REACTION OF N-VINYLAZOLES AND N-VINYLINDOLE WITH HALOHYDRINS

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The peculiarities of the reaction of chloro(bromo,fluoro)hydrins with N-vinylimidazole, -benzimidazole, -benzotriazole, and -indole are demonstrated. Vinyl and polymeric azoles with various functional groups (OH, Cl, Br, CNS, and NO_3) attached to the substituent in the 3 position of the five-membered ring were synthesized.

We have previously observed the effect of the structure of conjugated heterocyclic systems of aromatic character on their reactivities in an investigation of the reactions of N-vinylazoles and N-vinylindole with halogens, alkyl halides, and dialkyl sulfates [1-3]. In the present research we have studied the reaction of N-vinylimidazole (I), N-vinylbenzimidazole (II), N-vinylbenzotriazole (III), and N-vinylindole (IV) with ethylene chlorohydrin, tetramethylene-1,4-chlorohydrin, 1-chloropropylene-2,3-chlorohydrin, trimethylene-1,3-bromohydrin, and ethylene fluorohydrin. In the case of halohydrins, we investigated a new (for N-vinylazoles) series of organic electron acceptors that have active functional groups, owing to which the possibility of further modification of vinyl nitrogen-containing heterocycles in order to obtain biologically active substances is revealed.

In view of the rather significant differences in the electronic structures, one might have expected that the investigated five-membered heterocycles would behave differently on reaction with the hydrin. In fact, I-IV react with halohydrins in the most diverse directions to give quaternary salts and quaternized polymers; addition proceeds at the double bond of the vinyl group to give charge-transfer complexes (CTC).

The investigation of the reaction was carried out with variations in the temperature, time, and component ratio.

Regardless of the conditions under which the components are mixed, quaternary salts due to coordination of the hydrogens with the nitrogen in the 3 position are formed in the reaction of halohydrins with N-vinylimidazoles I and II. Compounds I and II react most actively with ethylene chlorohydrin. After 20 h at 90°C, they form quaternization products in 83 and 76% yields, respectively. When the temperature is lowered to 70° (after 50 h), the yield of quaternary salt II is reduced to 34%, while I under these conditions forms an oily reaction mixture, from which a total of 4% of a crystalline quaternized product can be isolated. Compounds I and II react less actively with trimethylene bromohydrin. In this case, II forms quaternary salts in 58% yield. The products of the reaction on the basis of I cannot be isolated because of the oily reaction mixture that is formed. Only traces of quaternization products (4-8%) are formed in the reaction of I and II with 1-chloropropylene-2,3-chlorohydrin and tetramethylene chlorohyrin. The fluorohydrins do not react with I and II even after 100 h at 90°. Like I and II, polyvinylimidazole and polyvinylbenzimidazole also react with ethylene chlorohydrin to give polymeric quaternary salts of the composition

$$(C_5H_6N_2 \cdot CH_2Cl{-}CH_2OH)_n \text{ and } [(C_9H_8N_2)_2 \cdot CH_2Cl{-}CH_2OH]_n.$$

The structure of the quaternization products based on I, II, and their polymers is confirmed by the results of elementary analysis and the IR spectra. Quaternized I and II contain absorption bands of a vinyl group at 1646 and 960 cm^{-1}. The shift in frequencies that correspond to the vibrations of the imidazole ring to

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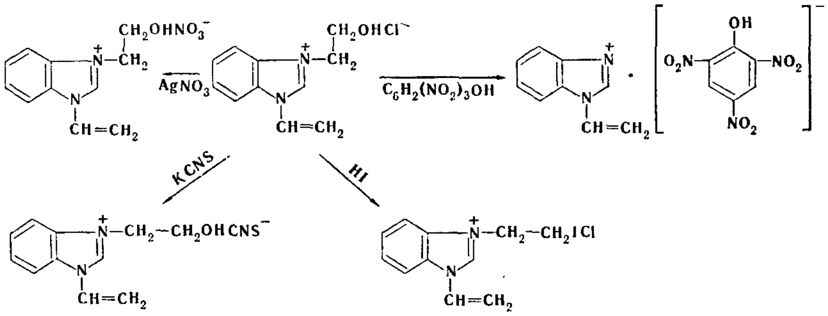
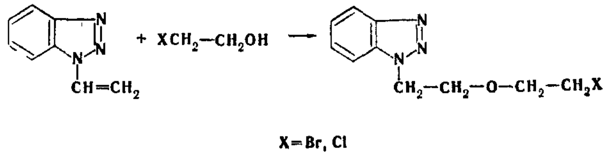
the short-wave region and the appearance of frequencies that are characteristic for hydroxyl (3400 cm^{-1}) and C—Hal (665-760 cm^{-1}) absorption attest to coordination with the hydrin. A similar pattern is also observed in the IR spectra of the quaternized polyvinylimidazoles. The structures of the quaternary salts of N-vinylimidazoles and the hydrins are confirmed by their chemical properties, particularly by exchange with picric acid with replacement of the acceptor and formation of N-vinylimidazole picrates via the scheme



The labilities of the halogen and hydroxyl atoms in the quaternization products of N-vinylimidazole are demonstrated by the ease of exchange by NO$_3$, CNS, and I on reaction with silver nitrate, potassium thiocyanate, and hydrogen iodide to give the corresponding modified vinyl quaternary salts based on I and II.

In contrast to I and II, addition of bromo- and chlorohydrin to the double bond of the vinyl group via the following scheme is the primary process in the reaction of N-vinylbenzotriazole (III) with the halohydrin:



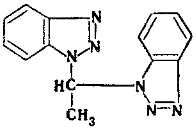
A similar reaction direction also predominates in the action of bromine and chlorine on III [4] and is in agreement with the results of quantum-mechanical calculation, which attests to a decrease in the basicity of III as compared with that of I and II.

Compound III reacts considerably more actively with bromohydrins. The reaction proceeds in 5 h at 70-80°. Longer heating is required to obtain products of the reaction of III with ethylene chlorohydrin. The absence in the IR spectrum of frequencies characteristic for the absorption of a vinyl group attests to the addition of the bromo- and chlorohydrin to the double bond of the vinyl group of III. The strong absorption at 1030, 1070, and 1170 cm^{-1} characterizes the C—O—C asymmetric stretching vibrations. The frequencies at 2870, 2925, and 2950 cm^{-1} are related to the absorption of the $-CH_2-CH_2-$methylene group, and no hydroxyl absorption band is present.

The PMR spectra of the products of the reaction of III with bromo- and chlorohydrins consist of two unsymmetrical triplets and a multiplet at weak field at 7.75-8.13 ppm. The latter attests to the presence of aromatic protons. The integral intensities of the signals were taken into account in the interpretation of the PMR spectra. The triplet belonged to the protons of the methylene groups bonded to the heteroatom, and the protons of two CH$_2$ groups positioned near the oxygen atom resonate at weaker field (δ 5.06 ppm). The signals of the protons of the methylene groups attached to the nitrogen and halogen atoms are superimposed at δ 4.19 ppm ($J_{CH_2\text{-}CH_2} = 5.0$ Hz). The triplet at strong field that is characteristic for the methyl group is absent in the spectrum. This form of the spectra makes it possible to assume that the addition of halohydrins to III proceeds at the vinyl group, counter to Markovnikov's rule.

It should be noted that, in contrast to the bromohydrins, ethylene chlorhydrin, in addition to the product of addition at the vinyl group, also reacts with III to give a product that does not contain chlorine. The IR spectrum of the latter does not contain the absorption band of the vinyl group double bond and the hydroxyl group. Its PMR spectrum consists of a doublet at strong field and a multiplet at weak field with an integral intensity ratio of 1 : 3. On the basis of the change in the multiplicity of the signals when double resonance is superimposed on the doublet (δ 2.65 ppm, J = 7 Hz), we confirmed its assignment to methyl protons, and we also confirmed the assignment of the quartet at weak field (δ 7.64 ppm) to the methylidyne proton.

The following structure can apparently be assumed for the product that does not contain chlorine on the basis of the results of elementary analysis and data from PMR and IR spectroscopy:



In contrast to III, benzotriazole and polyvinylbenzotriazole react with bromo- and chlorohydrin to give quaternary salts. Their IR spectra contain frequencies characteristic for the hydroxyl and C—Br (Cl) groups, which confirm coordination with the hydrin.

The reaction of N-vinylindole (IV) with the halohydrin, which is accompanied in all cases by vinyl polymerization with simultaneous quaternization and formation of brightly colored polymeric products of various composition, proceeds in a most complex manner. The absorption bands due to vibrations of the vinyl group vanish in the IR spectra of the products of reaction of IV with the hydrins, and new frequencies appear at 3400 (OH) and 615-740 cm^{-1} (C—Cl, C—Br).

New bands at 400-550 nm (λ_{max} 455 and 495 nm) appear in the electronic spectra of the quaternized polymeric products from IV. The deep color of the products of the reaction of IV with the hydrins, the appearance of new bands in their electronic spectra, the inability to undergo exchange with picric acid, and the insolubility in water provide a basis for assuming that they are similar in nature to CTC. We have previously observed the formation of similar polymeric CTC in the reaction of IV with halogens and hydrogen halides [5, 6].

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer at 400-3600 cm^{-1} with LiF, NaCl, and KBr prisms. The electronic spectra of dimethylformamide and alcohol solutions of the compounds were recorded with a Unicam SP-8000 spectrophotometer. The PMR spectra were recorded with a BS 487B spectrometer at room temperature with hexamethyldisiloxane (δ scale) as the internal standard. The chromatography was carried out in a thin layer of activity-II aluminum oxide. The chromatograms were developed with iodine vapors.

Synthesis of the Quaternary Salt of I with Ethylene Chlorohydrin. A mixture of 1 g (0.01 mole) of I and 1.6 g (0.02 mole) of ethylene chlorohydrin was heated in an ampul at 90° for 22 h. The reaction mixture was dissolved in DMF—ethanol (1 : 5) and reprecipitated with ether to give 1.5 g (83%) of a white powdery substance with mp 278-280°. Found: Cl 19.41%. $C_5H_6N_2 \cdot C_2H_5OCl$. Calculated: Cl 20.1%.

Quaternization of II with Trimethylene Bromohydrin. A mixture of 1 g (7 mmole) of II and 1.92 g (14 mmole) of trimethylene bromohydrin was heated in an ampul at 70° for 38 h to give 1.13 g (58%) of a white powder with mp 144-150°. Found: Br 29.7%. $C_9H_8N_2 \cdot C_3H_7BrO$. Calculated: Br 28.3%.

Exchange of Ethylene Chlorohydrin-Quaternized N-Vinylbenzimidazole (V) with Picric Acid. A solution of 0.1 g of V in 1 ml of ethanol was added to a saturated alcohol solution of picric acid, and the mixture was heated to the boiling point. The precipitate that formed on cooling was removed by filtration, washed with alcohol, and dried to give 0.05 g of a yellow powder with mp 194-196°. Found: C 48.78; H 3.37%. $C_9H_8N_2 \cdot C_6H_3N_3O_7$. Calculated: C 48.26; H 2.94%.

Reaction of V with $AgNO_3$. A solution of 0.1 g (0.4 mmole) of V in 1 ml of ethanol was added dropwise to an alcohol solution of 0.075 g (0.4 mmole) of $AgNO_3$, and the resulting white coagulated precipitate was removed by filtration. The alcohol filtrate was treated with ether to precipitate 0.07 g (62%) of a white powder with mp 124-125°. Found: C 51.93; H 5.36%. $C_9H_8N_2 \cdot C_2H_5NO_4$. Calculated: C 52.58; H 5.17%.

Replacement of the Chlorine in V by a CNS group. A solution of 0.086 g (0.8 mmole) of KCNS in 4 ml of ethanol was added to an alcohol solution of 0.2 g (0.8 mmole) of V. The precipitated KCl was removed by filtration, and the filtrate was treated with ether to precipitate 0.14 g (70%) of a white powder with mp 60-62°. Found: C 55.58; H 4.99%. $C_9H_8N_2C \cdot C_2H_5OCNS$. Calculated: C 56.03; H 5.04%.

Reaction of III with Trimethylene Bromohydrin. A mixture of 5 g (34 mmole) of III and 8.3 g (60 mmole) of trimethylene bromohydrin was heated at 70-80° for 5 h. The excess hydrin was removed by vacuum distillation, and the residue was dissolved in alcohol and reprecipitated by the addition of ether. Repeated reprecipitations yielded 5.7 g (57%) of a light-brown solid that deliquesced in air. Found: C 47.2; H 4.9; Br 28%. $C_{11}H_{14}N_3BrO$. Calculated: C 47.0; H 4.9; Br 28.1%. R_f 0.1 [benzene—hexane—chloroform (6 : 1 : 3)].

Reaction of III with Ethylene Chlorohydrin. A mixture of 5 g (34 mmole) of III and 5.4 g (67 mmole) of ethylene chlorohydrin was held in a sealed ampul at 90° for 20 h. The excess hydrin was then removed by vacuum distillation, and the residue was washed repeatedly with ether and dissolved in alcohol. Reprecipitation by the addition of ether yielded 4 g of crude powder. Found: C 53.3; H 5.6; Cl 15%. $C_{10}H_{12}N_3OCl$. Calculated: C 53.3; H 5.3; Cl 15.8%. Removal of the ether by distillation gave an oily residue, which was recrystallized from alcohol to give 5 g of a white crystalline product with mp 142-143°. Found: C 62.3; H 4.7%. The product did not contain chlorine and had R_f 0.3 [benzene—hexane—chloroform (6:1:3)].

Reaction of IV with Trimethylene Bromohydrin. A solution of 1 g (7 mmole) of IV in 3 ml of ether or CCl_4 was added gradually at 10-15° to 1 g (7 mmole) of trimethylene bromohydrin. After 30 min, the resulting mass was triturated in ether, and the crystalline precipitate was removed by filtration and dried to give 1.1 g (55%) of a dark cherry-red powder with mp 153-160°. Found: C 71.88; H 6.0; Br 11.9%. $(C_{10}H_9N)_4 \cdot C_3H_7BrO$. Calculated: C 72.5; H 5.9; Br 11.15%.

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