RESEARCH OF BENZIMIDAZOLE DERIVATIVES. XXXVI.* SYNTHESIS AND TRANSFORMATIONS OF N-PROPARGYL-SUBSTITUTED 2-AMINOBENZIMIDAZOLES

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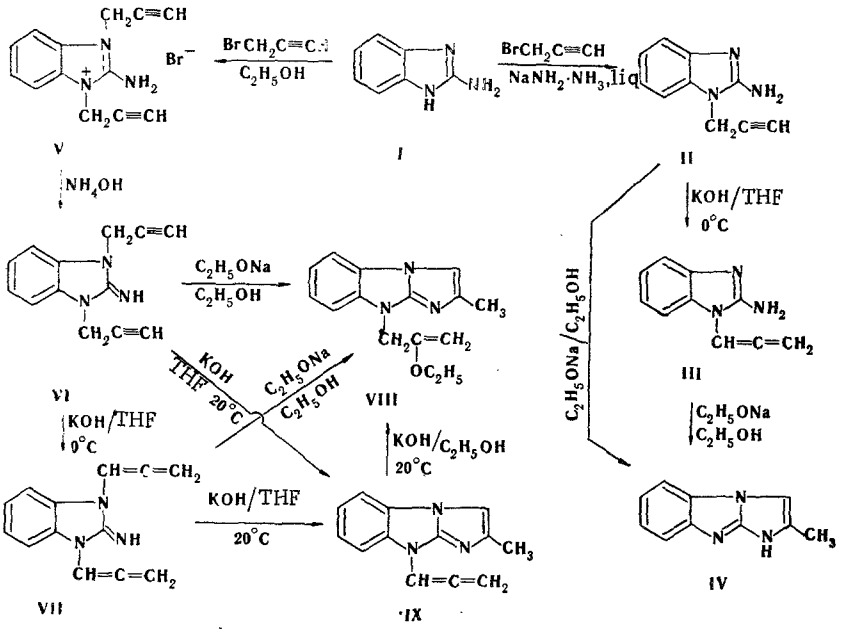
1-(2'-Propynyl)-2-aminobenzimidazole and 1,3-di(2'-propynyl)-2-iminobenzimidazoline, which are cyclized by the action of bases to imidazo[1,2-a]benzimidazole derivatives, were obtained by alkylation of 2-aminobenzimidazole with propargyl bromide. The cyclization proceeds with the formation of intermediate N-propadienyl derivatives.

The alkylation of 2-aminobenzimidazole (I) with propargyl bromide was studied under various conditions. It was found that 1-(2'-propynyl)-2-aminobenzimidazole (II) is formed in good yield in the reaction of I with propargyl bromide in liquid ammonia in the presence of an equimolecular amount of sodium amide. However, the reaction of I with propargyl bromide in refluxing ethanol gives 1,3-di(2'-propynyl)-2-iminobenzimidazoline (V), which is converted to base VI on treatment with concentrated ammonium hydroxide. The IR spectrum of II contains absorption bands at 3315 cm^{-1} (≡C–H) and 3400 and 3480 cm^{-1} (–NH_2), and the IR spectrum of VI contains bands at 3315 cm^{-1} (≡C–H) and 3360 cm^{-1} (=NH).



In contrast to I, the reaction of propargyl bromide with the less basic 4,5-diphenyl-2-aminoimidazole (X) in ethanol gives only monopropargyl-substituted XI. The IR spectrum

*See [1] for communication XXXV.

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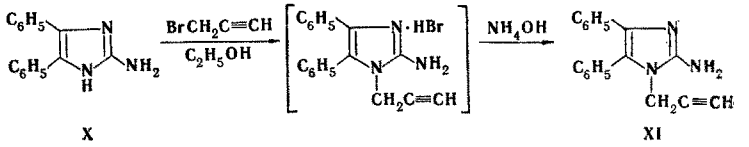
of XI contains absorption bands at 3310 (≡C–H) and 3365 and 3450 cm^{-1} (–NH_2).



X XI

The cyclization of propargyl-substituted II and VI to imidazo[1,2-a]benzimidazole derivatives (IV, VIII, and IX) proceeds through prototropic rearrangement of these compounds to allenes III and VII and subsequent addition of an amino group to the propadienyl radical. Thus the action of potassium hydroxide in tetrahydrofuran (THF) on II and VI at 0°C gives the corresponding propadienyl derivatives (III and VII), which are stable on brief storage. The ≡C–H band is absent in the IR spectra of these compounds, and absorption characteristic for the allene group appears at 1090 and 1980 cm^{-1}. Compound VIII can be isolated only by the action of sodium ethoxide in ethanol on V, VI, or VII and is formed during nucleophilic addition of an alcohol molecule to the initially formed allene (IX). In fact, treatment of VI or VII with potassium hydroxide in THF at 20° gives only IX, which is converted to VIII in alcoholic potassium hydroxide. The IR spectrum of IX contains absorption bands at 1095 and 1980 cm^{-1}(–CH=C=CH_2), whereas the spectrum of VIII contains only a band at 1600 cm^{-1} (C=C).

It should be noted that 1-(2'-propynyl)-2-aminobenzimidazole (II), in contrast to 1-alkyl-3-(2'-propynyl)-2-iminobenzimidazolines [1], is cyclized to derivative IV in ethanol in the presence of sodium ethoxide upon more prolonged refluxing. The rate of cyclization is probably determined by the rate of formation of the N-anion that attacks the propadienyl gorup, a rate that is higher in the case of 2-iminobenzimidazolines. The cyclization of II in THF in the presence of potassium hydroxide at 20° proceeds with considerable resinification.

EXPERIEMNTAL METHOD

The IR spectra of chloroform solutions of the compounds were recorded with a UR-20 spectrometer.

1-(2'-Propynyl)-2-aminobenzimidazole (II). A 1.32-g (0.01 mole) sample of I was added to a solution of 0.23 g (0.01 g-atom) of sodium metal in 50 ml of liquid ammonia. After 15 min, a solution of 0.8 ml (0.01 mole) of propargyl bromide in 3 ml absolute ether was added dropwise to the reaction mixture, and it was stirred at –70° for 1 h. Ammonium chloride (1g) was then added, and the mixture was allowed to stand until the ammonia had completely evaporated. The residue was treated with 20 ml of water, and the reaction product was removed by filtration to give 1.39 g (82%) of colorless prisms with mp 145-146° (from dioxane). Found %: C 69.8; H 5.8; N 24.6. $C_{10}H_9N_3$. Calculated %: C 70.2; H 5.3; N 24.5.

1-Propadienyl-2-aminobenzimidazole (III). A solution of 0.85 g (5 mmole) of II in 1 ml of THF was added to a cooled (to 0°) suspension of 0.56 g (0.01 mole) of calcined potassium hydroxide in 3 ml of absolute THF, after which the mixture was stirred at room temperature for 1.5 h. Water (20 ml) was then added, and the resulting precipitate was removed by filtration to give 0.8 g (94%) of colorless prisms with mp 132-133° (from aqueous ethanol); the product turned red on storage. Found %: C 70.0) H 5.7; N 24.5. $C_{10}H_9N_3$. Calculated %: C 70.2; H 5.3; N 24.5.

1(9)H-2-Methylimidazo[1,2-a]benzimidazole (IV). A) A 1.71-g (0.01 mole) sample of II was added to a solution of sodium ethoxide obtained from 0.23 g (0.01 g-atom) of sodium metal and 5 ml of absolute ethanol, after which the mixture was refluxed on a water bath for 5 h. It was then cooled, treated with 20 ml of water, and extracted with chloroform. The solvent was removed by distillation, and the residue was crystallized from benzene to give 1.43 g (83%) of colorless prisms with mp 195-196° [2].

B) Compound IV was similarly obtained from III in 76% yield.

2-Imino-1,3-di(2'-propynyl)benzimidazoline Hydrobromide (V). A solution of 1.32 g (0.01 mole) of I and 0.8 ml (0.01 mole) of propargyl bromide in 6 ml of ethanol was refluxed

on water bath for 1 h, after which it was cooled, and the resulting precipitate was removed by filtration and washed successively with alcohol and ether to give 1.33 g (46%) of colorless prisms with mp 235° (from water). Found %: C 53.3; H 4.6; Br 27.7; N 14.5. $C_{13}H_{12}N_3Br$. Calculated %: C 53.7; H 4.1; Br 27.6; N 14.5.

2-Imino-1,3-di(2'-propynyl)benzimidazoline (VI). A 0.45-g (1.5 mmole) sample of V was triturated thoroughly with 5 ml of concentrated ammonium hydroxide, after which the solid was removed by filtration and washed with water to give 0.28 g (95%) of colorless needles with mp 141-142° (from aqueous ethanol); the product was soluble in alcohol, chloroform, and acetone but insoluble in water. Found %: C 74.8; H 5.3; N 19.6. $C_{13}H_{12}N_3$. Calculated %: C 74.7; H 5.3; N 20.0.

2-Imino-1,3-dipropadienylbenzimidazole (VII). The procedure used to obtain III was used to prepare this compound from 0.4 g (2 mmole) of VI and 0.45 g (8 mmole) of potassium hydroxide in 5 ml of absolute THF at 0°. The yield of colorless prisms, which darkened on storage and had mp 96-97° (from aqueous ethanol) was 0.36 g (89%). The product was quite soluble in organic solvents. Found %: C 74.4; H 5.5; N 19.6. $C_{13}H_{11}N_3$. Calculated %: C 74.7; H 5.3; N 20.0.

2-Methyl-9-(β-ethoxyallyl)imidazo[1,2-a]benzimidazole(VIII). A) A 2.1-g (0.01 mole) sample of VI was added to a solution of sodium ethoxide obtained from 0.46 g (0.02 g-atom) of sodium metal and 8 ml of absolute ethanol, and the reaction mixture was refluxed for 1 h. It was then cooled, treated with 15 ml of water, and extracted with chloroform. The reaction product was purified by chromatography with a column filled with Al_2O_3 and elution with ether to give 1.68 g (80%) of VIII as colorless oil. The oil was quite soluble in organic solvents. The picrate was obtained as yellow needles with mp 193-194° (from ethanol). Found %: C 52.2; H 4.6; N 17.4. $C_{15}H_{17}N_3O \cdot C_6H_3N_3O_7$. Calculated %: C 52.1; H 4.2; N 17.4.

B) Compound VIII was similarly obtained from VII in 82% yield.

C) A 1-g (5 mmole) sample of IX and 1 g of potassium hydroxide were dissolved in 5 ml of ethanol, and the solution was allowed to stand overnight. It was then refluxed for 15 min, cooled, diluted with 20 ml of water, and extracted with chloroform to give 0.75 g (75%) of VIII.

The picrates of VIII obtained by methods A, B, and C were identical.

2-Methyl-9-propadienylimidazo[1,2-a]benzimidazole (IX). A) A 0.5-g (2.5 mmole) sample of VI was added to a suspension of 0.5 g of calcined potassium hydroxide in 3 ml of absolute THF, and the mixture was allowed to stand at room temperature for 2 h. Water (15 ml) was then added, and the reaction product was extracted with ether to give 0.25 g (50%) of colorless prisms with mp 67-69° (from aqueous ethanol); the product darkened rapidly in air. The picrate was obtained as yellow prisms with mp 178-179° (from ethanol). Found %: C 52.4; H 2.8; N 18.8. $C_{13}H_{11}N_3 \cdot C_6H_3N_3O_7$. Calculated %: C 52.0; H 3.2; N 19.2.

B) Compound IX was similarly obtained from VII in 72% yield.

1-(2'-Propynyl)-2-amino-4,5-diphenylimidazole (XI). A solution of 1.2 g (5 mmole) of X and 0.4 ml (5 mmole) of propargyl bromide in 6 ml of ethanol was refluxed for 8 h. The solvent was then removed by distillation, and the residue was treated with ammonium hydroxide. The reaction product was extracted with chloroform to give 0.88 g (65%) of a yellow oil, which was soluble in alcohol, chloroform, and acetone but insoluble in water. The picrate was obtained as yellow prisms with mp 245-246° (from ethanol). Found %: N 16.6. $C_{18}H_{15}N_3 \cdot C_6H_3N_3O_7$. Calculated %: N 16.7.

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