SYNTHESIS OF 1-(2-NAPHTHYL)DIHYDRO- AND 1-(2-NAPHTHYL)-2-THIODIHYDROURACILS AND THEIR TRANSFORMATIONS

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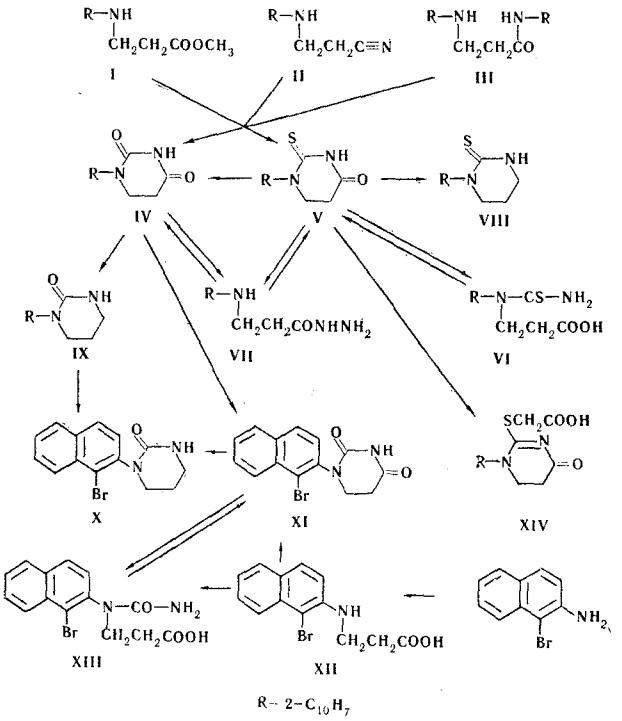
1-(2-Naphthyl)dihydro- and 1-(2-naphthyl)-2-thiodihydrouracils were obtained from N-(2-naphthyl)-β-alanine derivatives. The thiodihydrouracil was converted to a dihydrouracil. Bromination of 1-(2-naphthyl)dihydrouracil gave (1-bromonaphthyl)dihydrouracil. 1-(2-Naphthyl)-2-oxo-, 1-(2-naphthyl)-2-thio-, and 1-(1-bromo-2-naphthyl)-2-oxohexahydropyrimidines were obtained.

It is known that 1-substituted dihydro- and 2-thiodihydrouracils have a heat-stabilizing action on polycapramide [1, 2], and they can also be used as azo components [3].

In [4], one of us obtained 1-(2-naphthyl)dihydro- (IV) and 1-(2-naphthyl)-2-thiodihydrouracils (V) in 20-30% yields from N-(2-naphthyl)-β-alanine by the reaction of the latter with urea or potassium thiocyanate. The synthesis was then improved, and the yields of 1-aryldihydro- and 1-aryl-2-thiodihydrouracils were raised to 40-67% [5].



In the present study, IV and V were obtained from methyl ester I in ~85% yields. Dihydrouracils IV and V were also obtained by the same method from other β-alanine derivatives (II, III, and VII).

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Oxidation of thiodihydrouracil V with hydrogen peroxide converts it to dihydrouracil IV, while reaction with monochloroacetic acid gives carboxymethylthio derivative XIV.

Under the influence of alkalis [6], V is converted to thioureido acid VI, which forms V by the action of hydrochloric acid or heat. Hydrazide VII was obtained by the action of hydrazine on IV and V.

The keto group in the 4 position is subjected to the action of the reducing agent in the reduction of hydrouracils IV and V with lithium aluminum hydride in ether [7, 8], and the corresponding hexahydropyrimidines (IX and VIII) are formed. Bromination of 1-(2-naphthyl)-2-oxohexahydropyrimidine (IX) with bromine gives 1-(1-bromo-2-naphthyl)-2-oxohexahydropyrimidine (IX), which is also formed by the action of $LiAlH_4$ on XI. Compound XI was synthesized alternatively to prove its structure. The reaction of 1-bromo-2-aminonaphthalene with methyl acrylate and subsequent hydrolysis of the resulting methyl ester on N-(1-bromo-2-naphthyl)-β-alanine gave alanine XII, which was converted to 1-(1-bromo-2-naphthyl)-dihydrouracil (XI) by the method in [5]. Compound XI is decyclized during alkaline hydrolysis to form the corresponding β-ureido acid (XIII), which is converted to XI under the influence of hydrochloric acid.

The IR spectra of VIII and IX contain characteristic absorptions at 3235 and 3300 cm^{-1}, which correspond to the stretching vibrations of the NH groups in the presence of hydrogen bonds [9]. The bands at 1660 cm^{-1} correspond to the stretching vibrations of the C=O group of IX, the band at 1195 cm^{-1} corresponds to the C=S group of VIII, and the band at 1300-1310 cm^{-1} corresponds to the "tertiary amide" group.

EXPERIMENTAL

1-(2-Naphthyl)dihydrouracil (IV). A) A mixture of 11.46 g (0.05 mole) of I, 12 g (0.2 mole) of urea, and 20 ml of acetic acid was heated at 100° for 3 h, 6.5 ml of concentrated hydrochloric acid was added, and the mixture was heated for another 3 h at 120°. The mixture was cooled and filtered to give 9.7 g (85%) of a product with mp 242-243° (from acetic acid).

B) Compound IV (42-50%) was obtained via method A from 0.01 mole of II, III, or VII, 0.02 mole of urea, 6 ml of acetic acid, and 1.5 ml of hydrochloric acid.

C) A total of 3 ml of 30% H_2O_2 was added to a refluxing solution of 5.1 g (0.02 mole) of V in 100 ml of acetic acid, and the mixture was refluxed for 15 min. The hot solution was filtered, cooled, and diluted with water (to 1 : 2) to give 4.0 g (85%) of IV.

The samples of IV obtained by methods A-C did not depress the melting point of an authentic sample [10].

1-(2-Naphthyl)-2-thiodihydrouracil (V). A) Compound V [10.25 g (83%)] with mp 245-246° (from acetic acid) was similarly obtained via method A from 11.46 g (0.05 mole) of I, 7.6 g (0.1 mole) of ammonium thiocyanate, and 25 ml of acetic acid.

B) Compound V (30-60%) was obtained via method A from 0.01 mole of II, III, or VII, 2g of KCNS, 6 ml of acetic acid, and 5 ml of concentrated hydrochloric acid.

C) A mixture of 1.38 g (5 mmole) of VI and 5 ml of concentrated hydrochloric acid was heated at 100° for 10 min to give 1.21 g (96%) of V.

Samples of V obtained via methods A-C did not depress the melting point of a genuine sample [10].

N-(2-Naphthyl)-N-thiocarbamido-β-alanine (VI). A mixture of 2.56 g (0.01 mole) of V and 20 ml of 10% NaOH was allowed to stand overnight. It was then filtered and acidified with acetic acid. The precipitate was crystallized from 30% ethanol to give 2.3 g (85%) of a product with mp 109° (dec.). Found: N 10.3%. $C_{14}H_{14}N_2O_2$. Calculated: N 10.2%.

N-(2-Naphthyl)-β-alanine Hydrazide (VII). A) A mixture of 3 g (0.012 mole) of V, 25 ml of 25% hydrazine, and 10 ml of dioxane was refluxed for 7 h. It was then cooled, and water was added. The resulting crystals were removed by filtration to give 1.2 g (52%) of a product with mp 148.5-149° (from dioxane–benzene). Found: N 18.2; 18.5%. $C_{13}H_{15}N_3O$. Calculated: N 18.3%.

B) Compound VII [1.15 g (60%)] was similarly obtained from 2 g (8.4 mmole) of IV, 20 ml of 25% hydrazine, and 10 ml of dioxane. This product did not depress the melting point of the compound obtained via method A.

1-(2-Naphthyl)-2-thiohexahydropyrimidine (VIII). A total of 13 g (0.05 mole) of V was added in small portions to a solution of 2.5 g (0.066 mole) of $LiAlH_4$ in 200 ml of absolute ether, and the mixture was refluxed for 40 h and cooled. The excess $LiAlH_4$ was decomposed with ethanol–ether, the solvents were removed by distillation, and the residue was extracted with acetone. The acetone was removed by distillation, and the residue was crystallized from ethanol to give 10.8 g (87%) of a product with mp 207-207.5°. Found: C 69.8; 69.8; H 5.8; 5.8; N 11.5; 11.5%. $C_{14}H_{14}N_2S$. Calculated: C 69.4; H 5.8; N 11.5%.

1-(2-Naphthyl)-2-oxohexahydropyrimidine (IX). Compound IX [2.9 g (34%)] with mp 179.5-180° (from ethanol) was similarly obtained from 9 g (0.04 mole) of IV and 2 g of $LiAlH_4$ in 200 ml of ether. Found: N 12.5; 12.6%. $C_{14}H_{14}N_2O$. Calculated: N 12.4%.

1-(1-Bromo-2-naphthyl)-2-oxohexahydropyrimidine (X). A) A solution of 0.1 ml (2 mmole) of bromine in 1 ml of acetic acid was added to a solution of 0.45 g (2 mmole) of IX in 10 ml of acetic acid. After 7 h, the mixture was filtered and diluted with water (to 3 : 1). The precipitated X was removed by filtration to give 0.42 g (69%) of a product with mp 236.5-237.5° (from ethanol). Found: Br 26.3; 26.4; N 9.3; 9.4%. $C_{14}H_{13}BrN_2O$. Calculated: Br 26.2; N 9.2%.

B) Compound X [0.9 g (20%)] was obtained as in the case of IX from 6.35 g (0.02 mole) of XI by reduction with $LiAlH_4$ in ether (26 h).

The sample of X obtained by method B did not depress the melting point of the product of method A.

1-(1-Bromo-2-naphthyl)dihydrouracil (XI). A) A solution of 1.1 ml (0.021 mole) of bromine in 10 ml of acetic acid was added dropwise with stirring at 18-20° to 5 g (0.021 mole) of IV and 1.7 g of sodium acetate in 50 ml of acetic acid, and the mixture was allowed to stand for 2 days. The precipitated crystals were removed by filtration to give 4.55 g (68%) of a product with mp 292° (from acetic acid). Found: Br 25.1; 25.3; N 8.9; 9.0%. $C_{14}H_{11}BrN_2O_2$. Calculated: Br 25.3; N 8.8%.

B) Compound XI [0.22 g (69%)] was obtained as in the case of IV (method B) from 0.29 g (1 mmole) of XII, 0.25 g of urea, 0.75 ml of acetic acid, and 0.6 ml of concentrated hydrochloric acid.

C) A mixture of 0.5 g (1.5 mmole) of XIII and 2.5 ml of concentrated hydrochloric acid was heated at 100° for 10-15 min to give 0.42 g (89%) of XI.

No depression of the melting points was observed with mixtures of the samples of XI prepared by methods A-C.

N-(1-Bromo-2-naphthyl)-β-alanine (XII). A mixture of 11.5 g (0.05 mole) of 1-bromo-2-aminonaphthalene, 5 ml (0.055 mole) of methyl acrylate, and 0.5 ml of acetic acid was heated in an ampul at 115° for 12 h. The contents were then dissolved in 50 ml of ethanol, 40 ml of 30% NaOH was added, and the mixture was heated at 80-90° for 2 h. It was then cooled, filtered, and acidified with acetic acid to give 4.2 g (27%) of XII with mp 149.5-150° (from ether–petroleum ether). Found: Br 27.2; N 4.9%. $C_{13}H_{12}BrNO_2$. Calculated: Br 27.2; N 4.8%.

N-(1-Bromo-2-naphthyl)-N-carbamido-β-alanine (XIII). A mixture of 3.1 g (0.01 mole) of XI, 30 ml of ethanol, and 0.7 g of KOH was refluxed for 2 h. It was then cooled, 30 ml of water was added, and the mixture was acidified with acetic acid to give 2.93 g (87%) of a product with mp 175-175.5° (dec., from ethanol). Found: Br 23.9; N 8.3%. $C_{14}H_{13}BrN_2O_3$. Calculated: Br 23.7; N 8.3%.

1-(2-Naphthyl)-2-carboxymethylthio-4-oxo-1,4,5,6-tetrahydropyrimidine (XIV). Sodium acetate (7.2 g) was added to a solution of 2.5 g (0.01 mole) of V in 60 ml of acetic acid, a solution of 2 g of monochloroacetic acid in 10 ml of acetic acid was added in the course of 30 min, and the mixture was heated at 100° for 30 min. It was then cooled and filtered to give 1.2 g of the starting V. The filtrate was evaporated in vacuo, and the residue was recrystallized from ethanol–ether (1 : 1) to give 1.95 g (62%) of a product with mp 184.8-185.4°. Found: C 61.1; H 4.5; N 8.7%. $C_{16}H_{14}N_2O_3$. Calculated: C 61.1; H 4.4; N 8.9%.

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