The Synthesis and Properties of Certain *N*-Methylated 5-Diazouracils (1)

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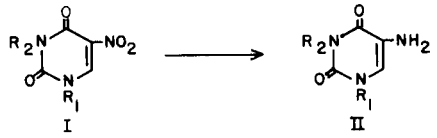
The reduction of 1-methyl-, 3-methyl- and 1,3-dimethyl-5-nitrouracil (Ia-c) to the corresponding 5-aminouracils (IIa-c) is described. Diazotization of 5-amino-1-methyluracil (IIa) and 5-amino-1,3-dimethyluracil (IIc) gave 5-diazouracils which were characterized as thermally stable C6 covalent hydrates (III and XIII). Diazotization of 5-amino-3-methyluracil (IIb) gave anhydro 5-diazo-3-methyluracil (X) which underwent covalent methanolation and thermally reversible covalent hydration. Treatment of III and XIII with hot methanol resulted in solvent exchange of the C6 hydroxyl groups by a mechanism which may involve initial formation of diazoethers. Treatment of the methanolates (IV, XI and XIV) with dimethylamine resulted in coupling at the diazo group with a concomitant expulsion of the C6 methoxyl groups to give 5-(3,3-dimethyl-1-triazeno)uracils (XVa-c).

Our recent investigations on 5-diazouracils have resulted in the revision of several structures (2). These investigations also included the discovery that some of these derivatives undergo hydrolytic (3,4) and thermal (5) ring contractions. We now wish to report on the synthesis of certain *N*-methylated-5-diazouracils and our subsequent studies on their chemical reactivity.



I II

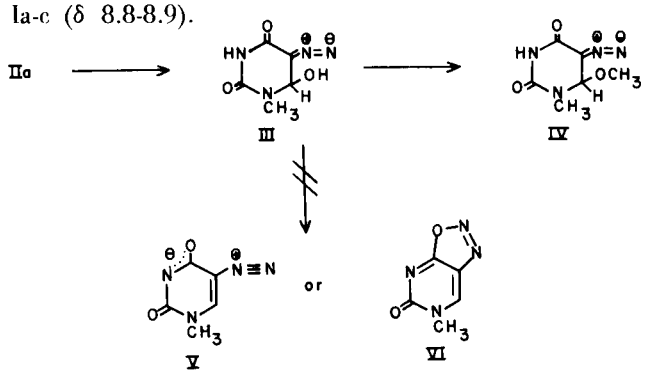
a) R_1=CH_3, R_2=H
b) R_1=H, R_2=CH_3
c) R_1=CH_3, R_2=CH_3

Several methods which have been reported for the preparation of 5-aminouracils include the treatment of 5-bromouracils with liquid ammonia (6,7) or alkylamines (8) and the reduction of 5-nitrouracils by catalytic hydrogenation (9-11) or by treatment with sodium hydrosulfite (12-14). In our hands, these methods were found to be unsatisfactory for the preparation of the requisite amines (IIa-c).

Treatment of 5-bromo-*N*-methylated uracils with liquid ammonia at 100° for several days gave only unreacted starting material. Atmospheric pressure catalytic hydrogenation of the 5-nitrouracils (Ia-c) gave low yields of the amines (IIa-c) which were contaminated by impurities and required purification as their hydrochlorides. Reduction of the 5-nitrouracils (Ia-c) with sodium hydrosulfite failed to give an isolable product.

This prompted us to study other methods for the reduction of these 5-nitrouracils. We have found that reduction of 5-nitrouracils (Ia-c) by treatment with hydrazine and palladium on charcoal in refluxing ethanol (15) provided a convenient preparation of the amines (IIa-c) and gave consistently high yields of products which were not contaminated by impurities.

The amines (IIa-c) were characterized by standard methods. In particular, their ultraviolet spectra showed a significant hypsochromic shift (approx. 35 nm) of the absorption maximum in absolute methanol as compared with *p*H 1 buffer. The pmr spectra (DMSO-d_6) of the amines (IIa-c) showed a broad exchangeable singlet (δ 4.1, NH_2) which integrated for two protons and a peak for the C6 protons of IIa-c was found significantly upfield (δ 6.8-6.9) from the peak observed for the C6 protons of Ia-c (δ 8.8-8.9).

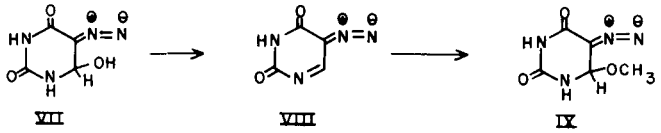


IIa III IV V or VI

Diazotization of 5-amino-1-methyluracil (IIa) gave a product which was recrystallized from water to furnish 5-diazo-1-methyluracil as a covalently bound hydrate (III). The structure was assigned on the basis of the following data: elemental analyses (CHN) were found to be consistent with the empirical formula $C_5H_6N_4O_3$; the infrared spectrum showed a strong absorption at 2140 cm^{-1} which has been reported (2) to be characteristic of the diazo group of other 5-diazouracils and the ultraviolet absorption maximum was observed at 265 nm which was very similar to the absorption maxima of similar 5-diazouracils (2).

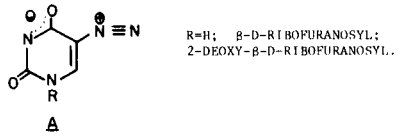
The pmr spectra (DMSO-d_6 and DMSO-d_6/deuterium oxide) of III revealed a peak (s) for the N1 methyl group (δ 2.93), two peaks (d) (δ 5.95 and δ 6.95, J = 8.0 Hz) and a broad exchangeable peak (s) (δ 10.4) which was assigned to a proton residing at N3. On the addition of deuterium oxide to the pmr sample, the peak (d) at δ 6.95 underwent exchange and the peak (d) at δ 5.95 collapsed to a singlet. This allowed assignment of the peak (d) at δ 6.95 to a covalently bonded hydroxyl group at C6 and the peak (d) at δ 5.95 to a proton residing at C6.

We found III to be thermally stable up to its melting point (16). Attempts to thermally dehydrate III to afford V or VI by heating a sample for 24 hours in an Abderhalden apparatus at the reflux temperature of toluene, under 0.5 Tr pressure, gave only unchanged III. This thermal stability was of considerable interest since we have previously (2) observed a facile dehydration of 5-diazouracil-6-hydrate (VII) to give 5-diazouracil (VIII) by merely drying VII at ambient temperature and pressure for several hours.



VII VIII IX

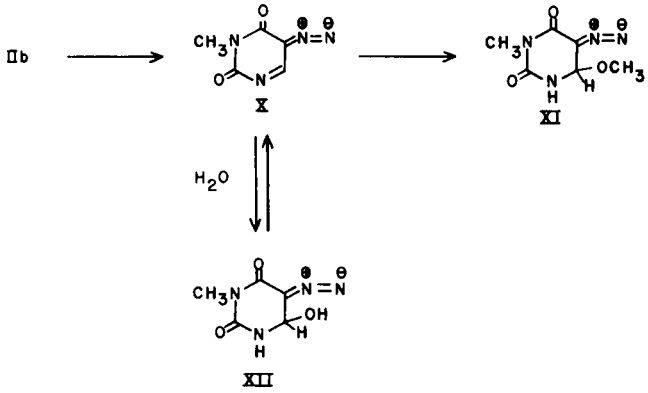
This was also of interest since it demonstrated that 5-diazouracils which are alkylated at N1 cannot be thermally converted to the "internal ion" species A, or to bicyclic structures similar to VI which were previously proposed (17-19) for the structures of certain 5-diazouracils. It also demonstrated that dehydration of VII cannot proceed *via* the initial formation of A (R=H) with a subsequent tautomeric shift to provide VIII.



A

We have previously shown (2) that the conversion of VIII to IX by recrystallization from methanol proceeded by an addition mechanism. We have also observed (2) a conversion of VII to IX by heating VII in methanol at reflux temperature. It was proposed (2) that this conversion proceeded by an elimination-addition mechanism on the basis of the facile dehydration observed for VII and the expectation that dehydration of VII should be rapid at the reflux temperature of methanol. In view of the thermal stability of III, it was of interest to determine whether an exchange of the C6 hydroxyl group by a methoxyl group would occur merely on the recrystallization of III from methanol. A methanolic solution of III was heated for a brief period to afford the C6 methoxyl derivative IV. The ultraviolet absorption maximum (263 nm) and infrared spectrum (2120 cm^{-1}, diazo) of IV were very similar to the data for III but elemental analyses gave the empirical formula $C_6H_8N_4O_3$. The pmr spectrum of IV also showed two methyl groups (δ 2.97 and δ 3.18), a broad exchangeable singlet (δ 10.6) for a proton residing at N3 and a singlet (δ 6.10) for the C6 proton. This established that recrystallization of III from methanol had resulted in an exchange of the C6 hydroxyl group by a methoxyl group. The mechanism of this exchange was investigated further by a study of the 1,3-dimethyl derivative (*vide infra*).

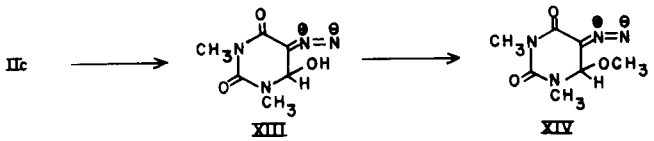
Diazotization of 5-amino-3-methyluracil (IIb) was complicated by the failure of XII to crystallize from aqueous solution. This necessitated the use of an extraction procedure to furnish a product which was assigned the structure 5-diazo-3-methyluracil (X) on the basis of elemental analyses ($C_5H_4N_4O_2$), an ultraviolet absorption maximum of 301 nm when determined in anhydrous



acetonitrile and a strong band (2150 cm^{-1}, diazo) in the infrared spectrum. A pmr spectrum of X (DMSO-d_6) revealed the presence of a methyl group (δ 3.20) and a peak for an aromatic proton (δ 9.19) with a chemical shift similar (2) to the chemical shift for the peak assigned to the C6 proton of VIII (δ 9.13).

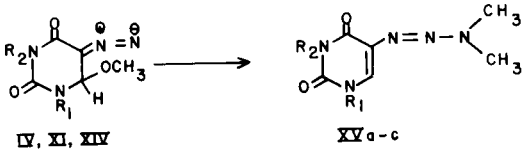
Recrystallization of X from methanol resulted in the addition of methanol to the 1,6 double bond to afford 5-diazo-3-methyluracil-6-methanolate (XI). The structural

assignment for XI was facilitated by observing two doublets (δ 5.72, J = 5.0 Hz; δ 8.82, J = 5.0 Hz) in the pmr spectrum (DMSO-d_6) for the C6 and N1 protons, respectively, and by observing an exchange of the doublet at δ 8.82 with the concomitant collapse of the doublet at δ 5.72 to a singlet when deuterium oxide was added to the pmr sample. To demonstrate that 1,6-double bond addition was reversible, the pmr spectrum of X was first determined in deuterium oxide solution with XII-d_2 being observed. The pmr sample was then evaporated *in vacuo* to dryness, redissolved in DMSO-d_6 and the spectrum again determined. This spectrum was identical to the spectrum of X and established that hydration of X occurs across the 1,6-double bond and that XII may then be thermally dehydrated to afford X. These studies have established that 5-diazo-3-methyluracil (X) is similar to 5-diazouracil (VIII) (2) in regards to addition-elimination reactions at the 1,6-double bond.



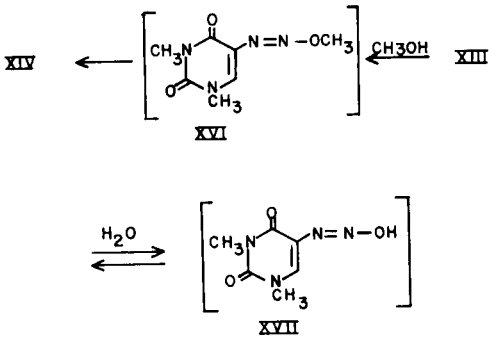
IIc XIII XIV

5-Amino-1,3-dimethyluracil (IIc) was diazotized and the product recrystallized from water to give a compound which was assigned the structure 5-diazo-1,3-dimethyluracil-6-hydrate (XIII) on the basis of ultraviolet and infared spectral data comparisons to the spectral data of III, as well as the elemental analyses which were found to be consistent with the empirical formula $C_6H_8N_4O_3$. The pmr spectrum of XIII (DMSO-d_6) showed peaks (singlets) (δ 2.96 and δ 3.08) for the N1 and N3 methyl groups and two doublets (δ 5.83 and δ 6.88. J = 8.0 Hz) which were assigned to the C6 proton and C6 hydroxyl group, respectively. The latter two assignments were confirmed by the addition of deuterium oxide to the pmr sample and observing an exchange of the doublet at δ 6.88 with the concomitant collapse of the doublet at δ 5.83 to a singlet. Recrystallization of XIII from methanol resulted in an exchange of the C6 hydroxyl group by a methoxyl group to give 5-diazo-1,3-dimethyluracil-6-methanolate (XIV). That an exchange had occurred was established by a method similar to that used for a determination of the structure for IV (*vide supra*).



IV, XI, XIV XVa-c

The *N*-methylated-5-diazouracil-6-methanolates (IV, XI and XIV) were found to undergo coupling at the diazo group when treated at room temperature with anhydrous dimethylamine for 1-3 days to give the 5-(3,3-dimethyl-1-triazeno)-*N*-methylated uracils (XVa-c). The appearance of a peak for two equivalent methyl groups (δ 3.3) in the pmr spectra and a downfield shift of the C6 proton from δ 5.7-6.1 to δ 7.2-7.5 established that coupling had indeed occurred to provide XVa-c. Similar reactions of 5-diazouracil-6-methanolate (IX) and the nucleosides 5-diazouridine and 5-diazo-2′-deoxyuridine have been reported (2). These reactions demonstrate that nucleophilic attack may occur at the diazo group of 5-diazouracils.



XIV XVI XIII XVII

When 5-diazo-6-hydroxy-1,6-dihydrouracils are heated in methanol at reflux temperature for a brief period, the C6 hydroxyl group is replaced by a methoxyl group. We have shown (*vide infra*) that when a proton is present at N1, this exchange can occur by an elimination-addition mechanism. If, however, a methyl group is located at N1, thermal dehydration does not occur and the exchange must proceed by a different mechanism. The reactions of 5-diazouracils with dimethylamine to give the triazeno derivatives suggested that the mechanism of these exchange reactions might involve the formation of an unstable diazoether. The diazoether XVI which could be formed in the reaction of XIII would be thermally unstable (20), decomposing with solvent capture at the C6 position to form XIV. If this was correct, there should be a detectible equilibrium between XIII and its corresponding diazotic acid (XVII) in aqueous solution. Spectral evidence for this equilibrium was obtained by the following experiment.

A dilute solution of XIII in water was prepared and examined by differential uv spectroscopy. Aliquots of the solution were placed in 1 cm uv cells and one of the samples placed in the reference compartment of the spectrophotometer. The other sample was heated in a water bath maintained at 77° for 3 minutes and then placed in the sample compartment of the spectrophotometer. The spectrum was determined immediately and

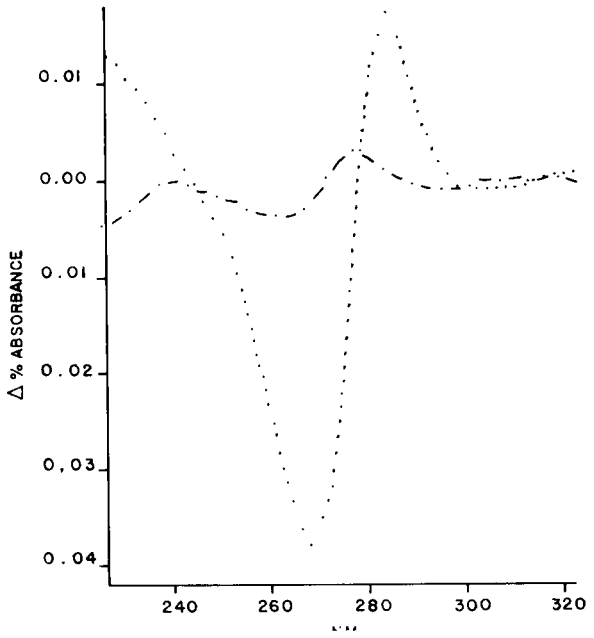


Figure 1. Differential uv spectrum of 5.8 x 10^{-5} *M* aqueous solution of 5-diazo-1,3-dimethyluracil-6-hydrate (XIII). - - - -, sample and reference at 26°; · · ·, reference at 26°; sample after heating at 77° for 3 minutes.

revealed that the heated sample had an increase in absorptivity at 283 nm while the absorptivity at 268 nm (the position of the maximum of XIII) had decreased with respect to the sample which had not been heated (Fig. 1). A gradual decrease in the absorption maxima was observed as the sample cooled, with the baseline being retraced when the sample had cooled to 27°. When this experiment was repeated, using acetonitrile as the solvent, the effect was not observed.

This data was consistent with the presence of a thermally mobile equilibrium between XIII and the corresponding diazotic acid (XVII). This would suggest that the exchange reactions of III and XIII may proceed *via* unstable diazoethers similar to XVI.

EXPERIMENTAL

Ultraviolet spectra were determined on a Beckman DK2 or a Beckman ACTA CIII recording spectrophotometer and ir spectra on a Beckman IR-8 spectrophotomer in compressed potassium bromide discs, unless otherwise indicated. Pmr spectra were obtained using a Varian A56/60 spectrometer in DMSO-d_6 or DMSO-d_6/D_2O solution at ambient temperature with sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as an internal standard and the chemical shifts are expressed as δ, parts per million from DSS. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Concentrations *in vacuo* were performed at or below 40°. Samples for analysis were dried in a Abderhalden apparatus, under 0.5 Tr vacuum using phosphorous pentoxide as the dessicant.

General Procedure for the Reduction of 5-Nitro-*N*-methylated Uracils (Ia-c).

The 5-nitro-*N*-methylated uracil [Ia or Ib (21), 10 g., Ic (22), 10.8 g.] was finely powdered in a mortar and then mixed with 5% palladium on carbon (6.6 g.). The mixture and reaction flask was then *thoroughly* (23) flushed with nitrogen. Ethanol (0°) was added and the contents of the flask were thoroughly mixed under a nitrogen atmosphere. Hydrazine (97%, 5.5 ml.) was added dropwise with vigorous stirring and the reaction mixture was slowly (about 1 hour) heated to reflux temperature. Reflux temperature was maintained for 3-4 hours and the catalyst was then removed from the hot mixture by filtration through a celite bed. The celite bed was washed with 400-600 ml. of hot ethanol. Isolation and purification of the amines (IIa-c) was performed as described below. Samples for elemental analyses were dried for 3-4 hours at the reflux temperature of toluene.

5-Amino-1-methyluracil (IIa).

Ethanol (1.42 l.) was used as the solvent. The filtrate and washings were concentrated *in vacuo* to 600 ml. The solid which had separated was redissolved by heating and on standing at room temperature for 18 hours, IIa (6.42 g., 78%) separated from solution as amber needles, m.p. 248-250°, uv λ max (*p*H 1): 268 nm (ε, 6,900), (methanol) 301 nm (ε, 5,900).

Anal. Calcd. for $C_5H_7N_3O_2$: C, 42.55; H, 5.00; N, 29.77. Found: C, 42.28; H, 5.01; N, 30.08.

5-Amino-3-methyluracil (IIb).

Ethanol (1.1 l.) was used as the solvent. The filtrate and washings were concentrated *in vacuo* to near dryness to give a damp white powder. This powder was recrystallized from hot ethanol (250 ml.) to give IIb (6.63 g., 81%) as colorless needles, m.p. 202-204°, uv λ max (*p*H 1): 260 nm (ε, 7,300), (methanol) 294 nm (ε, 5,220).

Anal. Calcd. for $C_5H_7N_3O_2$: C, 42.55; H, 5.00; N, 29.77. Found: C, 42.49; H, 4.97; N, 29.91.

5-Amino-1,3-dimethyluracil (IIc).

The following method for the reduction of 5-nitro-1,3-dimethyluracil (Ic) was found to be better than the previously reported (11) procedure. Ethanol (525 ml.) was used as the solvent. The filtrate and washings were concentrated *in vacuo* to dryness and the residue recrystallized from 250 ml. of xylene (120°) to give IIc (7.65 g., 85%), m.p. 136-137°, lit. (11) m.p. 136-138°; uv λ max (*p*H 1): 268 nm (ε, 7,600), (methanol) 301 nm (ε, 6,760); lit. (11) uv λ max (methanol): 302 nm (ε, 6,300).

Anal. Calcd. for $C_6H_9N_3O_2$: C, 46.45; H, 5.85; N, 27.08. Found: C, 46.41; H, 5.84; N, 27.12.

5-Diazo-6-hydroxy-1-methyl-1,6-dihydropyrimidin-2,4-(3*H*,6*H*)-dione. (5-Diazo-6-hydroxy-1-methyl-1,6-dihydrouracil) (III).

5-Amino-1-methyluracil (IIa, 4.78 g., 33.8 mmoles) was dissolved in 0.957 *N* hydrochloric acid (74.5 ml., 2.10 eq.) and the solution cooled to 0° in an ice-salt bath. A 6.9% aqueous sodium nitrite solution (39.4 ml., 1.10 eq.) was added dropwise with efficient stirring over a period of 18 minutes while maintaining the temperature at -2° to +1°. After the addition was complete the solution was stirred in the cold salt bath for 15 minutes and 0.99 *N* sodium hydroxide (34.1 ml., 1.00 eq.) was then added dropwise at such a rate that the temperature remained below 5°.

The solution was treated with Norit, the Norit was removed by filtration and the filtrate concentrated *in vacuo* to 50 ml. After standing at 5° for 18 hours, the solid which had separated from solution was collected by filtration, washed with water (10 ml. at 0°) and recrystallized from water (80 ml. at 60°) to afford pure III (5.04 g., 88%). A sample for analysis was dried for 7 hours at the reflux temperature of methanol, m.p. 155-158° melt and resolidfy, remelt at 235-238°; uv λ max (water): 265 nm (ε, 18,700); ir 2140 cm^{-1} (diazo).

Anal. Calcd. for $C_5H_6N_4O_3$: C, 35.30; H, 3.55; N, 32.93. Found: C, 35.24; H, 3.53; N, 32.79.

5-Diazo-6-hydroxy-1,3-dimethylpyrimidin-2,4-(6*H*)dione. (5-Diazo-6-hydroxy-1,3-dimethyl-1,6-dihydrouracil) (XIII).

5-Amino-1,3-dimethyluracil (IIc, 1.85 g.) was dissolved in 1 *N* hydrochloric acid (15 ml.) and the solution cooled to 0° in an ice-salt bath. A 6.9% aqueous sodium nitrite solution (13.7 ml.) was added dropwise with stirring over a period of 25 minutes while maintaining the temperature at 0-2°. After the addition was complete, the solution was stirred in the cold for 15 minutes and the *p*H of the solution was adjusted to 7 with 1 *N* sodium hydroxide. The solution was warmed to 60° and the temperature maintained at 60° until the color changed from red to light yellow (about 10 minutes). The solution was then concentrated *in vacuo* to 10 ml. and allowed to stand at 5° for 18 hours. The light yellow crystals which had separated from solution were collected by filtration, washed with water (2 x 2 ml. at 0°) and recrystallized from water (5 ml. at 50°) to give 1.8 g. (82%) of XIII, m.p. 96-99°. A small sample was recrystallized from water (50°) for analysis and dried for 5 hours at the reflux temperature of methanol, m.p. 101-102°; uv λ max (water): 268 nm (ε, 16,500); ir: 2110 cm^{-1} (diazo).

Anal. Calcd. for $C_6H_8N_4O_3$: C, 39.13; H, 4.38; N, 30.42. Found: C, 39.01; H, 4.58; N, 30.42.

5-Diazo-3-methylpyrimidin-2,4-(1*H*)dione. (5-Diazo-3-methyluracil) (X).

5-Amino-3-methyluracil (IIb, 500 mg.) was diazotized by the procedure described above for IIa. After removal of the Norit, the filtrate was concentrated *in vacuo* to 3 ml. and this solution was extracted with a 3:2 (v:v) mixture of chloroform:acetonitrile (4 x 8 ml.). The organic phases were combined and dried (magnesium sulfate) at 5° for 18 hours. The dried solution was concentrated *in vacuo* to afford a light yellow oil which crystallized on trituration with anhydrous diethylether (10 ml.) to give 363 mg. (68%) of X. A sample was dried for 2 hours at ambient temperature for analysis, m.p. 123-124°, uv λ max (acetonitrile): 301 nm (ε, 15,200); ir: 2150 cm^{-1} (diazo).

Anal. Calcd. for $C_5H_4N_4O_2$: C, 39.48; H, 2.65; N, 36.83. Found: C, 39.51; H, 2.76; N, 36.67.

5-Diazo-6-methoxy-1-methyl-1,6-dihydropyrimidin-2,4-(3*H*,6*H*)-dione. (5-Diazo-6-methoxy-1-methyl-1,6-dihydrouracil) (IV).

5-Diazo-1-methyluracil-6-hydrate (III, 5.50 g.) was added to methanol (40 ml.) and the mixture heated to reflux temperature and heating was continued for 15 minutes after III had dissolved. The solution was then allowed to stand at -30° for 18 hours to give IV (5.55 g., 93%), m.p. 121-123°. A sample for analysis was dried for 2 hours at the reflux temperature of methanol, m.p. unchanged; uv λ max (methanol): 263 nm (ε, 13,600); ir: 2120 cm^{-1} (diazo).

Anal. Calcd. for $C_6H_8N_4O_3$: C, 39.13; H, 4.38; N, 30.42. Found: C, 38.91; H, 4.11; N, 30.32.

5-Diazo-6-methoxy-3-methyl-1,6-dihydropyrimidin-2,4-(1*H*,6*H*)-dione. (5-Diazo-6-methoxy-3-methyl-1,6-dihydrouracil) (XI).

5-Amino-3-methyluracil (IIb, 2.86 g.) was diazotized, extracted and dried by the method described above for the preparation of X. The oil, instead of being directly crystallized, was dissolved in hot methanol and the solution heated at reflux temperature for 5 minutes and then allowed to stand at -30° for 18 hours. The light yellow needles which had separated from solution were collected by filtration, triturated with diethylether (15 ml. for 3 minutes) and dired for 1 hour at ambient temperature to give 2.45 g. (70%) of XI, m.p. 86-87°. A small sample was recrystallized from methanol for analysis and dried for 5 hours at ambient temperature, m.p. 95-97°; uv λ max (methanol): 268 nm (ε, 18,400); ir: 2140 cm^{-1} (diazo).

Anal. Calcd. for $C_6H_8N_4O_3$: C, 39.13; H, 4.38; N, 30.42. Found: C, 39.19; H, 4.51; N, 30.53.

5-Diazo-6-methoxy-1,3-dimethyl-1,6-dihydropyrimidin-2,4-(6*H*)-dione. (5-Diazo-6-methoxy-1,3-dimethyl-1,6-dihydrouracil) (XIV).

5-Diazo-1,3-dimethyluracil-6-hydrate (XIII, 3.25 g.) and methanol (100 ml.) were heated at reflux temperature for 18 hours and the solution was then concentrated *in vacuo* to dryness to give XIV as an analytically pure oil. The product (XIV) usually crystallized on standing at -30° for several days, m.p. 37-38°; uv λ max (methanol): 264 nm (ε, 20,800); ir (neat): 2120 cm^{-1} (diazo).

Anal. Calcd. for $C_7H_{10}N_4O_3$: C, 42.42; H, 5.09; N, 28.27. Found: C, 42.51; H, 5.20; N, 28.38.

5-(3,3-Dimethyl-1-triazeno)-1-methyluracil (XVa).

5-Diazo-6-methoxy-1-methyl-1,6-dihydrouracil (IV, 630 mg.) was placed in a 25 ml. round bottom flask and dimethylamine (approximately 18 ml.) was condensed into the flask under anhydrous conditions. The flask was tightly stoppered and allowed to stand at room temperature for 3 days. The mixture was then concentrated *in vacuo* to dryness and the residue triturated with anhydrous diethylether (10 ml. for 15 minutes). The insoluble material was collected by filtration, washed with diethylether (15 ml.) and recrystallized from dry acetonitrile to give 496 mg. (74%) of XVa, m.p. 185-187°. A small sample was recrystallized from acetonitrile for analysis and dried for 20 hours at the reflux temperature of toluene, m.p. 193-194°; uv λ max (methanol): 270 nm (ε, 10,100), 335 nm (ε, 12,200).

Anal. Calcd. for $C_7H_{11}N_5O_2$: C, 42.64; H, 5.62; H, 35.51. Found: C, 42.67; H, 5.60; N, 35.81.

5-(3,3-Dimethyl-1-triazeno)-3-methyluracil (XVb).

5-Diazo-6-methoxy-3-methyl-1,6-dihydrouracil (XI, 418 mg.) was dissolved in dry ethylacetate (5 ml.) and the solution cooled to the temperature of a dry-ice/methanol bath. Dimethylamine (2.5 ml.) was then condensed into the flask under anhydrous conditions. The reaction flask was tightly stoppered and allowed to stand at room temperature for two days. The mixture, containing tan needles, was cooled to -30° and the crystals collected by filtration, washed with anhydrous diethylether (3 x 5 ml.) and dried for 6 hours at ambient temperature to give 373 mg. (83%) of XVb, m.p. 167-169°; uv λ max (methanol): 266 nm (ε, 12,400), 331 nm (ε, 6,895). A second crop (34 mg., 91%, m.p. 163-165°) was obtained by allowing the filtrate and washings to stand for 8 days at -30° in a tightly stoppered flask.

Anal. Calcd. for $C_7H_{11}N_5O_2$: C, 42.64; H, 5.62; N, 35.51. Found: C, 42.39; H, 5.91; N, 35.39.

5-(3,3-Dimethyl-1-triazeno)-1,3-dimethyluracil (XVc).

5-Diazo-6-methoxy-1,3-dimethyl-1,6-dihydrouracil (XIV, 750 mg.) was placed in a 25 ml. round bottom flask and dimethylamine (approximately 15 ml.) condensed into the flask under anhydrous conditions. The flask was tightly stoppered, allowed to stand at room temperature for 18 hours and the mixture was then concentrated *in vacuo* to dryness. The white solid which remained was recrystallized from dry acetonitrile (4 ml.) and dried for 3 hours at the reflux temperature of methanol to give 741 mg. (93%) of XVc, m.p. 138-140°; uv λ max (methanol): 271 nm (ε, 11,600), 332 nm (ε, 13.200).

Anal. Calcd. for $C_8H_{13}N_5O_2$: C, 45.49; H, 6.20; N, 33.16. Found: C, 45.21; H, 6.19; N, 33.05.

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