**, 49372 (1971).
91. N. N. Sveshnikov, I. I. Levkoev, N. I. Shirokova and N. A. Damir, *Dokl. Akad. Nauk SSSR.*, **148**, 1091 (1963).
92. J. Liebscher and H. Hartmann, *Z. Chem.*, **14**, 189 (1974).
93. J. Liebscher and H. Hartmann, *Z. Chem.*, **12**, 417 (1972).
94. M. G. Voronkov, N. S. Vyazankin, E. N. Deryagina, A. S. Nakhmanovich and V. A. Usov, "Reactions of Sulfur with Organic Compounds" (Russ.), Novosibirsk, Nauka, 1979, p. 271.
95. A. E. Tschitschibabin and I. L. Knunjanz, *Ber.*, **62**, 3048 (1929).
96. A. Edinger, *Ber.*, **33**, 3769 (1900).
97. Kalle Co., Ger. Patent 120,586 (1901); Zbl. **B.1**, 1254 (1901).
98. A. Edinger, *J. Prakt. Chem.*, **64**, 196 (1901).

99. H. Hashitani and K. Katsuyama, *Japan Analyst,* **19,** 355 (1970).
100. M. S. Korobov, L. E. Nivorozhkin and V. I. Minkin, *Zh. Org. Khim.,* **9,** 1717 (1973).
101. M. Weissenfels and M. Pulst, *J. Prakt. Chem.,* **315,** 873 (1973).
102. M. Pulst, S. Steingrüber and E. Kleinpeter, *Z. Chem.,* **17,** 93 (1977).
103. L. E. Nivorozhkin, M. S. Korobov, B. Ya. Simkin and V. I. Minkin, *Zh. Org. Khim.,* **8,** 1677 (1972).
104. V. I. Minkin, Yu. A. Zhdanov, L. P. Olekhnovich, L. E. Nivorozhkin and M. I. Knyazhanskii, *Zh. Org. Khim.,* **6,** 348 (1970).
105. Ya. L. Gol'dfarb and M. A. Kalik, *Usp. Khim.,* **41,** 679 (1972).
106. I. Ya. Kvitko and N. B. Sokolova, *Khim. Geterotsikl. Soedin.,* 791 (1972).
107. I. Ya. Kvitko and B. A. Porai-Koshits, *Zh. Org. Khim.,* **5,** 1685 (1969).
108. L. N. Kurkovskaya, N. N. Shapet'ko, N. B. Sokolova and I. Ya. Kvitko, *Zh. Org. Khim.,* **11,** 1091 (1975).
109. E. A. Panfilova, I. Ya. Kvitko, L. N. Kurkovskaya and A. V. El'tsov, *Zh. Org. Khim.,* **14,** 2208 (1978).
110. V. A. Bren', V. I. Usachova, Zh. V. Bren', B. Ya. Simkin and V. I. Minkin, *Khim. Geterotsikl. Soedin.,* 631 (1974).
111. I. Ya. Kvitko, R. V. Khoseeva and A. V. El'tsov, *Khim. Geterotsikl. Soedin.,* 670 (1979).
112. S. Hauptmann, E. Uhlemann and L. Widmann, *J. Prakt. Chem.,* **38,** 101 (1968).
113. H. Behringer and A. Grimm, *Ann.,* **682,** 188 (1965).
114. V. A. Usov, L. V. Timokhina, L. I. Lavlinskaya and M. G. Voronkov, *Zh. Org. Khim.,* **15,** 2598 (1979).
115. G. Duguay, *C. R. Hebd. Seances Acad. Sci.,* **C 281,** 1077 (1975).
116. G. Duguay, C. Metayer and H. Quiniou, *Bull. Soc. Chim. Fr.,* 2507 (1974).
117. Ya. L. Gol'dfarb, M. A. Kalik and M. L. Kirmalova, *Izv. Akad. Nauk SSSR, Ser. Khim.,* 701 (1962).
118. Ya. L. Gol'dfarb and M. A. Kalik, *Izv. Akad. Nauk SSSR, Ser. Khim.,* 2072 (1973).
119. Ya. L. Gol'dfarb and Ya. L. Danyushevskii, *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1345 (1964).
120. Ya. L. Gol'dfarb and M. A. Kalik, *Khim. Geterotsikl. Soedin.,* 902 (1972).
121. C. Metayer and G. Duguay, *C. R. Acad. Sci. (Paris),* **C 273,** 1457 (1971).
122. E. L. Smutny, W. Turner, E. D. Morgan and R. Robinson, *Tetrahedron,* **23,** 3785 (1967).
123. H. Quiniou and N. Lozac'h, *Bull. Soc. Chim. Fr.,* 450 (1964).
124. E. Uhlemann and B. Zöllner, *Z. Chem.,* **14,** 245 (1974).
125. E. Uhlemann, *Z. Naturforsch.,* **21b,** 592 (1966).
126. H. Gotthardt, *Chem. Ber.,* **105,** 2004 (1972).
127. P. Sykes and H. Ullach, *J. Chem. Soc. Perkin,* I, 2305 (1972).
128. H. Ullach and P. Sykes, *Chem. Ind. (London),* 1162 (1973).
129. G. Duguay, H. Quiniou and N. Lozac'h, *Bull. Soc. Chim. Fr.,* 2763 (1967).
130. V. A. Usov, Ya. S. Tsetlin, K. A. Petriashvili and M. G. Voronkov, *Zh. Org. Khim.,* **12,** 1830 (1976).
131. Ya. S. Tsetlin, V. A. Usov, N. D. Sudakova, E. O. Tsetlina and M. G. Voronkov, *Zh. Org. Khim.,* **12,** 1828 (1976).
132. E. G. E. Hawkins, "Organic Peroxides, Their Formation and Reactions", Spon Ltd., London, 1961.
133. N. A. Korchevin, Dissertation, Moscow State University, 1976.
134. L. V. Timokhina, Ya. S. Tsetlin, E. O. Tsetlina, V. A. Usov and M. G. Voronkov, *Zh. Org. Khim.,* **14,** 666 (1978).
135. L. V. Timokhina, V. A. Usov and M. G. Voronkov, *Zh. Org. Khim.,* **14,** 2226 (1978).
136. V. A. Usov, N. A. Korchevin, K. A. Petriashvili, I. A. Dorofeev and L. A. Oparina, IXth International Symposium on Organic Sulfur Chemistry, Riga, USSR, 1980, Abstracts of Papers, p. 63.
137. N. A. Korchevin, V. A. Usov, L. A. Oparina, I. A. Dorofeev, Ya. S. Tsetlin and M. G. Voronkov, *Zh. Org. Khim.,* **16,** 1842 (1980).
138. O. Siimann and J. Fresco, *J. Amer. Chem. Soc.,* **92,** 2652 (1970).
139. L. I. Lavlinskaya and L. V. Timokhina, IXth International Symposium on Organic Sulfur Chemistry, Riga, USSR, 1980, Abstracts of Papers, p. 241.
140. V. A. Usov, L. V. Timokhina and M. G. Voronkov, *Zh. Org. Khim.,* **16,** 226 (1980).
141. R. E. Banks and R. N. Haszeldine, in "The Chemistry of Organic Sulfur Compounds", Vol. 2, edited by N. Kharasch and C. Y. Meyers, Pergamon Press, London, 1966, p. 156.
142. V. A. Usov, L. V. Timokhina, T. L. Usova and M. G. Voronkov, *Zh. Org. Khim.,* **17,** 1327 (1981).
143. D. H. Clemens, A. J. Bell and J. O. O'Brien, *J. Org. Chem.,* **29,** 2932 (1964).
144. G. Bianchetti, P. Della Croce and D. Pocar, *Gazz. Chim. Ital.,* **94,** 606 (1964).
145. W. Walter and K.-D. Bode, *Angew. Chem.,* **78,** 517 (1966).
146. J. E. Baldwin, G. V. Kaiser and J. A. Romersberger, *J. Amer. Chem. Soc.,* **87,** 4114 (1965).
147. S. Hünig, K. Hübner and E. Benzing, *Chem. Ber.,* **95,** 926 (1962).

148. J. Schoen and M. Barcik, *Rocz. Chem.*, **45**, 73 (1971).
149. R. W. J. Carney, J. Wojtkunski and G. de Stevens, *J. Org. Chem.*, **29**, 2887 (1964).
150. W. Walter and T. Fleck, *Ann.*, 670 (1976).
151. R. Fusco, G. Bianchetti and S. Rossi, *Gazz. Chim. Ital.*, **91**, 825 (1961).
152. J. Goerdeler and J. Gnad, *Chem. Ber.*, **98**, 1531 (1965).
153. J. Goerdeler and H. Poland, *Chem. Ber.*, **94**, 2950 (1961).
154. J. Goerdeler and H. Poland, *Chem. Ber.*, **96**, 526 (1963).
155. J. Moszew, A. Inasinski, K. Kubiczek and J. Zawrzykraj, *Rocz. Chem.*, **34**, 1169 (1960).
156. S. Rajappa and B. G. Advani, *Indian J. Chem.*, **9**, 759 (1971).
157. G. Le Coustumer and Y. Mollier, *Bull. Soc. Chim. Fr.*, 3349 (1973).
158. J. Chupp, US Patent 3,576,862 (1971); C. A. **75**, 35488 (1971).
159. G. Zigeuner, W.-B. Lintschinger, A. Fuchsgruber and K. Kollmann, *Monatsh. Chem.*, **107**, 155 (1976).
160. W. Walter, T. Fleck, J. Voss and M. Gerwin, *Ann.*, 275 (1975).
161. J. S. Walta, S. N. Bannore, A. S. Walia and L. Guillot, *Chem. Lett.*, 1005 (1974).
162. J. Brelivet and J. Teste, *Bull. Soc. Chim. Fr.*, 2289 (1972).
163. L. Legrand, Fr. Patent 1,539,834 (1968); C. A. **71**, 91543 (1968).
164. L. Legrand and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 3905 (1972).
165. L. Legrand and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 3892 (1972).
166. G. Wagner and L. Rothe, *Pharmazie*, **26**, 271 (1971).
167. A. P. Bhaduri, N. M. Khanna and M. L. Dhar, *Indian J. Chem.*, **2**, 159 (1964).
168. R. Mayer and H. Hartmann, *Chem. Ber.*, **97**, 1886 (1964).
169. C. Paulmier, Y. Mollier and N. Lozac'h, *Bull. Soc. Chim. Fr.*, 2463 (1965).
170. R. Boberg and W. Gentzkow, *J. Prakt. Chem.*, **315**, 965 (1973).
171. G. Le Coustumer, Y. Mollier and H. Normant, *C. R. Acad. Sci. (Paris)*, **267**, 1423 (1968).
172. H. E. Winberg, J. E. Carnahan, D. D. Coffman and M. Broun, *J. Amer. Chem. Soc.*, **87**, 2054 (1965).
173. F. Boberg and W. Gentzkow, *Ann.*, 247 (1973).
174. F. Boberg and W. Gentzkow, *J. Prakt. Chem.*, **315**, 970 (1973).
175. S. Scheithauer and R. Mayer, in "Topics in Sulfur Chemistry", Vol. 4, edited by A. Senning, Georg Thieme Publishers, Stuttgart, 1979, p. 36.
176. K. Mizuyama, Y. Tominaga and Y. Mutsuda, *J. Pharm. Soc.*, **94**, 702 (1974).
177. L. N. Kurkovskaya, N. N. Shapet'ko, I. Ya. Kvitko, Yu.N. Koshelev and E. M. Sof'ina, *Zh. Org. Khim.*, **9**, 821 (1973).
178. V. S. Bogdanov, M. A. Kalik, Ya. L. Danyushevskii and Ya. L. Gol'dfarb, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2782 (1967).
179. V. S. Bogdanov, M. A. Kalik, I. P. Yakovlev and Ya. L. Gol'dfarb, *Zh. Obshch. Khim.*, **40**, 2102 (1970).
180. U. Dabrowska and J. Dabrowski, *Adv. Mol. Relaxation Processes*, **5**, 81 (1973).
181. L. E. Nivorozhkin, M. S. Korobov and V. I. Minkin, *Zh. Org. Khim.*, **14**, 347 (1978).
182. A. Maquestiau, I. Van Haverbeke and J. C. Vanovervelt, *Bull. Soc. Chim. Belg.*, **84**, 741 (1975).
183. Ya. L. Gol'dfarb, I. N. D'yachenko and S. G. Mairanovskii, *Khim. Geterotsikl. Soedin.*, 309 (1975).
184. V. S. Bogdanov, V. P. Litvinov, Ya. L. Gol'dfarb, N. N. Petukhova and E. G. Ostapenko, *J. Prakt. Chem.*, **316**, 970 (1974).
185. V. S. Bogdanov, M. A. Kalik and Ya. L. Gol'dfarb, *Izv. Akad. Nauk SSSR., Ser. Khim.*, 598 (1974).
186. A. V. El'tsov, I. Ya. Kvitko, S. P. Fradkina and E. A. Panfilova, *Zh. Obshch. Khim.*, **49**, 417 (1979).
187. L. N. Kurkovskaya, N. N. Shapet'ko, I. Ya. Kvitko, Yu, M. Koshelev and E. D. Samartseva, *Zh. Org. Khim.*, **10**, 2210 (1974).
188. A. V. El'tsov, I. Ya. Kvitko, E. A. Panfilova and V. A. Amelichev, *Zh. Obshch. Khim.*, **48**, 2307 (1978).
189. L. N. Kurkovskaya, N. N. Shapet'ko, I. Ya. Kvitko, L. V. Alam, E. A. Panfilova and A. V. El'tsov, *Zh. Strukt. Khim.*, **19**, 620 (1978).
190. V. I. Minkin, B. Ya. Simkin and L. P. Olekhnovich, *Int. J. Sulfur Chem.*, **8**, 249 (1973).
191. V. S. Bogdanov, Ya. L. Danyushevskii and Ya. L. Gol'dfarb, *Izv. Akad. Nauk SSSR., Ser. Khim.*, 675 (1970).
192. V. I. Minkin, L. P. Olekhnovich. Yu. A. Zhdanov and Yu. A. Ostroumov, *Zh. Org. Khim.*, **6**, 549 (1970).
193. G. Klose, H. Müller and E. Uhlemann, *Z. Naturforsch.*, **19b**, 952 (1964).
194. E. Uhlemann and H. Müller, J. Prakt. Chem., **30**, 163 (1965).
195. G. Gattow and K. Hanewald, *Chem. Ber.*, **109**, 3243 (1976).

196. T. L. Usova, E. I. Kasitsina, L. V. Timokhina, V. A. Usov and M. G. Voronkov, *Izv. Akad. Nauk SSSR., Ser. Khim.*, 181 (1981).
197. A. Yogev and Y. Mazur, *J. Org. Chem.*, **32**, 2167 (1967).
198. L. V. Timokhina, T. L. Usova, V. A. Usov and M. G. Voronkov, *Khim. Geterotsikl. Soedin.*, 121 (1981).
199. E. Kleinpeter and M. Pulst, *J. Prakt. Chem.*, **322**, 575 (1980).
200. I. Ya. Kvitko, R. V. Khoseeva, N. S. Fedorova, G. M. Frolova and A. V. El'tsov, *Zh. Org. Khim.*, **12**, 1598 (1976).
201. L. N. Kurkovskaya, N. N. Shapet'ko, E. D. Smartseva, Yu. N. Koshelev, E. M. Sof'ina and I. Ya. Kvitko, *Zh. Org. Khim.*, **11**, 1734 (1975).
202. J. Dabrowski and K. Kamienska-Trela, *Org. Magn. Reson.*, **4**, 421 (1972).
203. E. Kleinpeter and M. Pulst, *Org. Magn. Reson.*, **9**, 308 (1977).
204. E. Kleinpeter and M. Pulst, *J. Prakt. Chem.*, **319**, 1003 (1977).
205. E. Kleinpeter, B. Heinrich and M. Pulst, *Z. Chem.*, **18**, 220 (1978).
206. E. Kleinpeter and M. Pulst, *Z. Chem.*, **17**, 339 (1977).
207. J. Dabrowski, K. Kamienska-Trela and L. Kozerski, *Org. Magn. Reson.*, **6**, 499 (1974).
208. M.-L. Filleux-Blanchard, H. Durand, M. T. Bergeou, F. Clesse, H. Quiniou and G. J. Martin, *J. Mol. Struct.*, **3**, 351 (1969).
209. J. Dabrowski and L. Kozerski, *Org. Magn. Reson.*, **4**, 137 (1972).
210. H. E. A. Kramer and R. Gompper, *Z. Phys. Chem. (Frankfurt)*, **43**, 292 (1964).
211. K. J. Dahlqvist and B. Forsén, *Acta Chem. Scand.*, **24**, 2075 (1970).
212. W. E. Stewart and T. H. Siddal, *Chem. Rev.*, **70**, 517 (1970).
213. H. Kessler, *Angew. Chem.*, **82**, 237 (1970).
214. W. Walter and T. Fleck. *Ann.*, 682 (1976).
215. J.-P. Sauve and N. Lozac'h. *Bull. Soc. Chim. Fr.*, 2016 (1970).
216. U. Dabrowska and J. Dabrowski, *Chem. Ber.*, **109**, 1779 (1976).
217. M. Saquet and A. Thuillier, *Bull. Soc. Chim. Fr.*, 2841 (1967).
218. E. J. Smutny, *J. Amer. Chem. Soc.*, **91**, 208 (1969).
219. G. Le Coustumer, Y. Mollier, D. Le Botlan and M.-L. Filleux-Blanchard, *Org. Magn. Reson.*, **6**, 454 (1974).