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**SYNTHESIS OF CERTAIN 4-METHYL-2-THIOURACIL DERIVATIVES
TO BE TESTED AS ANTI-TUMOR OR ANTI-THYROID AGENTS**

By

R.M.ABDEL-RAHMAN and A.M. ABDEL-HALIM

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Faculté des Sciences de l'Université d'Ankara
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SYNTHESIS OF CERTAIN 4-METHYL-2-THIOURACIL DERIVATIVES TO BE TESTED AS ANTI-TUMOR OR ANTI-THYROID AGENTS

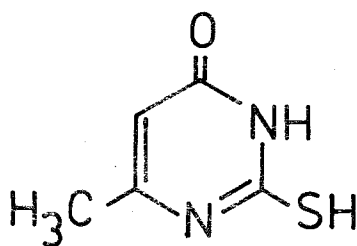
R.M. ABDEL-RAHMAN and A.M. ABDEL-HALIM

Chemistry Department, Faculty of Education, Ain-Shams University, Cairo, Roxy, A.R. Egypt

INTRODUCTION

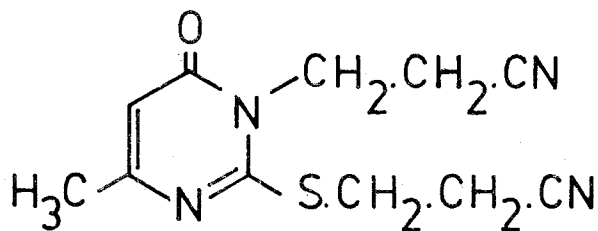
Uracil and its 5-methyl derivative; thymine, are biologically of great importance in fundamental metabolism. They derive their importance because certain of their derivatives are building blocks of RNA and DNA., 5-Fluorouracil is particularly effective in the treatment of advanced carcinoma especially of the breast and the gastrointestinal tract; thiouracil, used in treating hyperthyroidism and angina pectoris.

The wide applications of the diazines as chemotherapeutic agents aroused the interest of author to synthesize some derivatives of 4-methyl-2-thiouracil (I) that might have biological activity as antitumor or antithyroid agents.

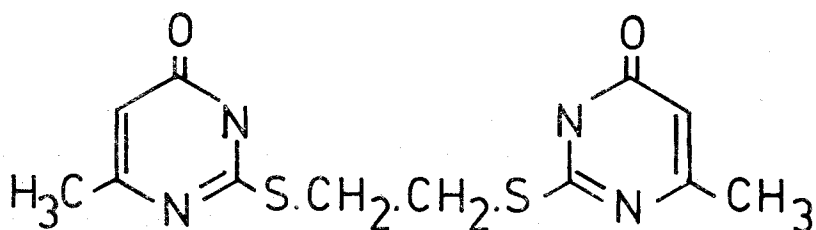


(I)

Thus, reaction of I with olefins, namely, acrylonitrile^{1,2,3} and ethylacrylate⁴ leads to the 1,2-bis (β-cyanoethyl)-4-methyl-2-methylthiouracil (II) and the bis (4-methyl-2-methylmercaptouracil) (III) respectively.



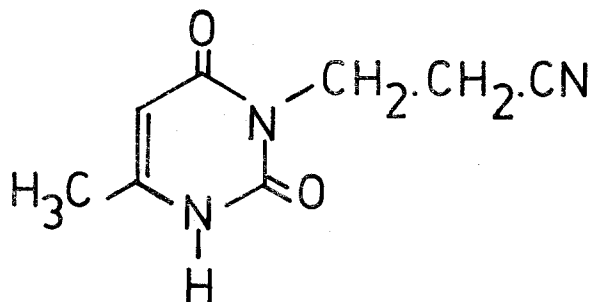
(II)



(III)

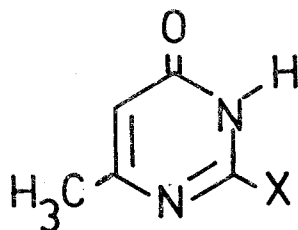
Compound (III) was also obtained by the action of 1,2-dibromoethane⁴ on I (direct comparison of m.p., m.m.p., and ir).

Acid hydrolysis^{1,2,3} of II affords N'-(β-cyanoethyl)-4-methyl uracil (IV) its structure is supported by correct analytical data (contains no sulfur) and ir spectra which coincide with its structure.



(IV)

The reactivity of the sulfur atom attached to uracil nucleus towards nucleophilic attack is greatly influenced by the type of sulfur, the nucleophilic agent and the reaction condition. Thus the course of the reaction of I with chloroacetic acid was studied in detail, the reaction being important for the transformation to S-alkylated analogs which cyclized readily, through the loss of one molecule of water, to give the corresponding thiazolo (1,2-b) 1,3-diazine derivatives. Thus, on refluxing I with chloroacetic acid in aqueous potassium hydroxide⁵ gave 4-methyl uracil (Va); whereas, 4-methyl-2-methyl-mercapto-1, 3- diazin-6- one (Vb) was isolated when I was fused with chloroacetic acid. Gentle boiling for few minutes of I with chloroacetic acid in aqueous KOH gave -carboxylethylmercapto-4-methyl-1,3-diazin-6- one (Vc).

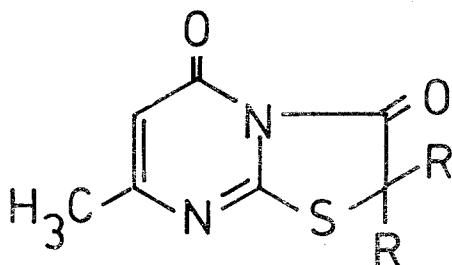


(V)

| | <u>X</u> | | <u>X</u> |
|----|-------------------------|---|------------------------------------|
| Va | OH | b | S.CH ₃ |
| c | S.CH ₂ .COOH | d | S.CO.C ₆ H ₅ |

The synthesis of thiazolo (1,2-b)1,3-diazine derivatives is usually achieved by the action of bifunctional compounds on I^{6,7,8}. The interaction of I with haloacids, and haloketones is now undertaken where condensed 1,3-diazine systems are synthesized. Thus, the reaction of I with chloroacetic acid in dry pyridine -DMF⁶ leads to the direct formation of 7-methyl-2-hydrothiazolo (1,2-b) 1,3-diazin-3,5-dione (VIa). The formation of 2-(2'-nitro or 4'-chlorobenzylidene)-7-methylthiazolo-(1,2-b)-1,3-diazine-3,5-dione (VIb,c) by treatment of I with chloroacetic acid in the presence of o-nitrobenzaldehyde and p-chlorobenzaldehyde⁷ res-

pectively, gives evidence for the structure of VIa. The reactions is believed to proceed via the formation of the intermediate VIa which readily condenses with the aldehyde to VIb, c.



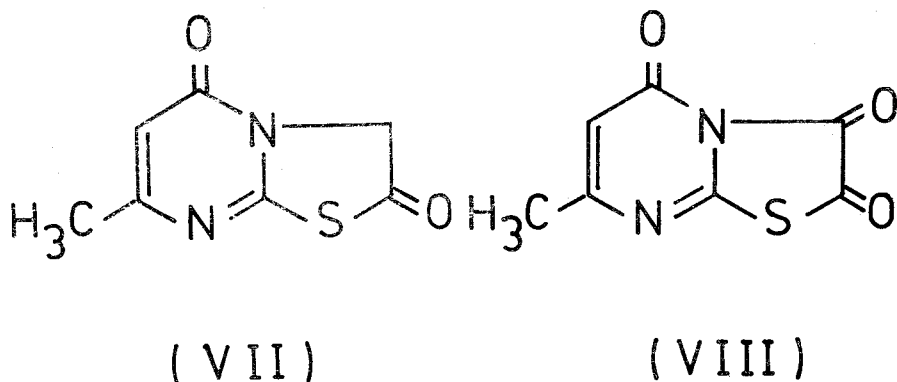
(VI)

| | |
|-----|---|
| | <u>R</u> |
| VIa | H |
| b | =CH.C ₆ H ₄ .NO ₂ (o-) |
| c | =CH.C ₆ H ₄ .Cl(p-) |

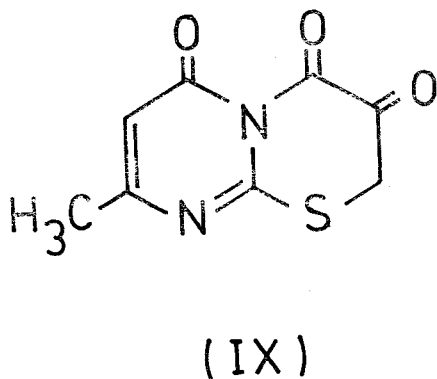
On the other hand, compound I react with acid halides, namely, bromoacetyl bromide⁸, and oxalyl chloride to give 7-methyl-3-hydrothiazolo (1,2-b)-1,3-diazin-2,5-dione (VII) and 7-methyl-thiazolo (1,2-b)-1,3=diazin-2,3,5- trione (VIII) respectively.

One possible approach to explain the direct formation of VII is the assumption that an intermediate monoacetyl derivative was formed firstly that cyclizes through the loss of one mole of HBr to give (VII).

Benzoylation of I using benzoyl chloride in pyridine gave 4-methyl-2-benzoylthiouracil (Vd) the structure of which was supported by analytical data as well as ir spectral analysis which reflects absorption bands at 3400, 3200, 1720 and 1620 cm⁻¹ due to NH, OH tautomeric structure, C=O of benzoyl and C=O in thiouracil moiety with disappearance of C=S band at 1190 cm⁻¹.



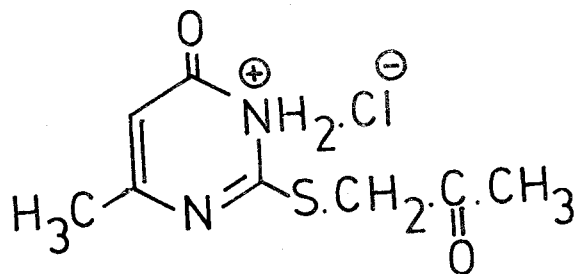
Reaction of I with bromopyruvic acid in pyridine -KOH media^{1,9} affording 7-methyl-1,3-thiazino (1,2b) -1,3-diazin-3,4,5-trione (IX).



Its ir spectrum reflects the disappearance of the -NH absorption band, while three successive C=O bands appear at lower frequencies in the region 1750-1650 cm^{-1} .

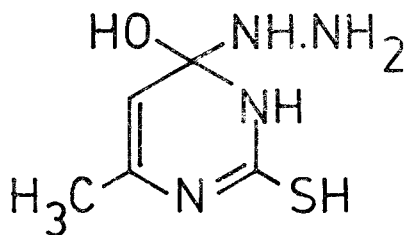
α -Haloketone, namely, chloroacetone reacts with I in pyridine¹⁰, to give 2-acetonyl-4-methylthiouracil hydrochloride (X).

The behavior of 4-methyl-2-thiouracil toward hydrazine hydrate at different experimental conditions was also studied. Thus, treatment of compound I with hydrazine hydrate at room temperature, leads to the addition of the hydrazine to the C=O double bond¹¹ affording compo-

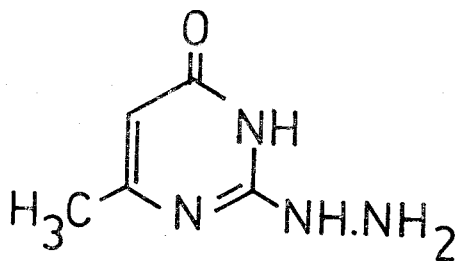


(X)

und (XI), whereas refluxing I with hydrazine hydrate in isopropyl alcohol¹² for 6 hrs, leads to 2-hydrazino-4-methyluracil (XII).

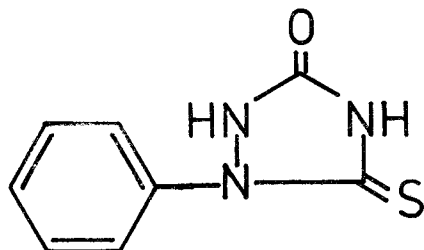


(XI)



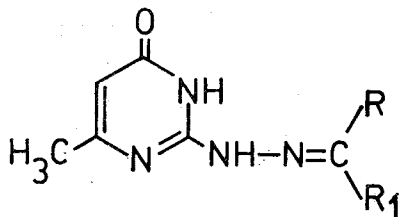
(XII)

Fusion of compound I with phenylhydrazine¹³ in an oil bath (200°C), for 1/2 hour gave compound (XIII) which was identified as 2-phenyl-3-thio-1,4-dihydro-1, 2,4-triazol-5- one.



(XIII)

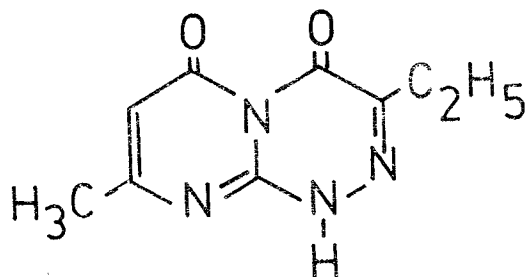
The reactivity of the hydrazino group in (XII) exhibits the normal characteristics of this group, thus, condensation of XII with different carbonyl compounds¹², namely, 2-oxobutyric acid, o-aceto-benzoic acid, o-benzoyl benzoic acid, acetylacetone and benzoylacetone gives the corresponding hydrazones (XIVa-e).



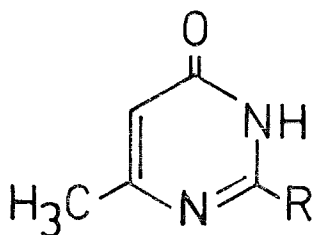
(XIV)

| | <u>R</u> | <u>R₁</u> |
|------|-------------------------------|---|
| XIVa | C ₂ H ₅ | COOH |
| b | CH ₃ | C ₆ H ₄ .COOH (o-) |
| c | C ₆ H ₅ | C ₆ H ₄ .COOH(o-) |
| d | CH ₃ | CH ₂ .CO.CH ₃ |
| e | CH ₃ | CH ₂ .CO.C ₆ H ₅ |

Cyclization of XIVa-c, through the loss of one mole of water leads to the formation of heterocyclic derivatives for 4-methyluracil⁸ XV, and XVIa-d.



(XV)

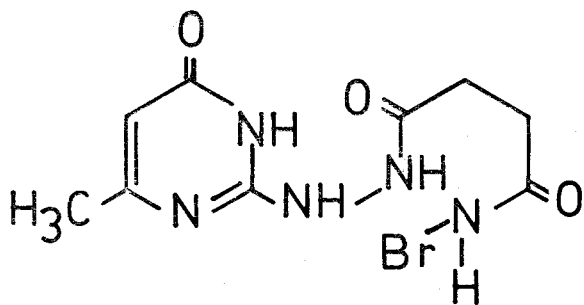
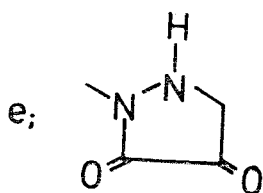
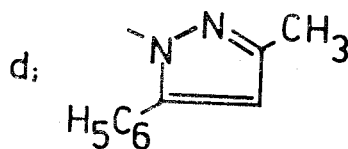
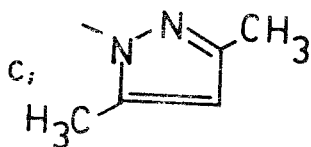
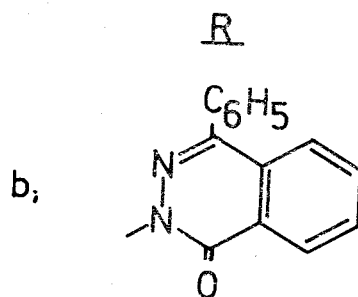
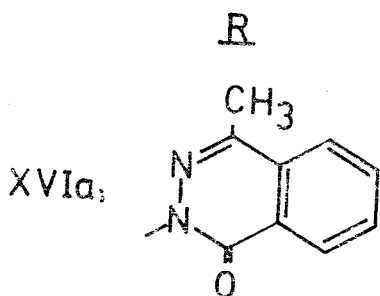


(XVI)

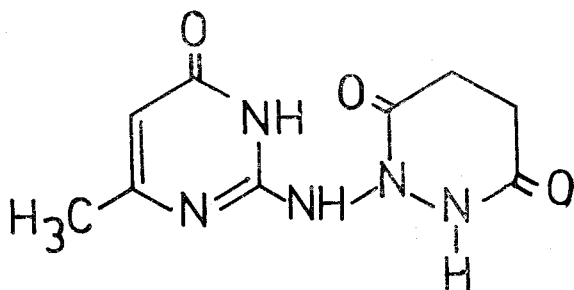
Reaction of XII with bromopyruvic acid in pyridine-ethanol¹⁴ gave (XVIe).

When XII was heated with-N-bromosuccinimide in pyridine¹⁴, the hydrazide derivative (XVII) was obtained.

Heating XVII with alcoholic KOH¹⁶ gave the pyridazin-1,4- dione derivative (XVIII). Its ir shows the appearance of the absorption band at 1800-1700 cm^{-1} characteristic for condensed 1-4-diones in addition to the absence of bromine in its elemental analysis.



(XVII)



(XVIII)

EXPERIMENTAL

The ir spectra were recorded with a Beckman IR 4 spectrophotometer using KBr pellet technique.

All melting points are not corrected.

The reagents and solvents used in the synthesis described in this paper were the purest grade.

REACTIONS OF 4-METHYL-2- THIOURACIL (I) WITH OLEFINS:

a) *Formation of II and III**General Procedure:*

Compound I (0.01 mole) was added to a mixture of phridine (50 ml.) and water (10 ml) containing acrylonitrile or ethyl acrylate (3 ml.). The reaction mixture was heated under reflux for 3 hr, cooled, diluted with water and the solid obtained was recrystallized from the proper solvent to give II and III respectively about 75 % yield (Table 1), ir (KBr) *compound II*, 3200-3100 (ν_{NH}), 1680 (br., ν_{CO}), 3500-3400 (ν_{OH}) and 2250 cm^{-1} ($\nu_{\text{C=N}}$); *compound III*, 3500-3300 (ν_{OH} , NH), 2936-2916 (ν_{VH_2}), 1620 ($\nu_{\text{V=O}}$) and 1440 cm^{-1} ($\nu_{\text{S-CH}_2}$).

Hydrolysis of II: Formation of IV:

A mixture of II (0.5 g) and dilute HCl (20 ml.) was heated under reflux for 2 hr. neutralized with sodium carbonate and the solid obtained was crystallized from ethanol to give IV as colourless crystals in about 60 % yield (Table 1), ir (KBr); 2940 ($\nu_{\text{C-H}_2}$), 2280 cm^{-1} ($\nu_{\text{C=N}}$).

REACTION OF I WITH MONOCHLOROACETIC ACID:*(a) Formation of Va:*

A mixture of I (0.01 mole); monochloroacetic acid (0.01 mole) and potassium hydroxide solution (50 ml., 20 %) was heated under reflux for 1 hr, cooled, acidified (HCl) and the solid obtained was crystallized from acetic acid to give Va as colourless crystals in about 80 % yield (Table 1), ir (KBr); 3240 (ν_{NH}) and 1680 cm^{-1} ($\nu_{\text{C=O}}$).

(b) Formation of Vb:

A mixture of I (0.01 mole) and monochloroacetic acid, (0.01 mole) was heated in an oil-bath at 200°C for 1 hr, cooled and the solid obtained was crystallized from methanol to give Vb as yellow crystals in about 85 % yield (Table 1), ir (KBr); 1440-1415 cm^{-1} ($\nu_{\text{S-CH}_2}$).

(c) Formation of Vc:

A mixture of I (0.01 mole), monochloroacetic acid (0.01 mole) and potassium hydroxide solution (50 ml., 5 %) was heated at 60° (water-bath) for 10 min., acidified (HCl) and the solid obtained was crystallized from methanol to give Vc as yellow crystals in about 70 % yield (Table 1); ir (KBr), 3333-2300 (vr., ν_{OH} bonded) and 1715 cm^{-1} (ν_{CO}).

(d) Formation of VIa:

(i) A mixture of Vc (0.01 mole), and sodium carbonate (50 ml., 10 %) was heated under reflux for 3 hr, cooled, and the solid obtained was crystallized from ethanol to give VIa as brownish-yellow crystals in about 80 % yield (Table 1), ir (KBr), 1680 ($\nu_{\text{C=O}}$).

(ii) A mixture of I (0.01 mole) and monochloroacetic acid (0.01 mole) in pyridine-DMF (25:25 ml), was heated under reflux for 30 min., cooled, then cold water was added and the solid obtained was treated as above to give VIa as brownish-yellow crystals in about 85 % yield, m.p. and m.m.p. with the product from (d-(i)) showed no depression.

Table 1. Physical Data of Compounds II-XIII

| Compound | °C | Recrystallization solvent | Yield % | Mol. Formula | Analysis (Found / Calc.) % | | | | |
|----------|------------|--|---------|--|----------------------------|-----------|-------------|-------------|------------|
| | | | | | C | H | N | S | X |
| II | 275-276° | C ₂ H ₅ OH | 70 | C ₁₁ H ₁₂ N ₂ SO | 54.0/53.22 | 5.0/4.83 | 23.2/22.58 | 12.8/12.90 | — |
| III | above 310° | C ₂ H ₅ OH | 70 | C ₁₂ H ₁₄ N ₂ S ₂ O ₂ | 46.4/46.45 | 4.1/4.51 | 18.9/18.06 | 20.4/20.64 | — |
| IV | above 310° | C ₂ H ₅ OH | 60 | C ₂ H ₅ N ₂ O ₂ | 53.9/53.93 | 4.3/4.49 | 23.8/23.59 | — | — |
| V a | 299-300° | CH ₃ COOH | 80 | C ₂ H ₆ N ₂ O ₂ | 48.0/47.62 | 4.6/4.70 | 23.0/22.22 | — | — |
| b | 298-299° | CH ₃ OH | 70 | C ₂ H ₆ N ₂ SO | 47.0/46.15 | 5.1/5.12 | 18.5/17.98 | 21.0/20.51 | — |
| c | above 310° | CH ₃ OH | 60 | C ₇ H ₈ N ₂ SO ₃ | 42.8/42.00 | 4.3/4.00 | 14.9/14.00 | 16.4/16.00 | — |
| d | 304-305° | C ₂ H ₅ OH | 90 | C ₁₂ H ₁₀ N ₂ SO ₂ | 58.9/58.53 | 3.85/4.06 | 11.5/11.38 | 13.7/13.00 | — |
| VI a | above 310° | C ₂ H ₅ OH | 90 | C ₇ H ₈ N ₂ SO ₂ | 46.6/46.15 | 3.00/3.29 | 15.0/15.38 | 17.7/17.58 | — |
| b | 214-215° | CH ₃ COOH | 80 | C ₄ H ₆ N ₂ SO ₄ | 52.6/53.33 | 2.35/2.85 | 13.2/13.33 | 9.50/10.15 | — |
| c | 125-126° | CH ₃ COOH | 90 | C ₄ H ₆ N ₂ SO ₄ Cl | 55.9/55.08 | 2.60/2.95 | 9.4/9.18 | 10.0/10.49 | 11.3/11.80 |
| VII | 235-236° | CH ₃ COOC ₂ H ₅ | 60 | C ₁₁ H ₁₂ N ₂ SO ₂ | 46.6/46.15 | 3.0/3.29 | 15.0/15.38 | 17.7/17.57 | — |
| VIII | above 310° | CH ₃ COOH | 60 | C ₂ H ₅ N ₂ SO ₂ | 43.0/42.85 | 2.0/2.04 | 13.9/14.28 | 16.0/16.32 | — |
| IX | 309-310° | CH ₃ COOH | 70 | C ₃ H ₄ N ₂ SO ₂ | 45.0/45.71 | 22./2.38 | 14.0/13.33 | 16.0/15.23 | — |
| X | above 310° | pyridine-water | 80 | C ₈ H ₈ N ₂ SClO ₂ | 41.0/40.35 | 4.2/4.68 | 12.0/11.91 | 12.99/13.61 | 14.9/15.10 |
| XI | 275-278° | C ₂ H ₅ OH | 90 | C ₅ H ₁₀ N ₂ SO | 35.0/34.48 | 5.5/5.74 | 31.60/32.19 | 18.6/18.39 | — |
| XII | 249-250° | Isopropyl alc | 70 | C ₂ H ₅ N ₂ O | 43.4/42.85 | 5.9/5.71 | 40.5/40.00 | — | — |
| XIII | 305-305° | CH ₃ OH | 60 | C ₈ H ₈ N ₂ SO | 49.0/49.74 | 3.6/3.64 | 20.8/21.75 | 16.80/16.57 | — |

(e) *Formation VIb, c:*

A mixture of equimolar amounts of I, monochloroacetic acid, o-nitro benzaldehyde or p-chlorobenzaldehyde and sodium acetate in acetic anhydride (30 ml.) was heated under reflux for 4 hr., cooled, cold water was then added and the solid obtained was crystallized from acetic acid to give VIb and VIc respectively. (Table 1).

REACTION OF I WITH HALO-COMPOUNDS: FORMATION OF Vd, VII, VIII, IX AND X:

General Procedure:

A mixture of I (0.01 mole) and halo-compound, namely, benzoyl chloride, bromoacetyl bromide, oxalyl chloride, bromopyruvic acid, and chloroacetone, (0.01 mole) was dissolved in the least amount of dry pyridine. The reaction mixture was refluxed for 1-2 hr. and the product was poured into ice-cold dilute HCl. The products were crystallized from the proper solvent to give compounds Vd, VII, VIII, IX and X respectively in about 60-80 % yield (Table 1), ir (KBr) for compound Vd; 3400 (ν_{OH}), 3200 (ν_{NH}), 1720 (ν_{CO} "benzoyl") and 1620 cm^{-1} ($\nu_{C=O}$ "in thiouracil moiety"); VII, 3500 (br. ν_{OH}) and 1700 cm^{-1} (ν_{CC}); VIII, 1680-1660 cm^{-1} (ν_{V-O}); IX, 1750-1650 cm^{-1} ($\nu_{C=O}$); X, 3250 (ν_{NH}), 2920 (ν_{CH_2}), 1680 ($\nu_{C=O}$), 1190 (ν_{SH}) and 2000-1800 cm^{-1} (ν_{NH_2} . Cl salt).

REACTION OF I WITH HYDRAZINE HYDRATE:

(a) *Formation of XI:*

A mixture of I (0.01 mole) and hydrazine hydrate (10 ml.) in isopropyl alcohol (20 ml) was left at room temperature for 24 hr., water was added and the solid precipitated was recrystallized from ethanol to give XI as colourless crystals, in about 80 % yield (Table 1), ir (KBr) 3500-3200 (br. ν_{NH_2} , OH), 3100 (ν_{NH}) and 1280-1250 cm^{-1} (s, $\nu_{C=S}$).

(b) *Formation of XII:*

A mixture of I (0.01 mole) and hydrazine hydrate (10 ml.) in isopropyl alcohol (100 ml.) was heated under reflux for 6 hr. cooled, diluted with water and the solid obtained was recrystallized from isopropyl alcohol to give XII as colourless crystals in about 80 % yield (Table 1), ir (KBr) 3500-3200 (br. ν_{NH_2} , OH) and 3100 cm^{-1} (ν_{NH}).

REACTION OF I WITH PHENYLHYDRAZINE: FORMATION OF XIII:

A mixture of compound I (0.01 mole) and phenylhydrazine (0.01 mole) was fused at 200° (oil-bath) for 30 min., cooled, triturated with methanol and the solid obtained was crystallized from methanol to give XIII as orange crystals, in about % 70 yield (Table 1); ir (KBr) 3200–3100 (ν_{NH}), 1680 ($\nu_{\text{C=O}}$), 1190 ($\nu_{\text{C=S}}$) and 1050 cm^{-1} (s, ν substituted benzene ring).

REACTION OF XII WITH CARBONYL COMPOUNDS: FORMATION OF XIVa-e:

A mixture of XII (0.01 mole) and the appropriate aldehyde, ketone, and / or 2-oxoacid (0.015 mole), in absolute ethanol (30 ml.) was heated under reflux for 30 min., cooled, poured into water, filtered and the solid obtained recrystallized from a proper solvent to give XIVa-e (Table 2); ir (KBr) 3400 ($\nu_{\text{OH, NH}}$), 2940 (ν_{CH_2}), 1580 ($\nu_{\text{C=N}}$) in addition to 1740 cm^{-1} ($\nu_{\text{C=O}}$) in case of XIVd, e.

CYCLIZATION OF XIVa-e:

(a) Formation of XV:

Compound XIVa (0.01 mole) in sodium carbonate solution (50 ml., 10%) was refluxed for 3 hr., cooled, neutralized with dilute HCl and the solid precipitated was filtered, washed with cold water and crystallized from ethyl alcohol to give XV as colourless crystals, in about 60 % yield (Table 2); ir (KBr) 1665 cm^{-1} characteristic for cyclic structure assigned for this compounds.

(b) Formation of XVIa-d:

Compound XIVb-e (0.01 mole) in acetic acid (30 ml.) was heated under reflux for 2 hr., cooled, poured on cold water, then filtered off and the solid obtained was recrystallized from the proper solvent to give XVIa-d (Table 2); ir (KBr) for compounds XVIa,b, 1630 cm^{-1} ($\nu_{\text{cyclic amide}}$); XVIc, 1570 (ν_{CN}), 1640 ($\nu_{\text{C=O}}$) and 3300 cm^{-1} (ν_{NH}).

(c) Formation of XVIe:

A mixture of equimolar amounts of XII and broxopyruvic acid in ethanol (30 ml.) and pyridine (30 ml.) was refluxed for 2 hr., cooled, then

Table 2. Physical Properties of Compounds

| Compound | M.P. °C | Recrystallization solvent | Yield % | Mol. formula | Analysis (Found / Calc.) % | | | |
|----------|------------|------------------------------------|---------|--|----------------------------|-----------|-------------|------------|
| | | | | | C | H | N | X |
| XIV a | 257—258° | CH ₃ COOH | 80 | C ₈ H ₁₂ N ₄ O ₃ | 48.50/48.21 | 5.00/5.35 | 24.50/25.00 | — |
| b | 245—246° | CH ₃ COOH | 80 | C ₈ H ₁₄ N ₄ O ₃ | 58.40/48.74 | 4.70/4.89 | 19.80/19.57 | — |
| c | 96—97° | CH ₃ COOH | 90 | C ₁₉ H ₁₆ N ₄ O ₃ | 65.20/65.51 | 4.30/4.59 | 16.90/16.09 | — |
| d | 114—115° | C ₂ H ₅ OH | 70 | C ₁₀ H ₁₄ N ₄ O ₂ | 54.20/54.05 | 6.00/6.30 | 25.90/25.22 | — |
| e | 153—154° | C ₂ H ₅ OH | 70 | C ₁₃ H ₁₆ N ₄ O ₂ | 63.70/63.38 | 5.20/5.63 | 19.90/19.72 | — |
| XV | 244—245° | C ₂ H ₅ OH | 80 | C ₉ H ₁₀ N ₄ O ₂ | 52.10/52.41 | 4.90/4.85 | 28.00/27.18 | — |
| XVI a | 122—123° | C ₂ H ₅ OH | 90 | C ₁₄ H ₁₂ N ₄ O ₂ | 63.00/62.68 | 4.17/4.47 | 21.00/20.88 | — |
| b | 297—298° | CH ₃ COOH | 80 | C ₁₁ H ₁₂ N ₄ O ₂ | 68.90/69.09 | 4.00/4.24 | 17.01/16.96 | — |
| c | 75—76° | CH ₃ CH ₂ OH | 90 | C ₁₀ H ₁₂ N ₄ O ₂ | 58.28/58.82 | 6.00/5.88 | 23.10/22.54 | — |
| d | 155—156° | C ₂ H ₅ OH | 80 | C ₈ H ₁₁ N ₄ O | 68.00/67.66 | 5.20/5.26 | 22.00/21.06 | — |
| e | 239—240° | pyridine | 60 | C ₁₃ H ₁₄ N ₄ O ₃ | 46.60/46.15 | 3.30/3.86 | 27.80/26.92 | — |
| XVII | above 300° | CH ₃ OH | 70 | C ₈ H ₈ N ₄ O ₃ Br | 33.30/33.96 | 3.50/3.77 | 21.80/22.01 | 25.1/25.15 |
| XVIII | above 310° | pyridine | 60 | C ₉ H ₁₁ N ₅ O ₃ | 46.00/45.56 | 4.14/4.64 | 30.60/29.53 | — |

poured into ice-cold dilute HCl. The solid obtained was crystallized from pyridine to give XVIe as orange crystals in about 80 % yield (Table 2), ir (KBr) 3350 (ν_{NH}), 2950 (ν_{CH_2} and 1770 cm^{-1} ($\nu_{\text{C=O}}$).

REACTION OF XII WITH N-BROMOSUCCINIMIDE: FORMATION OF XVII:

A mixture of XII (0.01 mole) and N-bromosuccinimide (0.015 mole) in dry pyridine (20 ml.) was shaken, at room temperature, for 15 min., poured into ice-cold dilute HCl, and the solid obtained was recrystallized from methanol to give XVII as yellowish-brown crystals in about 60 % yield (Table 2), ir (KBr) 3500-2920 (v. br., ν_{OH} , NH , CH_2) and 1700-1620 cm^{-1} ($\nu_{\text{C=O}}$)

CYCLIZATION OF XVII: FORMATION OF XVIII:

Compound XVII (0.01 mole) in alcoholic potassium hydroxide (50 ml., 5 %) was heated under reflux for 1 hr., cooled, neutralized with dilute HCl and the solid obtained was filtered, washed with little cold water and recrystallized from pyridine to give XVIII as yellow crystals in about 60 % yield (Table 2); ir (KBr) 1800-1700 cm^{-1} ($\nu_{\text{condensed 1:4-diones}}$).

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