RESEARCH ON UNSATURATED AZOLE DERIVATIVES.

VI.* SYNTHESIS OF SOME N-VINYLBENZIMIDAZOLES

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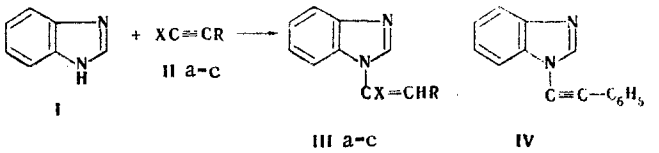
The reaction of benzimidazole with phenylacetylene, ethyl propiolate, and their β-bromo derivatives leads to the corresponding β-substituted N-vinylbenzimidazoles.

The vinylation of benzimidazole with acetylene has been described by Reppe [2] and Shostakovskii and co-workers [3]. We have studied the reaction of benzimidazole with some substituted acetylenes.

N-(β-Phenylvinyl)benzimidazole (IIIa) was obtained by refluxing benzimidazole (I) with phenylacetylene (IIa) in pyridine in the presence of cuprous chloride. Benzimidazole adds more readily to the activated C≡C bond of ethyl propiolate (IIb), and ethyl β-(N-benzimidazolyl)acrylate (IIIb) is formed in good yield without a catalyst (see [4]).

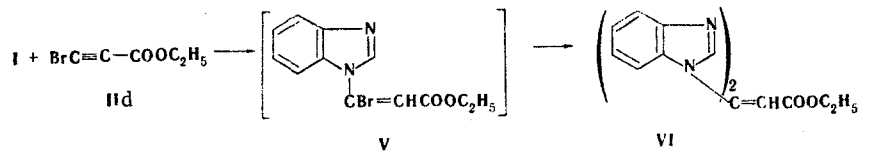
It is known that the alkylation of lithium salts of secondary amines with bromophenylacetylene (IIc) leads to enamines [5]. According to our data, 1-(1-bromo-2-phenylvinyl)benzimidazole (IIIc) is formed instead of the expected 1-(β-phenylethynyl)benzimidazole (IV) when the lithium or sodium salt of benzimidazole is heated with acetylene IIc in anisole or tetrahydrofuran (THF) or when alcohol solutions of I and IIc are refluxed in the presence of potassium hydroxide.



I III a-c IV

II-IIIa R = C_6H_5, X = H; b R = $COOC_2H_5$, X = H; c R = C_6H_5, X = Br

Instances of this sort of addition of amines to β-bromophenylacetylene are unknown [5]. In contrast to this, in the case of the reaction of benzimidazole with ethyl bromopropiolate (IId) the reaction does not stop with the addition of I to the activated C=C bond: The more labile halogen atom in the intermediate bromovinyl derivative (V) evidently readily undergoes nucleophilic substitution by a I molecule to give ethyl β,β'-di(1-benzimidazolyl)acrylate (VI).



V VI

The IR and PMR spectral data are in agreement with the proposed structure of VI. The ease of replacement of the halogen by heating I with β-chlorovinyl phenyl ketone in alcohol constitutes evidence in favor of the proposed mechanism; vinyl ketone VII is formed in high yield in this case.

The action of alcoholic alkali solution on 1-(α-bromo-β-phenylvinyl)benzimidazole (IIIc) in order to convert it to ynamine IV leads to resinification of the reaction products.

*See [1] for communication V.

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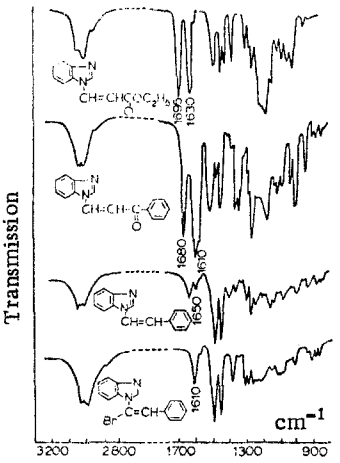
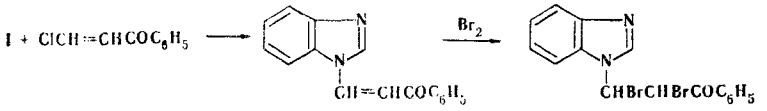


Fig. 1. IR spectra of enamines IIIa-c and VII.

1-Vinylbenzimidazoles IIIa, b, which are stable under ordinary conditions, form resinous low-molecular-weight polymeric compounds upon bromination. On the other hand, the rather stable 2,3-dibromopropanone VIII is formed by bromination of vinyl ketone VII; however, we were also unable to convert it to N-benzimidazolylethynyl phenyl ketone by treatment with a solution of potassium hydroxide in alcohol because of resinification of the reaction mixture.



VII VIII

Since stabilization of anion IX, formed as a result of β addition of I to acetylenic compounds IIa-d, promotes conjugation with electrophilic substituent R, the products of the reaction of I with acetylenes IIa-d have primarily a β structure (see [6]).

IX

The IR spectra of enamines IIIa-c and VII contain absorption bands at 895-900 cm^{-1}, and this constitutes evidence for the primary formation of trans β isomers (see Fig. 1).

EXPERIMENTAL

The IR spectra of $CHCl_3$ solutions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of CF_3COOH solutions were obtained with a Tesla RS-487C spectrometer.

1-(β-Phenylvinyl)benzimidazole (IIIa). A mixture of 1.18 g (0.01 mole) of benzimidazole and 1.5 g (0.015 mole) of phenylacetylene in 3 ml of pyridine was heated with a catalytic amount of cuprous chloride in a sealed ampule at 98°C for 8 h, after which it was cooled and poured into 30 ml of water. The liberated oil was extracted with ether, and the extract was shaken with 30 ml of 10% HCl. The hydrochloric acid layer was separated, washed with 10 ml of ether, and treated with aqueous sodium bicarbonate solution. The resulting precipitate was removed by filtration to give 1.63 g (74%) of colorless needles with mp 113-115°C (from petroleum ether). IR spectrum: 1650 cm^{-1} (C=C). Found, %: C 82.0; H 5.2; N 12.8. $C_{15}H_{12}N_2$. Calculated, %: C 81.8; H 5.5; N 12.7. The picrate was obtained as yellow prisms with mp 164-165°C (from ethanol).

Ethyl β-(1-Benzimidazolyl)acrylate (IIIb). A solution of 1.18 g (0.01 mole) of I and 1.2 g (0.012 mole) of ethyl propiolate in 7 ml of alcohol was refluxed on a water bath for 6 h, after which it was cooled and treated with 20 ml of water, and the precipitate was removed by filtration to give 1.96 g (91%) of colorless plates with mp 68°C (from petroleum ether). Found, %: C 67.0; H 5.3; N 14.6. $C_{12}H_{12}N_2O_2$. Calculated, %: C 66.7; H 5.6; N 14.8. IR spectrum: 1652 (C=C) and 1715 cm^{-1} (C=O).

1-(α-Bromo-β-phenylvinyl)benzimidazole (IIIc). A solution of 0.59 g (5 mmole) of I and 0.28 g (5 mmole) of KOH in 10 ml of alcohol was refluxed for 1 h with 1.08 g (6 mmole) of β-bromophenylacetylene, after which it was cooled, diluted with 40 ml of water, and extracted with ether. The extract was worked up as described in the preparation of IIIa to give a colorless oil (after vacuum distillation) that was readily soluble in water. The yield was 1.06 g (84.5%). IR spectrum: 1610 cm^{-1} (C=C). The picrate was obtained as yellow needles with mp 173-174°C (from alcohol). Found, %: C 47.8; H 3.0; Br 15.3; N 13.0. $C_{15}H_{11}BrN_2 \cdot C_6H_3N_3O_7$. Calculated, %: C 47.7; H 2.7; Br 15.2; N 13.3.

Ethyl β,β-Di(1-benzimidazolyl)acrylate (IV). A solution of 3.6 g (30 mmole) of benzimidazole and 1.77 g (10 mmole) of β-bromoethyl propiolate in 15 ml of alcohol was refluxed on a water bath for 5 h, after which the solvent was removed by distillation, and the residual oil was treated with chloroform. The chloroform solution of VI was separated from the hydrobromide of I and chromatographed with a column filled with activity II Al_2O_3 (elution with chloroform). The chloroform was removed by distillation, the residual oil was triturated with ether, and the resulting crystals were removed by filtration. The yield of product with mp 136°C (from alcohol—ether) was 1.8 g (56%). Found, %: C 69.5; H 5.2; N 16.6. $C_{19}H_{16}N_4O_2$. Calculated, %: C 69.6; H 4.8; N 16.9. The product had a molecular weight of 330 (by the Rast method in camphor). IR spectrum: 1720 cm^{-1} (C=O). PMR spectrum, δ: 0.8 (t, CH_3), 3.9 (q, CH_2), 7.0-7.62 (m, aromatic and olefinic* protons), and 9.42 ppm (benzimidazole ring 2-H).

1-(β-Benzoylvinyl)benzimidazole (VII). A 1.66-g (0.01 mole) sample of β-chlorovinyl phenyl ketone was added to a solution of 2.36 g (0.02 mole) of I in 15 ml of alcohol, and the reaction mixture was refluxed on a water bath for 30 min. It was then cooled, and the precipitate was removed by filtration and washed with alcohol and ether to give 2.24 g (90%) of colorless prisms of VII with mp 189-190°C (from alcohol). The product was quite soluble in chloroform and acetone. Found, %: C 77.8; H 4.8; N 11.2. $C_{16}H_{12}N_2O$. Calculated, %: C 77.4; H 4.8; N 11.3. IR spectrum: 1680 (C=O) and 1610 cm^{-1} (C=C).

3-(1-Benzimidazolyl)-2,3-dibromo-1-phenylpropane (VIII). A solution of 0.88 g (5.5 mmole) of bromine in 3 ml of chloroform was added with vigorous stirring at −5°C to a solution of 1.24 g (5 mmole) of VII in 15 ml of dry chloroform, and the mixture was stirred for 1 h. The solvent was then removed, and the residual oil was chromatographed with a column filled with activity II Al_2O_3 (elution with ether) to give 2 g (98%) of a viscous yellow oil. The picrate was obtained as yellow needles with mp 200-202°C (from alcohol). Found, %: C 56.3; H 3.6; Br 24.5; N 11.0. $C_{16}H_{12}Br_2N_2O \cdot C_6H_3N_3O_7$. Calculated, %: C 56.0; H 3.9; Br 24.3; N 10.7.

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*The value calculated by an additive scheme [7] is 7.55 ppm.