ADDITION OF MERCAPTANS TO N-VINYL DERIVATIVES OF INDOLE AND IMIDAZOLES

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Nine new N-(thioalkyl) ehtylindoles and imidazoles were synthesized. Analysis of the PMR spectra of these compounds showed that, in the presence of radical activators, mercaptans are mainly added to N-vinylindole and to N-vinylimidazoles contrary to Markovikov rule. Under the influence of cathionic catalysts, N-vinylimidazole reacts in accordance with that rule. N-vinylindole polymerizes under these conditions, but N-vinylbenzoimidazole in general does not react.

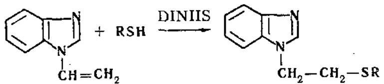
Little information is to be found in the literature [1, 2] on the sulfurization of N-vinyl nitrogen heterocycles. It deals mainly with thioderivatives of N-vinylcarbazole and points out to the possibility of obtaining, in analogy with it, products containing sulfur from N-vinylpyrrole and N-vinylindole. The addition of mercaptans to unsaturated compounds through ionic mechanism usually proceeds according to Markovnikov rule, but contrary to it when radical mechanisms are employed [3, 4].

This paper deals with the study of the reaction of various mercaptans with N-vinylindole (I), N-vinylimidazole (II), and N-vinylbenzoimidazole (III).

This reaction was studied taking as examples the reactions of I–III with ethyl-, propyl-, isopropyl-, n-butyl, and tertiary-butyl mercaptans (IV–VIII), under the conditions of free-radical activation at 70–80° C, and in the presence of dinitrylazoisobutyric acid (DINIIS). By sulfurizing I for 18 hr, the yield of sulfurized products attained 77%, and diminished to one-third as much due to appreciable resinification when the heating lasted 24 hr. In the absence of the activator, the addition of mercaptans to I at 80° C did not take place, and the initial components were fully recovered.

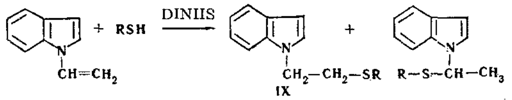
In the presence of DINIIS, II reacted very easily after 18 hr at 70° C with IV, V, and VII. The sulfurizing of III under similar conditions proceeded with a lower yield (38%) of reaction products when compared with II (94%). When the temperature was raised to 80° C and was kept at this level for 50 hr, the yield of N-(thioethyl)ethylbenzomidazole (XVI) increased to 51%. The table presents the properties of the synthesized compounds.

We presume that the sulfurizing reaction of I–III, in analogy with N-vinylcarbazole [1, 2] and under the conditions of radical activation, forms N-(β-thioalkyl)ethylindoles (IX–XI) and N-(β-thioalkyl)ethylimidazoles (XII, XIV–XVII) according to the following scheme:



XVI, XVII

Furthermore, the possibility that the reaction may follow Markovnikov rule cannot be excluded. Thus, we observed a somewhat anomalous reaction of I with mercaptans. By modifying the temperature conditions during the reaction, a mixture of both α- and β-addition compounds was obtained:



IX

The structure of the sulfurized compounds obtained from I–III was clearly proved by the proton magnetic resonance method. It was easy to identify the spectra obtained from IX, XII, XIII, and XVI. The signal of the substituent at the nitrogen atom of N-(β-thioethyl)ethylindole (IX) may be represented by four multiplets, among which three triplets (1.00; 2.57; 3.96 ppm) and a quartet (2.14 ppm). A similar picture exhibited the spectrum of N-(β-thioethyl)ethylimidazole (XII) (1.08; 2.71; 4.01; and 2.33 ppm), as shown in the figure. The integral intensities of the resonance lines of the multiplets were in the ratio 3 : 2 : 2 : 2, respectively, and the spin-spin constant of the interaction J of the protons of the corresponding nonequivalent groups was equal to 7 cps. Consequently, to compounds

Properties of N-[$\beta(\alpha)$-Thioalkyl]ethylindoles, Imidazoles, and Benzoimidazoles

Compound	Name	Mp, °C (mm)	n_D^{20}	d_4^{20}	MR_D		R_f*	Molecular formula	Found, %			Calculated, %			Yield, %
					Found	Calculated			C	H	S	C	H	S	
IX	N-(β-Thioethyl)ethylindole	138(1)	1.6020	1.0819	65.06	64.50	0.55	$C_{12}H_{15}NS$	71.56	7.22	15.76	71.24	7.37	15.60	72
X	N-(β-Thioisopropyl)ethylindole	161(2)	1.5870	1.0605	69.38	69.14	—	$C_{13}H_{17}NS$	71.60	7.52	13.92	71.23	7.76	14.61	77
XI	N-(β-tertiary-Thiobutyl)ethylindole	141—142(1)	1.5770	1.0325	74.76	73.97	—	$C_{14}H_{19}NS$	72.50	7.96	13.60	72.10	8.15	13.73	65
XII	N-(β-Thioethyl)ethylimidazole	129(1)	1.5350	1.0863	44.77	45.14	0.52	$C_7H_{12}N_2S$	53.48	7.70	20.67	53.84	7.69	20.51	74
XIII	N-(α-Thioethyl)ethylimidazole	114(4)	1.5270	1.0766	45.16	45.14	0.55	$C_7H_{12}N_2S$	53.58	7.69	20.60	53.84	7.69	20.51	61
XIV	N-(β-Thiopropyl)ethylimidazole	145(2)	1.5272	1.0586	49.38	49.81	0.50	$C_8H_{14}N_2S$	56.10	8.00	18.82	56.42	8.28	18.83	72
XV	N-(β-Thiobutyl)ethylimidazole	159(2)	1.5218	1.0377	54.01	54.34	0.54	$C_9H_{16}N_2S$	58.63	8.66	17.37	58.65	8.75	17.39	94
XVI	N-(β-Thioethyl)ethylbenzoimidazole	190—192(2)	1.6010	1.1409	61.56	61.50	0.61	$C_{11}H_{14}N_2S$	64.35	6.87	15.25	64.03	6.84	15.54	38
XVII	N-(β-Thiopropyl)ethylbenzomidazole	190—191(1)	1.5885	1.1162	66.46	66.02	0.62	$C_{12}H_{16}N_2S$	65.41	7.32	14.55	65.08	7.29	14.12	42

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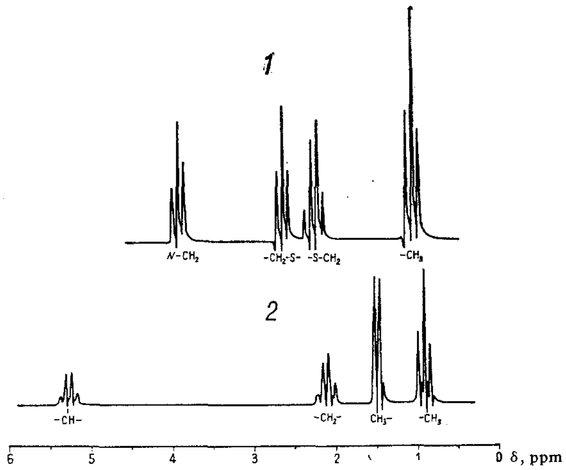
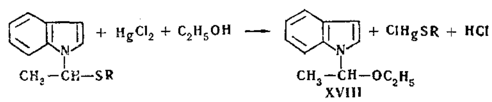
*Compound IX was chromatographed in the system hexane-benzene (3 : 2); the remaining ones, in the system hexane-benzene-acetone (3 : 2 : 1).

IX and XII may be assigned the structure of the β-addition product, in which the substituent at the nitrogen atom is the $-CH_2-CH_2-S-CH_2-CH_3$ group. Then the triplet at the strong field (1.08 ppm) belongs to the methyl group protons, and the quartet to the protons of the methylene group of the ethyl residue. Considering the significance of the chemical shift of the signal of the methylene group protons linked to the sulfur atom [6], as well as the δ signal of the CH_2 group protons in the PMR spectrum of ethylimidazole (3.88 ppm), the triplet with β = 2.71 ppm should be assigned to protons of the CH_2 group linked to the sulfur atom, and the triplet with δ = 4.01 ppm to the protons of the CH_2 group attached to the nitrogen atom.



PMR Spectra: 1)- N-(β-thioethyl)ethylimidazole;
2)- N-(α-thioethyl)ethylimidazole.

An analysis of the PMR spectrum of N-(β-thioethyl)ethylbenzoimidazole (**XVI**) showed that, similarly to the spectrum of XII, it consisted of three resonance band triplets (0.94;2.62;4.01 ppm) and a quartet (2.15 ppm). Taking into account the integral intensities of the signals and J = 7 cps, to the substituent at the nitrogen atom in compound **XVI** should also be assigned a β-structure $-CH_2-CH_2-S-CH_2-CH_3$. The α-addition products of mercaptans to I–III were not individually isolated, although separate fractions obtained during the sulfurizing of I in the presence of DINIIS did significantly differ in their physical constants. Their PMR spectra were complex, rich in numerous lines, and their deciphering was difficult. Yet the presence of α-addition products was confirmed by the reaction with alcoholic mercuric chloride and by the acidity which developed in this medium (38–85%). As is known, when the reaction proceeds contrary to Markovnikov rule, the β-addition products should not react with mercuric chloride according to the following scheme [3, 5]:

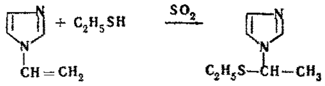


The constants of compound **XVIII**, which was separated by ether extraction from the reaction mixture, agreed with those of N-(α-ethoxy)ethylindole, synthesized by the interaction of I with ethanol [6]. The R_f value of **XVIII**, obtained by various methods, had the same magnitude (0.57) in the system hexane–benzene (3 : 2). The elementary composition of the precipitate which separated out confirmed the formation of chloromercuricthiolate and not the thioderivative of complex I with mercuric chloride. Furthermore, the individual β-addition product of ethylmercaptan to I, when reacting with alcoholic mercuric chloride, imparted a neutral reaction to the medium, and this distinguished it from the mixture under study.

The mercuric chloride method proved unsuitable to detect the presence of α-addition products when sulfurizing II and III. Similarly to the initial II and III, the products of their interaction with mercaptans easily formed white precipitates with alcoholic mercuric chloride, but exhibited a neutral reaction. Presumably this is due to the great activity of compounds of the imidazole series in forming complexes.

As a result of these experiments, a peculiar tendency was observed in the sulfurization of I–III according to an ionic mechanism. Thus, benzoderivatives of N-vinylpyrrole and of N-vinylimidazole, in the presence of SO_2 or of p-toluenesulfonic acid, do not in general add ethylmercaptan, in spite of variations in temperature from 0–70° C. The first one is converted to penta- and hexamers of I, and the second is recovered unchanged when the reaction mixture is distilled.

It is interesting that, among all the N-vinyl compounds (I–III) studied, only N-vinylimidazole (II) proved capable of adding mercaptans under the influence of an ionic catalyst. The addition of ethylmercaptan to II took place at 80° C in the presence of SO_2 or of p-toluenesulfonic acid, to form N-(α-thioethyl)ethylimidazole (XIII) according to the following scheme:



The structure of this α-addition product was convincingly shown by its PMR spectrum which contained four resonance bands: triplet (0.93 ppm), doublet (1.51 ppm) and two quartets (2.13 and 5.36 ppm). The ratio of the sums of the signal intensities was 3 : 3 : 2 : 1, and J = 7 cps. Such a type of spectra indicates that the substituent at the nitrogen atom in compound XIII has the $CH_3{-}CH{-}S{-}CH_2{-}CH_3$ structure.

Obviously, the triplet belongs to the methyl protons in the ethyl residue; the quartet with $\delta = 2.13$ ppm, to the CH_2 protons; and the doublet should be attributed to the second methyl group. Finally, the quartet with $\delta = 5.36$ ppm characterized the proton associated with the tertiary carbon atom. The difference between the PMR-spectra of the α- and the β-addition products of ethylmercaptans to II may be distinctly seen in the figure.

Thus, it was experimentally shown that, under the influence of radical activators, the addition of mercaptans to N-vinyl derivatives of indole and imidazole proceeds chiefly contrary to Markovnikov rule, in agreement with the literature data [1, 4].

The identification of all the products obtained in the sulfurizing of I–III was confirmed by thin-layer chromatography on aluminum oxide (activity II according to Brockmann). The R_f values are present in the table. All the thioderivatives of I–III were oily liquids heavier than water. Unlike the products of the reaction of mercaptans with simple vinyl ethers, N-(thioalkyl)ethylindoles, -imidazoles, and -benzoimidazoles did not hydrolyze when boiled with 50% sulfuric acid, probably on account of their great stability.

EXPERIMENTAL

In this research we employed freshly-distilled I–III, with bp., °C (mm), and n_D^{20} : I- 70 (1); 1.6330; II–80 (10); 1.5330; III–124 (3); 1.6220. Ethyl- and isopropylmercaptans IV and VI were obtained by the general synthetic method through S-alkylthiouronic salts [8].

Reaction of N-vinylindole(I) with ethylmercaptan (IV). Into an ampul containing 2.2 g (~1.5 mM) of I and while cooling, 1 g (~16 mM) of IV and 0.015 g of DINIIS twice recrystallized ex methanol were added. Nitrogen was bubbled through the cooled ampul, which was then sealed and placed for 18 hr in a thermostat at 70 ± 0.2° C. Upon distillation under vacuum, 2.28 g (72%) of N-(β-thioethyl)ethylindole (IX) was obtained. Bp 170–172° C (7 mm); d_4^{20} 1.0897; n_D^{20} 1.6020.

Similarly from 2.2 g of I, 1 g of IV and 0.015 g of DINIIS at 80° C during 18 hr, 0.9 g of product was obtained. Bp 135–138° C (1 mm); d_4^{20} 1.0819; n_D^{20} 1.6030.

X and XI were synthesized following a similar process. Their properties may be found in the table.

Reaction of N-(thioethyl)ethylindole with mercuric chloride. To 0.2 g of the ethylthioderivative I (obtained at 80° C for 18 hr) in an Erlenmeyer flask, 1 ml of 20% alcoholic mercuric chloride was added. A white precipitate of ethylmercuricchloride was formed at once. Methyl orange was added to the reaction mixture, followed by titration with 0.1 NaOH. The acidity of the medium was 42% of the theoretical. This reaction proceeded similarly with X and XI.

Sulfurization of N-vinylindole (I) in the presence of SO_2. 1.23 g (~8.5 mM) of IV were placed in an ampul. The reaction mixture was cooled by dry ice and acetone, then compressed nitrogen was bubbled through it, followed by

SO_2 during 2 min. After 48 hr, the reaction products were dissolved in 3 ml acetone and precipitated with 50 ml absolute ethanol. The white precipitate formed was separated by centrifuging and dried under vacuum to constant weight. 1.07 g (87%) of a white powder of polyvinylindole was obtained, mp 180–186° C. Found, %: N 9.45. Calculated for $(C_{10}H_9N)_n$, %: N 9.78.

Synthesis of N-(β-thiobutyl)ethylimidazole (XV). From 2.24 g (~18 mM) of II, 1.98 g (22 mM) of VII and 0.2 g of DINIIS, after 18 hr at 70 ± 0.2° C, 3.02 g of XV was obtained. Colorless liquid, bp 159° C (2 mm), n_D^{20} 1.5218.

In a similar way were obtained **XII**, **XIV–XVII**. The table presents the constants of the compounds synthesized in the presence of DINIIS.

N-(α-thioethyl)ethylimidazole (XIII). SO_2 was bubbled under cooling through a mixture of 2.37 g (~20 mM) of **II** and 1.5 g (~24 mM) of ethylmercaptan. The mixture was then kept at 80° C for 18 hr. 2.38 g (61%) of N-(α-thioethyl)-ethylimidazole was separated by vacuum distillation. Bp 113–114° C (4 mm); d_4^{20} 1.0766; n_D^{20} 1.5270.

Attempt to hydrolyze N-(β-thioisopropyl)ethylindole (X). 0.22 g of **IX** was placed in an 100-ml ampul together with 25 ml of 5% H_2SO_4. After heating in a thermostat at 100° C for 30 hr, the qualitative reaction with 2,4-dinitrophenylhydrazine on the hydrolysis products proved negative. The substance extracted with ether from the reaction mixture, after distilling of the solvent, had the same constants as the initial **X**, bp, 158–160° C (2 mm); n_D^{20} 1.5864.

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