

Oxidation of N,S-Divinyl-2-mercaptobenzimidazole (II). A 1.5-g (14 mmole) sample of 70% acetyl hydroperoxide was added dropwise at -10° to a solution of 1 g (5 mmole) of II in 20 ml of diethyl ether, after which the mixture was allowed to stand at $20-22^{\circ}$ for 2 days. The solvent was then removed by distillation, the residue was triturated with dry acetone, and the solid material was removed by filtration to give 0.5 g of polymer XIV with mp $250-280^{\circ}$. Found %: C 49.2; H 4.6; S 17.0. IR spectrum, cm^{-1} : 1040 (SO); 1130, 1320 (SO_2); 1150-1220 (SO_3H).

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BEHAVIOR OF N,S-DIVINYL-2-MERCAPTOBENZIMIDAZOLE IN THE THIYLATION REACTION

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N,S-Divinyl-2-mercaptobenzimidazole reacts with thiols under free-radical initiation conditions at both vinyl groups to give β -addition products, whereas it reacts with sulfur dioxide to give a stable complex. N-Vinylbenzimidazole-2-thione was obtained by heating the divinyl derivative of benzimidazole-2-thione in the presence of a mercaptan without a catalyst. The former on reaction with thiols under the influence of azobisisobutyronitrile readily forms N-(β -alkylthio)ethylbenzimidazole-2-thiones; in the presence of ionic catalysts, N-(α -alkylthio)ethylbenzimidazole-2-thiones are formed.

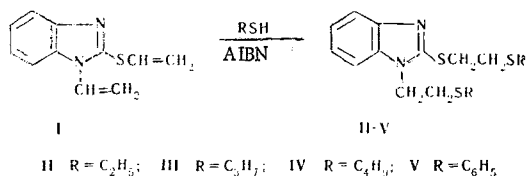
Thiols readily react with N-vinylbenzimidazole in the presence of free-radical initiators to give β -addition products [1]. The attachment of a vinyl group to the sulfur atom in the benzimidazole-2-thione molecule complicates the course of the thiylation reaction, in which connection one observes splitting out of the grouping in the 2 position of the heteroring [2]. The aim of the present research was the synthesis of a number of sulfides from N,S-divinyl-2-mercaptobenzimidazole (I) for subsequent testing of their biological activity. Moreover, we also proposed to obtain new sulfur-containing vinyl monomers, i.e., to direct the addition of the thiol to one of the vinyl groups of I in order to make it possible to subsequently synthesize polymeric preparations with prolonged action.

The thiylation of divinyl derivative I was investigated under homolytic and heterolytic conditions. Ethyl, propyl, butyl, and phenyl mercaptans were used as the thiols.

It was found primarily that disulfides of mercaptobenzimidazoles (II-V) are formed in yields up to 80% in the reaction of I with mercaptans in the presence of azobisisobutyronitrile (AIBN). Ultraviolet irradiation of the reaction mixture does not change the direction of the reaction.

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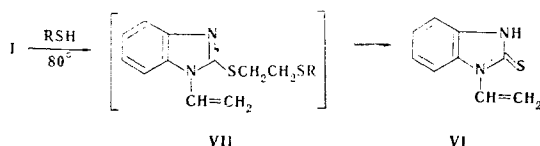
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An attempt to accomplish the reaction of divinyl derivative I with thiols in the presence of SO_2 as the catalyst did not give the desired result, inasmuch as a stable crystalline complex of I with sulfur dioxide is isolated under these conditions.

The absorption bands of vinyl groups bonded to sulfur and nitrogen atoms (1590 and 1632 cm^{-1}) vanish in the IR spectra of disulfides II-V, and intense absorption bands that characterize the stretching vibrations of methyl and methylene groups appear at $2870\text{--}2970\text{ cm}^{-1}$. The presence of $\text{>NCH}_2\text{CH}_2\text{S-}$ and $\text{-SCH}_2\text{CH}_2\text{S-}$ fragments is confirmed by the signals at $2.25\text{--}4.25\text{ ppm}$ in the PMR spectra of disulfides II-V.

We were unable to obtain monosulfides from I. However, a side reaction involving splitting out of the substituent in the 2 position to give N-vinylbenzimidazole-2-thione (VI) (10–20% yield) occurs under the conditions of homolytic thiylation of I. The appearance of thione VI in the reaction mixture is apparently associated with decomposition of the N-vinyl-S-(β -alkylthio)ethyl-2-mercaptobenzimidazole (VII) formed in the first step; this is in agreement with the literature data [3] on the increased reactivity of the double bond of vinyl sulfides under homolytic thiylation conditions.

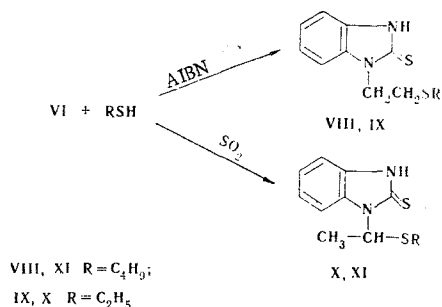


An investigation of the composition of the other side products of this reaction also confirmed the scheme presented above. Thus N-(β -butylthio)ethylbenzimidazole-2-thione (VIII) and dithioethylene glycol dibutyl ether were obtained and identified in the reaction of I with butyl mercaptan in the presence of AIBN.

The yield of thione VI can be increased considerably if a mixture of I and excess mercaptan is heated without a catalyst. Thus, whereas traces of thione VI are formed at 20° , the yields of VI at 40° and 80° are, respectively, 46% and 72%.

The IR spectrum of VI contains absorption bands at 1646 ($\text{C}=\text{C}$), 1512 ($\text{HN}-\text{C}=\text{S}$), and $2960\text{--}3430$ (NH) cm^{-1} . The presence of an $\text{N}-\text{C}=\text{S}$ group shows up in the electronic spectrum as an absorption maximum at 313 nm ($\log \epsilon$ 4.4) [4]. The protons of the vinyl group form an ABX spin system (δ_{A} 5.26, δ_{B} 5.65, and δ_{X} 7.46 ppm; $J_{\text{AB}} = 1.2$, $J_{\text{AX}} = 9.2$, and $J_{\text{BX}} = 16.0\text{ Hz}$).

Compound VI readily adds mercaptans via both free-radical and ionic mechanisms:



N-(β -Alkylthio)ethylbenzimidazole-2-thiones (VIII, IX) are formed in the reaction of thione VI with butyl and ethyl mercaptans in the presence of AIBN. In the presence of sulfur dioxide this thione reacts with mercaptan to give N-(α -alkylthio)ethylbenzimidazole-2-thiones (X, XI). The possibility of reaction in accordance with Markownikoff's rule is due to the mesomeric effect, which gives rise to the development of a partial negative charge on the β -carbon atom of the vinyl group. The presence of a quartet at δ 6.70 ppm and a doublet at δ 1.71 ppm in the PMR spectrum of sulfide X proves α addition of the mercaptan. The aromatic protons form a

TABLE 1. Characteristics of the Synthesized Compounds

Com- pound	bp, °C (mm)	n_D^{20}	d_4^{20}	M_{RD}		Empirical formula	Found, %			Calc., %			Yield, %
				found	calc.		C	H	S	C	H	S	
I	208—210 (2)	1,6133	1,1748	96,75	96,15	$C_{15}H_{22}N_2S_3$	55,4	6,7	29,2	55,3	6,7	29,5	67
III	229—230 (2)	1,5923	1,1406	104,95	104,35	$C_{17}H_{26}N_2S_3$	57,6	7,4	27,1	57,6	7,4	27,1	72
IV	243—244 (2)	1,5873	1,0990	117,03	116,50	$C_{19}H_{30}N_2S_3$	60,2	8,0	25,0	59,7	7,9	25,1	80
V	215—217 (1)	1,6530	1,2121	127,65	126,91	$C_{23}H_{28}N_2S_3$	65,6	5,1	22,6	65,4	5,2	22,7	69
VI	175	—	—	—	—	$C_9H_8N_2S$	61,5	4,6	18,2	61,3	4,6	18,2	72
VIII	114	—	—	—	—	$C_{13}H_{18}N_2S_2$	58,6	6,6	23,9	58,6	6,8	24,1	57
IX	135	—	—	—	—	$C_{11}H_{14}N_2S_2$	55,6	5,9	26,5	55,4	5,9	26,9	65
X	97	—	—	—	—	$C_{11}H_{14}N_2S_2$	55,5	5,9	26,7	55,4	5,9	26,9	75
XI	85	—	—	—	—	$C_{13}H_{18}N_2S_2$	58,7	6,9	24,3	58,6	6,8	24,1	74

multiplet ($\delta \sim 7.0$ and 7.4 ppm), whereas the ethyl group gives signals at $\delta 1.14$ (triplet) and $\delta 2.40$ ppm. The latter signal is a multiplet because of the anisochronicity of the diastereotopic methylene proton. This phenomenon is characteristic for acetals and hemoacetals [5].

Thus the two most important reactions of N,S-divinyl-2-mercaptobenzimidazole (I) under thiylation conditions are the synthesis of disulfides of 2-mercaptobenzimidazole (II-V) and decomposition of I to give a new monomer—N-vinylbenzimidazole-2-thione (VI). Up until now, the latter compound was unknown and could not be obtained by direct reaction of benzimidazole-2-thione with acetylene [6]. The thiylation of I is not accompanied by a change in the structure of the heteroring. However, the different pathways it takes and the formation of anomalous products are probably due to conjugation of the double bonds of the vinyl groups through the unshared pairs of electrons of the heteroatoms with the aromatic system of the benzimidazole ring and also to the ease of the tautomeric transformations in it.

EXPERIMENTAL

The IR spectra of KBr pellets of the compound and thin layers between NaCl and LiF plates were recorded with a UR-20 spectrometer. The UV spectra of ethanol solutions were recorded with a Pye-Unicam SP-8000 spectrophotometer. The PMR spectra of CCl_4 and $CDCl_3$ solutions of the compounds were recorded with a BS487B spectrometer at room temperature with hexamethyldisiloxane as the internal standard (δ scale). The course of the reactions and the separation of the reaction mixtures were monitored by means of thin-layer chromatography (TLC) and column chromatography, respectively, on activity II aluminum oxide.

The following R_f values were obtained: 0.72 for II, 0.80 for III, 0.81 for IV, 0.79 for V, 0.30 for VI, 0.24 for X, and 0.23 for XI. Freshly distilled N,S-divinyl-2-mercaptobenzimidazole (I) [6] and mercaptans were used.

N,S-Di(β -ethylthioethyl)-2-mercaptobenzimidazole (II). A 3.03-g (15 mmole) sample of I, 3.72 g (60 mmole) of ethyl mercaptan, and 0.35 g ($\sim 0.5\%$ of the weight of the mixture) of AIBN were placed in an ampule, after which the ampule was sealed and heated in a thermostat at 80° for 24 h. It was then cooled, and the excess mercaptan was removed by distillation. The residue was vacuum fractionated, and the resulting oil was subjected to chromatography [with a column filled with Al_2O_3 and elution with a hexane-benzene-acetone system (3:2:1)] to give 3.28 g (67%) of II and 0.45 g (17%) of thione VI. Compounds III-V were similarly obtained.

Disulfides II-V were obtained as light-yellow oily liquids that were soluble in most organic solvents. The characteristics of the synthesized compounds are presented in Table 1.

N-Vinylbenzimidazole-2-thione (VI). A mixture of 3.03 g (15 mmole) of I and 3.72 g (60 mmole) of ethyl mercaptan in a sealed ampule was heated at 80° for 24 h, after which it was cooled, and the resulting white acicular crystals were washed with hexane and recrystallized from benzene to give 1.9 g (72%) of VI.

N-(β -Ethylthio)ethylbenzimidazole-2-thione (IX). A mixture of 1.5 g (8.5 mmole) of thione VI, 5 ml of ethyl mercaptan, and 0.02 g of AIBN was heated in a sealed ampule at 80° for 24 h, after which the excess mercaptan was removed by distillation. The residue was recrystallized twice from benzene to give 1.3 g (65%) of IX. IR spectrum, cm^{-1} : 1510 (HN-C=S), 2870-2970 (CH_2 , CH_3), and 2840-3440 (NH). The linear structure of IX was confirmed by the $>NCH_2CH_2S-$ signals, which resonate in the form of two AA'XX' multiplets at $\delta 4.43$ and 2.95 ppm. The ethyl group forms a quartet and a triplet at 2.77 and 1.22 ppm, and the aromatic protons form a multiplet ($\delta \sim 7.0$ ppm).

Thione VIII was similarly obtained.

N-(α -Ethylthio)ethylbenzimidazole-2-thione (X). Dry SO_2 was bubbled for 30 sec into a mixture of 0.88 g (5 mmole) of thione VI and 5 ml of ethyl mercaptan, after which the ampule containing the mixture was sealed

and heated at 80° for 2 h. The excess mercaptan was removed by distillation, and the residue was dissolved in chloroform and purified with a column filled with Al₂O₃ (elution with CHCl₃) to give 0.9 g (75%) of X. Compound XI was similarly obtained.

Compounds VIII-X were obtained as white crystalline substances that were stable in air (Table 1).

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RESEARCH ON UNSATURATED AZOLE DERIVATIVES

V.* TRANSFORMATIONS OF 3-FORMYLINDAZOLES IN THE WITTIG REACTION

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3-Formylindazoles are converted to 1-methyl- and 2-methyl-substituted β -(3-indazolyl)acrylic and α -bromoacrylic acids by the Wittig reaction. Dehydrohalogenation of the β -(3-indazolyl)- α -bromoacrylic acid esters gave β -(3-indazolyl)propionic acids, the decarboxylation of which gives isomeric 1-methyl- and 2-methyl-substituted 3-ethynylindazoles.

Continuing our research on the synthesis of vinyl and ethynyl derivatives of azoles we subjected 1-methyl- and 2-methyl-3-formylindazoles (I, II) to reaction with carbomethoxy- and carbethoxymethylenetriphenylphosphoranes IIIa, b. The β -(1-methyl- and 2-methyl-3-indazolyl)acrylic acid esters (IVa, b and Va, b) obtained in this way were subsequently hydrolyzed to the corresponding β -(3-indazolyl)acrylic acids (VI, VII). β -(1-Methyl-3-indazolyl)- and β -(2-methyl-3-indazolyl)- α -bromoacrylic acid esters IVc and Vc were obtained in good yields by reaction of aldehydes I and II with the more reactive carbethoxybromomethylenetriphenylphosphorane (IIIc) at 17-20°C; the best yields of reaction products can be obtained when ethanol is used as the solvent. The action of alcoholic alkali on ethyl β -(1-methyl-3-indazolyl)- α -bromoacrylate (IVc) at 15-20° leads only to hydrolysis of the ester group to give β -(1-methyl-3-indazolyl)- α -bromoacrylic acid (VIII), whereas β -(2-benzimidazolyl)- α -bromoacrylic acid esters are converted under these conditions to 2-benzimidazolylpropionic acids [2]. A difficult-to-separate mixture of products was obtained in the hydrolysis of ethyl β -(2-methyl-3-indazolyl)- α -bromoacrylate (Vc) under these conditions.

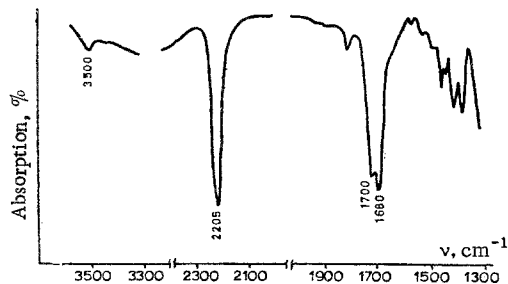


Fig. 1. IR spectrum of acid X.

A mixture of products, the IR spectrum of which contains absorption bands of the $-C\equiv C-$ bond of the corresponding β -(3-indazolyl)propionic acids (IX and X), is formed by the action of alcoholic alkali on esters IVc and Vc at 50-60°. Treatment of the mixture of esters IVc and Vc with aqueous alkali at 55-60° gave

*See [1] for communication IV.

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