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REACTION OF 3-MERCAPTOINDOLE AND ITS ETHYL DERIVATIVES WITH ACETYLENE

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1-Vinyl-3-vinylthioindole, 1-vinyl-3-ethylthioindole, and 1-ethyl-3-vinylthioindole, respectively, were obtained by the reaction of 3-mercaptoindole, 3-ethylthioindole, and 1-ethyl-3-mercaptoindole with acetylene. 3-Mercaptoindole reacts with acetylene in aqueous media to give 3-vinylthioindole. The structures of the vinyl derivatives of 3-mercaptoindole obtained were proved by means of IR and PMR spectroscopy and the results of elementary analysis.

Indole reacts with acetylene under pressure in the presence of an alkaline catalyst under rather severe temperature conditions to give 1-vinylindole [1]. There is no information in the literature regarding the synthesis of vinyl derivatives of 3-mercaptoindole. The introduction of an SH group in the 3 position of the indole molecule leads to the development of a new reaction center that is capable, together with the imino group, of reaction with acetylene.

We have found that the reaction of acetylene with indoles I-III under the conditions of the vinylation of indole (at 220 deg C for 30 min) proceeds with pronounced resinification. Vinyl derivatives were isolated in no greater than 3-5% amounts. Lowering the reaction temperature 40 deg C made it possible to obtain 1-vinyl-3-vinylthioindole (IV) and 1-vinyl-3-ethylthioindole (V) in good yields (up to 70%). A further decrease in the reaction temperature to 150-160 deg C reduces the yields of vinylthioindoles IV and V, respectively, to 35 and 23%; the formation of the product of the addition of one molecule of acetylene – 3-vinylthioindole (VII) – is observed in the case of 3-mercaptoindole. We were unable to obtain monovinyl derivative VII in high yield in dioxane. Vinyl sulfide VII was obtained in 60% yield in the reaction of 3-mercaptoindole with acetylene in water in the presence of an equimolar amount of KOH.

I-III

IV-VII

I $R=R'=H$; II $R=C_2H_5$, $R'=H$; III $R=H$, $R'=C_2H_5$; IV $R=R'=CH{=}CH_2$; V $R=CH{=}CH_2$, $R'=C_2H_5$; VI $R=C_2H_5$, $R'=CH{=}CH_2$; VII $R=H$, $R'=CH{=}CH_2$

We assume that, as in the case of cyclic thioamides, acetylene adds initially to the more nucleophilic sulfur atom in the vinylation of mercaptoindole I. Considerably milder conditions than in the reaction of indole with acetylene are necessary for this. Evidence for this is also provided by the relative ease of formation of 1-ethyl-3-vinylthioindole (VI), the yield of which at 120 deg C reaches 60%. Due to its electron-acceptor effect, the vinylthio grouping formed in the case of mercaptoindole I in the 3 position of the indole ring promotes greater polarizability of the N–H bond, as a consequence of which the addition of a second molecule of acetylene to the nitrogen atom occurs under milder conditions than addition to indole itself.

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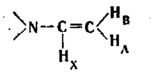
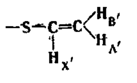
TABLE 1. Vinyl Derivatives of 3-Mercaptoindole

Compound	bp, °C (1-2 mm)	n_D^{20}	d_4^{20}	Found, %			Empirical formula	Calc., %			Yield, %
				C	H	S		C	H	S	
IV	130	1,6398	1,0949	71,8	5,7	15,9	$C_{12}H_{11}NS$	71,6	5,5	15,9	70
V	133	1,6120	1,0901	70,8	6,3	15,6	$C_{12}H_{13}NS$	70,9	6,4	15,7	70
VI	132	1,6182	1,0972	70,5	6,3	15,6	$C_{12}H_{13}NS$	70,9	6,4	15,7	60
VII	136	1,6551	1,1772	68,7	5,1	18,4	$C_{10}H_9NS$	68,5	5,1	18,3	60

TABLE 2. PMR Spectra of Vinyl Derivatives of 3-Mercaptoindole



$>N-C(H_X)=C(H_B)(H_A)$



$-S-C(H_{X'})=C(H_{B'})(H_{A'})$

Compound	Chemical shifts, δ, ppm										Spin—spin coupling constant						
	A—H	B—H	X-H	A′-H	B′-H	X′-H	2-H	CH_2	CH_3	Aromatic protons	J_{AX}	J_{BX}	J_{AB}	$J_{A'X'}$	$J_{B'X'}$	$J_{A'B'}$	CH_2CH_3
IV	4,74	5,16	7,11	5,08	4,88	6,30	7,49	—	—	7,10—7,63	8,80	15,40	1,40	9,50	16,40	0	—
V	4,71	5,14	7,13	—	—	—	7,43	2,70	1,23	7,08—7,79	8,60	15,60	1,40	—	—	—	7,20
VI	—	—	—	5,00	4,76	6,28	7,14	4,09	1,45	6,88—7,70	—	—	—	9,40	16,00	0	7,10
VII	—	—	—	5,02	4,78	6,30	7,16	—	—	7,12—7,58	—	—	—	9,60	16,60	0	—

The use of dimethyl sulfoxide (DMSO) and α-methylpyrrolidone as the solvent in place of dioxane made it possible to lower the temperature of the synthesis of IV and V to 120 deg C, and the yield as before is 60-70%.

The chemical shifts and spin–spin coupling constants (SSCC) of the olefin protons in the PMR spectra of IV-VII are characteristic for the vinyl groups attached to the sulfur and nitrogen heteroatoms [2]. The absorption at 1590 cm^{-1} in the IR spectra of IV and VI and at 1642 cm^{-1} for IV and V constitutes evidence for the presence of vinyl groups attached to the sulfur and nitrogen atoms, respectively. In addition, the absorption bands at 2530 and 3410 cm^{-1}, which are related to the stretching vibrations of the S–H and N–H bonds of I-III, vanish in the spectra of these compounds.

As in the case of the reduction of divinyl derivatives of cyclic thioamides [4, 5], reduction of only the vinylthio grouping is observed in the hydrogenation of the divinylthioindole over Raney nickel. As a result, 1-vinyl-3-ethylthioindole (V) is formed. Its properties are in complete agreement with the properties of V, obtained by direct reaction of acetylene with III.

EXPERIMENTAL

The IR spectra of microlayers of the compound were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in CCl_4 were recorded with a BS-487-B spectrometer with hexamethyldisiloxane as the internal standard.

3-Mercaptoindole (I). This compound, with mp 102-103 deg C (from water) [mp 103 deg C (CCl_4) [5]], was obtained in 60% yield by reaction of indole with thiourea in the presence of iodine [5].

1-Ethyl-3-Mercaptoindole (II). A solution of 7.62 g of I_2 and 7.5 g of KI in 10 ml of water was added dropwise in a stream of nitrogen at 20 deg C to a mixture of 4.32 g (30 mmole) of 1-ethylindole [6] and 2.28 g (30 mmole) of thiourea in 75 ml of methanol, and the mixture was heated at 50-55 deg C for 3 h, after which the alcohol was removed by distillation. The crystalline precipitate was washed repeatedly with ether, and the ether was decanted away from the precipitate. A total of 100 ml of 4 N NaOH was added to the precipitate, and this mixture was heated at 95-96 deg C for 10 min. The resulting small amount of bis(1-ethyl-3-indolyl) disulfide was separated, and the alkaline solution was acidified with acetic acid. The liberated thioindole II was extracted with chloroform. Vacuum distillation gave 2.7 g (51% of mercaptoindole II with bp 136-137 deg C (3 mm) and n_D^{20} 1.6245. IR spectrum: 2530 (SH); 2870, 2935, and 2980 cm^{-1} (CH_2CH_3). Found: C 67.7; H 6.0; S 18.0%. $C_{10}H_{11}NS$. Calculated: C 68.0; H 6.2; S 18.0%.

3-Ethylthioindole (III). Ethyl iodide was added to a mixture of 7.45 g (50 mmole) of mercaptoindole I and 20.7 g (150 mmole) of anhydrous K_2CO_3 in 50 ml of absolute acetone, and the mixture was stirred at room temperature for 4 h. It was then filtered, and the solvent was removed from the filtrate by vacuum distillation. The residue was chromatographed with a column filled with Al_2O_3 (elution with $CHCl_3$) to give 8.85 g (56.5%) of thioindole III with n_D^{20} 1.6300. IR spectrum: 3410 (NH); 2870, 2935, and 2980 cm^{-1} (CH_2CH_3). Found: C 67.2; H 6.1; S 17.7%. $C_{10}H_{11}NS$. Calculated: C 67.7; H 6.2; S 18.0%.

1-Vinyl-3-vinylthioindole (IV). An autoclave was charged with 6 g (40 mmole) of mercaptoindole I, 1.8 g (4.5 mmole) of KOH, and 100 ml of dioxane, acetylene was fed in at an initial pressure of 15 gage atm, and the reaction mixture was heated at 180 deg C for 1 h. The solvent was removed by distillation, and the residue was vacuum distilled to give 5.6 g (70%) of divinylthioindole IV.

1-Vinyl-3-ethylthioindole (V). A) This compound was obtained from 3.5 g (20 mmole) of 3-ethylthioindole III and 1.05 g (20 mmole) of KOH in 50 ml of dioxane, as in the preceding experiment. The yield was 2.8 g (70%).

B) Vinylthioindole IV was reduced in the presence of Raney nickel [4], the alcohol was removed by distillation, and the resulting V was vacuum distilled. The constants of vinylthio derivative V obtained by methods A and B were identical. The yields were also close.

1-Ethyl-3-vinylthioindole (VI). An autoclave was charged with 3.5 g (20 mmole) of mercaptoindole II and 1.05 g (20 mmole) of KOH in 50 ml of dioxane, acetylene was fed in at an initial pressure of 15 gage atm, and the mixture was heated to 120 deg C and maintained at this temperature for 30 min. Vacuum distillation gave 2.4 g (60%) of VI with bp 132 deg C (1-2 mm).

3-Vinylthioindole (VII). A mixture of 6.0 g (40 mmole) of mercaptoindole I, 120 ml of water, and 4.5 g (80 mmole) of KOH was saturated with acetylene in an autoclave (0.5 liter). The autoclave was heated at 120 deg C for 1 h, after which the contents were distilled in vacuo to give 4.3 g (60%) of 3-vinylthioindole VII, which was a crystallizable liquid with mp 37 deg C.

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