STRUCTURE AND PROPERTIES OF IMIDAZOLE-2-THIONES (REVIEW)

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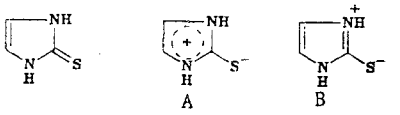
Literature data on the structure, physicochemical properties, and transformations of imidazole-2-thiones and their benzo analogs are correlated.

The interest in imidazole-2-thiones, which are cyclic analogs of thiourea, is associated with the broad spectrum of their biological action and their valuable technical properties. Diverse methods for obtaining these compounds have been developed, and definite advances have been made in the study of the peculiarities of the structure and reactivity of this series of imidazole derivatives. At the same time, monographs on the chemistry of heterocyclic compounds contain rather scanty and fragmentary data on the properties of imidazole-2-thiones. In our review we attempted to systematize numerous literature data on the structure and chemical properties of imidazole-2-thiones and their benzo analogs.

STRUCTURE AND PHYSICOCHEMICAL PROPERTIES OF IMIDAZOLE-2-THIONES

The principal structural peculiarity of imidazole-2-thiones is the presence of a thiouredine fragment. The results of quantum-chemical calculations constitute evidence for a nonuniform distribution of the π-electron density in the imidazole-2-thione molecule and for the presence of the maximum negative charge on the exocyclic sulfur atom [1]. The molecular structures of imidazole-2-thione [2] and 1,3-dimethylimidazole-2-thione [3] were studied by x-ray diffraction analysis. The imidazolethione molecule is planar. A strong mesomeric shift of the electron pairs of the nitrogen atoms to the sulfur atom leads to partial double-bond character of the N–C–N system. The length of the C–N bond is 1.345 Å; this is very close to the length of the C–N partial double bond in nitrogen-containing heterocyclic systems (1.352 Å). According to the calculations in [1], the order of the C–S bond in imidazolethione is less than two, and its length is 1.70 Å [2], which is greater than the length of the C=S bond (1.61 Å). Thus, the state of the imidazole-2-thione molecule can be represented most satisfactorily by resonance hybrid A. The data on the bond lengths and orders [1-3] constitute evidence that dipolar form B predominates in the resonance hybrid.



A B

The benzimidazole-2-thione molecule is planar and aromatic [4]. The lengths of the bonds in the condensed imidazole ring are greater than in the free imidazole system. There are no substantial differences in the lengths of the two types of C–N bonds (1.362 and 1.383 Å). The degree of double-bond character of the C–S bond is 80%, and its length is 1.671 Å. The bond angles are in good agreement with the data in [2].

The large values of the dipole moments of imidazole-2-thione and benzimidazole-2-thione (5.67 and 4.14 D, respectively, in dioxane) can be explained by the large contribution of the limiting dipolar form to the structure of the molecule [5]. The introduction of a condensed benzene decreases the dipole moment appreciably; this is associated with π conjugation of the imidazole and benzene rings.

The ionization potentials of imidazole-2-thione have been calculated by the CNDO (complete neglect of differential overlap) method, and the bands in the photoelectronic spectra of 1-methyl- and 1,3-dimethylimidazole-2-thione [6] and 1,3-dimethylbenzimidazole-2-thione

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[7] have been assigned. It was shown that the highest occupied molecular orbital (HOMO) is a bonding π MO and that the next occupied orbital is a nonbonding nσ MO; both of these orbitals are strongly localized on the sulfur atom of the thiocarbonyl group.

Imidazolethiones are weak organic bases that are protonated when they are dissolved in acids. The pK_{BH^+} values of imidazolethiones range from −1.1 to −2.2 H_0 units [1], while the pk_{BH^+} value of benzimidazole-2-thione is about −2.69 H_0 units [8]. Imidazolethiones are NH acids. The results of measurements showed the existence of two constants of acidic dissociation of benzimidazolethione in water, viz., pK_1 9.18 and pK_2 10.98, which, in the opinion of Lomakina and Alimarin [9], characterize dissociation of the NH and SH groups. In an investigation of the effect of the pH of the medium and the solvent on the UV spectra of benzimidazolethione derivatives it was established that deprotonation in an alkaline medium occurs through the NH^+ group, whereas protonation in a strongly acidic medium takes place at S^- [10].

Two absorption maxima at 217 and 270 nm are observed in the UV spectrum of imidazole-2-thione in CH_2Cl_2 [11]. The introduction of alkyl substituents into the 1 and 3 positions causes virtually no shift of the long-wave absorption maximum. The effect of the volume of the substituent is manifested in the spectrum commencing with the tert-butyl group. The presence of an aromatic substituent attached to the nitrogen atom leads to an 18-20 nm bathochromic shift of this maximum. A significant bathochromic shift is observed in the imidazolethione–benzimidazolethione series: the absorption maxima of the latter in ethanol lie at 246 and 304 nm [12]. Quantum-chemical calculations of the electronic spectra of imidazolethiones made it possible to assign all of the observed transitions to transitions of the $\pi \rightarrow \pi^*$ type [11].

The most nearly complete analysis of the IR spectra of imidazole-2-thione and alkyl-substituted imidazole-2-thiones was given in [2, 13-17]. A comparison of the spectra of imidazole-2-thione and its N,N'-deuterated, oxygen, and selenium analogs and S-methyl derivative and calculations of the observed band with respect to the type of symmetry and the approximate form of the internal vibrations made it possible to assign the band at 520 cm^{-1} to vibrations of the C=S group [13]. In the case of 1-alkylimidazolethiones the bands at 1150-1220 (ν C=S) and 515-550 cm^{-1} (δ C=S or ring +ν C=S) were assigned to vibrations of the thiocarbonyl group [14]. Raper and coworkers [15-17] examined a number of bands due to vibrations of the HN–C=S fragment in the IR spectra of imidazolethiones. Four bands, viz., 1480, 1228, 1070, and 740 cm^{-1}, were assigned to the vibrations of the thioamide fragment in the case of imidazole-2-thione. The following thioamide bands were ascertained from benzimidazolethione: 1508 (ν N–C=S), 1270 (δ N–H), and 1180 cm^{-1} (ν C=S) [18, 19]. A comparison of the IR spectra of benzimidazole-2-thione and benzimidazole-2-selenone made it possible to assign the band at 598 cm^{-1} to vibrations of the C=S bond [20].

Imidazole-2-thiones are associated by means of intermolecular hydrogen bonds of the N–H...S type [21-23]. Evidence for this is provided by the rather high melting points of imidazole-2-thiones and the significant decrease in them for the N- and S-substituted compounds. The IR spectra of imidazolethiones in CCl_4 contain two absorption bands: the narrow band at 3400-3470 cm^{-1} corresponds to vibrations of free NH groups, while the broad band at 2900-3200 cm^{-1} corresponds to vibrations of associated NH groups [21]. It was established by x-ray diffraction analysis that each sulfur atom in benzimidazole-2-thione is associated by means of hydrogen bonding with two NH groups of adjacent molecules (N...S 3.366, S...H 2.42 Å) [4]. The H–N...S bond angle (22°) indicates small deviation from linearity.

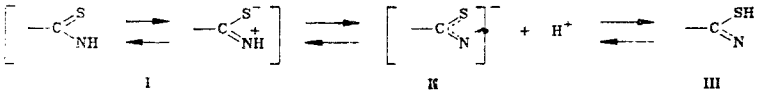
Imidazole-2-thiones can exist in two tautomeric forms, viz., thione and thiol:

It has been demonstrated by means of the dipole moments [5] and IR [13-20, 24], UV [11, 12, 24], and ^1H [3], ^{13}C [25], and ^{15}N [26] NMR spectroscopy, as well as x-ray diffraction analysis [2, 4], that imidazolethiones exist in the thione form in the crystalline state and in solutions. According to ^{15}N NMR data, 1-methylimidazole-2-thione exists in DMSO exclusively in the form of the thione tautomer, whereas for benzimidazole-2-thione the percentage of the latter is 92% [26]. The ionization constants of the tautomeric and model methylated compounds were used in [1] to investigate the tautomeric equilibria of imidazolethiones. The equilibrium constant of the tautomeric reaction thiol ⇄ thione was found to be 10^8. The

stabilization of the thione form is associated to a considerable extent with interaction of the π-electron system of the heteroring with the electron shell of the sulfur atom..

CHEMICAL PROPERTIES

Imidazole-2-thiones are classified as so-called "ambifunctional nucleophilic compounds" and readily undergo reactions with electrophilic reagents. The ambident anion of these compounds, which contain a thioamide group, that is formed as a result of splitting out of a proton is represented by triad II with a negative charge that is distributed nonuniformly between its ends [27].



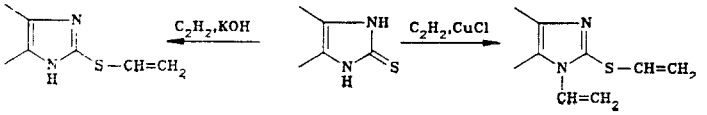
I II III

Two factors, viz., electrostatic attraction and polarizability, affect the interaction of the ambient anion with the electrophilic reagent [27]. In reactions of the nucleophile with the polar electrophilic reagent the reaction is realized at the more electronegative nitrogen atom, which has the highest electron density. In reactions that proceed through a step involving the formation of a transition state a valence bond is formed with the readily polarizable sulfur atom.

Nucleophilic Addition

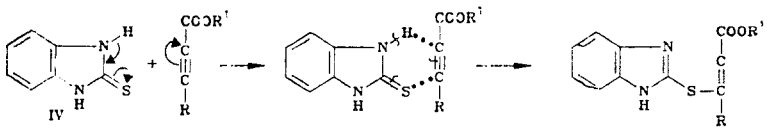
Reactions with Acetylenes. One of the most interesting, in our opinion, chemical properties of imidazole-2-thiones is nucleophilic addition to a carbon–carbon triple bond, which, depending on the reaction conditions and the nature of the reagents, leads to the formation of S- or N-substituted derivatives.

Benzimidazole-2-thione and 4,5-diphenylimidazole-2-thione react with acetylene at high temperatures and pressures in dioxane in the presence of potassium hydroxide or metal salts (cuprous chloride, cadmium acetate) [28-30]. S-Mono- or N,S-divinyl derivatives are obtained, depending on the nature of the catalyst.



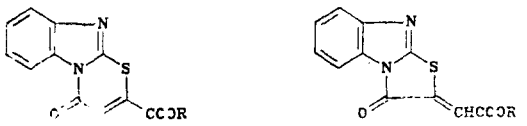
The introduction of activating groupings (COOH, COOR, COR, CN) at the triple bond of acetylenes, on the one hand, increases its electrophilicity and makes it possible to realize the addition of imidazolethiones under milder conditions, and, on the other hand, it expands the synthetic possibilities of this reaction due to intramolecular cyclization.

The reaction of benzimidazole-2-thione (IV) with acetylenecarboxylic acids and their esters has been studied quite thoroughly [31-39]. Thione IV reacts smoothly with propiolic acid and its esters on heating in ethyl acetate [31, 32] or benzene in the presence of basic or acidic catalysts [33] with the formation of unsaturated sulfides. In the opinion of Grinblat and Postovskii [31, 32] the reaction proceeds with migration of the reaction center through an intermediate cyclic complex:



IV

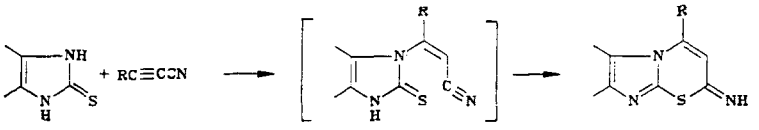
2-Phenyl-4H-[1,3]thiazino[3,2-a]benzimidazol-4-one was obtained by reaction of thione IV with ethyl phenylpropiolate by heating (200°C) for 12 h [37]. The addition of thione IV to acetylenecarboxylic acid esters is realized in methanol or acetic acid at the readily polarizable sulfur atom with the formation of a mixture of 1,3-thiazine[3,2-a]benzimidazolone and thiazolo[3,2-a]benzimidazolone derivatives in a ratio of ~1:1 [35, 36, 38]; these products are capable of interconversion on refluxing in methanol in the presence of sulfuric acid. Carrying out the same reaction in dry acetonitrile leads only to a thiazolidone derivative, whereas the reaction in dry methanol leads to a thiazinone derivative [39].



The reaction of thione IV and 4,5-diphenylimidazol-2-thione with α-acetylenic ketones and dibenzoylacetylene in methanol or acetonitrile with heating leads, depending on the reagent ratio, to acyl vinyl sulfides or N,S-diadducts [40, 41].

The preparation of unsaturated sulfides from imidazole- and benzimidazole-2-thiones and ethynylchlorobenzenes has been described [42].

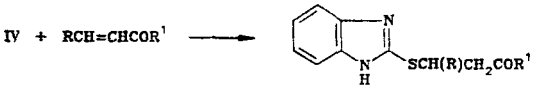
Imidazole-2-thiones react with phenylcyanoacetylene [43, 44] and tertiary cyanoacetylenic alcohols [45-47]. The activating effect of the cyano group and basic catalysis promote the addition of thione IV and 4,5-diphenylimidazole-2-thione to acetylenes at the hard base center of the ambident anion – the nitrogen atom. The reaction is accompanied by intramolecular cyclization with the formation of substituted 7-iminoimidazo[2,1-b][1,2]thiazines.



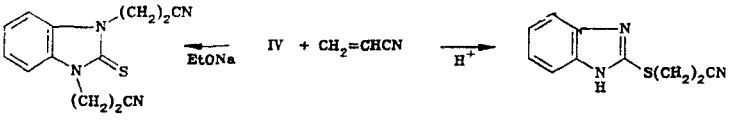
The mechanism of the formation of 1,3-thiazinobenzimidazoles has been studied by PMR and IR spectroscopy, and addition at the N atom was demonstrated unequivocally [48]. The reaction of imidazolethiones with a twofold excess of phenylcyanoacetylene leads to N,S-dicyanovinyl derivatives [44].

Addition to an Activated Double Bond. Products of addition to the double bond rather than acylation products are formed in the reaction of benzimidazole-2-thione (IV) with acrylic acid and its chloride under mild conditions; the reaction takes place at the sulfur atom [49].

The addition of thione IV to α,β-unsaturated aldehydes and ketones in the presence of HCl also leads to adducts at the S atom [50, 51].



Only patent data on the cyanoethylation of imidazole-2-thione are available [52]. The behavior of thione IV in this reaction has been studied quite thoroughly. A diadduct, viz., N,N'-bis(cyanoethyl)benzimidazole-2-thione, was obtained in its reaction with acrylonitrile in dioxane in the presence of triethylbenzylammonium hydroxide hydrate [53]. However, in [54, 55] it is asserted that, depending on the nature of the catalyst, the reaction can be directed to either nucleophilic center. Selective cyanoethylation at the sulfur atom is carried out in an acidic medium, while selective cyanoethylation at the nitrogen atoms is carried out in the presence of a basic catalyst.



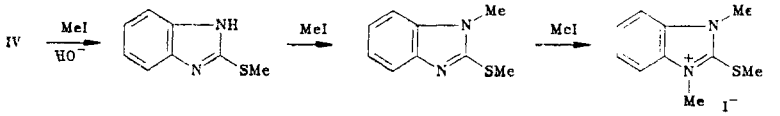
The possibility of the synthesis of an N-monoadduct of thione IV with acrylonitrile has been demonstrated [56].

N,N'-Bis- and N-mono[2-(2-pyridyl)ethyl]benzimidazole-2-thiones were obtained when thione IV was heated with 2-vinylpyridine in glacial acetic acid [57].

Nucleophilic Substitution

Alkylation and Arylation. The alkylation of imidazolethiones with alkyl halides [58-67], dialkyl sulfates [65-72], phosphoric and phosphorous acid esters [71-73], and diazomethane [69, 70] has been studied rather thoroughly. Alkylation is usually carried out in an alcohol, aqueous alcohol, or aqueous medium in the presence of alkali metal hydroxides

or carbonates for tying up the liberated hydrogen halide. The more nucleophilic sulfur atom is initially alkylated with the formation of 2-alkylthioimidazoles, treatment of which with excess alkyl halide gives dialkyl-substituted products and quaternary salts.

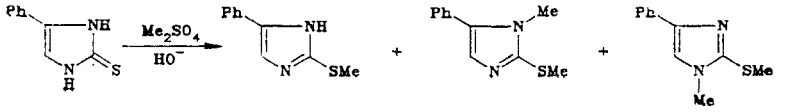


1-Methylbenzimidazole-2-thione was isolated in good yield when the quaternary salt was refluxed in pyridine [58].

The rate of the reaction of 1-methylimidazole-2-thione and 1-methylbenzimidazole-2-thione with methyl iodide or isopropyl iodide is described by a second-order equation; benzimidazolethione reacts slower by a factor of 10-20 than imidazolethione [74].

Interphase catalysis has been used in the last decade for the exhaustive alkylation of imidazolethiones [75, 76]; this makes it possible to use not only alkyl iodides but also alkyl bromides and chlorides in this reaction [77].

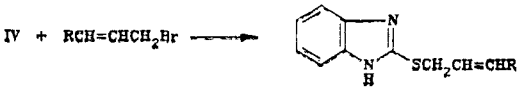
In the case of alkylation with dimethyl sulfate, in addition to exhaustive methylation [65, 67], one observes the formation of a mixture of mono- and disubstituted imidazoles [69].



The use of dimethylformamide dimethylacetal as the alkylating agent is interesting [78]. Either mono- or disubstituted benzimidazoles can be obtained in high yields, depending on the reaction time.

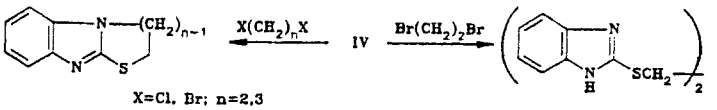
2-Alkylthioimidazoles and carbon dioxide are formed when alkyl-2-thioxoimidazole-4(5)-carboxylates are heated [79]. Jones [79] suggests intermolecular alkylation of the ester group with the subsequent loss of CO_2 by the resulting acid. This is confirmed by the reaction of imidazolethione with alkyl benzoates, as a result of which alkylthioimidazoles and benzoic acid were obtained [80].

The reaction of thione IV with allyl bromides occurs in a few minutes and gives an S-allylation product [81].



Thione IV reacts with propargyl bromide to give 2-propargylthiobenzimidazole [82-85]. 1-Propargyl-2-propargylthiobenzimidazole is formed with excess propargyl bromide in acetone in the presence of potassium carbonate [84].

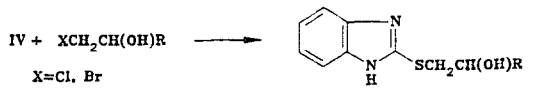
The reaction of thione IV with dihaloalkanes takes place simultaneously at the sulfur and nitrogen atoms and leads to derivatives of thiazolo- or thiazinobenzimidazoles, depending on the structure of the starting halogen-containing hydrocarbon [86-92].



X=Cl, Br; n=2,3

However, 1,2-bis(2-mercaptobenzimidazolyl)ethane was isolated in the case of refluxing with excess dibromoethane in toluene or heating 2 moles of thione IV with 1 mole of dibromoethane in ethanol in the presence of an alkali [87].

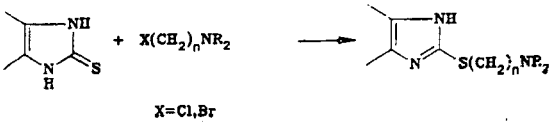
The S-hydroxyalkylation of thione IV with β- and γ-halo alcohols in the presence of an alkali has been described [87, 93-96].



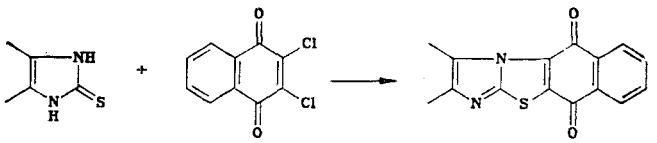
2-(2-Hydroxyethylthio)imidazoles can also be obtained from imidazolethiones and ethylene oxide [97, 98].

A hydroxy-substituted 1,3-thiazinobenzimidazole was isolated in the reaction of thione IV with epichlorohydrin; this product develops via intramolecular cyclization of the initially formed alkylation product [99, 100].

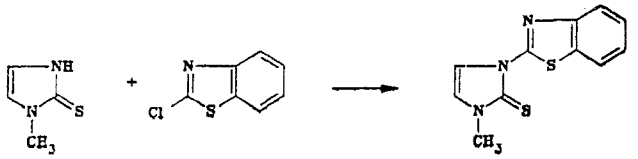
The introduction of an amino function into the side chain of imidazolethiones is realized by reaction with haloalkylamines [93, 101-104].



One should note some reactions with halo derivatives of aromatic compounds [105-107] that expand the synthetic possibilities of imidazolethiones. Imidazolethiones react with 2,3-dichloro-1,4-naphthoquinone to give dioxo derivatives of condensed azole systems [108].

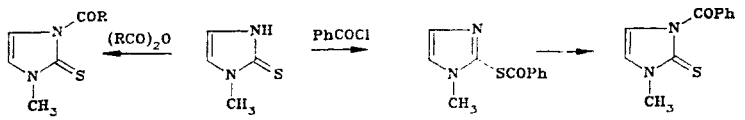


The reaction of imidazole-2-thiones with halo-substituted heterocycles [109-114] leads to the formation of hetarylthioimidazoles, among which preparations with high pharmacological activity have been found [111, 112]. However, 1-methyl-3-(2-benzothiazolyl)imidazole-2-thione was isolated when 1-methylimidazole-2-thione was fused with 2-chlorobenzothiazole [113].



Acylation

The medium and the reaction conditions play a large role in the acylation of imidazolethiones [115-117]. N-Acylimidazolethiones were synthesized by the reaction of imidazolethione and substituted imidazolethiones with benzoyl chloride and aliphatic carboxylic acid anhydrides in pyridine [117]. Benzoylthioimidazoles were obtained in absolute alcohol.



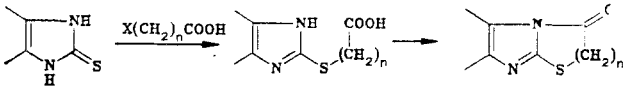
The possibility of the migration of an acyl substituent from the sulfur atom to the nitrogen atom with the formation of the more stable N-acylimidazolethione has been established.

N-Acylbenzimidazolethiones have been synthesized using acid chlorides and anhydrides, as well as isocyanates in the absence of bases, as the acylating agents [118-121]. Thione

IV reacts with oxalyl chloride in a neutral medium to give S,S'-bis(2-benzimidazolyl)-1,2-dithiooxalate [122].

Reaction with Halo Carbonyl Compounds

The reactions of imidazolethiones with bifunctional compounds such as halo-substituted acids and their derivatives has attracted the attention of numerous researchers in connection with the possibility of the synthesis of reactive synthones [59, 94, 105-107, 123-131], the subsequent modification of which may lead, in particular, to condensed imidazothiazoles and imidazothiazines [92, 124, 127, 128, 131-141].



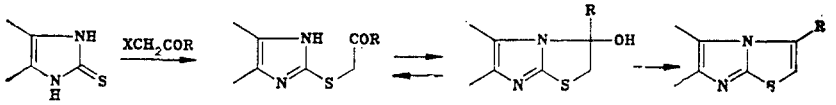
X=Cl,Br; n= 1-3

The reaction of thione IV with 2-bromopropionic acid gave 2-(benzimidazolylthio)propionic acid, which could be separated into enantiomers [125].

The nucleophilic substitution of cis- and trans-β-chloroacrylic acids by thione IV proceeds with complete retention of the configuration [124].

To expand the number of biologically active compounds, in addition to halo-substituted carboxylic acids, their derivatives, viz., amides [64, 102, 142], esters [102, 142-147], and nitriles [85, 142, 148, 149], are used in reactions with imidazolethiones; the corresponding 2-thio-subtituted compounds are obtained in all cases.

The reaction of imidazolethiones with α-halo ketones has become widely used [92, 150-154]; this is also explained by the possibility of the further intramolecular cyclization of the resulting 2-[β-ketoalkyl(aryl)]thioimidazoles [155-160]. According to the data in [150, 153-156, 159], the latter exist in equilibrium with the tautomeric cyclic form:



X=Cl,Br

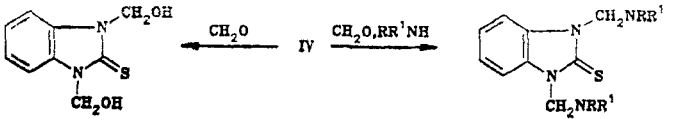
In the case of acidic catalysis water is eliminated from the cyclic imidazothiazoline intermediate, and imidazothiazoles are formed. Thus, imidazolylthio ketones should be regarded as intermediates in the synthesis of thiazoles via the Hantzsch method [155]. The shift of the equilibrium to one or the other side depends on the structures of the starting components and the reaction conditions [150, 153, 159]. In an alkaline medium the equilibrium is shifted completely to favor the open form, whereas in an acidic medium it is shifted to favor the cyclic isomer.

Thiazolo[3,2-a]benzimidazoles and intermediate noncyclic products were synthesized from thione IV and ketones in the presence of iodine [129]. This method has preparative value, since it makes it possible to use ketones instead of α-halo ketones, which are difficult to obtain in some cases.

Imidazolylacetaldehydes could not be isolated in the reaction of 4(5)-substituted imidazolethiones with bromoacetaldehyde – the corresponding 3-hydroxyimidazo[2,1-b]thiazolines were obtained [161, 162]. However, (imidazolylthio)acetaldehyde dialkylacetals were synthesized in the reaction with acetals. Simple preparative methods have been developed for obtaining (benzimidazolythio)acetaldehydes and their acetals, as well as 3-hydroxythiazolino-[3,2-a]benzimidazole and substituted derivatives of the latter, by the reaction of thione IV with α-halo aldehydes and their acetals [163].

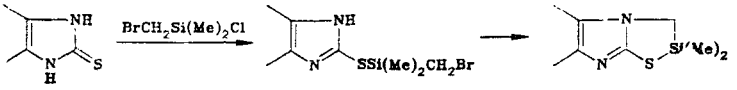
Other Reactions

Hydroxymethylation and aminomethylation have been studied chiefly in the case of thione IV. Thus N,N'-bis(hydroxymethyl)benzimidazole-2-thione was obtained by condensation of IV with formaldehyde [70, 164, 165]. N,N-Dialkyl(aryl, hetaryl)aminomethylbenzimidazolethiones are formed in the Mannich reaction of thione IV with formaldehyde and primary and secondary amines [70, 164, 166-169].



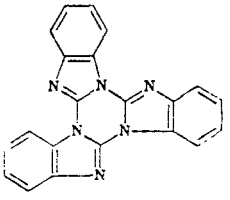
A large number of 1,3-aminomethyl derivatives of imidazole-2-thione have been synthesized [166, 170] in connection with the detection of the cytostatic activity of some hydroxymethyl and aminomethyl derivatives [166, 170].

Silylation of benzyimidazolethiones is also realized at the nitrogen atoms [171, 172]. However, the reaction of imidazolethiones and benzimidazolethiones with bromomethyldimethylchlorosilane in tetrahydrofuran leads to the corresponding S-silyl derivatives, which are capable of undergoing rearrangement to silaazoles [173].



Depending on the nature of the oxidizing agent and the reaction conditions, the corresponding disulfides and sulfinic or sulfonic acids can be obtained in the oxidation of imidazolethiones. Air oxygen [174], halogens [164, 175], hydrogen peroxide [175-179], and potassium permanganate [175, 180-182], as well as tert-butyl peroxide [183], acetyl peroxide [179], and benzoyl peroxide [184], have been used as the oxidizing agents. In some cases the oxidation of imidazolethiones has preparative value in the synthesis of the corresponding imidazoles that are formed as a result of the elimination of sulfur during oxidation [59].

Unexpected results were obtained when thione IV was heated with phosphorus oxychloride [185] and DMSO [186]. The principal reaction product in both cases is tris(benzimidazo)-s-triazine.



A new reaction was observed in the benzimidazole series, viz., replacement of the mercapto group by chlorine by the action of thionyl chloride on substituted benzimidazole-2-thiones [187].

Benzimidazole is formed in high yield when thione IV is heated with Raney nickel in butanol [188]. Desulfuration also occurs when elementary sulfur [189] and nickel and cobalt or their salts [188, 190] are used as the catalysts.

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OXIRANYL-β-AMINOVINYL KETONES.

2.* SYNTHESIS OF 3(2H)-FURANONES

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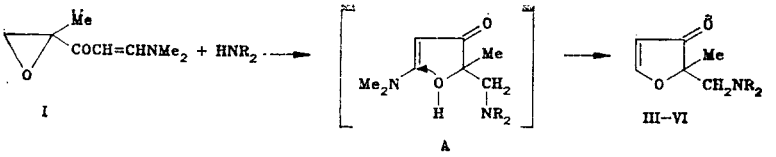
The reaction of oxiranyl-β-dimethylaminovinyl ketones with secondary amines, hydrochloric, and hydrobromic acids leads to the formation of the corresponding 2-aminomethyl- and 2-halomethyl-3-(2H)-furanones.

The 3(2H)-furanone ring is found as a structural fragment of several natural compounds [2-6]. One of the few methods available for the synthesis of 3(2H)-furanones consists in the intramolecular cyclization of γ-hydroxy-β-aminovinyl ketones [6-8] and α'-bromo- [9] or α'-hydroxy-β-aminovinyl ketones [10, 11]. In many cases, opening of the epoxide ring of epoxyketones by nucleophilic or electrophilic reagents leads to the formation of substituted α-hydroxyketones. Hence it might be expected that the opening of the epoxide ring of oxiranyl-β-aminovinyl ketones, leading to the formation of a hydroxyketone fragment, would be accompanied by intramolecular cyclization to the corresponding 3(2H)-furanones. It has, in fact, been shown that in the reaction of 1-dimethylamino-4-methyl-4,5-epoxy-1-penten-3-one (I) with dimethyl- and diethylamine, piperidine, and morpholine, the products of the opening of the epoxide ring cyclize under the conditions of the reaction of 2-aminomethyl-3(2H)-furanones III-VI in yields of 31-54%. The cyclization of the intermediate A apparently takes place via the Michael addition of the hydroxyl group to the double bond of the aminovinyl ketone with subsequent splitting off of dimethylamine and the formation of the 3(2H)-furanone.



III R=Me; IV R=Et; V R—R=$(CH_2)_5$; VI R—R=$(CH_2)_2O(CH_2)_2$

Cyclization of α'-hydroxy-β-aminovinyl ketones to 3(2H)-furanones is generally carried out in an acid medium [10, 11]. In the present case, acidification of the reaction mixture after the disappearance of the oxiranyl-β-dimethylaminovinyl ketone (TLC) did not result in any increase in the yield of 3(2H)-furanones III-VI. At the same time, 1-dimethylamino-4-methyl-4,5-epoxy-1-hexen-3-one (II), containing an epoxide ring which is less reactive with respect to amines, when reacted with morpholine did not form the corresponding furanone,

*For Communication 1, see [1].

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