ISOMERISATION, ALKYLATION, AND CYCLISATION OF GLYOXYLIC ACID SEMICARBAZONE DERIVATIVES*

H.HŘEBABECKÝ and J.BERÁNEK

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague

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The (*Z*)- and (*E*)-isomers of methyl glyoxylate semicarbazone and methyl glyoxylate 4-phenylsemicarbazone have been prepared. Isomerisation of compound *Ia* (*IIa*) by the action of hydrogen chloride in acetonitrile affords a mixture of 14% (31%) of the (*Z*)-isomer *Ib* (*IIb*) and 86% (69%) of the (*E*)-isomer *Ia* (*IIa*). Thermal isomerisation in dimethyl sulfoxide at 150°C results in a mixture of compounds *Ib* (8%) and *Ia* (92%). Cyclisation of the (*Z*)-isomer *Ib* (*IIb*) with sodium methoxide takes place at room temperature to afford quantitatively compound *XX* (*XXI*). Compound *Ia* is not cyclised under analogous conditions while at 150°C 6-azauracil (*XX*) is obtained *via* the previous isomerisation of *Ia* to compound *Ib*. Reaction of methyl iodide or benzyl chloride with the sodium salt of the semicarbazone *Ia* (*IIa*) in dimethylformamide affords the 2-alkyl derivatives *III* and *IV* (*V* and *VI*). Compound *III* (*IV*) is converted to the acid *X* (*XI*) on alkaline hydrolysis and to the amide *XII* (*XIII*) on ammonolysis. By reaction with sodium hydride, the 2-alkylsemicarbazone *III* (*IV*) undergoes a quantitative cleavage with the formation of sodium cyanate and the 2-alkylhydrazone *XIV* (*XV*) which may be converted to the acetylhydrazone *XVI* (*XVII*) by acetylation. The dependence between the cyclisation rate of 2-alkylsemicarbazones *III* and *IV* and the substitution at position 2 is more pronounced when sodium methoxide (at 65°C) is used as the cyclisation agent than in the case of sodium acetate–acetic anhydride agent (at 140°C). Reaction of ethyl chloroacetate with the sodium salt of the semicarbazone *Ia* affords 4% of the semicarbazone derivative *VII* and 69% of the hydantoin derivative *IX*.

Systematic investigations on alkylation and ribosylation[1,2] of methyl glyoxylate semicarbazone (*Ia*) as well as cyclisation of the resulting derivatives along with examinations on the influence of substituents and configuration of the starting semicarbazones on the rate and readiness of the cyclisation reaction are object of the present paper and two subsequent communications. The whole work has been motived by the aim to develop an alternative in the preparation of 6-azauridine, *i.e.*, a nucleoside analogue which has been paid considerable attention in this Laboratory (for references see[1]). The present paper reports on alkylation of methyl glyoxylate semicarbazone (*Ia*) and cyclisation of the resulting alkyl derivatives to 1-substituted 6-azauracils with a special respect to the future glycosylations. The present work is based on the earlier investigations[3] on the substituent effect in cyclisations of acyl cyanide semicarbazones

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to 5-alkyl-6-azacytosines and on the earlier syntheses of 6-azauracil[4-6] and its alkyl derivatives[6-8].

The starting methyl glyoxylate semicarbazone (*Ia*) was prepared by reaction[9] of semicarbazide hydrochloride with chloral hydrate in refluxing methanol as an analogy of the earlier reported[10] preparation of glyoxylic acid semicarbazone by reaction of chloral hydrate with semicarbazide hydrochloride in aqueous medium. In the earlier syntheses of 6-azauracil[4,5], the starting glyoxylic acid semicarbazone was cyclised by aqueous sodium hydroxide[4] (10%, at 100°C) in a low yield or methyl glyoxylate semicarbazone was subjected to cyclisation by the action of sodium ethoxide in ethylene glycol[5] as solvent (24 h at 150°C). In the analogous cyclisation of 5-alkyl-6-azacytosines[3], an attempt has been made to replace ethylene glycol by isoamyl alcohol and thus decrease the reaction temperature to 130°C.

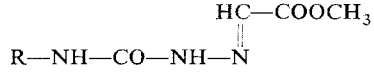
Despite the detailed investigations[11] on 6-azauracil as important antimetabolite and intermediate in the production of the medicament 6-azauridine, no attention has been so far paid to isomerisation of the starting compound in its synthesis, *i.e.*, of methyl glyoxylate semicarbazone (*Ia*) or to isolation of the (*Z*)- and (*E*)-isomers* (*Ia* and *Ib*) or to cyclisation of the individual isomers to 6-azauracil (*XX*). The preparation of both geometrical isomers of ethyl glyoxylate 4-phenylsemicarbazone has been reported[12] only, namely, by reaction of phenyl isocyanate with the corresponding (*Z*)- and (*E*)-isomers of ethyl glyoxylate hydrazone. In the same paper[12], an observation is also mentioned on the exclusive formation of the (*E*)-isomer of ethyl glyoxylate semicarbazone by reaction of phenylsemicarbazide with ethyl glyoxylate. The isomerisation of acetophenone semicarbazone and benzaldehyde semicarbazone by the action of UV radiation and isolation of both (*Z*)- and (*E*)-isomers has been recently reported[13]. In the equilibrium mixture, the ratio of the (*Z*)-isomer to the (*E*)-isomer was 1 : 1·2 in the case of acetophenone semicarbazone and 1 : 5 with benzaldehyde semicarbazone. In another paper on cyclisation of arylidene semicarbazones to oxadiazoles, the isomerisation of the (*E*)-isomer to the (*Z*)-isomer is assumed as the rate-controlling step on the basis of kinetic measurements[14]; the individual isomers have not been however isolated.

On the basis of reported data[12-14], the preparation and isolation of (*Z*)- and (*E*)-isomers of methyl glyoxylate semicarbazone (*Ia*) has been now attempted. Thus, the reaction of semicarbazide hydrochloride with chloral hydrate in methanol was found to yield a single isomer which was assigned the (*E*)-configuration *Ia*. The isomerisation of the semicarbazone *Ia* by the action of acids was observed to be strongly influenced by the character of the solvent. In methanol as solvent, the equilibrium is strongly shifted in favour of the (*E*)-isomer *Ia*; this finding explains formation of the practically homogeneous (*E*)-isomer *Ia* in the synthesis of methyl glyoxylate semicarbazone. In acetonitrile as a dipolar aprotic solvent, the ratio of the (*Z*)-isomer to the (*E*)-isomer is more favourable since the equilibrium mixture contains 14% of the (*Z*)-isomer *Ib* and 86% of the (*E*)-isomer *Ia*. The thermal isomerisation of the semicarbazone *Ia* has also been examined. After 150 min in dimethyl sulfoxide at

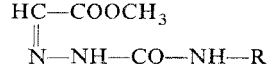
* In the earlier literature[12,13], the (*Z*)-isomer is designated as *syn* and the (*E*)-isomer as *anti*.

150°C, the equilibrium mixture was found to contain 8% of the (*Z*)-isomer and 92% of the (*E*)-isomer. At temperatures up to 120°C, no isomerisation could be observed under the experimental conditions applied. Both (*Z*)- and (*E*)-isomers were isolated in pure state from the equilibrium mixture by chromatography on silica gel. The IR and NMR spectra were in accordance with the expected structure. An unequivocal proof on the configuration of the (*Z*)-isomer *Ib* was supplied by the cyclisation test with methanolic sodium methoxide. Thus, the (*Z*)-isomer *Ib* is cyclised to 6-azauracil (*XX*) by the action of 0·1M methanolic sodium methoxide at room temperature for 90 min in a quantitative yield while the cyclisation of the (*E*)-isomer *Ia* does not occur at all under these conditions; compound *Ia* does not cyclise even in refluxing methanol. The literature[5] reports on cyclisation of the semicarbazone *Ia* in ethylene glycol as solvent in the presence of ethanolic sodium ethoxide at 150°C for 24 h. As it may be inferred from the above mentioned results, the temperature of 150°C brings about isomerisation of the (*E*)-isomer to the (*Z*)-isomer; consequently, the cyclisation is also in this case preceded by the formation of the (*Z*)-isomer and the thermal isomerisation of the (*E*)-isomer *Ia* to the (*Z*)-isomer *Ib* represents the rate-controlling step.

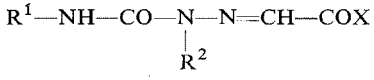
Analogous results were obtained in isomerisation of the 4-phenylsemicarbazone *IIa* and the appropriate cyclisation reaction. The starting methyl glyoxylate 4-phenylsemicarbazone (*IIa*) was prepared similarly to the semicarbazone *Ia*. Reaction of the 4-phenylsemicarbazide hydrochloride with chloral hydrate in refluxing methanol affords a 75% yield of the (*E*)-isomer *IIa*. In contrast to the literature[12], the mother liquors were found to contain a small amount of the (*Z*)-isomer *IIb*. In accordance with this observation, isomerisation of the 4-phenyl derivative *IIa* furnished a higher



Ia, R = H
IIa, R = Ph



Ib, R = H
IIb, R = Ph



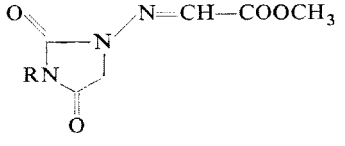
III, R^1 = H, R^2 = CH_3, X = OCH_3
IV, R^1 = H, R^2 = CH_2Ph, X = OCH_3
V, R^1 = Ph, R^2 = CH_3, X = OCH_3
VI, R^1 = Ph, R^2 = CH_2Ph, X = OCH_3
VII, R^1 = H, R^2 = CH_2COOEt, X = OCH_3
X, R^1 = H, R^2 = CH_3, X = OH
XI, R^1 = H, R^2 = CH_2Ph, X = OH
XII, R^1 = H, R^2 = CH_3, X = NH_2
XIII, R^1 = H, R^2 = CH_2Ph, X = NH_2

XIV, R^1 = H, R^2 = CH_3
XV, R^1 = H, R^2 = CH_2Ph
XVI, R^1 = $COCH_3$, R^2 = CH_3
XVII, R^1 = $COCH_3$, R^2 = CH_2Ph

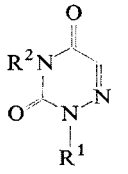
yield of the (Z)-isomer *IIb* when compared with the unsubstituted substance *Ia*. Treatment with hydrogen chloride in acetonitrile at room temperature resulted in an equilibrium mixture containing 31% of the (Z)-isomer *IIb* and 69% of the (E)-isomer *IIa*. Similarly to compound *Ib*, the (Z)-isomer *IIb* is cyclised to 3-phenyl-6-azauracil (*XXI*) in 84% yield when treated at room temperature with 0·1M methanolic sodium methoxide for 20 min. On the other hand, the (E)-isomer of the 4-phenylsemicarbazone *IIa* does not undergo cyclisation by the action of methanolic sodium methoxide at room temperature and decomposes at higher temperatures. The behaviour of the 2-benzyl-4-phenylsemicarbazone *VI* is analogous.

The preparation of the 2-substituted alkyl derivatives of glyoxylic acid semicarbazone is reported in the literature[8] in the case of glyoxylic acid 2-benzylsemicarbazone and of the corresponding alkyl ester only along with the subsequent alkaline cyclisation at 120°C for 3·5 h with the formation of 1-benzyl-6-azauracil. As reported[15], the benzaldehyde semicarbazone reacts in the form of a nucleophilic anion when condensed with ethyl chloroacetate in the presence of sodium ethoxide.

Analogously to this observation[15], treatment of methyl glyoxylate semicarbazone in anhydrous medium with a strong base, *e.g.*, with methanolic sodium methoxide, affords a strongly nucleophilic semicarbazone anion which reacts with alkyl halides with the formation of 2-alkylsemicarbazone. Reaction of the semicarbazone *Ia* with one equivalent of sodium methoxide affords the sodium salt of the semicarbazone *Ia* from which compound *Ia* may be regenerated by neutralisation with acetic acid. The alkylation occurs more readily and in higher yields when performed in a dipolar aprotic solvent as it may be expected on the basis of the literature[16]. By reaction of the semicarbazone *Ia* sodium salt with methyl iodide or benzyl chloride in dimethylformamide, there was prepared the 2-methylsemicarbazone *III* and the 2-benzylsemicarbazone *IV* in 73% and 90% yields, resp. By an analogous alkylation of the 4-phenylsemicarbazone *IIa* sodium salt with methyl iodide or benzyl chloride in dimethylformamide, there were obtained the 2-methyl-4-phenylsemicarbazone *V* and the 2-benzyl-4-phenylsemicarbazone *VI*, resp. Reaction of the semicarbazone *Ia*



VIII, R = H
IX, R = CH_2COOEt



XVIII, $R^1 = CH_3$, $R^2 = H$
XIX, $R^1 = CH_2Ph$, $R^2 = H$
XX, $R^1 = R^2 = H$
XXI, $R^1 = H$, $R^2 = Ph$

sodium salt with ethyl chloroacetate affords under analogous conditions the 2-ethoxycarbonylmethyl derivative *VII* as the minor product and 1-methoxycarbonylmethyleneamino-3-ethoxycarbonylmethylhydantoin (*IX*) as the main product. It is of importance to note that under conditions of the substitution reaction, the 2-ethoxycarbonylmethylsemicarbazone *VII* is fastly cyclised with the formation of the hydantoin derivative *VIII*. The acidity of the hydantoin derivative *VIII* is higher than that of the semicarbazone *Ia*; consequently, compound *VIII* is instantaneously transformed by the action of the semicarbazone anion into the hydantoin anion which reacts with a further molecule of ethyl chloroacetate with the formation of the disubstituted hydantoin *IX*.

The esters of 2-alkylsemicarbazones *III* and *IV* were converted by alkaline hydrolysis into the free glyoxylic acids *X* and *XI*. By hydrolysis in aqueous 80% methanol at room temperature, the acids *X* and *XI* were obtained in yields above 80% and the hydrolysis was not accompanied by cyclisation to the 6-azauracil derivative. The 4-phenylsemicarbazone of glyoxylic acid was obtained analogously in 90% yield.

Ammonolysis (18% methanolic ammonia at room temperature) of esters *III* and *IV* afforded the amides *XII* and *XIII*, resp., which were isolated in yields above 90% (no competitive cyclisation took place).

The additional alkylation of 2-substituted semicarbazones (*e.g.*, *III* and *IV*) at position 4 failed but a side reaction was observed. The reaction mixture contained a new substance which was different both from the starting material and the expected disubstituted derivative. This substance was identified as a 2-alkylhydrazone which is formed on degradation of the semicarbazone portion of the molecule by the action of a base. To a lesser extent, such a degradation has also been observed in cyclisations of 2-substituted semicarbazones *III* and *IV* to 1-alkyl-6-azauracils *XVIII* and *XIX* by the action of sodium methoxide or on treatment with a mixture of acetic anhydride and sodium acetate. By the action of a strong base on 2-alkylsemicarbazones, an alkylsemicarbazone anion is probably formed as the primary intermediate which is then rapidly decomposed with the formation of an alkylhydrazone and cyanate anion. Thus, the methylhydrazone *XIV* is formed by reaction of the methylsemicarbazone *III* with an equimolar amount of sodium hydride in dimethylformamide. Similarly, the benzylsemicarbazone *IV* afforded the benzylhydrazone *XV*. The resulting cyanate anion was proved by conversion into urea. The quantitative determination of the CNO^- ions in the reaction mixture was performed polarographically on the basis[17] of the anodic wave of the cyanate with mercury. It has been found that one equivalent of the cyanate is released and that the reaction is practically quantitative. The semicarbazone which is not substituted at position 2 (such as compound *Ia*) does not undergo this degradation even in the presence of two equivalents of sodium hydride. When the (*Z*)- or (*E*)-isomer of methyl glyoxylate 4-phenylsemicarbazone was refluxed with a mixture of acetic anhydride and sodium acetate, a mixture was

obtained from which acetanilide was isolated. Since the 4-phenylsemicarbazone *IIa* (in contrast to the 2-alkyl derivatives) is not cleaved with sodium hydride it is assumed that the reaction conditions lead first to acetylation of the N^2 nitrogen atom and then degradation to phenyl isocyanate which is converted by the reaction medium into acetanilide. Virtually, an authentic specimen of phenyl isocyanate afforded acetanilide under analogous reaction conditions.

The effect of substitution on the cyclisation of acyl cyanide semicarbazones to 5-substituted 6-azacytosines has been recently examined[3]. In this connection it was of interest to evalueate the effect of substituents at position 2 of the semicarbazone moiety on cyclisation to 6-azauracil derivatives, namely on cyclisation of the 2-methylsemicarbazone *III* and the 2-benzylsemicarbazone *IV* by the action of sodium methoxide or acetic anhydride in the presence of sodium acetate. The cyclisation in acetic anhydride was examined with a special respect to the preparation of triacetyl-6-azauridine as reported in the subsequent communication[1]. When refluxed in 0·1M methanolic sodium methoxide for 7 h, the methylsemicarbazone *III* affords 1-methyl-6-azauracil (*XVIII*) in 21% yield. In addition to the cyclisation product *XVIII*, there is isolated 9% of the methylhydrazone *XIV*. Under analogous conditions, the cyclisation of the benzylsemicarbazone *IV* is accomplished within 2·5 h and affords 1-benzyl-6-azauracil (*XIX*) in 70% yield. When performed in acetic anhydride, the cyclisation requires the reflux temperature to proceed by a satisfactory rate. Also the yields of 1-alkyl-6-azauracils *XVIII* and *XIX* are rather low (about 28%) and do not differ from each other. The low yields are due to the above mentioned side reaction consisting in removal of cyanate from the alkylsemicarbazone *III* and *IV* with the formation of the alkylhydrazone *XIV* and *XV* which is immediately acetylated to the alkylhydrazone acetyl derivative *XVI* and *XVII*, resp. The acetyl derivatives *XVI* and *XVII*, isolated from the crude cyclisation mixtures, may also be prepared from the alkylsemicarbazone *III* and *IV* on treatment with sodium hydride and the subsequent acetylation of the resulting alkylhydrazone *XIV* and *XV*, resp. Conclusively, the 2-benzylsemicarbazone *IV* is cyclised farly more readily and in a higher yield than the 2-methylsemicarbazone *III*. The effect of the tribenzoylribofuranosyl residue as the substitutent at position 2 of the semicarbazone is even more favourable since the cyclisation with sodium methoxide occurs at room temperature in an almost quantitative yield[1].

It may be inferred from the above results that cyclisation of the semicarbazone unsubstituted at position 2 depends on configuration of the starting material *Ia*, *Ib*, *IIa*, and *IIb*, the cyclisation of the (*E*)-isomer being preceded by isomerisation of the starting material to the (*Z*)-isomer. In the case of the 2-alkylsemicarbazones *III*, *IV*, *V*, and *VI*, the two isomers have been neither isolated nor detected (*e.g.*, by spectral measurements). It might be expected that cyclisation of the pure (*Z*)-form of 2-substituted semicarbazones at room temperature would be even easier than cyclisation of the (*Z*)-isomers of semicarbazones unsubstituted at position 2 (compounds *Ib*

and *IIb*); this was not observed. Notwithstanding, the influence of substituents at position 2 (or 4) is not negligible since the substituted derivatives are cyclised farly more readily than the unsubstituted (*E*)-isomers *Ia* and *IIa*.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). Analytical samples were dried at 25°C/0·01 Torr for 8 h. Thin-layer chromatography (Table I) was performed on fluorescent indicator-containing ready-for-use Silufol UV_{254} silica gel foils (Kavalier Glassworks, Votice, Czechoslovakia) in the solvent systems S_1, benzene–acetone (3 : 2), and S_2, benzene–ethyl acetate (2 : 1). The UV spectra were measured on an Optica Milano CF 4 apparatus, IR spectra were recorded on a Zeiss Model UR 10 apparatus, and NMR spectra were taken on a Varian HA 100 apparatus at 100 MHz. Polarographic measurements were performed on a LP 7 polarograph with attached recording millivoltmeter EZ 7.

Methyl Glyoxylate (*Z*)-Semicarbazone (*Ib*)

A) A stirred suspension of the semicarbazone[9] *Ia* (435 mg; 3 mmol) and 0·5M hydrogen chloride in acetonitrile (10 ml) was maintained at 50°C for 1·5 h and at room temperature for 1 h and then evaporated under diminished pressure. The residue was coevaporated with acetonitrile (20 ml) and chromatographed on a column of silica gel (particle size, 30–60 μ; 140 g) in the solvent system chloroform–ethanol (8 : 1). Yield, 54 mg (12·4%) of the (*Z*)-isomer *Ib*, m.p. 177–179°C (toluene), along with 325 mg (74·7%) of the starting semicarbazone *Ia*. UV spectrum of *Ib* (ethanol): λ_{max} 224 nm and 262 nm (log ε 3·73 and 3·94), λ_{min} 233 nm (log ε 3·70). IR spectrum (deuteriochloroform): 1702 cm^{-1} (CO), 3297 cm^{-1} (NH intramol. bridge), 3420 cm^{-1} (NH_2 sym.), 3539 cm^{-1} (NH_2 asym.). For $C_4H_7N_3O_3$ (145·1) calculated: 33·10% C, 4·86% H, 28·95% N; found: 32·90% C, 4·73% H, 28·65% N.

B) A solution of the semicarbazone *Ia* (435 mg; 3 mmol) in dimethyl sufoxide (20 ml) was heated at 150°C for 2·5 h and evaporated under diminished pressure. Column chromatography of the residue on silica gel yielded 31 mg (7%) of the (*Z*)-isomer *Ib* and 360 mg (83%) of the starting (*E*)-isomer *Ia*.

Methyl Glyoxylate (*E*)-4-Phenylsemicarbazone (*IIa*)

A solution of 4-phenylsemicarbazide hydrochloride (9·38 g; 50 mmol) and chloral hydrate (8·25 g; 50 mmol) in methanol (150 ml) was refluxed for 10 h and concentrated under diminished pressure to the volume of 75 ml. The concentrate was kept at +3°C to deposit crystals which were collected with suction and washed with methanol. Yield, 5·50 g of compound *IIa*, m.p. 181–184°C. The mother liquors were concentrated to the volume of 30 ml and kept at +3°C for 12 h to deposit an additional crop (2·81 g). Overall yield, 75% of compound *IIa*, m.p. 182·5 to 184·5°C (after recrystallisation from ethanol). UV spectrum (ethanol): λ_{max} 233 nm and 282 nm (log ε 4·11 and 4·05), λ_{min} 253 nm (log ε 3·99). IR spectrum (chloroform): 1539 cm^{-1} (amide II), 1597 cm^{-1} (C=N + ring), 1702 cm^{-1} (amide I dimer), sh 1723 cm^{-1} (CO ester), 3343 cm^{-1} (N^2H), 3395 cm^{-1} (N^4H). NMR spectrum (deuteriochloroform–hexadeuteriodimethyl sulfoxide, tetramethylsilane as internal standard): 3·76 (s, 3 H, $-COOCH_3$), 6·94–7·65 (m, 6 H, arom. protons + —CH=), 8·45 (broad s, 1 H, —NH—), 11·28 (broad s, 1 H,—NH—). For $C_{10}H_{11}N_3O_3$ (221·2) calculated: 54·29% C, 5·01% H, 19·00% N; found: 54·17% C, 5·05% H, 19·03% N.

Methyl Glyoxylate (*Z*)-4-Phenylsemicarbazone (*IIb*)

A solution of the phenylsemicarbazone *IIa* (221 mg; 1 mmol) in 0·5M hydrogen chloride in acetonitrile (10 ml) was maintained at 40°C for 20 min and at room temperature for 1 h. The acetonitrile was evaporated under diminished pressure, the residue coevaporated with fresh acetonitrile (5 ml), and chromatographed on a column of silica gel (particle size, 30—60 μ; 25 g) in chloroform. Yield, 63 mg (28·5%) of the (*Z*)-isomer *IIb*, m.p. 146—148°C (5 : 1 benzene–acetone) along with 139 mg (62·9%) of the recovered starting (*E*)-isomer *IIa*. UV spectrum of *IIb* (ethanol): λ_{max} 232 nm and 287 nm (log ε 4·02 and 4·02), sh 262 nm (log ε 3·97), λ_{min} 214 nm and 245 nm (log ε 3·79 and 3·92). Infrared spectrum (chloroform): 1 538 cm^{-1} (amide II), sh 1 584 cm^{-1}, 1 598 cm^{-1}, sh 1 604 cm^{-1} (C=N + ring), 1 704 cm^{-1} (CO), sh 1 723 cm^{-1} (amide I), 3 293 cm^{-1} (N^2H), 3 395 cm^{-1} (N^4H). NMR spectrum (deuteriochloroform–hexadeuteriodimethyl sulfoxide, tetramethylsilan as internal standard; chemical shifts in p.p.m.): 3·80 (s, 3 H, —$COOCH_3$), 6·94—7·62 (m, 6 H, arom. protons + —CH=), 8·25 (broad s, 1 H, —NH—), 11·12 (broad s, 1 H, —NH—). For $C_{10}H_{11}N_3O_3$ (221·2) calculated: 54·29% C, 5·01% H, 19·00% N; found: 54·05% C, 5·07% H, 19·11% N.

Methyl Glyoxylate 2-Methylsemicarbazone (*III*)

To a stirred suspension of the semicarbazone *Ia* (1·45 g; 10 mmol) in dimethylformamide (20 ml) there was added 1M methanolic sodium methoxide (10 ml). Methanol was removed by coevaporation with two 20 ml portions of toluene under diminished pressure. The thus-obtained suspension of the sodium salt of the semicarbazone *Ia* in dimethylformamide was treated with methyl iodide (0·8 ml), the whole mixture stirred at room temperature for 2 h, and evaporated under diminished pressure. The residue was crystallised from water to afford 1·16 g (73%) of compound *III*, m.p. 166—167°C. Ultraviolet spectrum (water): λ_{max} 272 nm (log ε 4·21), λ_{min} 227 nm (log ε 3·55). Infrared spectrum (chloroform): 1 556 cm^{-1} (amide II), 1 590 cm^{-1} (C=N), 1 710 cm^{-1} (CO), 1722 cm^{-1} (amide I), 3 417 cm^{-1} (NH_2 sym.), 3 536 cm^{-1} (NH_2 asym.). For $C_5H_9N_3O_3$ (159·15) calculated: 37·74 C, 5·70% H, 26·40% N; found: 37·80% C, 5·70% H, 26·11% N.

Methyl Glyoxylate 2-Benzylsemicarbazone (*IV*)

To a stirred mixture of the sodium salt of the semicarbazone *Ia* (10 mmol) and dimethylformamide (20 ml) prepared analogously to the preceding paragraph (compound *III*), there was added benzyl chloride (1·5 ml). The resulting solution was kept at room temperature for 3 h and evaporated under diminished pressure. The residue was triturated with chloroform (80 ml), the insoluble portion filtered off and washed with two 5 ml portions of chloroform. The filtrate and washings were combined and evaporated under diminished pressure. Crystallisation of the residue from ethanol yielded 1·86 g of compound *IV*, m.p. 188—189·5°C. Work-up of mother liquors yielded additional 260 mg of the product. Total yield, 90% of compound *IV*. UV spectrum (ethanol): λ_{max} 272 nm (log ε 4·09), λ_{min} 229·5 nm (log ε 3·48). IR spectrum (chloroform): 1 556 cm^{-1} (amide II), 1 593 cm^{-1} (C=N), 1 712 cm^{-1} (CO), 3 417 cm^{-1} (NH_2 sym.), 3 535 cm^{-1} (NH_2 asym.). For $C_{11}H_{13}N_3O_3$ (235·2) calculated: 56·16% C, 5·57% H, 17·86% N; found: 55·97% C, 5·52% H, 17·75% N.

Methyl Glyoxylate 2-Methyl-4-phenylsemicarbazone (*V*)

To a stirred mixture of the sodium salt of the phenylsemicarbazone *IIa* (2 mmol) and dimethylformamide (5 ml) prepared analogously to the procedure given above in the case of compound *III*, there was added methyl iodide (0·16 ml). The resulting mixture was stirred at room tempera-

ture for 30 min and evaporated under diminished pressure. The residue was dissolved in chloroform (10 ml), the insoluble portion filtered off and extracted with two 2 ml portions of chloroform. The filtrate and extracts were washed with two 5 ml portions of water, dried over magnesium sulfate, and evaporated under diminished pressure. Crystallisation of the residue from ether–light petroleum yielded 343 mg (73%) of compound *V*, m.p. 70—70·5°C. UV spectrum (ethanol): λ_{max} 233 nm and 288 nm (log ε 3·94 and 3·87), λ_{min} 214 nm and 252 nm (log ε 3·62 and 3·74). IR spectrum (chloroform): 1531 cm^{-1} (amide II), 1594 cm^{-1} (C=N), 1711 cm^{-1} (CO), 3390 cm^{-1} (NH). For $C_{11}H_{13}N_3O_3.0{\cdot}5\,H_2O$ (244·25) calculated: 54·10% C, 5·78% H, 17·20% N; found: 54·26% C, 5·77% H, 17·19% N.

Methyl Glyoxylate 2-Benzyl-4-phenylsemicarbazone (*VI*)

The title compound *VI* was prepared from the 4-phenylsemicarbazone *IIa* (442 mg; 2 mmol) and benzyl chloride (0·6 ml) analogously to the 2-methyl-4-phenylsemicarbazone *V*. The reaction mixture was stirred at room temperature for 3 h and evaporated under diminished pressure. The residue was dissolved in acetone (5 ml), the insoluble portion filtered off, and washed with acetone (2 ml). The filtrate and washings were evaporated under diminished pressure and the residue was crystallised from ethanol to yield 548 mg (88%) of compound *VI*, m.p. 153—154°C. UV spectrum (ethanol): λ_{max} 233 nm and 288 nm (log ε 4·18 and 4·00), λ_{min} 218 nm and 267 nm (log ε 4·01 and 3·92). IR spectrum (chloroform): 1531 cm^{-1} (amide II), 1595 cm^{-1} (C=N), 1710 cm^{-1} (CO), 3389 cm^{-1} (NH). For $C_{17}H_{17}N_3O_3$ (311·3) calculated: 65·58% C, 5·50% H, 13·50% H; found: 65·67% C, 5·47% H, 13·53% N.

Methyl Glyoxylate 2-Ethoxycarbonylmethylsemicarbazone (*VII*)
and 1-Methoxycarbonylmethyleneamino-3-ethoxycarbonylmethylhydantoin (*IX*)

To a stirred mixture of the sodium salt of the semicarbazone *Ia* (10 mmol) and dimethylformamide (10 ml) there was added ethyl chloroacetate (2·12 ml; 20 mmol). The mixture was kept at room temperature for 2 h and evaporated under diminished pressure. The residue was triturated with chloroform (80 ml), the insoluble solid collected with suction, washed with two 10 ml portions of chloroform, and crystallised from water to afford 634 mg of the starting semicarbazone *Ia*. The chloroform filtrate and washings were combined, evaporated under diminished pressure, and the residue crystallised from benzene to yield 835 mg of the hydantoin derivative *IX*, m.p. 146 to 149°C. UV spectrum (ethanol): λ_{max} 263 nm (log ε 4·00), λ_{min} 223 nm (log ε 3·47). IR spectrum (chloroform): 1597 cm^{-1} (C=N), sh 1710 cm^{-1}, sh 1724 cm^{-1} (CO ester), 1750 cm^{-1} (C^4O), 1815 cm^{-1} (C^2O). NMR spectrum (deuteriochloroform–hexadeuteriodimethyl sulfoxide, hexamethyldisiloxane as internal standard; referred to tetramethylsilane, chemical shifts in p.p.m.): 1·21 (t, 3 H, $\underline{CH_3}$—CH_2—, $J_{CH_3-CH_2}$ = 7·0 Hz), 3·78 (s, 3 H, —COO$\underline{CH_3}$), 4·15 (q, 2 H, CH_3—$\underline{CH_2}$—), 4·26 (s, 2 H, N—$\underline{CH_2}$), 4·47 (s, 2 H, N—$\underline{CH_2}$), 7·20 (s, 1 H, =CH—). For $C_{10}H_{13}N_3O_6$ (271·2) calculated: 44·28% C, 4·83% H, 15·49% N; found: 44·43% C, 4·85% H, 15·46% N.

The mother liquors remaining after crystallisation of compound *IX* were chromatographed on a column of silica gel (particle size, 30—60 μ; 30 g) in the solvent system benzene–acetone (1 : 1). Evaporation of the absorbing fraction 1 yielded additional 190 mg of compound *IX*. Total yield of compound *IX*, 69% (referred to the reacted semicarbazone *Ia*). The absorbing fraction 2 was evaporated and the residue crystallised from benzene to afford 50 mg (4%) of the semicarbazone *VII*, m.p. 134—137°C. UV spectrum (ethanol): λ_{max} 268 nm (log ε 4·03), plateau 210—225 nm (log ε 3·53). IR spectrum (chloroform): 1559 cm^{-1} (amide II), 1599 cm^{-1} (C=N), sh 1711 cm^{-1}, 1721 cm^{-1}, sh 1746 cm^{-1}, (CO + amide I), 3418 cm^{-1} (NH_2 sym.), 3536 cm^{-1} (NH_2 asym.). For $C_8H_{13}N_3O_5$ (231·2) calculated: 41·56% C, 5·67% H, 18·17% N; found: 41·59% C, 5·65% H,

17·95% N. Evaporation of absorbing fraction 3 afforded additional 20 mg of the starting semicarbazone *Ia*.

Glyoxylic Acid 2-Methylsemicarbazone (*X*)

The 2-methylsemicarbazone *III* (159 mg; 1 mmol) was dissolved in hot 80% aqueous methanol (10 ml), the solution treated with 1M methanolic sodium methoxide (1 ml), the whole kept at room temperature for 30 min, and applied to a column (1·2 × 12 cm) of Dowex 50 (H^+) ion exchange resin. The column was eluted with water, the eluate evaporated, and the residue crystallised from ethanol to afford 91 mg of compound *X*, m.p. 202°C (decomp.). Work-up of mother liquors yielded additional 27 mg of the same substance. Total yield, 81% of compound *X*. UV spectrum (ethanol): λ_{max} 268 nm (log ε 4·06), λ_{min} 222 nm (log ε 3·63). IR spectrum (KBr): 1571 cm^{-1} (amide II), 1584 cm^{-1} (C=N), sh 1694 cm^{-1}, 1710 cm^{-1}, sh 1725 cm^{-1} (CO + + amide I), 2540 cm^{-1} (OH), 3342 cm^{-1} (NH_2 sym.), 3481 cm^{-1}, 3497 cm^{-1} (NH_2 asym.). For $C_4H_7N_3O_3$ (145·1) calculated: 33·10% C, 4·86% H, 28·96% N; found: 33·31% C, 4·94% H, 29·13% N.

Glyoxylic Acid 2-Benzylsemicarbazone (*XI*)

Analogously to the preparation of the semicarbazone *X*, the 2-benzylsemicarbazone *IV* (235 mg; 1 mmol) was converted into 193 mg (87·5%) of compound *XI*, m.p. 203°C (decomp.). UV spectrum (ethanol): λ_{max} 267 nm (log ε 4·00), λ_{min} 228 nm (log ε 3·57). IR spectrum (KBr): 1551 cm^{-1} (amide II), 1593 cm^{-1} (C=N + ring), 1695 cm^{-1}, sh 1712 cm^{-1} (CO + amide I), 3293 cm^{-1}, sh 3310 cm^{-1} (NH_2 sym.), 3480 cm^{-1} (NH_2 asym.). For $C_{10}H_{11}N_3O_3$ (221·2) calculated: 54·29% C, 5·01% H, 19·00% N; found: 54·57% C, 5·11% H, 19·29% N.

Glyoxylic Acid Amide 2-Methylsemicarbazone (*XII*)

A solution of the 2-methylsemicarbazone *III* (79 mg; 0·5 mmol) in 18% methanolic ammonia (15 ml) kept at room temperature for 1·5 h and evaporated under diminished pressure. Crystallisation of the residue from ethanol yielded 50 mg of compound *XII*, m.p. 229·5—231·5°C. Work-up of mother liquors afforded additional 18 mg of the substance. Total yield, 93·5% of compound *XII*. UV spectrum (ethanol): λ_{max} 227 nm and 268 nm (log ε 3·88 and 4·12), λ_{min} 233 nm (log ε 3·87). IR spectrum (KBr): 1585 cm^{-1} (C=N), sh 1612 cm^{-1} (amide II), 1662 cm^{-1}, sh 1680 cm^{-1}, 1705 cm^{-1} (amide I), 3290 cm^{-1}, 3400 cm^{-1} (NH_2). For $C_4H_8N_4O_2$ (144·1) calculated: 33·33% C, 5·59% H, 38·87% N; found: 33·53% C, 5·56% H, 38·86% N.

Glyoxylic Acid Amide 2-Benzylsemicarbazone (*XIII*)

Analogously to the preparation of compound *XII*, the 2-benzylsemicarbazone *IV* (118 mg; 0·5 mmol) was converted into 103 mg (93·5%) of compound *XIII*, m.p. 206·5—209·5°C. UV spectrum (ethanol): λ_{max} 266 nm (log ε 4·00), λ_{min} 229 nm (log ε 3·72). IR spectrum (KBr): 1586 cm^{-1}, 1606 cm^{-1} (C=N + amide II + ring), 1666 cm^{-1}, 1694 cm^{-1} (amide I), 3212 cm^{-1}, sh 3260 cm^{-1}, 3311 cm^{-1}, sh 3335 cm^{-1}, 3433 cm^{-1} (NH_2). For $C_{10}H_{12}N_4O_2$ (220·2) calculated: 54·54% C, 5·49% H, 25·44% N; found: 54·74% C, 5·58% H, 25·22% N.

Methyl Glyoxylate 2-Methylhydrazone (*XIV*)

Sodium hydride (55 mg) was added with stirring to a solution of the 2-methylsemicarbazone *III* (318 mg; 2 mmol) in dimethylformamide (5 ml), the stirring continued for 10 min, the mixture

treated with 1M acetic acid in methanol (2 ml), and evaporated under diminished pressure. The residue was triturated with chloroform (10 ml), the insoluble portion filtered off, and washed with three 5 ml portions of chloroform. The combined filtrate and washings were evaporated under diminished pressure and the residue chromatographed on a column of silica gel (particle size, 30–60 μ; 25 g) in the solvent system chloroform–acetone (4 : 1). The greatest absorbing fraction was evaporated to afford 155 mg of a residue. Crystallisation of the residue from ether–light petroleum yielded 103 mg of compound *XIV*, m.p. 58·5–59·5°C. Work-up of mother liquors furnished additional 29 mg of the substance of an identical melting point value. Total yield, 57% of compound *XIV*. UV spectrum (ethanol): λ_{max} 273 nm (log ε 4·09), λ_{min} 218 nm (log ε 3·20). IR spectrum (chloroform): 1 580 cm^{-1} (C=N), 1 709 cm^{-1}, sh 1 721 cm^{-1} (CO), 3 454 cm^{-1} (NH). NMR spectrum (deuteriochloroform, tetramethylsilane as internal standard, chemical shifts in p.p.m.): 2·97 (s, 3 H, N—CH_3), 3·81 (s, 3 H, —$COOCH_3$), 6·68 (s, 1 H, =CH—), 7·0 (broad r, 1 H, —NH—). For $C_4H_8N_2O_2$ (116·1) calculated: 41·37% C, 6·94% H, 24·13% N; found: 41·23% C, 6·86% N, 24·13% N.

Determination of cyanate. Sodium hydride (14 mg) was added with stirring to a solution of the 2-methylsemicarbazone *III* (79·6 mg; 0·5 mmol) in dimethylformamide (1·25 ml), the stirring continued for 10 min, and the mixture diluted with water to the volume of 25 ml. The cyanate content was 0·453 mmol as determined polarographically from the wave height by means of a calibration curve.

Methyl Glyoxylate 2-Benzylhydrazone (*XV*)

Analogously to the preparation of the 2-methylhydrazone *XIV*, the 2-benzylsemicarbazone *IV* (470 mg; 2 mmol) was converted into the title compound *XV*. The dimethylformamide was evaporated, the residue triturated with water (2 ml), the insoluble portion filtered off, and washed with two 2 ml portions of water. Crystallisation from di-n-propyl ether yielded 244 mg (63·5%) of compound *XV*, m.p. 85·5–86·5°C. UV spectrum (ethanol): λ_{max} 278 nm (log ε 4·10), λ_{min} 230 nm (log ε 3·42). IR spectrum (chloroform): 1 576 cm^{-1} (C=N), sh 1 604 cm^{-1} (ring), 1 709 cm^{-1}, sh 1 721 cm^{-1} (CO), 3 428 cm^{-1}, 3 452 cm^{-1} (NH). NMR spectrum (deuterio-

TABLE I
Thin-Layer Chromatography

Compound	S_1	S_2	Compound	S_1	S_2
Ia	0·16	0	*IX*	0·66	0·21
Ib	0·34	0·07	*XIV*	0·50	0·17
IIa	0·62	0·27	*XV*	0·71	0·41
IIb	0·78	0·62	*XVI*	0·74	0·42
III	0·35	0·07	*XVII*	0·84	0·64
IV	0·46	0·14	*XVIII*	0·52	0·22
V	0·82	0·46	*XIX*	0·69	0·43
VI	0·91	0·70	*XX*	0·41	0·11
VII	0·42	0·10	*XXI*	0·65	0·35

chloroform, hexamethyldisiloxane as internal standard, referred to tetramethylsilane; chemical shifts in p.p.m.): 3·51 (s, 3 H, —COOC$\underline{H}_3$), 3·69 (s, 3 H, —COOC$\underline{H}_3$), 4·33 (s. 2 H, —C$\underline{H}_2$—), 4·54 (d, 2 H, —C$\underline{H}_2$—NH, J_{CH_2-NH} = 4·5 Hz), 6·39 (s, 1 H, —C$\underline{H}$=), 6·69 (s, 1 H, —C$\underline{H}$=), 7·25 (m, 5 H, arom. protons), 10·55 (broad s, 1 H, —NH—). For $C_{10}H_{12}N_2O_2$ (192·2) calculated: 62·48% C, 6·30% H, 14·58% N; found: 62·65% C, 6·37% H, 14·76% N. The cyanate content was 0·495 mmol when 0·5 mmol of the 2-benzylsemicarbazone *IV* was used as reactant.

Methyl Glyoxylate 2-Acetyl-2-methylhydrazone (*XVI*)

To a solution of the 2-methylhydrazone *XIV* (23·2 mg; 0·2 mmol) in acetic anhydride (0·5 ml there was added sodium acetate (3 mg), the mixture heated at 65°C for 1 h, and the acetic anhydride removed by coevaporation with toluene under diminished pressure. Crystallisation of the residue from cyclohexane yielded 22 mg of compound *XVI*, m.p. 62—63°C. Work-up of mother liquors afforded additional 6 mg of the substance of the same melting point. UV spectrum (ethanol): λ_{max} 263 nm (log ε 3·74), λ_{min} 213 nm (log ε 2·96). IR spectrum (chloroform): 1 587 cm^{-1} (C=N), sh 1 696 cm^{-1}, 1 706 cm^{-1}, 1 743 cm^{-1} (CO). For $C_6H_{10}N_2O_3$ (158·2) calculated: 45·56% C, 6·37% H, 17·72% N; found: 45·74% C, 6·46% H, 17·73% N.

Methyl Glyoxylate 2-Acetyl-2-benzylhydrazone (*XVII*)

Analogously to the preparation of compound *XVI*, the 2-benzylhydrazone *XV* (38·5 mg; 0·2 mmol) was converted (reaction time, 2 h in this instance) into 45 mg of compound *XVII*, m.p. 93—94°C (cyclohexane). UV spectrum (ethanol): λ_{max} 261 nm (log ε 3·99), λ_{min} 224 nm (log ε 3·54). IR spectrum (chloroform): 1 590 cm^{-1} (C=N), 1 703 cm^{-1}, 1 741 cm^{-1} (CO). For $C_{12}H_{14}N_2O_3$ (234·25) calculated: 61·52% C, 6·02% H, 11·96% N; found: 61·47% C, 6·06% H, 12·04% N.

1-Methyl-6-azauracil (*XVIII*)

A) A solution of the 2-methylsemicarbazone *III* (159 mg; 1 mmol) in 0·1M methanolic sodium methoxide (20 ml) was refluxed for 7 h, cooled down, neutralised with Dowex 50 (H^+) ion exchange resin (prewashed with methanol), the resin filtered off, and washed with three 10 ml portions of methanol. The filtrate and washings were combined, evaporated, and the residue chromatographed on a column of silica gel (particle size, 30—60 μ; 40 g) in the solvent system chloroform–acetone (3 : 1). The absorbing fraction 1 was evaporated and the residue crystallised from ether–light petroleum to afford 10 mg of a substance, m.p. 58—59°C, undepressed on admixture with authentic 2-methylhydrazone *XIV*; the UV and IR spectra of both substances were also identical. The residue after evaporation of the absorbing fraction 2 was crystallised from water to afford 27 mg (21%) of compound *XVIII*, m.p. 156—157°C, undepressed on admixture with authentic 1-methyl-6-azauracil[18]; the UV and IR spectra of both specimens were also identical

B) A mixture of the 2-methylsemicarbazone *III* (318 mg; 2 mmol), sodium acetate (30 mg), and acetic anhydride (4 ml) was refluxed for 4 h and the acetic anhydride removed by coevaporation with toluene under diminished pressure. The residue was chromatographed on a column of silica gel (particle size, 30—60 μ; 50 g) in the solvent system benzene–acetone (3 : 1). The absorbing fraction 1 was evaporated and the residue crystallised from cyclohexane to afford 102 mg of a substance, m.p. 62—63°C, undepressed on admixture with authentic acetylmethylhydrazone *XVI*; the IR spectra of both specimens were also identical. Work-up of the absorbing fraction 2 and crystallisation of the residue from water yielded 60 mg of 1-methyl-6-azauracil (*XVIII*). The absorbing fraction 3 was evaporated and the residue crystallised from ethanol to afford 37 mg

of the starting 2-methylsemicarbazone *III*. When referred to the reacted 2-methylsemicarbazone *III*, the yield of 1-methyl-6-azauracil (*XVIII*) was 27%.

1-Benzyl-6-azauracil (*XIX*)

A) A solution of the 2-benzylsemicarbazone *IV* (235 mg; 1 mmol) in 0·1M methanolic sodium methoxide (20 ml) was refluxed for 2·5 h, cooled down, and neutralised with Dowex 50 (H^+) ion exchange resin (prewashed with methanol). The resin was filtered off and washed with three 10 ml portions of methanol. The filtrate and washings were combined and evaporated under diminished pressure. The residue was crystallised from 2-propanol to yield 123 mg of compound *XIX*, m.p. 189—190·5°C. Work-up of mother liquors by chromatography on a column of silica gel (particle size, 30—60 μ; 20 g) in the solvent system benzene–ethyl acetate (1 : 4) afforded additional 28 mg of the substance. Total yield, 74% of compound *XIX*. UV spectrum (pentanol): λ_{max} 276 nm (log ε 3·82), λ_{min} 238 nm (log ε 3·36). IR spectrum (KBr): 1 580 cm^{-1} (C=N), 1 693 cm^{-1}, sh 1 714 cm^{-1}, sh 1 733 cm^{-1} (CO), 3 100 cm^{-1}, 3 155 cm^{-1} (NH). For $C_{10}H_9N_3O_2$ (203·2) calculated: 59·11% C, 4·46% H, 20·68% N; found: 59·25% C, 4·46% H, 20·90% N.

B) A mixture of the 2-benzylsemicarbazone *IV* (470 mg; 2 mmol), sodium acetate (20 mg), and acetic anhydride (4 ml) was refluxed for 2 h and the acetic anhydride removed by coevaporation with toluene under diminished pressure. Crystallisation of the residue from 2-propanol (3 ml) yielded 112 mg of compound *XIX*, m.p. 188·5—190·5°C, undepressed on admixture with authentic specimen; the IR spectra of both substances were identical. The mother liquors were processed by chromatography on a column of silica gel (particle size, 30—60 μ; 50 g) in the solvent system chloroform–ethyl acetate (4 : 1). Fraction 1 was evaporated and the residue crystallised from cyclohexane to afford 73 mg of a substance, m.p. 93—94°C, undepressed on admixture with the acetylbenzylhydrazone *XVII*; the IR spectra of both specimens were identical. Fraction 2 was also evaporated and the residue crystallised from ethanol to afford 67 mg of the starting benzylsemicarbazone *IV*. The yield of 1-benzyl-6-azauracil (*XIX*) was 32% (referred to the reacted benzylsemicarbazone *IV*).

Cyclisation of the (*Z*)-Isomer *Ib* to 6-Azauracil (*XX*)

A solution of the (*Z*)-semicarbazone *Ib* (29 mg; 0·2 mmol) in 0·1M methanolic sodium methoxide (2 ml) was kept at room temperature for 1·5 h and then neutralised with Dowex 50 (H^+) ion exchange resin (prewashed with methanol). The resin was filtered off and washed with two 1 ml portions of methanol. The filtrate and washings were combined and evaporated under diminished pressure to afford 21 mg of compound *XX*, m.p. 268—270°C, undepressed on admixture with an authentic[6] specimen of 6-azauracil; the IR spectra of both substances were identical.

3-Phenyl-6-azauracil (*XXI*)

A solution of the (*Z*)-phenylsemicarbazone *IIb* (221 mg; 1 mmol) in 0·1M methanolic sodium methoxide (10 ml) was kept at room temperature for 20 min and then neutralised with Dowex 50 (H^+) ion exchange resin (prewashed with methanol). The resin was filtered off and washed with two 5 ml portions of methanol. The filtrate and washings were combined and evaporated under diminished pressure. Crystallisation of the residue from ethanol yielded 120 mg of compound *XXI*, m.p. 255—256°C. Work-up of mother liquors yielded additional 40 mg of the substance. Total yield, 84·5% of compound *XXI*. UV spectrum (ethanol): λ_{max} 262 nm (log ε 3·76), λ_{min} 225 nm (log ε 3·40). IR spectrum (KBr): 1 592 cm^{-1} (C=N), 1 656 cm^{-1}, 1 736 cm^{-1} (CO),

3110 cm^{-1}, 3172 cm^{-1}, 3220 cm^{-1} (NH). For $C_9H_7N_3O_2$ (189·2) calculated: 57·14% C, 3·73% H, 22·21% N; found: 57·04% C, 3·78% H, 22·03% N.

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