# NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES. CXXXV.*

## N-SUBSTITUTION OF 5-BROMO-6-AZAURACIL AND 5-BROMOURACIL

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Cyanoethylation of 5-bromo-6-azauracil (*I*) in aqueous triethylamine at room temperature affords 5-bromo-1-(2-cyanoethyl)-6-azauracil (*II*). 5-Bromo-1-(2-cyanoethyl)uracil (*VII*) is obtained from 5-bromouracil (*VI*) by an analogous procedure in the presence of alkali. Cyanoethylation of compound *I* in aqueous pyridine at an elevated temperature and prolonged reaction period of time affords 5-bromo-1,3-bis(2-cyanoethyl)-6-azauracil (*III*). 5-Bromo-1,3-bis(2-cyanoethyl)-uracil (*VIII*) is formed by cyanoethylation of compound *VI* in aqueous triethylamine in the absence of alkali. Partial decyanoethylation of compound *VIII* with sodium methoxide in methanol affords the monocyanoethyl derivative *XI*. Total decyanoethylation of both monocyanoethyl derivatives *VII* and *XI* as well as the bis(cyanoethyl) derivative *VIII* with excess sodium methoxide leads to compoud *VI*. Benzylation of compoud *I* with one mol of benzyl chloride in dilute aqueous sodium hydroxide affords 5-bromo-3-benzyl-6-azauracil (*V*). Benzylation with two mol of benzyl chloride leads to the formation of 5-bromo-1,3-dibenzyl-6-azauracil (*XII*). Benzylation of compound *VI* with both one and two mol of benzyl chloride affords exclusively 5-bromo-1,3-dibenzyluracil (*XIV*). Reaction of compound *XIV* with sodium methoxide leads to 5-methoxy-1,3-dibenzyluracil (*XV*) while with dilute aqueous sodium hydroxide degradation occurs under the formation of 1,3-dibenzylurea (*XVIII*).

As reported in an earlier paper[1] of this Series, cyanoethylation of 6-azauracil in aqueous triethylamine affords 1-(2-cyanoethyl)-6-azauracil; 1,3-bis(2-cyanoethyl)-6-azauracil is formed on refluxing with an excess of acrylonitrile. Cyanoethylation of uracil, 2-thiouracil, and their 5-methoxy derivatives does not proceed selectively, leading to a mixture of mono- and bis(cyanoethyl) derivatives. Norwithstanding, in the presence of alkali, pure 1-(2-cyanoethyl) derivatives were obtained[2]. The corresponding 3-(2-cyanoethyl) derivatives are formed by partial decyanoethylation of 1,3-bis(2-cyanoethyl) derivatives while in the 6-azauracil series the partial decyanoethylation of 1,3-bis(2-cyanoethyl) derivatives affords 1-(2-cyanoethyl)-6-azauracil[3]. Thus, the partial decyanoethylation takes place at position 3 in the latter case and

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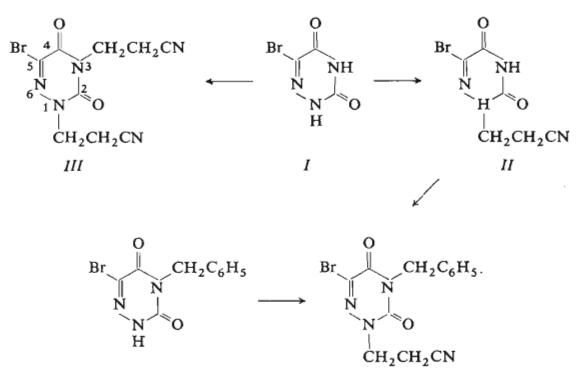
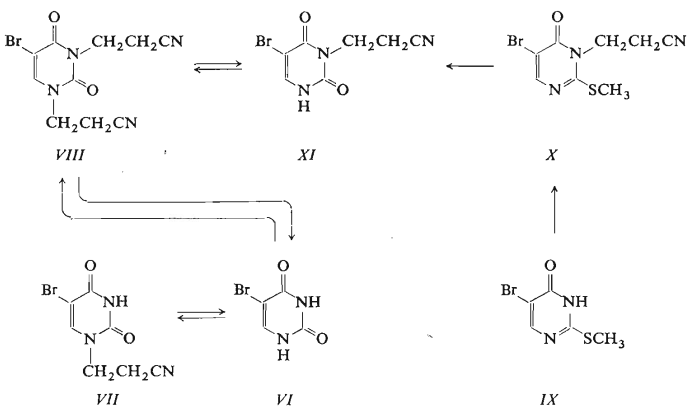
at position 1 in the former. In all cases, the total decyanoethylation led to the parent compounds. As an approach to the preparation of some further alkyl and glycosyl derivatives of 6-azauracil and uracil substituted at position 5, we wish to report in the present paper the cyanoethylation and benzylation of 5-bromo-6-azauracil (*I*) and 5-bromouracil (*VI*).

Reaction of compound *I* with excess acrylonitrile in aqueous triethylamine at room temperature affords the monocyanoethyl derivative *II* the benzylation of which leads to 5-bromo-3-benzyl-1-(2-cyanoethyl)-6-azauracil (*IV*), identical with a specimen obtained by cyanoethylation of 5-bromo-3-benzyl-6-azauracil (*V*). Consequently, the monocyanoethyl derivative *II* possesses the structure of 5-bromo-1-(2-cyanoethyl)-6-azauracil. In contrast to the cyanoethylation of 6-azauracil[2], the addition of alkali or the use of the sodium salt of 5-bromo-6-azauracil does not exert any influence on the reaction course. Consequently, the nucleophilicity of nitrogen atom at position 1 must be considerably higher than that at position 3. Due to the inductive effect of bromine atom at position 5, electrons are withdrawn from the carbonyl group carbon atom at position 4. Consequently, an increased interaction may be assumed between the loose electron pair at the nitrogen atom in position 3 and the carbonyl group in position 4. This assumption is unequivocally confirmed by the cyanoethylation to the second degree. In contrast to 6-azauracil[1] and uracil[2], the additional cyanoethylation of 5-bromo-6-azauracil (*I*) is difficult. Thus, in the preparation of the corresponding 5-bromo-1,3-bis(2-cyanoethyl)-6-azauracil (*III*), compound *I* has to be refluxed for 20 hours in an excess of acrylonitrile and in the presence of aqueous pyridine. The 1,3-bis(2-cyanoethyl) derivative *III* is obtained also by the additional cyanoethylation of the monocyanoethyl derivative *II* under analogous conditions.



Reaction of 5-bromouracil (*VI*) with excess acrylonitrile in aqueous triethylamine and in the presence of alkali affords at room temperature the monocyanoethyl derivative *VII*. On the other hand in the absence of sodium hydroxide under otherwise the same conditions, 5-bromo-1,3-bis(2-cyanoethyl)uracil (*VIII*) is exclusively formed. The course of cyanoethylation is thus identical with that of uracil and its derivatives[2]. Contrarily, the cyanoethylation of 6-azauracil[1] and 5-bromo-6-azauracil proceeds selectively at position 1 even in the absence of alkali. Consequently, the nucleophilicity difference of nitrogen atoms at position 1 and 3 is low both with uracil[2] and 5-bromouracil (*VI*).

Partial decyanoethylation of 5-bromo-1,3-bis(2-cyanoethyl)-uracil (*VIII*) with dilute methanolic sodium methoxide affords the monocyanoethyl derivative *XI* which is different from the monocyanoethyl derivative *VII*. The structure of compound *XI* was verified by cyanoethylation of 5-bromo-2-methylthiouracil (*IX*; prepared by bromination of 2-methylthiouracil[4]) in aqueous pyridine leading to 5-bromo-2-methylthio-3-(2-cyanoethyl)-uracil (*X*) the reflux of which in dilute hydrochloric acid afforded the identical substance *XI*, namely, 5-bromo-3-(2-cyanoethyl)-uracil. Consequently, the structure of the monocyanoethyl derivative *VII* is that of 5-bromo-1-(2-cyanoethyl)uracil. These assumptions are in accordance with results of a further cyanoethylation of monocyanoethyl derivatives *VII* and *XI* (prolonged heating in aqueous triethylamine or aqueous pyridine) under the formation of the same bis(cyanoethyl) derivative *VIII*. The course of partial decyanoethylation of 5-bromo-1,3-bis(2-cyanoethyl)uracil is analogous to that of uracil bis(cyanoethyl) derivative[3] but differs from partial decyanoethylation of 6-azauracil bis(cyanoethyl)




*VIII* *XI* *X*

*VII* *VI* *IX*

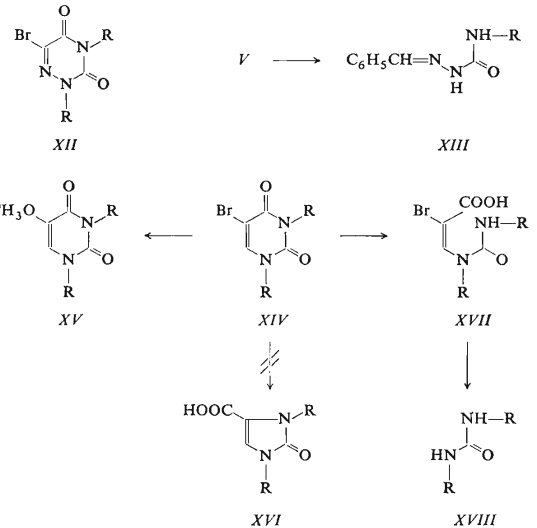
derivative. With the use of excess sodium methoxide and a longer reaction period, each of the monocyanoethyl derivatives *VII* and *XI* or the bis(cyanoethyl) derivative *VIII* suffers a total decyanoethylation under the formation of the starting 5-bromouracil (*VI*). Consequently, the reversible removal of the 2-cyanoethyl group may be also used in the 5-bromouracil series.

The reaction of 5-bromo-6-azauracil (*I*) with 1 mol of benzyl chloride in dilute aqueous sodium hydroxide affords 5-bromo-3-benzyl-6-azauracil (*V*). It may be seen that benzylation occurs under the above conditions at position 3 while the position 1 is involved in the case of 6-azauracil[5] itself. Benzylation of 5-bromo-6-azauracil sodium salt also differs from that of 6-azauracil sodium salt[6]. In ethylene glycol as solvent, the former salt affords a mixture consisting predominantly of 5-bromo-1,3-dibenzyl-6-azauracil (*XII*) while the latter salt affords under analogous conditions exclusively 3-benzyl-6-azauracil (*V*). Position of the benzyl group in the monobenzyl derivative *V* was unequivocally confirmed by ring cleavage with 1M-NaOH under the formation of 4-benzylsemicarbazide[5] which was isolated in the form of the benzylidene derivative *XIII*. Reaction of compound *I* with two mol of benzyl chloride in dilute aqueous sodium hydroxide affords the derivative *XII*. The same product is obtained by an additional benzylation of the monobenzyl derivative *V*. The attempted preparation of 5-bromo-1-benzyl-6-azauracil by a direct benzylation failed. Benzylation of 5-bromouracil (*VI*) in dilute aqueous sodium hydroxide affords under analogous conditions exclusively 5-bromo-1,3-dibenzyluracil (*XIV*). The attempted preparation of pure 1-benzyl and 3-benzyl derivatives by a direct benzylation with one mol of benzyl chloride failed both in aqueous and anhydrous media. Consequently, the difference in nucleophilicity of two nitrogen atoms in 5-bromouracil (*VI*) is too, small to ensure a selective reaction in contrast to 5-bromo-6-azauracil (*I*).

Contrary to 5-bromo-1,3-bis(2-cyanoethyl)-6-azauracil[5], the 5-bromo-1,3-bis(2-cyanoethyl)uracil (*VIII*) does not undergo under analogous conditions by the action of sodium methylate the nucleophilic substitution of the bromo atom by the methoxy group. The lower reactivity of the bromo atom in compound *VIII* does not surprise because of a decrease of the positive charge at carbon 5 by an interaction of the free electron pair on nitrogen atom at position 1 with the carbonyl group at position 4 through the mediation of the double bond between carbon atoms 6 and 5. Such an interaction is absent in the case of the 6-aza compound, namely, 5-bromo-1,3-bis(2-cyanoethyl)-6-azauracil. On the contrary, in the latter compound an opposite polarisation is preferred of the double bond between the carbon atom at position 5 and the nitrogen atom at position 6 leading to an increase of the positive charge at the carbon atom 5.

Under analogous conditions, 5-methoxy-1,3-dibenzyluracil (*XV*) is obtained from 5-bromo-1,3-dibenzyluracil (*XIV*). In contrast to 5-bromo-1,3-dibenzyl-6-azauracil[5] (*XII*), compound *XIV* does not undergo ring-contraction (formation of a five-membered ring) in spite of the fact that such a contraction has been observed with

some uridine derivatives[7]. This finding is in accordance with our earlier idea[5] that the contraction of this system depends both on the magnitude of the positive charge on the carbon atom at position 5 and on the character of substituents at positions 1 and 3.




In formulae *XII*–*XVIII*, R = $CH_2C_6H_5$

By the action of dilute aqueous sodium hydroxide, the ring of compound *XIV* is opened between the positions 3 and 4. The ring opening to compound *XVII* is followed by degradation to 1,3-dibenzylurea (*XVIII*). On the other hand, the ring opening of 5-bromo-1,3-dibenzyl-6-azauracil[5] (*XII*) between positions 3 and 4 is followed by an intramolecular nucleophilic substitution between the terminal nitrogen atom of the carbamoyl group and the carbon atom bearing the bromo atom. An analogous intramolecular nucleophilic substitution under the formation of the five-membered ring compound *XVI* cannot occur in the case of compound *XIV* because of a decreased positive charge at the carbon atom bearing the bromo substituent, owing to an interaction of the free electron pair at the nitrogen atom and the carboxylic group of compound *XVII*. Instead of a recyclisation, the bromo atom of compound *XVII* is substituted by a hydroxy group; this substitution is then followed by degradation to the urea derivative *XVIII*.

It may be seen from comparison of some reactions of 6-azauracil derivatives and uracil derivatives that the presence of a third nitrogen atom at position 6 of the former compounds considerably increases the nucleophilicity of the nitrogen atom at position 1 and hence the selectivity of reactions proceeding at nitrogen atoms or under their participation.

## EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler-block). Analytical samples were dried at 60°C/20 Torr.

5-Bromo-1-(2-cyanoethyl)-6-azauracil (*II*)

A mixture of 5-bromo-5-azauracil (*I*; 9·6 g; 0·05 mol), water (40 ml), triethylamine (40 ml), and excess acrylonitrile (15 ml) was stirred at room temperature for 6 hours, kept overnight, and evaporated on a steam bath under diminished pressure. The residue was diluted with water (200 ml), acidified with dilute (1 : 1) hydrochloric acid to pH 4, the solution filtered while hot (active charcoal), and the filtrate allowed to cool. The precipitate was collected with suction and recrystallised from water (235 ml) to yield 10·5 g (77·5%) of compound *II*,, m.p. 212—214°C. For $C_6H_5BrN_4O_2$ (245·0) calculated: 29·40% C, 2·05% H, 22·86% N; found: 29·50% C, 2·12% H, 22·63% N.

5-Bromo-1,3-bis(2-cyanoethyl)-6-azauracil (*III*)

*A*. A mixture of 5-bromo-6-azauracil (*I*; 9·6 g; 0·05 mol), water (40 ml), pyridine (40 ml), and excess acrylonitrile (20 ml) was refluxed for 20 hours, evaporated to dryness under diminished pressure, and the residue recrystallised (active charcoal) from water (1250 ml). An additional recrystallisation from water afforded 13·15 g (88·5%) of compound *III*, m.p. 143—145°C. For $C_9H_8BrN_5O_2$ (298·1) calculated: 36·26% C, 2·70% H, 26·80% Br, 23·49% N; found: 36·01% C, 2·60% H, 26·69% Br, 23·31% N.

*B*. 5-Bromo-1-(2-cyanoethyl)-6-azauracil (*II*, 2·45 g; 0·01 mol) afforded by an analogous procedure 2·55 g (85·6%) of compound *III*, m.p. 144—145°C (water), undepressed on admixture with a specimen obtained by procedure *A*.

5-Bromo-3-benzyl-1-(2-cyanoethyl)-6-azauracil (*IV*)

*A*. A refluxing mixture of water (100 ml), 5-bromo-1-(2-cyanoethyl)-6-azauracil (*II*; 4·9 g; 0·02 mol), and benzyl chloride (6·36 g; 0·05 mol) was treated dropwise under stirring over one hour with a solution of sodium hydroxide (2 g; 0·05 mol) in water (50 ml) and then refluxed for additional 5 hours. During this period of time, there was added 10 ml of 0·5M-NaOH. The resulting solution was cooled down to 20°C and the oily product extracted with benzene (70 ml). The extract was washed with water (40 ml) and evaporated to dryness from a steam bath under diminished pressure. The residue was recrystallised twice from 50% aqueous ethanol (30 ml) to afford 4·79 g (71·5%) of compound *IV*, m.p. 104—106°C. For $C_{13}H_{11}BrN_4O_4$ (335·2) calculated: 46·58% C, 3·31% H, 23·84% Br, 16·71% N; found: 46·37% C, 3·22% H, 23·65% Br, 16·56% N.

*B*. A mixture of 5-bromo-3-benzyl-6-azauracil (*V*; 2·82 g; 0·01 mol), triethylamine (20 ml), acrylonitrile (10 ml), and water (20 ml) was stirred at room temperature for 20 hours, evaporated under diminished pressure, the residue acidified with dilute (1 : 1) hydrochloric acid to pH 4,

and recrystallised twice from ethanol (30 ml) to afford 2·46 g (73·4%) of compound *IV*, m.p. 105—107°C, undepressed on admixture with a specimen obtained by procedure *A*.

5-Bromo-1-(2-cyanoethyl)uracil (*VII*)

Into a solution of sodium hydroxide (1 g; 0·025 mol) in water (100 ml) there was added 5-bromouracil (*VI*; 4·77 g; 0·025 mol), triethylamine (16 ml), and excess acrylonitrile (2·65 g; 0·05 mol). The mixture was stirred at room temperature for 8 hours and filtered (active charcoal) at 50°C. After cooling to 10°C, the filtrate was acidified with dilute hydrochloric acid to pH 2, the precipitate collected with suction, and recrystallised from water (200 ml) to afford 4·42 g (72·5%) of compound *VII*, m.p. 232—234°C. For $C_7H_6BrN_3O_2$ (244·0) calculated: 34·45% C, 2·47% H, 32·74% Br, 17·22% N; found: 34·28% C, 2·49% H, 32·61% Br, 17·01% N.

5-Bromo-1,3-bis(2-cyanoethyl)uracil (*VIII*)

A mixture of 5-bromouracil (*VI*; 4·77 g; 0·025 mol), water (20 ml), triethylamine (20 ml), and excess acrylonitrile (7 ml) was stirred at room temperature for 8 hours and then kept overnight. The precipitate was collected with suction, washed with water, and recrystallised from water to afford 5·57 g (75%) of compound *VIII*, m.p. 167—168°C. For $C_{10}H_9BrN_4O_2$ (297·1) calculated: 40·42% C, 3·05% H, 26·96% Br, 18·89% N; found: 40·51% C, 3·10% H, 26·83% Br, 18·72% N.

5-Bromo-2-methylthio-3-(2-cyanoethyl)uracil (*X*)

A mixture of 5-bromo-2-methylthiouracil (*XI*; 4·42 g; 0·02 mol), pyridine (80 ml), water (80 ml), and excess acrylonitrile (20 ml) was refluxed for 8 hours, evaporated to dryness under diminished pressure, and the residue recrystallised from ethanol (80 ml) to afford 4·11 g (75%) of compound *X*, m.p. 127—129°C. For $C_8H_8BrN_3OS$ (274·1) calculated: 35·05% C, 2·94% H, 29·14% Br, 15·32% N, 11·68% S; found: 34·98% C, 2·86% H, 29·01% Br, 15·13% N, 11·49% S.

5-Bromo-3-(2-cyanoethyl)uracil (*XI*)

*A*. 5-Bromo-1,3-bis(2-cyanoethyl)uracil (*VIII*; 5·94 g; 0·02 mol) was refluxed for 4 hours in methanolic sodium methoxide, prepared from 1·38 g of sodium (0·06 gramatom) and methanol (100 ml). The resulting solution was neutralised with hydrochloric acid to pH 7, evaporated to dryness under diminished pressure, the residue diluted with 50% aqueous ethanol (25 ml), the solution acidified with hydrochloric acid to pH 4, and filtered while hot. Recrystallisation from 50% aqueous ethanol afforded 3·41 g (70%) of compound *XI*, m.p. 176—178°C. For $C_7H_6BrN_3O_2$ (244·0) calculated: 34·45% C, 2·47% H, 32·74% Br, 17·22% N; found: 34·38% C, 2·42% H, 32·65% Br, 17·08% N.

*B*. A mixture of 5-bromo-2-methylthio-3-(2-cyanoethyl)uracil (*X*; 2·74 g; 0·01 mol) and 3% aqueous hydrochloric acid (40 ml) was refluxed for 5 minutes, filtered, and the filtrate allowed to crystallise. The precipitate was collected with suction and recrystallised from water (20 ml) to afford 1·65 g (68%) of compound *XI*, m.p. 166—168°C, undepressed on admixture with a specimen obtained by procedure *A*.

*Decyanoethylation*. Compound *XI* (2·44 g; 0·01 mol) was refluxed for 8 hours in methanolic sodium methoxide, prepared from sodium (0·92 g; 0·04 gramatom) and methanol (40 ml). The reaction mixture was acidified with hydrochloric acid to pH 7, evaporated to dryness under diminished pressure, the residue diluted with water (50 ml), the solution acidified with hydrochloric acid to pH 2, and the precipitate recrystallised from water to afford 1·27 g (69%) of com-

pound *VI*, m.p. 315–318°C, undepressed on admixture with an authentic specimen[8]. 5-Bromo-1-(2-cyanoethyl)uracil (*VII*) and 5-bromo-1,3-bis(2-cyanoethyl)-uracil (*III*) afforded by an analogous procedure 71% and 67%, resp., of compound *VI*.

5-Bromo-3-benzyl-6-azauracil (*V*)

Benzyl chloride (3·18 g; 0·025 mol) was added dropwise to a solution of compound *I* (4·8 g; 0·025 mol) in aqueous sodium hydroxide, prepared from 1 g (0·025 mol) of sodium hydroxide and 60 ml of water. The mixture was refluxed under stirring on a steam bath for 4 hours, then stirred at room temperature for one hour, and finally cooled down to 10°C. The precipitate was collected with suction and recrystallised from 50% aqueous ethanol (60 ml). After an additional crystallisation there was obtained 5·95 g (84·5%) of compound *V*, m.p. 150–152°C. For $C_{10}H_8BrN_3O_2$ (282·1) calculated: 42·57% C, 2·85% H, 28·32% Br, 14·89% N; found: 42·71% C, 2·73% H, 28·19% Br, 14·71% N.

5-Bromo-1,3-dibenzyl-6-azauracil (*XII*)

*A*. Benzyl chloride (7·62 g; 0·06 mol) was added dropwise to a solution of compound *I* (4·8 g; 0·025 mol) in aqueous sodium hydroxide, prepared from 2·4 g of sodium hydroxide (0·06 mol) and 120 ml of water. The mixture was heated on a steam bath for 4 hours and then adjusted at room temperature to pH 7 by the addition of aqueous sodium hydroxide. The precipitate was collected with suction at 10°C and recrystallised from 50% aqueous ethanol (250 ml). An additional crystallisation afforded 7·7 g (83%) of compound *XII*, m.p. 130–132°C. For $C_{17}H_{14}BrN_3O_2$ (372·2) calculated: 54·88% C, 3·78% H, 21·47% Br, 11·29% N; found: 54·69% C, 3·70% H, 21·39% Br, 11·08% N.

*B*. A solution of compound *I* (9·6 g; 0·05 mol) in aqueous sodium hydroxide (2 g; 0·05 mol; and 50 ml of water) was treated portionwise at 50°C with ethanol (350 ml) and cooled down to 10°C. The precipitate was collected with suction and dried at 60°C to afford 8·3 g (88·5%) of the sodium salt of 5-bromo-6-azauracil which did not melt up to 300°C. A mixture of this salt (4·28 g; 0·02 mol), ethylene glycol (50 ml), and benzyl chloride (2·54 g; 0·02 mol) was heated for 4 hours at 120°C. The reaction mixture was then diluted at 50°C with water (200 ml) and brought to pH 9 by the addition of aqueous sodium hydroxide. The precipitate was collected with suction and recrystallised from 50% aqueous ethanol to afford 3·3 g (45%) of compound *XII*, m.p. 129 to 131°C, undepressed on admixture with the specimen obtained by procedure *A*. The alkaline filtrate was acidified with hydrochloric acid to pH 3, the precipitate collected with suction, and recrystallised from 50% aqueous ethanol to afford 0·5 g of a substance showing an unsharp melting point. As shown by chromatography, the by-product contained a small amount of 5-bromo-3-benzyl-6-azauracil (*V*) along with the starting compound.

*C*. 5-Bromo-3-benzyl-6-azauracil (*V*; 2·82 g; 0·01 mol) was processed analogously to paragraph *A*. Yield, 2·85 g (76·5%) of compound *XII*, m.p. 131–132°C, undepressed on admixture with the specimen obtained by procedure *A*.

5-Bromo-1,3-dibenzyluracil (*XIV*)

A mixture of 5-bromouracil (*VI*; 9·55 g; 0·05 mol), benzyl chloride (15·4 g; 0·122 mol), sodium hydroxide (4·88 g; 0·122 mol), and water (240 ml) was heated under stirring on a steam bath for 4 hours and cooled down to 20°C. The aqueous layer was decanted, the residue purified by decantation with fresh water, and recrystallised from 50% aqueous ethanol (350 ml) to afford 12·9 g (70%) of compound *XIV*, m.p. 124–127°C. For $C_{18}H_{15}BrN_2O_2$ (371·2) calculated: 57·96% C, 4·07% H, 21·52% Br, 7·27% N; found: 57·81% C, 4·01% H, 21·32% Br, 7·31% N.

5-Methoxy-1,3-dibenzyluracil (*XV*)

5-Bromo-1,3-dibenzyluracil (*XIV*; 3·7 g; 0·01 mol) was refluxed for 7 hours in methanolic sodium methoxide, prepared from 1·38 g (0·06 gramatom) of sodium and 100 ml of methanol. The resulting solution was acidified with hydrochloric acid to pH 7, evaporated to dryness under diminished pressure, and the residue recrystallised from 70% aqueous ethanol to afford 2·28 g (71%) of compound *XV*, m.p. 116–118°C. For $C_{19}H_{18}N_2O_3$ (322·3) calculated: 70·79% C, 5·63% H, 8·69% N; found: 70·41% C, 5·46% H, 8·57% N.

1,3-Dibenzylurea (*XVIII*)

A mixture of 5-bromo-1,3-dibenzyluracil (*XIV*; 3·7 g; 0·01 mol), 1M-NaOH (30 ml), and ethanol (30 ml) was refluxed for 5 hours, filtered (active charcoal), and the filtrate acidified with hydrochloric acid to pH 2·5. The precipitate was collected with suction, washed with water, and recrystallised twice from 50% aqueous ethanol (60 ml). Yield, 1·5 g (66%) of compound *XVIII*, m.p. 168–171°C, undepressed on admixture with an authentic specimen[9].

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