9*H*-Pyrimido[4,5-*b*]indole-2,4-diones. The Acid-catalyzed Cyclization of 6-(Phenylhydrazino)uracils

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6-(Phenylhydrazino)uracils undergo facile Fischer-type cyclization in both *N* hydrochloric acid and in formic acid at reflux to give 9*H*-pyrimido[4,5-*b*]indole-2,4-diones. Yields appear to be related to substituent effects and side reactions, and these are discussed in light of the mechanism of this reaction. In the reaction of 6-(phenylhydrazino)uracil itself with hydrochloric acid, the major competing reaction is hydrolysis to barbituric acid and phenylhydrazine, whereas in formic acid a novel cyclization occurs to give 1-phenyl-3-carboxamidomethyl-1,2,4-triazole as the major product. Nmr spectra of pyrimido[4,5-*b*]indole-2,4-diones provide interesting examples of *peri* effects on proton chemical shifts.

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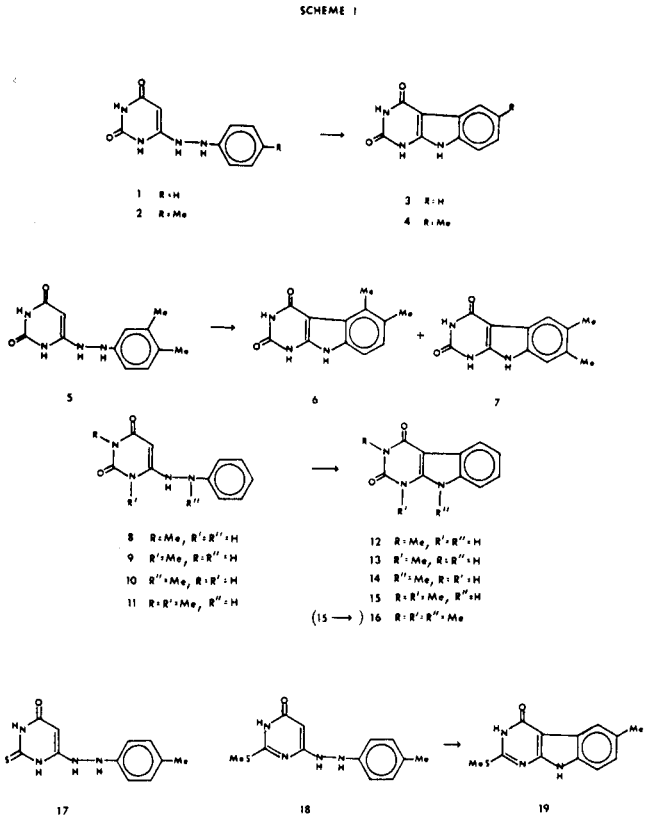
Our studies of the chemistry of 6-(arylhydrazino)pyrimidines, potent inhibitors of *Bacillus subtilis* DNA polymerase III (1,2), prompted us to examine the acid sensitivity of several 6-(phenylhydrazino)uracils. When **1** was dissolved in hot formic acid and the solution was diluted with an equal volume of water and chilled, a low yield of product was obtained which had a molecular ion 17 mass units lower than that of the starting compound. Its nmr spectrum (DMSO-d_6) showed three exchangeable resonances between 10.5 and 12.0 δ and unresolved multiplets in the aromatic region corresponding to four protons. These data suggested its structure to be 9*H*-pyrimido-[4,5-*b*]indole-2,4-dione (**3**), apparently resulting from a Fischer-type cyclization. Although the 9*H*-pyrimido-[4,5-*b*]indole ring system has been synthesized primarily by photochemical cyclization of 4-anilinopyrimidines (3a, 3b,4), one example exists where 1,3-dimethyl-6-(phenylhydrazino)uracil was cyclized thermally to 1,3-dimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (4). An analogous cyclization of phenylhydrazinopyridones has recently been reported (5). It was of interest to explore the generality of this reaction and its utility in the synthesis of 9*H*-pyrimido[4,5-*b*]indole-2,4-diones and related compounds.

When *C*-methyl-6-(phenylhydrazino)uracils were heated at reflux with either formic acid or *N* hydrochloric acid for 1 hour, the expected pyrimidoindoles were obtained. The yield of a given pyrimidoindole, with the exception of **3**, was always higher in hydrochloric acid than in formic acid. This was not a result of incomplete reaction in formic acid since no starting material was detected in either case. The yield was also found to increase with *C*-methyl substitution: whereas the yield of **3** from reaction in hydrochloric acid was only 21%, that of **4** was 64% and that of *C*-dimethyl isomer mixture (**6**,**7**) was 84%.

SCHEME I

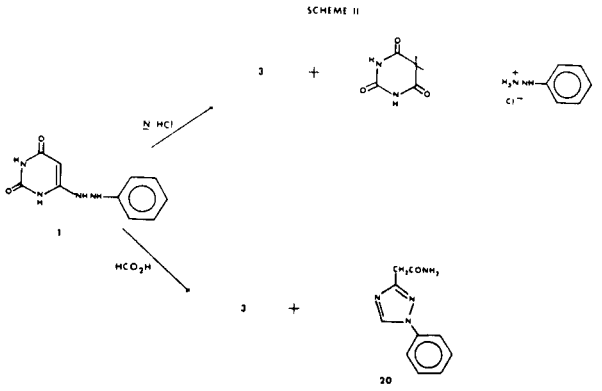


This reaction is analogous to the classical Fischer indole synthesis (6). The mechanism probably involves initial *N*-protonation followed by nucleophilic attack by an *ortho* phenyl carbon on the uracil 5-carbon and cleavage of the *N*-*N* bond. Loss of a hydrogen ion and tautomerization would give a diamine which could undergo ring closure by expulsion of the *uracil* amino group. That the uracil amino group and not the anilino is displaced in the final step is clear from the formation of **14** from **10**, where the *N*-methyl group is retained in the product. While the thermal cyclization of 4-pyrimidylhydrazones is best represented as a concerted [3,3]sigmatropic shift (7). the effects of electron-releasing methyl groups described above suggest that the phenyl ring provides the attacking electron pair. Observed yields, however, might be more directly related to competing reactions (see below), and could simply reflect the increased basicity of the anilino nitrogen with *C*-methyl substitution.

The above pyrimidoindoles proved to be rather intractible solids: indeed, several gave consistently poor elemental analyses (see Experimental). In contrast, pyrimidoindoles derived from ring *N*-methylated 6-(phenylhydrazino)uracils were crystallizable from methanol and, except for **15**, were obtained in high yields. Two compounds, in fact, seemed to spontaneously cyclize. When crude **9** was purified for elemental analysis, both analytical results and nmr suggested that such samples were mixtures of **9** and **13**. Also, under the conditions of synthesis of 1,3-dimethyl-6-(phenylhydrazino)uracil (**11**) from 1,3-dimethyl-6-aminouracil and phenylhydrazine, the isolated product consisted of a mixture of both **11** and the corresponding pyrimidoindole **15**. Upon crystallization from methanol, only **15** was obtained, indicating an unusually facile thermal cyclization of **11**. (It had been reported (4), however, that **11** was crystallized from methanol intact.) 1,3,9-Trimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (**16**), obtained by treating **15** with dimethyl sulfate, had a melting point identical to that previously reported (4).

A 2-thiouracil analog behaved differently. Attempted cyclization of **17** in both formic and hydrochloric acids gave products which are as yet unidentified, but which do not appear to be the 2-thiopyrimidoindole. However, 6-(*p*-tolylhydrazino)-2-methylmercapto-4-pyrimidone (**18**) gave a 66% yield of the pyrimidoindole **19** after 15 minutes of reflux in *N* hydrochloric acid. When the reaction was prolonged to 1 hour, hydrolysis of 2-SMe occurred giving **4** as the only product. Similarly, when **19** was boiled in *N* sodium hydroxide for 1 hour, the hydrolyzed product **4** was isolated.

SCHEME II



Side Reactions.

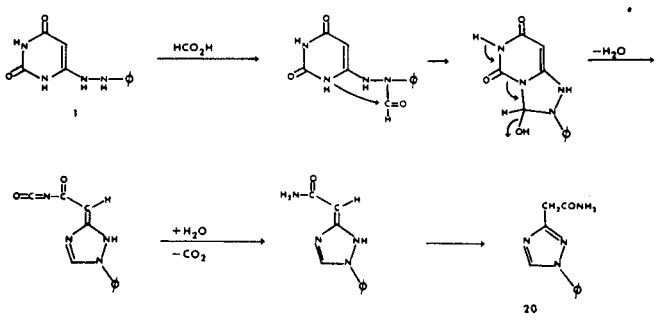
Relatively low yields of **3** and the inability to detect any starting material after even a brief (10 minutes) exposure to boiling acid led us to examine the reactions of **1** with both hydrochloric and formic acids in some detail (Scheme II).

When the filtrate remaining after isolation of **3** from a reaction of **1** with *N* hydrochloric acid was concentrated, a crystalline material was obtained. Its nmr spectrum and melting point indicated that it was barbituric acid (47% yield). Evaporation of the remaining filtrate produced a mass which was crystallized from methanol-ether; the colorless solid proved to be phenylhydrazine hydrochloride (50% yield). Apparently, hydrolysis of **1** is the major competing reaction under these conditions. Similarly, workup of a reaction of **2** with *N* hydrochloric acid gave smaller amounts of barbituric acid and *p*-tolylhydrazine hydrochloride.

The competing reaction of **1** in formic acid took a different course. In addition to the pyrimidoindole a crystalline compound was obtained, m.p. 204-206°, in 48% yield. Its nmr spectrum (DMSO-d_6) indicated the presence of five phenyl protons in a complex multiplet, a single proton peak at 9.16 δ and a two proton singlet at 3.57 δ. The only exchangeable resonance corresponded to two equivalent protons at 7.01 δ, suggesting the absence of the intact uracil ring and the presence of an amino group. An even number of nitrogens in this substance was inferred from the value of the molecular ion (m/e 202). When boiled in *N* sodium hydroxide, the odor of ammonia could be detected; acidification of this solution produced a new compound, m.p. 189-191°, whose nmr spectrum differed only in the absence of the exchangeable resonance at 7.01 δ and in the occurrence of a new exchangeable peak at 12.50 δ due to one proton.

Collectively, these data, in addition to the elemental analysis, led us to assign the structure of 1-phenyl-3-carboxamidomethyl-1,2,4-triazole (**20**) to this product. (Thus the product of its hydrolysis is 1-phenyl-3-carboxymethyl-1,2,4-triazole). The mechanism of formation of **20** can readily be rationalized (Scheme III). Formylation of the anilino nitrogen of **1** followed by attack by *N*-1 would produce a bicyclic system; its conjugate elimination of

SCHEME III



water as depicted would result in cleavage of the uracil ring, producing an acyl isocyanate. Subsequent hydration, decarboxylation and tautomerism could than lead to the observed product.

It was reasoned that the above sequence might produce a 5-methyltriazole when **1** was heated in glacial acetic acid. Reflux of **1** in acetic acid gave only starting material after 1 hour, but after 21 hours, 42% of the pyrimidoindole **3** was isolated as well as a small amount of a crystalline product, m.p. 110-112°. Its mass spectrum, nmr spectrum, and mixed melting point with an authentic sample showed that this substance was simply acetanilide. It most likely arises from cleavage of acetylated **1** (Scheme III) which, in view of the failure to isolate an analogous triazole, seems to support acylation of **1** as the first step in its unusual cyclization to **20**. Furthermore, **10**, with a methyl group on the anilino nitrogen, gives only the pyrimidoindole **14** in 81% yield with no evidence of a triazole side product.

The reaction of **2** with boiling formic acid yielded a compound, m.p. 186-189°, whose nmr spectrum is consistent with its being 1-(*p*-tolyl)-3-carboxamidomethyl-1,2,4-triazole. The mechanism of this cyclization and the chemistry of these products are being examined and will be reported later.

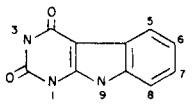
Nmr Spectra.

The proton nmr spectra of 9*H*-pyrimido[4,5-*b*]indole-2,4-diones are summarized in the Table. In addition to providing evidence for the structure of these compounds, unusual chemical shifts of certain protons can be observed. The 5-hydrogen of each compound consistently appears at lower field than the other hydrogens of the *benzo* ring. This is due to its close proximity to the 4-oxo group of the *pyrimido* ring where it lies in the deshielding region of that group. The chemical shifts of the methyl protons of **6** and **7** confirm this assignment: whereas both methyl groups appear at 2.27 δ in **7**, one of them is shifted considerably downfield (2.84 δ) in **6**, undoubtedly the 5-Me lying close to the 4-oxo group. Other *benzo* ring hydrogens appear within a relatively narrow range of chemical shifts, although H-8 would seem generally to be the most deshielded (see Table).

Peri effects (8) also distinguish chemical shifts of the N-H resonances. Whereas the 3-H resonances appear in the normal range for uracil N-H protons, *e.g.*, 10.3 δ in 6-aminouracil, 10.3-10.4 δ in 6-(phenylhydrazino)uracils (1), 1-H and 9-H exert mutual anisotropic deshielding effects of approximately 1 ppm relative to 3-H. While we have assigned the further downfield of these resonances to 1-H, this assignment is by no means unequivocal. We base the assignment on the small upfield shifts of the resonance at 11.60 δ in **3** upon *C*-methyl substitution and the lack of significant shifts of the one at *ca.* 11.8 δ. Similar mutual deshielding of 1- and 9-NMe protons is

Table

Nmr Chemical Shifts of Pyrimido[4,5-*b*]indole-2,4-diones (DMSO-d_6; δ ppm)



Compound	Substituents	1H	3H	9H	5H	6H	7H	8H	1Me	3Me	9Me	C-Me
3	---	11.86	10.63	11.60	7.73	(	7.2	)	---	---	---	---
4	6-Me	11.85	10.65	11.43	7.55	---	6.94	7.27	---	---	---	2.37
6	5,6-diMe	11.83	10.50	11.44	---	---	6.94	7.10	---	---	---	5Me: 2.84 6Me: 2.27
7	6,7-diMe	11.8	10.5	11.4	7.52	---	---	7.15	---	---	---	6,7Me: 2.27
12	3-Me	12.25	---	11.63	7.77	(	7.21	)	---	3.24	---	---
13	1-Me	---	10.90	12.09	7.79	(	7.24	)	3.47	---	---	---
14	9-Me	11.92	10.73	---	7.78	(	7.3	)	---	---	3.75	---
15	1,3-diMe	---	---	12.09	7.86	(	7.25	)	3.53	3.28	---	---
16	1,3,9-triMe	---	---	---	7.84	(	7.35	)	3.82	3.28	4.02	---

evident in the spectrum of **16**: comparison of the positions of the analogous methyls of **13** and **14** with those of **16** show downfield shifts of *ca.* 0.3 ppm arising from this interaction.

EXPERIMENTAL

Melting points were determined on a Fischer-Johns apparatus and are uncorrected. Nmr spectra were obtained with a Perkin-Elmer R-12B instrument equipped with a Nicolet TT7 Fourier Transform Accessory. Spectra were obtained in DMSO-d_6 solution (Stohler Isotope Chemicals) and chemical shifts are reported in ppm (δ) from internal TMS. Mass spectra were obtained with a Dupont 21-490 instrument *via* direct inlet. Elemental analyses were performed by Het-Chem-Co., Harrisonville, MO, (C,H,N) and by PCR Inc., Gainesville, FL (S), Several pyrimidoindoles (**3**, **6**, **7**) were difficult to purify and gave poor elemental analyses. Starting materials available commercially were used without further purification; 3,4-dimethylphenylhydrazine hydrochloride was made by diazotization and reduction of the aniline (9).

2-Methylmercapto-3-methyl-6-amino-4-pyrimidone.

A solution of methyl iodide (11.8 g., 0.083 mole) in absolute ethanol (40 ml.) was added during 45 minutes to a refluxing solution of 6-amino-2-thiouracil (5.0 g., 0.035 mole) and potassium hydroxide (4.6 g. of 85%, 0.070 mole) in absolute ethanol (80 ml.). After 3.5 hours, the solvent was removed under reduced pressure, and cold water (20 ml.) was added to the residue. The product was filtered with suction and crystallized from water giving 4.1 g. (68%), m.p. 253-255°, lit. (10) m.p. 255°; nmr: 6.39 δ (NH_2), 4.99 δ (5-*H*), 3.39 δ (NCH_3), 2.50 δ (SCH_3).

3-Methyl-6-aminouracil.

2-Methylmercapto-3-methyl-6-amino-4-pyrimidone (0.5 g., 0.0029 mole) was heated at reflux in 10% sodium hydroxide solution (15 ml.) for 1 hour. The solution was neutralized with *N* hydrochloric acid and chilled overnight. The colorless product was filtered with suction and crystallized from water giving 0.35 g. (85%), m.p. > 300°, lit. (11) m.p. 327°; nmr: 6.40 δ (NH_2), 4.54 δ (5-*H*), 3.0 δ (CH_3).

1-Methyl-6-aminouracil.

6-Aminouracil (2 g., 0.0157 mole) was dissolved in a solution of sodium hydroxide (0.65 g., 0.0157 mole) in water (20 ml.). Dimethyl sulfate (1.98 g., 0.0157 mole) was added dropwise with stirring. After 1 hour the mixture was chilled and the precipitate filtered with suction. The solid was heated with concentrated ammonium hydroxide for several minutes, the mixture chilled, and the product filtered with suction and washed with cold water giving 0.92 g. (41%), m.p. 308-310°, lit. (12) m.p. 305°; nmr: 10.07 δ (3-N*H*), 6.74 δ (NH_2), 4.58 δ (5-*H*), 3.18 δ (CH_3).

1,3-Dimethyl-6-aminouracil.

Dimethylsulfate (26.8 g., 0.213 mole) and a solution of sodium hydroxide (8.52 g., 0.213 mole) in water (100 ml.) were added during 4 hours to a stirred suspension of 6-aminouracil (10 g., 0.079 mole) in water (40 ml.). After stirring for an additional 19 hours, the mixture was chilled and filtered with suction giving 9.1 g. (74%) of off-white solid, m.p. 280-289°. Crystallization from water raised the m.p. to 292°, lit. (13) m.p. 293°; nmr: 6.76 δ (NH_2), 4.72 δ (5-*H*), 3.22 δ (1-CH_3), 3.05 δ (3-CH_3).

6-(Phenylhydrazino)uracils.

The synthesis of several compounds (**1, 2, 10**) has been reported (1). The general reaction involved reflux in aqueous solution of the appropriate 6-aminouracil or 6-amino-2-thiouracil, phenylhydrazine (2 moles) and acetic acid (2 moles). In the cases where phenylhydrazine hydrochlorides were used, an equivalent volume of *N* sodium hydroxide was added to a reaction mixture prior to reflux, followed by acetic acid. Purification of these products, which take on dark colors as a result of partial oxidation to the corresponding azo compounds, was effected by dissolving in *N* sodium hydroxide solution, filtering, decolorizing with aqueous sodium dithionite and adjusting to *p*H 8 with glacial acetic acid. The precipitated products were filtered with suction, washed thoroughly with water and dried *in vacuo* over phosphorus pentoxide.

6-(3',4'-Dimethylphenylhydrazino)uracil (**5**).

After 4 hours at reflux, 87% of tan solid was obtained, m.p. > 300°; nmr: 10.19 δ (1,3-*H*), 8.07 δ (6-N*H*), 7.53 δ (1'-N*H*), 6.94 δ (d, 6'-*H*, J = 8 Hz), 6.52 δ (s, 2'-*H*), 6.45 δ (d, 5'-*H*, J = 8 Hz), 4.56 δ (5-*H*), 2.12 δ (3',4'-CH_3).

Anal. Calcd. for $C_{12}H_{14}N_4O_2 \cdot H_2O$: C, 54.54; H, 6.10; N, 21.20. Found: C, 54.40; H, 6.04; N, 21.33.

3-Methyl-6-(phenylhydrazino)uracil (**8**).

After 3 hours at reflux, 63% of off-white powder was obtained, m.p. > 300°; nmr: 10.6 δ (1-*H*), 8.24 δ (6-N*H*), 7.85 δ (1'-N*H*), 6.6-7.5 δ (multiplet, -C_6H_5), 4.79 δ (5-*H*), 3.06 δ (CH_3).

Anal. Calcd. for $C_{11}H_{12}N_4O_2 \cdot 0.5\ H_2O$: C, 54.76; H, 5.43; N, 23.22. Found: C, 54.61; H, 5.36; N, 23.23.

1-Methyl-6-(phenylhydrazino)uracil (**9**).

After 4 hours at reflux, 41% of light purple solid was isolated, m.p. > 300°; nmr: 10.48 δ (3-*H*), 8.84 δ (6-N*H*), 7.90 δ (1'-N*H*), 6.6-7.5 δ (multiplet, -C_6H_5), 4.71 δ (5-*H*), 3.49 δ (CH_3). [The results of several elemental analyses and nmr showed that purified and dried (*in vacuo*) samples of **9** consisted of mixtures of **9** and the corresponding pyrimidoindole (**13**)].

6-(*p*-Tolylhydrazino)-2-thiouracil (**17**).

Six hours at reflux were required to give 40% of light brown powder, m.p. > 300°; nmr: 8.08 δ (6-N*H*), 7.80 δ (1'-N*H*), 7.04 δ (d, 2',6'-*H*, J = 7.8 Hz), 6.67 δ (d, 3',5'-*H*, J = 7.8 Hz), 4.88 δ (5-*H*), 2.18 δ (CH_3); M^+: m/e 248.

Anal. Calcd. for $C_{11}H_{12}N_4OS \cdot 2H_2O$: C, 46.46; H, 5.67; N, 19.70; S, 11.28. Found: C, 46.65; H, 5.36; N, 19.35; S, 11.01, 11.49.

2-Methylmercapto-6-(*p*-tolylhydrazino)-4-pyrimidone (**18**).

To a solution of **17** (0.75 g., 0.003 mole) in *N* sodium hydroxide (15 ml.) was added methyl iodide (0.47 g., 0.033 mole). After stirring for 1 hour at room temperature, the dark solution was filtered through glass wool and treated with a solution of sodium dithionite (0.5 g.) in water (5 ml.). After acidification with glacial acetic acid and chilling, the product was filtered with suction and washed with cold water giving 0.62 g. (78%) of light tan solid, m.p. 195-199°; nmr: 11.7 δ (3-*H*), 8.71 δ (6-N*H*), 7.66 δ (1'-N*H*), 7.03 δ (d, 2',6'-*H*, J = 7.8 Hz), 6.66 δ (d, 3',5'-*H*, J = 7.8 Hz), 5.08 δ (5-*H*), 2.44 δ (-SCH_3), 2.20 δ (4'-CH_3).

Anal. Calcd. for $C_{12}H_{14}N_4OS \cdot 2H_2O$: C, 48.30; H, 6.08; N, 18.78. Found: C, 48.10; H, 5.95; N, 19.03.

1,3-Dimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (**15**).

1,3-Dimethyl-6-aminouracil (1.0 g., 0.0064 mole), phenylhydrazine (1.4 g., 0.0129 mole) and acetic acid (0.4 g., 0.0067

mole) were heated at reflux in water (25 ml.) for 6 hours. The reddish solution was taken to dryness *in vacuo* and boiled down three times with benzene. Methanol (10 ml.) was added to the dark red residue and the solution stood overnight. The light purple precipitate was filtered with suction and washed with cold methanol. Crystallization from methanol gave 0.27 g. (18%) of colorless fibers, m.p. >300°, lit. (4) m.p. >300°.

1,3,9-Trimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (**16**).

Compound **15** (0.18 g., 0.00079 mole) was dissolved in 2 ml. of *N* sodium hydroxide solution. Dimethyl sulfate (0.11 g., 0.00087 mole) was added, and the solution was stirred at room temperature for 1 hour. The mixture, which had formed a colorless precipitate, was made strongly alkaline with 5*N* sodium hydroxide solution and filtered with suction. The product was washed with water giving 0.11 g. (57%). Crystallization from methanol afforded needles, m.p. 246-248°, lit. (4) m.p. 248°.

Cyclization of 6-(Phenylhydrazino)uracils.

a) In Formic Acid.

The starting compound was heated at reflux in 98% formic acid (25 ml. per g.). After 1 hour an equal volume of water was added and the solution was chilled. The precipitated product was filtered with suction and washed thoroughly with water.

b) In Hydrochloric Acid.

The starting compound was heated at reflux in *N* hydrochloric acid (25 ml. per g.) for 1 hour. The mixture was chilled and the product filtered with suction and washed with water.

9*H*-Pyrimido[4,5-*b*]indole-2,4-dione (**3**).

Method a) gave 23% and method b) 21% of off-white solid, m.p. >300° (from DMSO-water); M^+: m/e 201.

6-Methyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (**4**).

Method a) afforded 35% while method b) gave 64% of tan solid, m.p. >300° (from DMSO-water); M^+: m/e 215.

Anal. Calcd. for $C_{11}H_9N_3O_2 \cdot H_2O$: C, 56.65; H, 4.75; N, 18.01. Found: C, 56.27; H, 5.05; N, 18.25.

5,6-Dimethyl- and 6,7-Dimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4-diones (**6** and **7**).

Method b) produced an approximately equimolar mixture (nmr) of **6** and **7**, total yield 84%. The brownish solid (300 mg.) was treated with DMSO (20 ml.), and the insoluble material was filtered with suction and washed repeatedly with water giving **7** as a colorless solid, m.p. >300°.

Anal. Calcd. for $C_{12}H_{11}N_3O_2 \cdot 0.67\ H_2O$: C, 59.74; H, 5.15; N, 17.41. Found: C, 59.98; H, 4.75; N, 16.91.

The above filtrate was diluted with water (10 ml.) and the precipitate was filtered with suction and washed repeatedly with water giving **6** as a light brown solid, m.p. >300°.

3-Methyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (**12**).

Method b) produced 72% of colorless solid, m.p. >300° (from methanol).

Anal. Calcd. for $C_{11}H_9N_3O_2 \cdot 0.33\ H_2O$: C, 59.74; H, 4.40; N, 19.00. Found: C, 60.05; H, 4.56; N, 18.90.

1-Methyl-9*H*-pyrimido[4,5-*b*]indole-2,4-dione (**13**).

Method b) gave 65% of colorless crystals, m.p. >300° (from methanol).

Anal. Calcd. for $C_{11}H_9N_3O_2 \cdot 1.5\ H_2O$: C, 54.54; H, 4.99, N, 17.35. Found: C, 54.45; H, 5.25; N, 17.33.

9-Methyl-9*H*-pyrido[4,5-*b*]indole-2,4-dione (**14**).

Method a) gave 81% and method b) gave 54% of colorless solid, m.p. >300° (from DMSO-water); M^+: m/e 215.

Anal. Calcd. for $C_{11}H_9N_3O_2 \cdot 2\ H_2O$: C, 52.58; H, 5.21; N, 16.72. Found: C, 52.55; H, 5.14; N, 17.11.

2-Methylmercapto-6-methyl-9*H*-pyrimido[4,5-*b*]indol-4-one (**19**).

Method b) after reflux for 15 minutes, produced 66% of light brown solid, m.p. > 300° (from DMSO-water); nmr (deuterioacetone/DMSO-d_6): 11.79 δ (3*H* or 9*H*), 7.79 δ (s, 5-*H*), 7.36 δ (d, 8-*H*, J = 7.8 Hz), 7.10 δ (d, 7-*H*, J = 7.8 Hz), 2.63 δ (SCH_3), 2.44 δ (6-CH_3).

Anal. Calcd. for $C_{12}H_{11}N_3OS \cdot 0.2\ H_2O$: C, 57.90; H, 4.62; N, 16.88. Found: C, 58.21; H, 4.80; N, 16.67.

Reaction of **1** with *N* Hydrochloric Acid.

6-(Phenylhydrazino)uracil (**1**) (2.7 g., 0.0124 mole) was heated at reflux in *N* hydrochloric acid (75 ml.) for 1 hour. After standing overnight, the light brown solid was filtered with suction and washed with water giving 0.52 g. (21%) of **3**. The filtrate was reduced to about one-third its volume under reduced pressure and bright yellow crystals formed. The mixture was chilled and the solid filtered with suction giving 0.75 g. (47%) of barbituric acid. One crystallization from water gave colorless crystals, m.p. 257-259°; an authentic sample had m.p. 256-257°.

The second filtrate was evaporated to dryness under reduced pressure. Crystallization from methanol-ether gave 0.9 g. (50%) of phenylhydrazine hydrochloride, m.p. 245-248°; an authentic sample melted at 246-248°.

Reaction of **1** with 98% Formic Acid.

A solution of **1** (1.0 g., 0.0046 mole) in 98% formic acid (25 ml.) was heated at reflux for 1 hour. An equal volume of water was added and, after chilling overnight, 0.21 g. (23%) of **3** was isolated by filtration. The filtrate was reduced *in vacuo* to a dark oil. Water (10 ml.) was added and a copious yellow precipitate appeared. It was filtered with suction and crystallized from methanol affording 0.45 g. (48%) of **20** as colorless needles, m.p. 204-206°; nmr: 9.16 δ (s, 1H), 7.4-7.8 δ (m, 5H), 7.01 δ (bd s, 2H), 3.57 δ (s, 2H); M^+: m/e 202.

Anal. Calcd. for $C_{10}H_{10}N_4O$: C, 59.40; H, 4.98; N, 27.71. Found: C, 57.60; H, 5.14; N, 28.07.

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