LITERATURE CITED

1. L. P. Slesarchuk, V. T. Kolesnikov, and B. V. Boldyrev, Zh. Organ. Khim., 9, 2155 (1973).
2. West German Patent No. 1114194 (1959); Chem. Abstr., 56, 4740 (1962).
3. C. Shellhammer and S. Petersen, Liebigs Ann., 624, 108 (1959).
4. V. Pratt and N. Drake, J. Amer. Chem. Soc., 82, 1155 (1960).
5. T. Urbański and S. Krzyżanowski, Roczniki Chem., 27, 390 (1953).

RESEARCH ON UNSATURATED AZOLE DERIVATIVES

IV.* ALKYLATION OF INDAZOLE WITH PROPARGYL BROMIDE

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The alkylation of indazole with propargyl bromide and 2,3-dibromo-1-propene was investigated. It is shown that the ratio of the resulting isomeric 1- and 2-propargyl indazoles is determined by the reaction conditions. 1-(2'-Propynyl)indazole is readily isomerized in the presence of potassium hydroxide to 1-propadienylindazole.

It is well known that the alkylation of indazoles gives isomeric 1- and 2-alkyl derivatives, the ratio of which depends on the indazole compound and the synthetic conditions [2]. However, the reaction of indazole with unsaturated alkyl halides has not been studied, and only the synthesis of 1-allylindazole has been described [3]. Continuing our research on the synthesis of propargyl-substitited azoles [4, 5], we studied the reaction of indazole with propargyl bromide.

We found that indazole (I) readily reacts with propargyl bromide in liquid ammonia in the presence of sodium amide to give 1- and 2-propargylindazoles II and III in a ratio of 13:3, respectively. Alkylation of the sodium salt of indazole by refluxing it with propargyl bromide in toluene is accompanied by resinification. The ratio of isomers II and III in this case is 5:2. Replacement of the toluene by benzene or tetrahydrofuran (THF) reduces resinification, but it lowers the yields of the reaction products; the ratio of the isomers also changes to favor the formation of isomer II. Refluxing the silver salt of indazole with propargyl bromide in toluene gives a mixture of isomers II and III in a ratio of 6:5. Indazole reacts extremely smoothly with propargyl bromide on refluxing in a neutral medium (ethanol or butanol). In this case exclusively isomer III is formed. Structures II and III were assigned to the isomers obtained in this study on the basis of a comparison of their UV spectra with the spectra of 1-methyl- and 2-methylindazole [6].

The reaction of I with 2,3-dibromo-1-propene in alcoholic alkali gives only 1-(β-bromoallyl)indazole (IV), the dehydrobromination of which with sodium amide in liquid ammonia gives II.

Like 1-propargylbenzimidazole, II is readily isomerized by the action of potassium hydroxide in THF at 0°C to 1-propadienylindazole V, which can also be obtained under these conditions from IV. The IR spectrum of V contains ν_{as} bands at 1960 (−C=C=C−) and 890 cm^{-1} (>C=CH_2 out-of-plane deformation vibrations), which are characteristic for terminal allenes [7].

1-(β-Ethoxyallyl)indazole (VI) is formed in the dehydrobromination of IV in alcoholic potassium hydroxide. The reaction evidently proceeds through the intermediate formation of allene V, the nucleophilic addition of alcohol to which also leads to VI (see [5]). This conclusion is confirmed by the conversion of II and V to VI by the action of alcoholic potassium hydroxide.

*See [1] for communication III.

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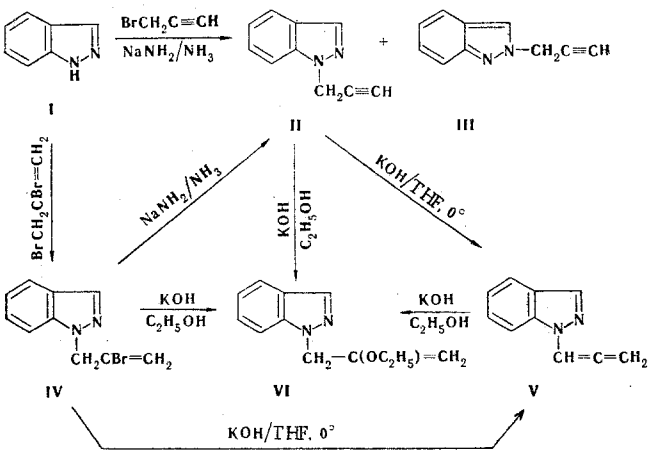

The position of the ethoxy group in structure VI was assigned on the basis of its IR spectrum and data on the addition of nucleophilic reagents to allenes [8].

EXPERIMENTAL

The IR spectra of chloroform solutions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of methanol solutions of the compounds were recorded with an SF-4A spectrophotometer.

Reaction of Indazole with Propargyl Bromide. A) A 0.59-g (5 mmole) sample of I was added to a solution of 0.11 g (5 mg-atom) of sodium metal in 40 ml of liquid ammonia, and 30 min later, a solution of 0.4 ml (5 mmole) of propargyl bromide in 3 ml of absolute ether was added dropwise. The mixture was then held at −70° for 1 h, after which it was allowed to stand at room temperature until the ammonia had evaporated. The residue was treated with 20 ml of water and extracted with ether. The solvent was removed by distillation, and the reaction products (II and III) were separated by chromatography on aluminum oxide (elution with ether) to give 0.51 g (65%) of II as a colorless oil. The picrate was obtained as yellow prisms with mp 128-129° (from ethanol). The yield of III, which was obtained as a colorless oil, was 0.12 g (15.5%). The picrate was obtained as yellow prisms with mp 138-139° (from ethanol). Found: C 49.8; H 2.7; N 17.8%. $C_{10}H_8N_2 \cdot C_6H_3N_3O_7$. Calculated: C 49.9; H 2.9; N 18.1%. A $\nu_{(\equiv CH)}$ band at 3315 cm^{-1} is present in the IR spectra of II and III.

B) A 2.36-g (0.02 mole) sample of I was added to a solution of sodium ethoxide obtained from 0.46 g (0.02 g-atom) of sodium metal and 15 ml of absolute ethanol, after which the alcohol was removed by vacuum distillation, and 20 ml of absolute toluene and 1.6 ml (0.02 mole) of propargyl bromide was added to the residual salt. The reaction mixture was then refluxed for 2 h, and the solid material was removed by filtration. The solvent was removed by distillation, and the residue was chromatographed on aluminum oxide (elution with ether) to give 0.62 g (40%) of II and 0.25 g (16%) of III.

C) A 0.8-ml (0.01 mole) sample of propargyl bromide was added to a suspension of 2.25 g (0.01 mole) of the silver salt of indazole in 15 ml of absolute toluene, and the mixture was refluxed for 3 h. The reaction products were isolated as in method B. The yield of II was 0.4 g (26%), and the yield of III was 0.31 g (20%).

D) A solution of 1.18 g (0.01 mole) of I and 0.8 ml (0.01 mole) of propargyl bromide in 15 ml of ethanol was refluxed on a water bath for 1.5 h. It was then cooled, 50 ml of water was added, and the liberated oil (III) was extracted with ether to give 0.65 g (42%) of product.

1-(β-Bromoallyl)indazole (IV). A solution of 6 g (0.03 mole) of 2,3-dibromo-1-propene in 4 ml of ethanol was added dropwise to a vigorously stirred solution of 3.54 g (0.03 mole) of I and 2 g (0.03 mole) of potassium hydroxide in 40 ml of ethanol, after which the mixture was stirred at room temperature for 1.5 h. The solid material was removed by filtration, and the solvent was removed by distillation. Ether (30 ml) was added to the residue, and the ether solution was dried over sodium sulfate and vacuum distilled to give 5.4 g (76%) of a colorless oil with bp 148-150° (14 mm). IR spectrum: $\nu_{C=C}$ 1630 cm^{-1}. The picrate was obtained as yellow prisms with mp 121-122° (from ethanol). Found: C 40.9; H 2.7; Br 16.8; N 14.7%. $C_{10}H_9N_2Br \cdot C_6H_3N_3O_7$. Calculated: C 41.2; H 2.6; Br 17.1; N 15.1%.

1-(2'-Propynyl)indazole (II). A solution of 2.37 g (0.01 mole) of IV in 5 ml of absolute ether 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 1 h, after which it was allowed to stand at room temperature until the ammonia had evaporated. The residue was treated with 30 ml of water and extracted with ether to give 1 g (68%) of product.

1-Propadienylindazole (V). A) A 1.56-g (0.01 mole) sample of II was added with vigorous stirring to a cooled (to 0°) suspension of 1.7 g (0.03 mole) of potassium hydroxide in 15 ml of THF (or ether), after which the mixture was held at 0° for 1 h. It was then treated with 50 ml of water and extracted with ether to give 1.48 g (95%) of colorless oil that was quite soluble in organic solvents, insoluble in water, and unstable on storage. The picrate was obtained as yellow prisms with mp 174-175° (from ethanol). Found: C 50.2; H 2.5; N 18.0%. $C_{10}H_8N_2 \cdot C_6H_3N_3O_7$. Calculated: C 49.9; H 2.9; N 18.1%.

B) This compound was also obtained in 80% yield from IV by method A.

1-(β-Ethoxyallyl)indazole (VI). A) A solution of 1.2 g (5 mmole) of IV and 2 g of potassium hydroxide in 10 ml of ethanol was held at room temperature for 8 h, after which the solid material was removed by filtration, the solvent was removed by distillation, and the residual oil was chromatographed on Al_2O_3 (elution with ether) to give 1.84 g (91%) of a colorless oil that was quite soluble in ether, chloroform, and acetone but insoluble in water. IR spectrum: $\nu_{C=C}$ 1628 cm^{-1}. The picrate was obtained as yellow needles with mp 179-180° (from ethanol). Found: C 50.5; H 4.5; N 16.6%. $C_{12}H_{14}N_2O \cdot C_6H_3N_3O_7$. Calculated: C 50.1; H 3.9; N 16.2%.

B) This compound was obtained as described in method A from V and potassium hydroxide by gentle heating (at 45-50°) of the reactants. The yield was 88%.

C) Compound VI was obtained by refluxing II in an alcohol solution of potassium hydroxide for 3 h. The yield was 67%.

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

LITERATURE CITED

1. A. A. Zubenko, I. I. Popov, and A. M. Simonov, Khim. Geterotsikl. Soedin., 1544 (1974).
2. R. Elderfield, Heterocyclic Compounds, Vol. 5, Wiley (1950-1957).
3. K. Auwers and W. Schaich, Ber., 54, 1738 (1921).
4. I. I. Popov, P. V. Tkachenko, and A. M. Simonov, Khim. Geterotsikl. Soedin., 551 (1974).
5. P. V. Tkachenko, I. I. Popov, and A. M. Simonov, Khim. Geterotsikl. Soedin., 1540 (1975).
6. Zhao Ér-Chan and M. N. Shchukina, Zh. Obshch. Khim., 1012 (1959).
7. J. H. Wotiz and D. E. Maucuse, J. Org. Chem., 22, 207 (1957).
8. L. R. Byrd and M. C. Caserio, J. Org. Chem., 37, 36 (1972).