SYNTHESIS OF 1-(4-BROMO-1-NAPHTHYL)-DIHYDROURACIL AND SOME OF ITS TRANSFORMATIONS

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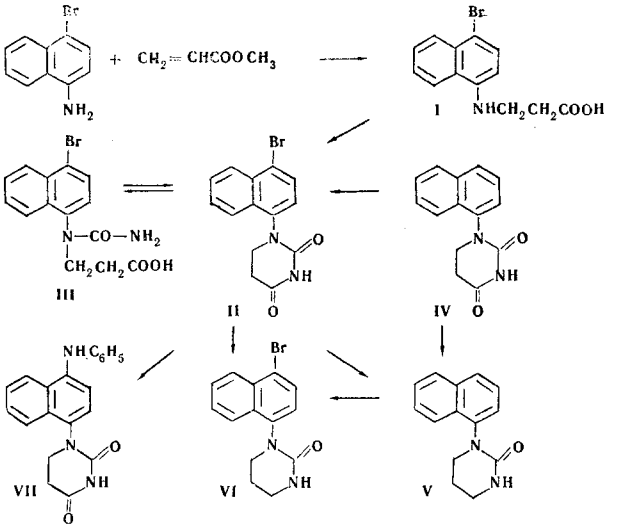
1-(4-Bromo-1-naphthyl)dihydrouracil, which is also obtained from 1-(4-bromo-1-naphthyl)-β-alanine, is formed by the bromination of 1-(1-naphthyl)dihydrouracil. Hydrogenation of 1-(4-bromo-1-naphthyl)dihydrouracil with lithium aluminum hydride yields either 1-(1-naphthyl)-2-oxohexahydropyrimidine or 1-(4-bromo-1-naphthyl)-2-oxohexahydropyrimidine, depending on the solvent used. 1-(4-Bromo-1-naphthyl)-2-oxohexahydropyrimidine is formed by the bromination of 1-(1-naphthyl)-2-oxohexahydropyrimidine.

1-(1-Naphthyl)-5-bromodihydrouracil is obtained by the bromination of 1-(1-naphthyl)dihydrouracil (IV) in acetic acid [1]. However, we have found that the bromine in the bromination product cannot be cleaved by the nucleophilic reagents which are suitable for the dehydrohalogenation of 1-phenyl-5-bromodihydrouracils [1, 2]. Assuming that the bromine is located in the naphthalene ring, we carried out the alternative synthesis of 1-(4-bromo-1-naphthyl)dihydrouracil (II) from 4-bromo-1-naphthylamine.



N-(4-Bromo-1-naphthyl)-β-alanine (I) is obtained by the reaction of the latter with methyl acrylate in the presence of acetic acid with subsequent hydrolysis of the ester thus formed. Compound II, which is identical to the compound synthesized from IV by the method in [1], was then isolated by the method in [3]. Unchanged II is isolated from the bromination of II with bromine in acetic acid, and only the monobromo derivative of II is isolated from the bromination of IV under the same conditions with double the amount of bromine. β-Ureido acid III is isolated from the decyclization of II. From this it can be assumed that the compound that we described in [7] as N-(1-naphthyl)-N-carbamido-α-bromo-β-aminopropionic acid is compound III.

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1-Aryl-2-oxo(thio)hexahydropyrimidines [4-6] are formed by the reduction of 1-aryldihydro- and 1-aryl-2-thiodihydrouracils with lithium aluminum hydride in ether. Reduction of II with lithium aluminum hydride in diethyl ether yielded VI, while the product in tetrahydrofuran was V, which is also formed by the reduction of IV in ether. Compound VI is obtained by the bromination of V with bromine in acetic acid. Phenylamine derivative VII is formed by refluxing II with aniline.

EXPERIMENTAL

N-(4-Bromo-1-naphthyl)-β-alanine (I). A mixture of 11.5 g (0.05 mole) of 4-bromo-1-naphthylamine, 5 ml (0.055 mole) of methyl acrylate, and 0.5 ml of acetic acid was heated in an ampule at 110-115° for 8-10 h. After cooling, the precipitated crystals were filtered and heated for 2 h with 25 ml of 30% NaOH at 100°. The solution was cooled, 50 ml of water was added, and the mixture was filtered. Acidification of the alkaline filtrate with acetic acid yielded I, which was filtered and crystallized from ethanol to give 3.7 g (25%) of a product with mp 137-137.5° (decomp.). Found %: N 4.67, 4.76. $C_{13}H_{12}BrNO_2$. Calculated %: N 4.82.

1-(4-Bromo-1-naphthyl)dihydrouracil (II). A. Compound IV [8] [4 g (1.6 mmole)] was dissolved in 40 ml of acetic acid, 2.4 g of sodium acetate was added, 0.81 ml (1.6 mmole) of bromine in 10 ml of acetic acid was added dropwise with stirring at room temperature, and the mixture was allowed to stand overnight. It was then diluted with water (1:2), and 4.09 g (75.5%) of a substance with mp 275-276° was filtered. Two crystallizations from acetic acid or ethanol gave II with mp 290°. Found %: Br 25.11, 25.55; N 8.77, 8.88. $C_{14}H_{11}BrN_2O_2$. Calculated %: Br 25.35; N 8.77.

B. A mixture of 0.6 g (2.1 mmole) of I, 0.6 g of urea, and 2 ml of acetic acid was heated at 100° for 4 h, 0.6 ml of concentrated HCl was added, and heating was continued for another hour. The crystals which precipitated on cooling were filtered and washed with ether and water to give 0.5 g (77%) of a product with mp 290° (from acetic acid).

C. A mixture of 0.5 g (1.5 mmole) of III and 2 ml of concentrated HCl was heated at 100° for 30 min, cooled, diluted with water (1:1), and 0.45 g (96%) of II with mp 290° was filtered. A sample of this product did not depress the melting point of samples of II obtained via methods A, B, and C, and the IR spectra were identical.

N-4-Bromo-1-naphthyl)-N-carbamido-β-alanine (III). A mixture of 3.19 g (0.01 mole) of II, 30 ml of water, and 0.8 g of KOH was refluxed for 3 h, cooled, and filtered. The filtrate was acidified with acetic acid, and the resulting precipitate was crystallized from ethanol to give 3.3 g (97.6%) of a product with mp 177-178° (decomp.). Found %: N 8.44, 8.49. $C_{14}H_{13}BrN_2O_3$. Calculated %: N 8.31.

1-(1-Naphthyl)-2-oxohexahydropyrimidine (V). A. A solution of 3.0 g (0.08 mole) of lithium aluminum hydride in 150 ml of absolute tetrahydrofuran was heated to boiling with stirring, 6.38 g (0.02 mole of II was added in small portions, and the mixture was refluxed for 4 h. The excess lithium aluminum hydride was decomposed with a moist ethanol–ether mixture, the solvent was removed by distillation, and the residue was dried and extracted with acetone (Soxhlet apparatus). The acetone extract was evaporated to give 2.47 g (54.7%) of V with mp 253.5-255° (from ethanol). Found %: N 12.27, 12.37. $C_{14}H_{14}N_2O$. Calculated %: N 12.37.

B. A total of 9 g (0.0375 mole) of IV was added in small portions to 4 g (0.1 mole) of lithium aluminum hydride in 250 ml of absolute ether, and the mixture was refluxed for 60 h. Compound V [4.5 g (53%)] was isolated as in method A. A sample of this product did not depress the melting point of a sample of V obtained by methods A and B.

1-(4-Bromo-1-naphthyl)-2-oxohexahydropyrimidine (VI). A. A total of 9.6 g (0.03 mole) of II was added in small portions with stirring to a boiling solution of 2 g (0.05 mole) of lithium aluminum hydride in 250 ml of absolute diethyl ether. The mixture was then refluxed for 35 h, and 2.5 g (27.3%) of VI with mp 220-221° (from ethanol) was isolated in the same way as was used to isolate V. Found %: Br 25.89, 26.09; N 9.38, 9.42. $C_{14}H_{13}BrN_2O$. Calculated %: Br 26.18; N 9.18.

B. Compound V [0.45 g (2 mmole)] was dissolved in 5 ml of acetic acid, 0.16 g of sodium acetate was added, and 0.1 ml (2 mmole) of bromine in 1 ml of acetic acid was then added dropwise. The mixture was allowed to stand overnight at room temperature. It was then diluted (1:1) with water, and 0.5 g (82%) of VI was filtered. A sample of this product did not depress the melting point of samples of VI obtained by methods A and B.

1-(4-Anilino-1-naphthyl)dihydrouracil (VII). Compound II [6.38 g (0.02 mole)] was refluxed for 10 h with 25 ml of aniline. The mixture was cooled, treated with ether, and 2.2 g (32.8%) of a product with mp 238.5-239° (from ethanol) was crystallized from ether–petroleum ether (1 : 2). Found %: N 12.77, 12.95. $C_{20}H_{17}N_3O_2$. Calculated %: N 12.68.

LITERATURE CITED

1. N. W. Gabel and S. B. Binkley, J. Org. Chem., 23, 644 (1958).
2. R. S. Baltrushis and I. I. Marioshyus, Khim. Geterotsikl. Soedin., 954 (1968).
3. R. S. Baltrushis and I. I. Marioshyus, USSR Author's Certificate No. 197,595; Byull. Izobr., No. 13 (1967).
4. R. S. Baltrushis, I. I. Marioshyus, and Z. G. Beresnevichyus, USSR Author's Certificate No. 232,269; Byull. Izobr., No. 1 (1969).
5. R. Baltrushis and I. Marioshyus, Khim. Geterotsikl. Soedin., No. 1, 120 (1969).
6. F. J. Marshall, J. Am. Chem. Soc., 78, 3696 (1956).
7. Z. G. Beresnevichyus, I. Marioshyus, and R. Baltrushis, Data from Papers Presented at the 18th Republic Scientific-Technical Conference in Kaunas [in Russian], (1968), p. 71.
8. A. K. Purenas and R. S. Baltrushis, Trudy AN LitSSR, Ser. B., 3(26), 203 (1961).