RESEARCH ON BENZIMIDAZOLE DERIVATIVES

XXXIV.* SOME TRANSFORMATIONS OF N-ALKENYL- AND N-ALKYNYL-SUBSTITUTED BENZIMIDAZOLES

P. V. Tkachenko, I. I. Popov, and A. M. Simonov

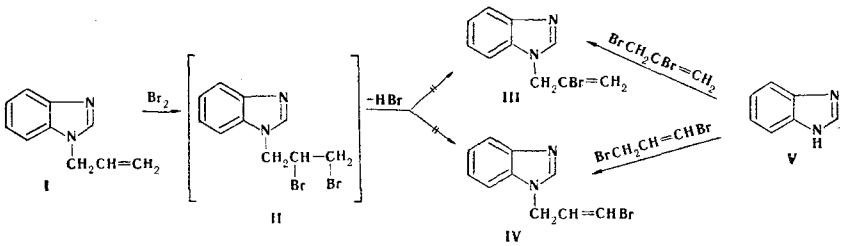
UDC 547.785.5:542.953

Benzimidazole was alkylated with 1,3-dibromo-1-propene, 2,3-dibromo-1-propene, and 1,2,3-tribromopropane, and some of the properties of the N-substituted benzimidazoles obtained were examined. It is shown that 1-(2'-propynyl)benzimidazole is readily rearranged to the 1-propadienyl derivative under the conditions of the Favorskii reaction.

Only the syntheses of N-vinyl- [2] and N-allylbenzimidazole [3] have been described in the benzimidazole series. In the present research we have continued our study of methods for the introduction of unsaturated radicals into the benzimidazole ring [4].

The readily accessible 1-allyl benzimidazole (I) could not be used as the starting material for the synthesis of 1-(2-propynyl)benzimidazole, inasmuch as all attempts to brominate it under various conditions – by varying the temperature conditions (–10, 0, and +20°C) and the solvents (CCl_4, $CHCl_3$, and CH_3COOH) – did not give positive results. Viscous oils with a variable bromine content that did not form picrates were isolated from the reaction mixtures in all cases.

It might have been assumed that the initially formed dibromo derivative II is dehydrobrominated under the influence of heteroring to monobromo derivatives III or IV, which then undergo polymerization. However, III and IV, which we obtained by direct alkylation of benzimidazole V with 2,3-dibromo-1-propene and 1,3-dibromo-1-propene in alcoholic alkali solution at room temperature, proved to be stable.

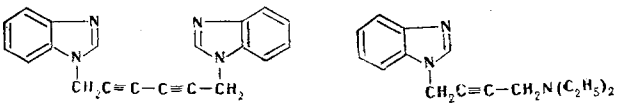


We were unable to synthesize dibromo derivative II by the action of 1,2,3-tribromopropane on benzimidazole V in refluxing toluene. In this case, as in the alkylation of 1,2-dibromoethane [5], two molecules of benzimidazole V enter into the reaction to give 1,3-(di-N-benzimidazolyl)-2-bromopropane (VI).

Compounds III and IV are converted smoothly by the action of sodium amide in liquid ammonia to 1-(2-propynyl)benzimidazole (VII), which we described in [4]. It has all of the properties of monosubstituted acetylenes. It reacts with copper and silver hydroxide in ammonia solution to give the corresponding acetylides. Oxidative dimerization of VII under the conditions of the Glaser coupling reaction gives diyne VIII. We obtained amino derivative IX in the Mannich reaction with diethylamine.

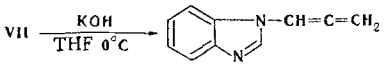
* See [1] for communication XXXIII.

Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1540-1543, November, 1974. Original article submitted December 4, 1974.



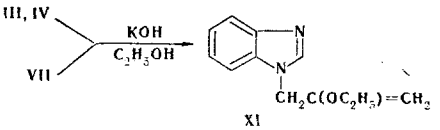
VIII IX

Moreover, VII could not be made to undergo reaction with acetone in the presence of potassium hydroxide, inasmuch as acetylene–allene rearrangement to give 1-propadienylbenzimidazole (X) proceeds at a high rate under the conditions of the Favorskii reaction, as attested to by the disappearance of the $\nu_{\equiv CH}$ band at 3310 cm^{-1} in the IR spectrum and the appearance of the absorption of propadienyl group at 1090 and 1970 cm^{-1}.



X

When acetylene VII is refluxed in an alcohol solution of potassium hydroxide, it adds alcohol to give 1-(β-ethoxyallyl)benzimidazole (XI). The ease of vinylation of VII as compared with phenylacetylene [6] is explained by the participation of intermediate structure X in this transformation. The formation of XI instead of VII on treatment of 1-(β-bromoallyl)benzimidazole (III) or 1-(α-bromoallyl)benzimidazole (IV) with potassium hydroxide solution in alcohol can also be explained by this participation. The structure of XI is assigned in conformity with the position of the nucleophilic addition to allenes [7].



XI

It is important to note that attempts to realize the rearrangement of terminal acetylene VII or allene X to a disubstituted acetylene were unsuccessful. Polymeric resins are formed in all cases when the reaction is carried out at room temperature in tetrahydrofuran (THF) solution in the presence of potassium hydroxide.

EXPERIMENTAL

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

1-(β-Bromoallyl)benzimidazole (III). A solution of 11.7 g (58 mmole) of 2,3-dibromo-1-propene in 10 ml of ethanol was added dropwise to a vigorously stirred solution of 6.9 g (58 mmole) of benzimidazole V and 3.28 g (58 mmole) of potassium hydroxide in 50 ml of ethanol, and the mixture was stirred at room temperature for 2 h. The resulting precipitate was removed by filtration, and the filtrate was diluted with 50 ml of water and extracted with ether. The ether extract was dried with calcium chloride, the ether was evaporated, and the residue was vacuum distilled to give 11.4 g (82%) of product. The colorless needles, with mp 95-96° (from petroleum ether), had bp 192-193° (11 mm), were quite soluble in chloroform and ethanol, and had limited solubility in ether and benzene. IR spectrum: $\nu_{C=C}$ 1620, ν_{C-Br} 550 cm^{-1}. Found, %: C 50.9; H 4.0; Br 33.6; N 12.0. $C_{10}H_9BrN_2$. Calculated, %: C 50.6; H 3.8; Br 33.8; N 11.8.

1-(α-Bromoallyl)benzimidazole (IV). This compound was similarly obtained from 11.8 g (0.1 mole) of benzimidazole V, 5.6 g (0.1 mole) of potassium hydroxide, and 20 g (0.1 mole) of 1,3-dibromo-1-propene. The yield was 20.1 g (85%). The colorless oil had bp 203-204° (11 mm) and was quite soluble in organic solvents. Found, %: C 50.5; H 4.1; Br 34.0; N 12.1. $C_{10}H_9BrN_2$. Calculated, %: C 50.6; H 3.8; Br 33.8; N 11.8. The picrate was obtained as yellow prisms with mp 192-194° (from ethanol). IR spectrum: $\nu_{C=C}$ 1600, ν_{C-Br} 540 cm^{-1}.

1,3-Di-N-benzimidazolyl)-2-bromopropane (VI). A mixture of 9.44 g (0.08 mole) of benzimidazole V, 5.6 g (0.02 mole) of 1,2,3-tribromopropane, and 30 ml of absolute toluene was refluxed for 8 h. It was then cooled, and the precipitated hydrobromide of V was removed by filtration. The solvent was removed by vacuum distillation, and the residue was chromatographed with a column filled with Al_2O_3 with elution by ether to give 4.5 g (63%) of a colorless oil. The picrate was obtained as yellow prisms with mp 173-175° (from ethanol). Found, %: C 47.0; H 3.3; Br 13.9; N 16.9. $C_{17}H_{15}BrN_4 \cdot C_6H_3N_3O_7$. Calculated, %: C 47.3; H 3.1; Br 13.7; N 16.8.

1-(2-Propynyl)benzimidazole (VII). A) A 2.37-g (0.01 mole) sample of III was added to a solution of 0.46 g (0.02 g-atom) of sodium metal in 50 ml of liquid ammonia, and the mixture was held at −70° for 2 h, after which the ammonia was allowed to evaporate. The residue was treated with 20 ml of water and extracted with ether to give 1.16 g (75%) of product. The picrate had mp 201-202° [4] (from ethanol). IR spectrum: $\nu_{\equiv CH}$ 3310 cm^{-1}.

B) Compound VII was obtained from benzimidazole IV as described in method A. The yield was 72%.

1,6-(Di-N-benzimidazolyl)-2,4-hexadiyne (VIII). A mixture of 0.47 g (3 mmole) of benzimidazole VII and 0.75 g of cuprous chloride in 11 ml of dry pyridine and 3 ml of methanol was shaken in an oxygen atmosphere until oxygen absorption ceased (~2 h). The mixture was then poured into 200 ml of water, and the resulting precipitate was removed by filtration and washed with water to give 0.37 g (80%) of colorless plates with mp 191-192° (dec., from ethanol or methanol), which was soluble in chloroform and acetone. Found, %: C 77.7; H 4.4; N 18.4. $C_{20}H_{14}N_4$. Calculated, %: C 77.4; H 4.5; N 18.1.

1-(4-Diethylamino-2-butynyl)benzimidazole (IX). A mixture of 0.78 g (5 mmole) of VII, 0.3 g of paraformaldehyde, 0.75 ml of diethylamine, and 0.075 g of cuprous chloride in 5 ml of absolute dioxane was refluxed for 4 h. The mixture was then cooled, 20 ml of water was added, and the reaction product was extracted with ether to give 0.86 g (72%) of product. The picrate was obtained as yellow needles with mp 179-180° (from ethanol). Found, %: C 53.4; H 4.6; N 17.8. $C_{15}H_{19}N_3 \cdot C_6H_3N_3O_7$. Calculated, %: C 53.6; H 4.7; N 17.9.

1-Propadienylbenzimidazole (X). A) A 0.47-g (3 mmole) sample of VII in 1 ml of THF was added to a suspension of 0.84 g (15 mmole) of potassium hydroxide (which had been previously calcined and ground to a powder) in 11 ml of absolute THF, and the mixture was stirred at 0° for 2 h. Water (20 ml) was then added, and the reaction product was extracted with ether to give 0.45 g (97%) of a colorless oil that was soluble in organic solvent, insoluble in water, and turned red on storage. The picrate was obtained as yellow prisms with mp 164-165° (from ethanol). Found, %: C 50.0; H 3.2; N 18.3. $C_{10}H_8N_2 \cdot C_6H_3N_3O_7$. Calculated, %: C 49.9; H 2.9; N 18.1.

B) Compound X was similarly obtained from III or IV. The yields were 88.6 and 91.3%, respectively. No melting-point depression was observed for a mixture of the picrates of X obtained by methods A and B.

1-(β-Ethoxyallyl)benzimidazole (XI). A) A 1.2-g (5 mmole) sample of benzimidazole III was added to a solution of 3 g of potassium hydroxide in 15 ml of ethanol, and the mixture was allowed to stand overnight. The precipitate was removed by filtration, the ethanol was evaporated, and the residue was chromatographed with a column filled with Al_2O_3 with elution by ether to give 0.94 g (94%) of a colorless oil that was quite soluble in the ordinary organic solvents and insoluble in water. Found, %: C 71.0; H 7.0; N 13.4. $C_{12}H_{14}N_2O$. Calculated, %: C 71.3; H 6.9; N 13.8. IR spectrum: $\nu_{C=C}$ 1615 cm^{-1}. The picrate was obtained as yellow prisms with mp 168-169° (from ethanol). Found, %: C 50.3; H 3.6; N 16.5. $C_{12}H_{14}N_2O \cdot C_6H_3N_3O_7$. Calculated, %: C 50.1; H 3.9; N 16.2.

B) Compound XI was similarly obtained in 93% yield from IV.

C) A 0.2-g (1.2 mmole) sample of benzimidazole VII in 10 ml of 15% alcoholic potassium hydroxide was heated on a water bath for 1 h. The mixture was cooled, 10 ml of water was added, and the reaction product was extracted with ether to give 0.17 g (85%) of XI. The picrates of the compounds obtained by methods A, B, and C were identical.

LITERATURE CITED

1. V. N. Komissarov and A. M. Simonov, Khim. Geterotsikl. Soedin., 1402 (1974).
2. M. F. Shostakovskii, G. G. Skvortsova, N. P. Glazkova, and E. S. Domnina, Khim. Geterotsikl. Soedin., 1070 (1969).
3. A. F. Pozharskii and A. M. Simonov, Zh. Obshch. Khim., 33, 179 (1963).
4. I. I. Popov, P. V. Tkachenko, and A. M. Simonov, Khim. Geterotsikl. Soedin., 551 (1973).
5. A. M. Simonov and A. F. Pozharskii, Zh. Obshch. Khim., 31, 3970 (1961).
6. C. Moureu, Comptes Rend., 138, 286 (1904).
7. L. R. Byrd and M. C. Caserio, J. Org. Chem., 37, 36 (1972).