NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES. CXLI.* SOME REACTIONS OF 5-BROMO-6-AZAURACIL

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The reaction of 5-bromo-1,3-bis(2-cyanoethyl)-6-azauracil (*Ib*) with sodium alkoxides affords the 5-alkoxy-1-(2-cyanoethyl) derivatives *IIIa—c*. Under analogous conditions, 5-bromo-6-azauracil (*Ia*), 5-bromo-1-(2-cyanoethyl)-6-azauracil (*Id*), and 5-bromo-3-benzyl-6-azauracil (*Ic*) do not react with alkoxides. Treatment of 5-bromo-1,3-dimethyl-6-azauracil (*Ih*) with sodium ethoxide affords 5-ethoxy-1,3-dimethyl-6-azauracil (*XII*). Compounds *Ia—c* react with aqueous sodium hydroxide under ring opening and partial degradation to afford the corresponding semicarbazones *IXa—c*. Under analogous conditions, compound *Id* does not undergo any cleavage. The reaction of 5-bromo-1,3-dibenzyl-6-azauracil (*Ie*) both with ethanolic sodium ethoxide and with aqueous sodium hydroxide is accompanied by ring contraction under the formation of 2,4-dibenzyl-3,4-dihydro-1,2,4-triazol-3-one (*XI*). The structure of the above compounds was confirmed by synthesis and infrared spectra.

In an earlier paper of this Series[1], we have investigated the cyanoethylation of 5-bromo-6-azauracil (*Ia*) from the standpoint of a reversible introduction of the 2-cyanoethyl group. In the present paper, we have studied the relations between the replacement of the bromo atom at position 5 of the 6-azauracil nucleus and substituents on nitrogen atoms at positions 1 and 3.

As shown by experiments, no reaction takes place between 5-bromo-6-azauracil (*Ia*) and sodium methoxide or ethoxide in excess methanol or ethanol even after refluxing for 10 hours. 5-Bromo-1-(2-cyanoethyl)-6-azauracil[1] (*Id*) and 5-bromo-3-benzyl-6-azauracil[1] (*Ic*) also do not react under analogous conditions. On the other hand, 5-bromo-1,3-bis(2-cyanoethyl)-6-azauracil[1] (*Ib*) reacts readily with ethanolic sodium ethoxide but, contrary to expectations, under the formation of 5-ethoxy-1-(2-cyanoethyl)-6-azauracil (*IIIb*) and not 5-ethoxy-1,3-bis(2-cyanoethyl)-6-azauracil (*II*). Consequently, a simultaneous decyanoethylation at position 3 took place. The

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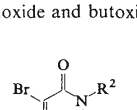
structure of compound *IIIb* was confirmed by an additional benzylation to afford compound *IV*. The authentic specimen of compound *IV* was obtained by reaction of 5-bromo-3-benzyl-1-(2-cyanoethyl)-6-azauracil[1] (*If*) with sodium ethoxide in excess ethanol (this reaction was accompanied by decyanoethylation at position 1) to afford compound *V* and the subsequent cyanoethylation of the latter. The required bis(2-cyanoethyl) derivative *II* was prepared by an additional cyanoethylation of compound *IIIb*. Similarly, the sodium ethoxide treatment of 5-bromo-3-methyl-1-(2-cyanoethyl)-6-azauracil (*Ig*; obtained by methylation of compound *Id* with dimethyl sulfate in alkali) afforded 5-ethoxy-3-methyl-6-azauracil (*VIa*) under simultaneous decyanoethylation. Compounds *IIIa* and *IIIc* were prepared by an analogous treatment of compound *Ib* with sodium methoxide and butoxide, respectively.



I

a, $R^1 = R^2 = H$
b, $R^1 = R^2 = CH_2CH_2CN$
c, $R^1 = H$; $R^2 = C_6H_5CH_2$
d, $R^1 = CH_2CH_2CN$; $R^2 = H$
e, $R^1 = R^2 = C_6H_5CH_2$
f, $R^1 = CH_2CH_2CN$; $R^2 = C_6H_5CH_2$
g, $R^1 = CH_2CH_2CN$; $R^2 = CH_3$
h, $R^1 = R^2 = CH_3$
i, $R^1 = C_6H_5CH_2$; $R^2 = H$

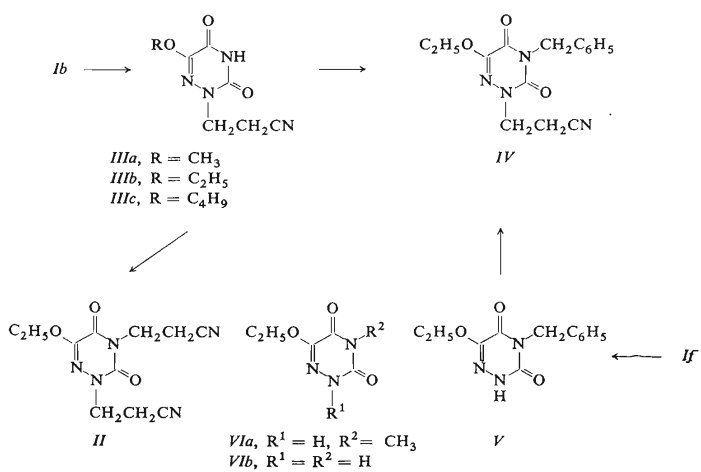
As it may be seen from the above results, the nucleophilic replacement of the bromo atom in 5-bromo-6-azauracil (*Ia*) is considerably facilitated by substitution of both nitrogen atoms at positions 1 and 3. The ethoxide reaction does not take place when only one of these nitrogen atoms is substituted. It has been also shown that the alkoxylation is accompanied by removal of one 2-cyanoethyl group. This removal, however, must occur as the secondary reaction, *i.e.*, after the primary alkoxylation since both 5-bromo-1-(2-cyanoethyl)-6-azauracil (*Id*) and 5-bromo-3-benzyl-6-azauracil (*Ic*) do not react with alkoxides under the aforementioned conditions.

The easier removal of the 2-cyanoethyl group at position 3 accompanying the alkoxylation of compound *Ib*, is in accordance with findings on decyanoethylation of 1,3-bis(2-cyanoethyl)-6-azauracil[2] since the 2-cyanoethyl group is less firmly fixed to the nitrogen atom at position 3 than to the more nucleophilic nitrogen atom at position 1. Consequently, higher concentrations of the alkoxide are necessary to remove the 2-cyanoethyl group from compound *IIIb* and to afford 5-ethoxy-6-azauracil (*VIb*). On the contrary, the alkoxylation of compound *Ig* is accompanied by

a ready removal of the 2-cyanoethyl group from the position $N_{(1)}$. The nucleophilicity of the $N_{(3)}$ nitrogen atom is increased by the presence of the methyl group which cannot be removed during the alkoxylation. Consequently, the carbonyl group at position 2 withdraws electrons from the nitrogen atom at position 1, the nucleophilicity of which is decreased. Furthermore, the bond between the nitrogen atom at position 1 and the 2-cyanoethyl group is weakened.

The nucleophilic substitution of the bromo atom in compound *Ia* and its derivatives by the action of aqueous sodium hydroxide is unexpectedly ready (in contrast to the treatment with sodium ethoxide) and is accompanied by ring cleavage. Thus, in 1M-NaOH at room temperature, compound *Ia* is cleaved into a semicarbazide which was isolated (after acidification of the reaction mixture) in the form of the benzylidene derivative *IXa*. The cleavage is considerably accelerated by higher temperatures. In the presence of zinc, no cleavage occurs in 1M-NaOH even at 90°C. 6-Azauracil[3] resulting by the primary dehydrohalogenation is stable under the reaction conditions and is not cleaved to the semicarbazide.

As reported earlier[4], 5-amino-6-azauracil is hydrolysed in refluxing 1M-NaOH into 5-hydroxy-6-azauracil. The attempted preparation of the latter compound by hydrolysis of the derivative *Ia* under analogous conditions failed. All attempts (even at lower concentrations of sodium hydroxide) resulted in the ring cleavage under the formation of the semicarbazide. This behaviour might be explained by the



inductive effect of the bromo atom. By the action of sodium hydroxide, the ring is opened between atoms 3 and 4 and the bromo atom is rapidly substituted. The resulting keto acid derivative *VIII* undergoes an additional cleavage to the semicarbazide.

Compound *Ib* reacts readily with a solution of sodium hydroxide under the formation of 2,4-bis(2-cyanoethyl)semicarbazide which was isolated in the form of the benzylidene derivative *IXb*. Compound *Ic* reacts somewhat slowly to afford 4-benzylsemicarbazide which was identified as the benzylidene derivative *IXc*. The attempted cleavage of compound *Id* to the known[5] semicarbazide *IXd* failed under analogous conditions. It may be seen that the 1,3-disubstituted derivatives are cleaved most readily in accordance with the course of the alkoxylation. The 3-substituted derivatives are cleaved by aqueous sodium hydroxide but do not react with sodium alkoxides. These findings are in accordance with the earlier[5] observation on the hydrolytical ring opening of uracil derivatives at the position 3–4: the ring opening is facilitated by substitution of the nitrogen atom at position 3. Noteworthy is the considerable stability of compound *Id* which does not react either with sodium ethoxide or aqueous sodium hydroxide. Owing to the substitution at position 1, the hydrogen atom on the nitrogen atom at position 3 of compound *Id* is probably of a more acidic nature. This circumstance is responsible for the decreased positive charge on the carbon at position 4 in contrast to compound *Ia*.

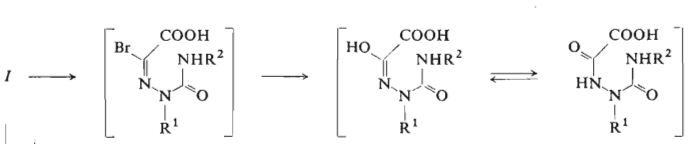
5-Bromo-1,3-dibenzyl-6-azauracil (*Ie*) is not affected by 1M-NaOH because of its insolubility. On the other hand, in refluxing 1M-NaOH and ethanol, compound *Ie* affords a crystalline substance (*XI*) which cannot be converted to the semicarbazone *IXe*. An authentic sample of the semicarbazone *IXe* was prepared from 4-benzyl-1-benzylidenesemicarbazide[6,7] (*IXc*) and benzyl chloride in alkali. The novel substance *XI* is also obtained from compound *Ie* on treatment with methanolic sodium methoxide, ethanolic sodium ethoxide or with 1M-NaOH in pyridine, and by reaction of 2,4-dibenzyl-1-benzylidenesemicarbazide (*IXe*) with formic acid. Finally, the novel substance was identified as 2,4-dibenzyl-3,4-dihydro-1,2,4-triazol-3-one (*XI*). Its formation from compound *Ie* might be explained by ring opening at position 3–4, intramolecular nucleophilic substitution involving the terminal nitrogen atom of the carbamoyl group and the carbon atom at position 5, removal of hydrogen bromide (or sodium bromide), contraction to the five-membered ring, and decarboxylation of the acid *X*. The decarboxylation is obviously facilitated by the formation of an internal salt of the carboxyl and the hetero atom.

5-Bromo-1,3-dimethyl-6-azauracil (*Ih*) does not react analogously to compound *Ie*. Treatment with sodium ethoxide results in alkoxylation at position 5, *i.e.*, in the formation of 5-ethoxy-1,3-dimethyl-6-azauracil (*XII*), the structure of which was confirmed by infrared spectra.

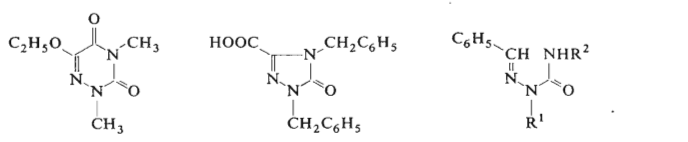
In connection with the different behaviour of compounds *Ib* and *Ih* on the one hand and compound *Ie* on the other to alkoxides, we have investigated the reaction

of formic acid with 2,4-dibenzyl-1-benzylidenesemicarbazide (*IXe*), 2-benzyl-1-benzylidenesemicarbazide[8,9] (*IXi*), 4-benzyl-1-benzylidenesemicarbazide (*IXc*) and benzylidenesemicarbazide (*IXa*). Only compound *IXe* undergoes cyclisation to compound *XI* possessing a five-membered ring. In refluxing formic acid, compound *IXi* splits off the carbamoyl group under the formation of 2-benzyl-2-formyl-1-benzylidenehydrazine (*XIII*). Compounds *IXc* and *XIb* are not affected by this treatment. When refluxed in formic acid, benzylidenesemicarbazide (*IXa*) splits off the carbamoyl group under the formation of N,N'-dibenzylidenehydrazine (*XIV*).

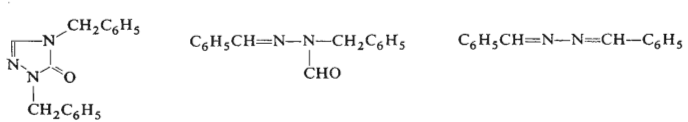
Consequently, the condition for a successful cyclisation of substituted semicarbazides to a five-membered ring consists in the presence of a benzyl group on both nitrogen atoms at positions 2 and 4. The cyclisation does not take place when only



VII *VIII*



XII *X* *IX*



XI *XIII* *XIV*

In formulae *I* to *IX*: *a*, $R^1 = R^2 = H$; *b*, $R^1 = R^2 = CH_2CH_2CN$; *c*, $R^1 = H$, $R^2 = C_6H_5CH_2$; *d*, $R^1 = CH_2CH_2CN$, $R^2 = H$; *e*, $R^1 = R^2 = C_6H_5CH_2$; *f*, $R^1 = C_6H_5CH_2$, $R^2 = H$.

one of these nitrogen atoms is substituted by the benzyl group or when both nitrogen atoms are substituted by the 2-cyanoethyl group.

The present investigations represent also contribution to the knowledge on cleavage of the carbamoyl group discussed earlier[6] in the case of some urea and hydrazine derivatives. With compound *IXi*, the terminal nitrogen atom of the carbamoyl group is not substituted and cannot cyclize because of a poor nucleophilic ability; consequently, the carbamoyl group is split off. Compound *IXa* behaves similarly. The formation of the hydrazine *XIV* instead of the expected formyl derivative analogous to compound *XIII* might be explained by a great stability of the system, caused by mesomeric effect of two aromatic nuclei. On the other hand, in the case of compound *IXc* (substituted terminal nitrogen atom, free nitrogen atom at position 2) we cannot expect either cyclisation or cleavage of the carbamoyl group.

It may be seen from the above results that the reaction of compound *Ie* with sodium alkoxides and sodium hydroxide strongly depends on the increased nucleophilicity of both nitrogen atoms due to substitution. In view of different course of an analogous reaction with compound *Ih*, however, it is also necessary to take into account the bulkiness of the substituent and the stability of the intermediary anion.

The structure of some reaction products was confirmed by infrared spectra. For a survey of characteristic infrared absorption bands in chloroform (compounds *IIIa–c*, *V*, *XI*, *XII*) see Table I. The 5-alkoxy derivatives *IIIa–c* display the band of a free NH group practically in the same region as that of 1-methyl-6-azauracil[10] (3374 cm^{-1}) when measured under analogous conditions. In other words, the unsubstituted NH group is at position 3. On the other hand, compound *V* obtained from 5-bromo-3-benzyl-1-(2-cyanoethyl)-6-azauracil (*If*) on treatment with sodium ethoxide exhibits the band due to a free NH group in the same region as 3-methyl-

TABLE I
Some Characteristic Infrared Bands

Compound	Free $\nu(N^1—H)$	Free $\nu(N^3—H)$	Bonded $\nu(N—H)$	$\nu(C\equiv N)$	$\nu(C—O)$		ν(ring)
IIIa[a]	—	3 370 vw		2 255 vw	1 736 w	1 711 m	1 613 w
IIIb	—	3 370 w	3 180 m	2 260 w	1 733 vs	1 710 vs	1 610 s
IIIc	—	3 370 w	3 180 m	2 255 w	1 733 s	1 710 vs	1 608 s
V	3 430 m	—	3 230 w	—	1 730 m	1 677 vs	1 622 m
XII	—	—	—	—	1 719 s	1 669 vs	1 612 s
XI	—	—	—	—	1 704 vs		1 556 s

[a] A saturated solution, $c \ll 2\%$.

6-azauracil[10] (at 3424 cm^{-1}). Furthermore, compound *V* lacks the stretching vibration band of the nitrile group at 2260 cm^{-1}. Consequently, the 2-cyanoethyl group was split off from the nitrogen atom at position 1. The ν(C=O) values of 5-ethoxy-1,3-dimethyl-6-azauracil (*XII*) are very close to those of 1,3-dimethyl-6-azauracil[10] (1722, 1680, and 1667 cm^{-1}), but the carbonyl band at 1669 cm^{-1} forms a doublet in the spectrum of compound *XII*. There are not suitable model compounds to confirm reliably by their spectra the structure of compound *XI*. The ν(C=O) value of 2,5-disubstituted 3,4-dihydro-1,2,4-triazol-3-one derivatives in solid state[11] is situated at about 1720 cm^{-1}. Substitution on both nitrogen atoms in α-position to the carbonyl group should result in a lower ν(C=O) value. The carbonyl band of compound *XI* in solid state is situated at 1690 cm^{-1} in accordance with this assumption.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). Analytical samples were dried at 60°C/20 Torr. Infrared spectra were taken in chloroform solutions (concentration, 2—3%) on a Zeiss UR-10 spectrophotometer.

5-Ethoxy-1-(2-cyanoethyl)-6-azauracil (*IIIb*)

A mixture of compound *Ib* (5·96 g; 0·02 mol) and ethanolic sodium ethoxide (from 1·38 g *i.e.* 0·06 gramatom of sodium and 100 ml of ethanol) was refluxed for 4 hours, adjusted with dilute (1 : 1) hydrochloric acid to pH 7 and evaporated to dryness under diminished pressure. The residue was diluted with water (5 ml), acidified with hydrochloric acid to pH 4 and filtered while hot (active charcoal). The filtrate deposited crystals which were collected with suction and recrystallised from water (10 ml). Yield, 3·05 g of compound *IIIb*, m.p. 143—145°C. For $C_8H_{10}N_4O_3$ (210·2) calculated: 45·71% C, 4·80% H, 26·66% N; found: 45·49% C, 4·65% H, 26·38% N.

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

A. A mixture of compound *IIIb* (2·1 g; 0·01 mol) and water (100 ml) was treated under stirring with a solution of sodium hydroxide (2 g; 0·05 mol) in water (50 ml). When the solid dissolved, there was added an excess of benzyl chloride (6·36 g; 0·05 mol). The whole mixture was refluxed under stirring for 4 hours, cooled down to 20°C, and the aqueous layer decanted from the sticky residue. Recrystallisation of the residue from 60% aqueous ethanol (50 ml) afforded 2·17 g (72·5%) of compound *IV*, m.p. 75—76°C. For $C_{15}H_{16}N_4O_3$ (300·3) calculated: 59·99% C, 5·37% H, 18·66% N; found: 59·58% C, 5·29% H, 18·43% N.

B. A mixture of compound *V* (2·47 g; 0·01 mol), pyridine (50 ml), water (50 ml) and acrylonitrile (50 ml) was refluxed on a steam bath for 15 hours, evaporated to dryness under diminished pressure, and the residue recrystallised from 50% aqueous ethanol (60 ml) Yield, 2·23 g (75%) of compound *IV*, m.p. 74—76°C, undepressed on admixture with a specimen obtained according to the procedure *A*.

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

A mixture of compound *If* (3·35 g; 0·01 mol) and ethanolic sodium ethoxide (from 0·7 g *i.e.* 0·03 gramatom of sodium and 50 ml of ethanol) was refluxed for 8 hours, cooled down to 20°C,

adjusted with dilute (1 : 1) hydrochloric acid to pH 7, and evaporated to dryness under diminished pressure. The residue was recrystallised from 50% aqueous ethanol (60 ml). Yield, 1·77 g (71·5%) of compound *V*, m.p. 166–168°C. For $C_{12}H_{13}N_3O_3$ (247·3) calculated: 58·29% C, 5·30% H, 17·00% N; found: 58·08% C, 5·21% H, 16·85% N.

5-Ethoxy-1,3-bis(2-cyanoethyl)-6-azauracil (*II*)

A mixture of compound *IIIb* (2·1 g; 0·01 mol), pyridine (12 ml), water (12 ml), and acrylonitrile (6 ml) was refluxed for 15 hours. The solution was evaporated to dryness under diminished pressure and the residue recrystallised twice from ethanol (15 ml). Yield, 1·89 g (72%) of compound *II*, m.p. 67–68°C. For $C_{11}H_{13}N_5O_3$ (263·3) calculated: 50·18% C, 4·98% H, 26·61% N; found: 50·42% C, 4·75% H, 26·43% N.

5-Bromo 3-methyl-1-(2-cyanoethyl)-6-azauracil (*Ig*)

Compound *Id* (2·45 g; 0·01 mol) was added portionwise under stirring to a solution of sodium hydroxide (0·8 g; 0·02 mol) in water (100 ml) The mixture was then treated dropwise in the course of 5 minutes with dimethyl sulfate (2 ml; 0·02 mol) and stirred at room temperature for 2½ hours The precipitate was collected with suction, washed with water until neutral, and recrystallised from water (35 ml). Yield, 2·03 g (78·5%) of compound *Ig*, m.p. 113–115°C. For $C_7H_7BrN_4O_2$ (259·1) calculated: 32·44% C, 2·72% H, 12·35% Br, 21·62% N; found: 32·18% C, 2·67% H, 12·14% Br, 21·41% N.

5-Ethoxy-3-methyl-6-azauracil (*VIa*)

A mixture of compound *Ig* (2·59 g; 0·01 mol) and ethanolic sodium ethoxide (from 0·4 g *i.e.* 0·01 gramatom of sodium and 120 ml of ethanol) was refluxed for 3 hours. The resulting solution was cooled down to 20°C, neutralised with dilute (1 : 1) hydrochloric acid to pH 7, and evaporated to dryness under diminished pressure. The residue was diluted with water (15 ml), acidified with hydrochloric acid to pH 4·5, and filtered while hot (active charcoal). Recrystallisation from water (10 ml) afforded 1·2 g (70·5%) of compound *VIa*, m.p. 198–200°C. For $C_6H_9N_3O_3$ (171·2) calculated: 42·10% C, 5·30% H, 24·55% N; found: 42·31% C, 5·05% H, 24·39% N.

5-Methoxy-1-(2-cyanoethyl)-5-azauracil (*IIIa*)

A mixture of compound *Ib* (5·96 g; 0·02 mol) and methanolic sodium methoxide (from 1·38 g *i.e.* 0·06 gramatom of sodium and 100 ml of methanol) was refluxed for 5 hours and then processed analogously to the preparation of compound *IIIb*. Yield, 2·76 g (70·5%) of compound *IIIa*, m.p. 172–174°C. For $C_7H_8N_4O_3$ (196·2) calculated: 42·86% C, 4·11% H, 28·56% N; found: 42·45% C, 4·02% H, 28·31% N. An analogous treatment of compound *Ib* (5·96 g; 0·02 mol) with butanolic sodium butoxide (from 1·38 g *i.e.* 0·06 gramatom of sodium and 100 ml of butanol) afforded 3·37 g (71%) of 5-butoxy-1-(2-cyanoethyl)-6-azauracil (*IIIc*), m.p. 142–144°C. For $C_{10}H_{14}N_4O_3$ (238·2) calculated: 50·42% C, 5·92% H, 23·52% N; found: 50·15% C, 5·81% H, 23·39% N.

5-Ethoxy-6-azauracil (*VIb*)

A mixture of compound *IIIb* (4·2 g; 0·08 mol) and ethanolic sodium ethoxide (from 1·84 g *i.e.* 0·08 gramatom of sodium and 80 ml of ethanol) was refluxed for 5 hours, adjusted with dilute (1 : 1) hydrochloric acid to pH 7, and evaporated to dryness under diminished pressure. The residue was

crystallised from water (13 ml) to afford 2·18 g (69·5%) of compound *VIb*, m.p. 218—219°C. For $C_5H_7N_3O_3$ (157·1) calculated: 38·22% C, 4·49% H, 26·74% N; found: 38·01% C, 4·36% H, 26·60% N.

1-Benzylidenesemicarbazide (*IXa*)

A mixture of 5-bromo-6-azauracil (*Ia*; 9·6 g; 0·05 mol) and 1M-NaOH (120 ml) was heated at 90°C for 2 hours, cooled down to 5°C, acidified with dilute (1 : 1) hydrochloric acid to pH 2·5, and concentrated under diminished pressure to a half of the original volume. The concentrate was refluxed with ethanol (50 ml) and benzaldehyde (12 ml) for 10 minutes, filtered while hot (active charcoal), and the filtrate cooled down (20°C) to deposit a solid which was collected with suction and recrystallised from 50% aqueous ethanol (180 ml). Yield, 6·4 g (79%) of compound *IXa*, m.p. 215—219°C, undepressed on admixture with an authentic specimen[12]. — An analogous treatment of compound *Ib* (8·94 g; 0·03 mol) with 50 ml of 1M-NaOH (1 hour at 90°C) afforded 5·68 g (70·5%) of 2,4-bis(2-cyanoethyl)-1-benzylidenesemicarbazide (*IXb*), m.p. 135—137°C. For $C_{14}H_{15}N_5O$ (269·3) calculated: 62·44% C, 5·61% H, 26·01% N; found: 62·01% C, 5·62% H, 25·91% N. An analogous treatment of compound *Ic* (2·82 g; 0·01 mol) afforded 1·82 g (72%) of compound *IXc* melting without depression when admixed with an authentic specimen[6,7].

2,4-Dibenzyl-1-benzylidenesemicarbazide (*IXe*)

A mixture of compound *IXc* (2·53 g; 0·01 mol), aqueous sodium hydroxide (from 0·96 g *i.e.* 0·024 mol of sodium hydroxide and 120 ml of water), and benzyl chloride (2·94 g; 0·024 mol) was heated on a steam bath for 6 hours under stirring and then cooled down (20°C) to deposit a solid which was recrystallised twice from 50% aqueous ethanol (150 ml). Yield, 2·2 g (68%) of compound *IXe*, m.p. 125—126·5°C. For $C_{22}H_{21}N_3O$ (343·4) calculated: 76·94% C, 6·16% H, 12·24% N; found: 76·71% C, 6·02% H, 12·13% N.

2,4-Dibenzyl-3,4-dihydro-1,2,4-triazol-3-one (*XI*)

A. A mixture of compound *Ie* (3·72 g; 0·01 mol), 1M-NaOH (35 ml), and ethanol (35 ml) was refluxed for 7 hours, cooled down (20°C), and acidified with dilute (1 : 1) hydrochloric acid to pH 2·5. The precipitate was collected with suction, washed with water, and recrystallised from 50% aqueous ethanol (25 ml) to afford 1·92 g of compound *XI*, m.p. 91—93°C. For $C_{16}H_{15}N_3O$ (265·3) calculated: 72·43% C, 5·70% H, 15·84% N; found: 72·21% C, 5·67% H, 15·69% N.

B. Compound *Ie* (3·72 g; 0·01 mol) and ethanolic sodium ethoxide (from 1·38 g *i.e.* 0·06 gramatom of sodium and 100 ml of ethanol) was refluxed for 4 hours and then processed analogously to procedure *A*. Yield, 1·99 g of compound *XI*, m.p. 92—93°C, undepressed on admixture with the specimen obtained by the procedure *A*.

C. A mixture of compound *IXe* (3·23 g; 0·01 mol) and excess concentrated formic acid (200 ml) was refluxed for 6 hours, evaporated to dryness under diminished pressure, and the residue recrystallised twice from 50% aqueous ethanol to afford 1·82 g (68·5%) of compound *XI*, m.p. 92—94°C, undepressed on admixture with the specimen obtained by the procedure *A*.

5-Bromo-1,3-dimethyl-5-azauracil (*Ih*)

Compound *Ia* (4·8 g; 0·025 mol) was dissolved in a solution of sodium hydroxide (2·4 g; 0·06 mol) in water (150 nl). Dimethyl sulfate was then added dropwise in the course of 10 minutes (7·5 g; 0·06 mol). The stirring was continued for additional 6 hours at room temperature (pH value

7·5—8·0). The precipitate was collected with suction, washed with water, and recrystallised from water (55 ml). Yield, 4·29 g (78%) of compound *Ih*, m.p. 101·5—102·5°C. For $C_5H_6BrN_3O_2$ (220·0) calculated: 27·29% C, 2·74% H, 36·32% Br, 19·09% N; found: 27·45% C, 2·82% H, 36·21% Br, 19·21% N.

5-Ethoxy-1,3-dimethyl-6-azauracil (*XII*)

A mixture of compound *Ih* (2·2 g; 0·01 mol) and ethanolic sodium ethoxide (from 0·23 g *i.e.* 0·01 gramatom of sodium and 100 ml of ethanol) was refluxed for 3 hours, adjusted with dilute (1 : 1) hydrochloric acid to pH 7, and evaporated to dryness under diminished pressure. The residue was adjusted to pH 5 with hydrochloric acid and recrystallised from water (5 ml). Yield, 1·29 g (70%) of compound *XII*, m.p. 94—95°C. For $C_7H_{11}N_3O_3$ (185·2) calculated: 45·40% C, 5·99% H, 22·69% N; found: 45·21% C, 5·87% H, 22·47% N.

2-Benzyl-2-formyl-1-benzylidenehydrazine (*XIII*)

A mixture of compound *IXi* (5·06 g; 0·02 mol) and concentrated formic acid (100 ml) was refluxed for 6 hours and evaporated to dryness under diminished pressure. The residue was coevaporated with 30 ml of ethanol and the recrystallised twice from 50% aqueous ethanol. Yield, 3·23 g (68%) of compound *XIII*, m.p. 90—91°C. For $C_{15}H_{14}N_2O$ (238·3) calculated: 75·60% C, 5·92% H, 11·76% N; found: 75·37% C, 5·93% H, 11·61% N.

N,N'-Dibenzylidenehydrazine (*XIV*)

A mixture of compound *IXa* (4·07 g; 0·02 mol) and concentrated formic acid (100 ml) was refluxed for 6 hours and then processed analogously to compound *XIII*. Yield, 2·78 g (67%) of compound *XIV*, m.p. 92—94°C, undepressed on admixture with an authentic specimen[13].

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