REACTIVITIES OF VINYL DERIVATIVES OF 3-MERCAPTOINDOLE IN REACTIONS WITH ALCOHOLS

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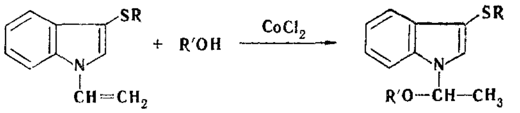
The addition of alcohols to 1-vinyl-3-vinylmercapto- and 1-vinyl-3-ethylmercaptoindole was accomplished in the presence of cobalt chloride. It was established that in the case of the divinyl derivative the addition of alcohols takes place only at the vinyl group attached to the nitrogen atom to give 1-(α-alkoxyethyl)-3-vinylmercaptoindoles. The relative reactivities of the vinylmercaptoindoles as a function of the substituent in the 3-position of the indole ring were studied kinetically.

Under the conditions of the reaction to form acetals, which is well known for vinyl ethers, the addition of alcohols to 1-vinylindole is hindered by the competitive polymerization of the starting monomer [1]. We were able to direct the reaction to favor the synthesis of alkoxyethylindoles only when we used a mixture of acetic acid, boric acid, and copper acetate as the catalyst [2, 3].

In the present research we studied the catalytic reaction of alcohols with 1-vinyl-3-vinylmercaptoindole (I) and 1-vinyl-3-ethylmercaptoindole (II). It was shown that the introduction of a vinylmercapto or ethylmercapto grouping in the 3-position of the 1-vinylindole molecule promotes even higher rates of their polymerization in reactions with alcohols in the presence of the catalysts that we used previously.

The ability of salts of transition metals to catalyze the hydrolysis of substituted imidazoles [4, 5] and the addition of alcohols to vinyl derivatives of carbazole [6] were studied. Catalysts of this sort can change the reactivities of unsaturated compounds due to their possible coordination with the metal [7]. In this connection, we used the salt of a transition metal as the catalyst in the present research in the addition of alcohols to vinyl derivatives of 3-mercaptoindole (I and II). We established that in the presence of cobalt chloride the alcohols react with vinylmercaptoindoles I and II at the double bond of the vinyl group in conformity with the Markownikoff rule, and 1-(α-alkoxyethyl)-3-vinylmercaptoindoles (III and IV) and 1-(α-propoxyethyl)-3-ethylmercaptoindole (V) are obtained in high yields. It should be noted that in the case of vinyl(vinylmercapto)indole I the addition of ethanol and propanol proceeds selectively only at the double bond of the vinyl group attached to the nitrogen atom.



I, II

III-V

I, III, IV R=CH=CH$_2$; II, V R=C$_2$H$_5$; III R′=C$_2$H$_5$; IV, V R′=C$_3$H$_7$

The structures of the synthesized compounds were proved by means of their IR and PMR spectra. The band at 1640 cm^{-1} that is characteristic for the stretching vibrations of a vinyl group attached to a nitrogen atom vanishes in the IR spectra of III-V. The absorption band at 1588 cm^{-1}, which belongs to the stretching vibrations of the C=C bond attached to the sulfur atom, is retained in the spectra of alkoxyethylvinylmercaptoindoles III and IV. An intense band at 1120 cm^{-1}, which is due to asymmetrical stretching vibrations of the resulting C—O—C bond, appears in the spectra of the products of addition of the alcohols. An

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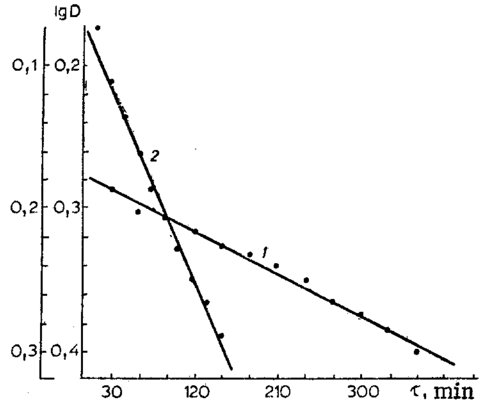

Fig. 1. Dependence of the concentration of 1-vinyl-3-vinylmercaptoindole (1) and 1-vinyl-3-ethylmercaptoindole (2) on time (K_1 = 0.024 ± 0.003; K_2 = 0.090 ± 0.01 h^{-1}).

analysis of the PMR spectra of III and V shows that the addition of alcohol to the double bond of the vinyl group proceeds with the formation of α-addition products. The signals of the protons of the ethylidene ($CH-CH_3$) grouping that is formed in this case are represented in the spectrum by a quartet (δ 5.51 ppm) and a doublet at stronger field (1.68 ppm). The protons of the vinyl group attached to the sulfur atom of III form an ABX spin system (δ_A = 4.98, δ_B = 4.78, and δ_X = 6.24 ppm).

The activating role of cobalt chloride is evidently due to its ability to enter into a donor-acceptor interaction with starting vinylmercaptoindoles I and II. The formation of an intermediate complex gives rise to redistribution of the electron density along the conjugation chain, leads to a change in the magnitudes of the electron charges on the carbon atoms for the $N-CH=CH_2$ group, and promotes the nucleophilic addition of the alkoxy ion to the α-carbon atom of the vinyl group. The sulfur atom evidently hinders the transmission of conjugation, the $S-CH=CH_2$ group is not activated in this reaction, and the alcohol adds selectively only to the vinyl group attached to the nitrogen atom.

The kinetics of the addition of propanol to I and II were investigated spectrophotometrically from the consumption of the substrate in a solution of propanol in the case of a large molar excess of cobalt chloride. The analytical wavelengths (320 and 310 nm, respectively) were selected beforehand by comparison of the UV spectra of starting vinylmercaptoindoles I and II and the reaction products.

A first-order reaction in vinylmercaptoindole I or II is confirmed by the rectilinearity of the semilogarthmic dependence of the change in the concentrations of I and II on time (Fig. 1). A comparison of the rate constants for the addition of propanol to vinyl(vinylmercapto)indole I (K = 0.024 h^{-1}) and vinyl(ethylmercapto)indole II (K = 0.090 h^{-1}) shows that the reaction of I with alcohol is hindered as compared with II. This is evidently due to the different inductive effects of the vinyl and ethyl groups attached to the sulfur atom. The ethyl group, which has a positive electron-donor effect, promotes the formation of a more stable intermediate complex of the starting substrate with cobalt chloride. In this connection, the equilibrium in the reaction system is shifted to favor an increase in its concentration, as a consequence of which the rate of reaction of alcohol with vinyl(ethylmercapto)indole II is higher than in the case of the reaction with vinyl(vinylmercapto)indole I.

EXPERIMENTAL

Compounds I and II were obtained by the reaction of 3-mercaptoindole with acetylene by the method in [8] and were purified by distillation and column chromatography on aluminum oxide. The UV spectra of solutions (0.07-0.14 mmole/liter) of the compounds were recorded with a Specord UV-vis spectrophotometer. 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. The IR spectra of microlayers of the compounds were recorded with a UR-20 spectrometer.

1-(α-Ethoxyethyl)-3-vinylmercaptoindole (III). A mixture of 0.4 g (2 mmole) of vinyl-(vinylmercapto)indole I and 0.5 g (2 mmole) of $CoCl_2 \cdot 6H_2O$ in 10 ml of ethanol was stirred at 70°C for 6 h, after which the excess ethanol was removed in vacuo, and the residue was washed repeatedly with ether. The ether extracts were combined, the ether was removed by distillation, and the residual light-colored oil was chromatographed with a column filled with Al_2O_3 (elution with chloroform) to give 0.2 g (54%) of vinylmercaptoindole III with d_4^{20} 1.0202 and n_D^{20} 1.5907. IR spectrum: 2880, 2933, 2985 (CH_2CH_3); 1588 ($S{-}CH{=}CH_2$; 1120 cm^{-1} (C—O—C). Found %: C 68.1; H 7.0; S 13.0. $C_{14}H_{17}NOS$. Calculated %: C 68.0; H 6.9; S 12.9.

1-(α-Propoxyethyl)-3-vinylmercaptoindole (IV). A mixture of 0.8 g (4 mmole) of vinyl-(vinylmercapto)indole I, 0.94 g (4 mmole) of $CoCl_2 \cdot 6H_2O$, and 15 ml of propanol was stirred at 62°C for 5.5 h, after which it was worked up as in the preceding experiment to give 0.9 g (86.5%) of vinylmercaptoindole IV with d_4^{20} 1.0890 and n_D^{20} 1.6000. IR spectrum : 2878, 2935, and 2963 ($CH_2{-}CH_2{-}CH_3$); 1582 ($S{-}CH{=}CH_2$); 1119 cm^{-1} (C—O—C). Found %: C 69.3; H 7.1; S 12.4. $C_{15}H_{19}NOS$. Calculated %: C 68.9; H 7.3; S 12.3.

1-(α-Propoxyethyl)-3-ethylmercaptoindole (V). The synthesis was carried out as in the preceding case, except that the heating time was 9 h. After workup of the reaction products, the ether extract was chromatographed on aluminum oxide [elution with ether—petroleum ether (1:3)] to give V, with d_4^{20} 1.0550 and n_D^{20} 1.5655, in 60% yield. IR spectrum: 2965, 2935, and 2875 ($CH_2{-}CH_2{-}CH_3$); 1120 cm^{-1} (C—O—C). Found %: C 68.7; H 7.8; N 5.0; S 11.7. $C_{15}H_{21}NOS$. Calculated %: C 68.4; H 8.0; N 5.3; S 12.2.

Kinetic Measurements. The changes in the concentration of the starting substrate with time were followed with an SF-4A spectrophotometer. The starting solution was prepared by dissolving a weighed sample of the vinylmercaptoindole and cobalt chloride in n-propanol in a pycnometer with a definite volume. The measurements were made in a thermostatted cuvette, which was simultaneously the reaction vessel, at 70 ± 0.1°C. Each constant was measured no less than five times. The rate constants were calculated by the standard method [9].

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