The Synthesis of Trypanocides. Part IV. The Attempted Preparation of 4-Amino-6-(6-amino-1 : 2-dimethylpyrimidinium-4-amino)-1 : 2-dimethylquinolinium Di-iodide.*

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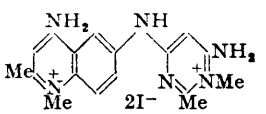
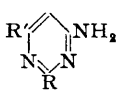
[Reprint Order No. 6150.]

The attempted preparation of the isomer of " Antrycide " in which the methyl group in the 6-position of the pyrimidine ring and the amino-group in the 2-position are interchanged, is described. The structure of the products of quaternisation of 6-amino-4-chloro-2-methylpyrimidine is established by degradation of 4-amino-6-chloro-1 : 2-dimethylpyrimidinium iodide, the major product, to 1 : 4-dihydro-1 : 2-dimethyl-4-oxopyrimidine which has been related to 1 : 6-dihydro-1-methyl-6-oxopyrimidine, synthesised by an unambiguous route. An account is also given of some exploratory work on alternative structural proofs.

FOR the preparation of the isomer (I) of " Antrycide " in which the methyl group in the 6-position of the pyrimidine ring and the amino-group in the 2-position are interchanged, the most direct method seemed to be reaction between a 6-amino-4-chloro-1 : 2-dimethylpyrimidinium salt, *e.g.* (III; R = Me, R′ = Cl), and a 4 : 6-diamino-1 : 2-dimethylquinolinium salt.



(I)



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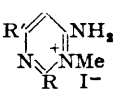

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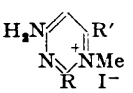


(IV)

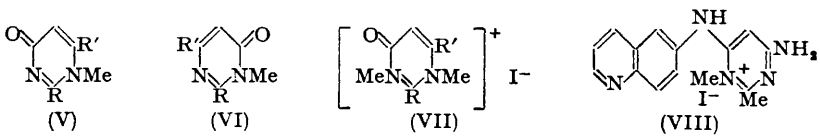
6-Amino-4-chloro-2-methylpyrimidine (II; R = Me, R′ = Cl) (Baddiley, Lythgoe, McNeil, and Todd, *J.*, 1943, 383), with methyl iodide in 2-ethoxyethanol under reflux, gave a mixture of two isomeric quaternary iodides (III and IV; R = Me, R′ = Cl), the second being by far the more abundant constituent.† These exchanged chlorine for an aniline residue, giving the iodides (III and IV; R = Me, R′ = NHPh), both of which were also obtained by the action of methyl iodide on 6-amino-4-anilino-2-methylpyrimidine (II; R = Me, R′ = NHPh). The proof of the constitution of these two pairs of quaternary derivatives is the main subject of this paper.

The first stage in this proof was the reduction of the chloro-compound (IV; R = Me, R′ = Cl) by zinc dust to 4-amino-1 : 2-dimethylpyrimidinium iodide (IV; R = Me, R′ = H), which was also obtained from 4-amino-2-methylpyrimidine (Gabriel, *Ber.*, 1904,

* Part III, preceding paper.

† Preparation of these quaternary derivatives is described in B.P. 634,417.

37, 3638) and methyl iodide and on alkaline hydrolysis gave 1 : 4-dihydro-1 : 2-dimethyl-4-oxopyrimidine (V; R = Me, R′ = H). The isomeric 6-oxo-compound (VI; R = Me, R′ = H) was obtained from 4-hydroxy-2-methylpyrimidine (Gabriel, *loc. cit.*; Cheruliez and Stavritch, *Helv. Chim. Acta*, 1922, **5**, 267) by methylation. That these products (V and VI; R = Me, R′ = H) were isomers of the type postulated was proved when with methyl iodide under pressure they gave the same 1 : 4-dihydro-1 : 2 : 3-trimethyl-4-oxopyrimidinium iodide (VII; R = Me, R′ = H).



The further work on the proof of the structure was carried out on the compound (VI; R = Me, R′ = H) since this was the more readily available isomer. An attempt at its unambiguous synthesis was unsuccessful. Cheruliez and Stavritch (*loc. cit.*) had prepared 4-hydroxy-2-methylpyrimidine by decarboxylation of 6-hydroxy-2-methylpyrimidine-4-carboxylic acid, which was obtained by the ring closure of the Schiff's base from acetaldehyde and the ω-amide of aspartic acid. However, the ring closure of the Schiff's base from acetaldehyde and the methylamide of aspartic acid could not be accomplished. Attention was therefore turned to relating the compound to a pyrimidine or uracil derivative of proved structure, in particular to elimination of the 2-methyl group. The 2-methyl group in (VI; R = Me, R′ = H) was remarkably stable to oxidising agents; it was not attacked by fuming nitric acid or neutral potassium permanganate. Attempts at side-chain bromination failed to give recognisable products capable of hydrolysis to known compounds. However, with benzaldehyde and zinc chloride, the compound gave the 2-styryl derivative (VI; R = CH:CHPh, R′ = H) (cf. Kondo and Yanoi, *J. Pharm. Soc. Japan*, 1937, **57**, 747; 1938, **58**, 397), which on oxidation with potassium permanganate in dry acetone followed by sublimation of the product in a high vacuum gave 1 : 6-dihydro-1-methyl-6-oxopyrimidine (VI; R = R′ = H) the structure of which has been proved by Brown, Hoerger, and Mason (*J.*, 1955, 213). Methylation of 4-hydroxypyrimidine (Wheeler, *Amer. Chem. J.*, 1909, **42**, 301) and desulphurisation of 1 : 6-dihydro-1-methyl-2-methylthio-6-oxopyrimidine with Raney nickel also gave this substance. Thus the constitutions of the compounds (VI; R = Me, R′ = H) and (IV; R = Me, R′ = Cl) were established.

Owing to the very small proportion of the isomer (III; R = Me, R′ = Cl) in the products of quaternisation of 6-amino-4-chloro-2-methylpyrimidine, the synthesis of the " Antrycide " analogue (I) was not attempted from this intermediate. Some reactions of the other isomer (IV; R = Me, R′ = Cl) with 6-aminoquinoline derivatives were, however, attempted. With 6-aminoquinoline itself it gave 4-amino-1 : 2-dimethyl-6 : 6′-quinolylaminopyrimidinium iodide (VIII), but with 4 : 6-diamino-2-methylquinoline and its methiodide no analogous product was obtained.

In the preliminary exploration of alternative structural proofs, an unsuccessful attempt was made to obtain 1 : 6-dihydro-1-methyl-6-oxopyrimidine by removal of the 4-methyl group from the 1 : 4-dimethyl compound (VI; R = H, R′ = Me). This was obtained either by methylation of 6-hydroxy-4-methylpyrimidine (Gabriel and Colman, *Ber.*, 1899, **32**, 2921) or by the treatment of 1 : 6-dihydro-1 : 4-dimethyl-2-methylthio-6-oxopyrimidine (Wheeler and McFarland, *Amer. Chem. J.*, 1909, **42**, 106) with Raney nickel. Its structure was confirmed by heating it with methyl iodide under pressure; it gave 1 : 4-dihydro-1 : 3 : 6-trimethyl-4-oxopyrimidinium iodide (VII; R = H, R′ = Me) identical with that obtained by a similar process from the isomeric 1 : 4-dihydro-1 : 6-dimethyl-4-oxopyrimidine (V; R = H, R′ = Me), which was synthesised in the following way. Reduction of 4-amino-2-chloro-1 : 6-dimethylpyrimidinium iodide (IV; R = Cl, R′ = Me) (previous paper) with hydriodic acid gave 4-amino-1 : 6-dimethylpyrimidinium iodide (IV; R = H, R′ = Me), also obtained either by quaternisation of 4-amino-6-methylpyrimidine (Gabriel and Colman, *loc. cit.*) or by the action of Raney nickel on 4-amino-1 : 2-dihydro-1 : 6-dimethyl-2-thiopyrimidine (the corresponding 2-methylthio-compound could not be used). Alkaline

hydrolysis of the product (IV; R = H, R′ = Me) gave 1 : 4-dihydro-1 : 6-dimethyl-4-oxopyrimidine (V; R = H, R′ = Me). The 4-methyl group in 1 : 6-dihydro-1 : 4-dimethyl-6-oxopyrimidine was unattacked by oxidising agents such as nitric acid, potassium permanganate, and selenium dioxide, and no styryl compound could be obtained.

When work on the orientation of these pyrimidine derivatives was first undertaken, it was planned to convert 1 : 4-dihydro-1 : 2-dimethyl-4-oxopyrimidine (V; R = Me, R′ = H) into 1 : 4-dihydro-1-methyl-4-oxopyrimidine (V; R = R′ = H), an authentic sample of which would be prepared from 1 : 4-dihydro-1 : 6-dimethyl-4-oxopyrimidine (V; R = H, R′ = Me). The low yields of (V; R = Me, R′ = H and R = H, R′ = Me) made this impracticable, but experiments were carried out on the preparation of (V; R = R′ = H). 4-Aminopyrimidine (Büttner, *Ber.*, 1903, **36**, 2227; Wheeler and Johnson, *J. Biol. Chem.*, 1907, **3**, 183) and methyl iodide in 2-ethoxyethanol under reflux gave 4-amino-1-methylpyrimidinium iodide (IV; R = R′ = H). Subsequent alkaline hydrolysis gave 1 : 4-dihydro-1-methyl-4-oxopyrimidine (V; R = R′ = H), and the relation between this compound and the isomer (VI; R = R′ = H) previously described was demonstrated by conversion of both into 1 : 4-dihydro-1 : 3-dimethyl-4-oxopyrimidinium iodide (VII; R = R′ = H).

Experimental

4-Amino-6-chloro-1 : 2-dimethylpyrimidinium Iodide (IV; R = Me, R′ = Cl).—6-Amino-4-chloro-2-methylpyrimidine (Baddiley *et al.*, *loc. cit.*) (25·8 g.), 2-ethoxyethanol (100 c.c.), and methyl iodide (27·2 c.c.) were heated on the steam-bath for 6 hr. After filtration, the *pyrimidinium iodide* was washed with boiling ethyl acetate and crystallised from water as flat prisms, m. p. 244—246° (decomp.) (10·1 g.) (Found: C, 25·1; H, 3·0; N, 14·35%; 1 mg. equiv. to 1·31 mg. of Ag halide. $C_6H_9N_3ClI$ requires C, 25·2; H, 3·2; N, 14·7%; 1 mg. equiv. to 1·28 mg. of Ag halide).

6-Amino-4-chloro-1 : 2-dimethylpyrimidinium Iodide (III; R = Me, R′ = Cl).—The 2-ethoxyethanol solution remaining after filtration of the iodide (IV; R = Me, R′ = Cl) (see above) was evaporated in a vacuum and the isomeric *pyrimidinium iodide* purified by crystallisation from water: it had m. p. 232—234° (decomp.) (Found: C, 24·9; H, 3·05%; 1 mg. equiv. to 1·32 mg. of Ag halide).

6-Amino-4-anilino-2-methylpyrimidine (II; R = Me, R′ = NHPh).—6-Amino-4-chloro-2-methylpyrimidine (2·4 g.), aniline (1·5 c.c.), water (10 c.c.), and concentrated hydrochloric acid (0·1 c.c.) were heated under reflux for 1 hr. The cooled solution was diluted with water and made alkaline with ammonia. The precipitated solid was filtered off and dissolved in aqueous-alcoholic ammonia. The crude *pyrimidine* was precipitated by dilution with water and crystallised from chlorobenzene as plates, m. p. 190—191° (Found, in material dried in a vacuum at 100°: C, 65·75; H, 5·8; N, 27·75. $C_{11}H_{12}N_4$ requires C, 66·0; H, 6·0; N, 28·0%).

4-Amino-6-anilino-1 : 2-dimethylpyrimidinium Iodide (IV; R = Me, R′ = NHPh).—(*a*) 6-Amino-4-anilino-2-methylpyrimidine (7·5 g.), methanol (50 c.c.) and methyl iodide (12 c.c.) were heated under reflux for 4 hr. The resulting solution was evaporated to dryness, and the residue was treated with ethyl acetate and filtered. Crystallisation of the residue first from alcohol–ethyl acetate and then from water gave *4-amino-6-anilino-1 : 2-dimethylpyrimidinium iodide* as prisms, m. p. 274—276° (Found: C, 41·75; H, 4·35; N, 16·75; I, 36·8. $C_{12}H_{15}N_4I$ requires C, 42·1; H, 4·4; N, 16·4; I, 37·1%).

(*b*) 4-Amino-6-chloro-1 : 2-dimethylpyrimidinium iodide (2·9 g.), aniline (1·8 g.), and water (10 c.c.) were heated under reflux for 2 hr. The solid which separated crystallised from water and had m. p. and mixed m. p. 274—276°.

6-Amino-4-anilino-1 : 2-dimethylpyrimidinium Iodide (III; R = Me, R′ = NHPh).—(*a*) The alcohol–ethyl acetate liquors [see (*a*) above] were evaporated to dryness; the *pyrimidinium iodide* crystallised from water as colourless prisms, m. p. 228—230° (Found: C, 41·85; H, 4·6; N, 16·15; I, 36·75%).

(*b*) 6-Amino-4-chloro-1 : 2-dimethylpyrimidinium iodide (0·85 g.), aniline (0·5 c.c.), and water (5 c.c.), as above, gave the preceding compound, m. p. and mixed m. p. 230—232° (from water).

4-Amino-1 : 2-dimethylpyrimidinium Iodide (IV; R = Me, R′ = H).—(*a*) 4-Amino-6-chloro-1 : 2-dimethylpyrimidinium iodide (2·0 g.), zinc dust (20 g.), and water (200 c.c.) were boiled together for 1·5 hr. The suspension was filtered, and the filtrate evaporated to dryness in a

vacuum. 4-*Amino*-1 : 2-*dimethylpyrimidinium iodide* thus obtained had m. p. 246—248° after crystallisation from alcohol (Found : C, 28·7; H, 3·85; N, 16·85; I, 50·5. $C_6H_{10}N_3I$ requires C, 28·7; H, 4·0; N, 16·75; I, 50·6%).

(*b*) 4-Amino-2-methylpyrimidine (Gabriel, *loc. cit.*) (8·2 g.), 2-ethoxyethanol (15 c.c.), and methyl iodide (10·5 c.c.), as above, gave the same salt (11·9 g.), m. p. and mixed m. p. 246—248° (from 75% aqueous alcohol; prisms).

1 : 4-*Dihydro*-1 : 2-*dimethyl*-4-*oxopyrimidine* (V; R = Me, R′ = H).—4-Amino-1 : 2-dimethylpyrimidinium iodide (2·5 g.), potassium hydroxide (0·56 g.), and water (20 c.c.) were heated under reflux for 1 hr. The solution was evaporated to dryness in a vacuum and the residue extracted with dry acetone. Evaporation of the acetone solution gave 1 : 4-dihydro-1 : 2-dimethyl-4-oxopyrimidine. It formed a *picrate*, m. p. 178—180° (from 2-ethoxyethanol) (Found : C, 41·1; H, 3·6; N, 19·55. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1; N, 19·8%).

1 : 6-*Dihydro*-1 : 2-*dimethyl*-6-*oxopyrimidine* (VI; R = Me, R′ = H).—4-Hydroxy-2-methylpyrimidine (Gabriel, *loc. cit.*; Cheruliez and Stavritch, *loc. cit.*) (3·3 g.) was dissolved in a solution of potassium hydroxide (1·68 g.) in alcohol (25 c.c.). Methyl iodide (2·1 c.c.) was added and the mixture warmed on the steam-bath until the solution no longer gave an alkaline reaction on Brilliant-yellow paper. After cooling, the solution was filtered, the filtrate evaporated to dryness in a vacuum, and the residue sublimed in a high vacuum. 1 : 6-*Dihydro*-1 : 2-*dimethyl*-6-*oxopyrimidine* was a hygroscopic white solid (Found : C, 57·9; H, 6·4. $C_6H_8ON_2$ requires C, 58·1; H, 6·5%). Addition of concentrated nitric acid to an acetone solution precipitated the *nitrate*, m. p. 162° (decomp.) (from methanol) (Found : C, 38·3; H, 4·15; N, 22·2. $C_6H_8ON_2,HNO_3$ requires C, 38·5; H, 4·8; N, 22·4%). Similarly, hydrochloric acid gave the *hydrochloride*, plates, m. p. 250° (decomp.) (from methanol) (Found : C, 44·25; H, 5·45; N, 16·9. $C_6H_8ON_2,HCl$ requires C, 44·9; H, 5·6; N, 17·4%), and methanolic picric acid the *picrate*, parallelepipeds, m. p. 172° (from 2-ethoxyethanol) (Found : C, 40·55; H, 3·15; N, 19·65. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1; N, 19·8%).

1 : 4-*Dihydro*-1 : 2 : 3-*trimethyl*-4-*oxopyrimidinium Iodide* (VII; R = Me, R′ = H).—1 : 6-Dihydro-1 : 2-dimethyl-6-oxopyrimidine (2·4 g.) and methyl iodide (1·24 c.c.) were heated in a sealed tube at 100° for 6 hr. The *pyrimidinium iodide* crystallised from alcohol as plates, m. p. 224° (decomp.) (Found : C, 31·95; H, 4·45; N, 10·75. $C_7H_{11}ON_2I$ requires C, 31·6; H, 4·1; N, 10·5%). The same compound was obtained from 1 : 4-dihydro-1 : 2-dimethyl-4-oxopyrimidine and methyl iodide.

1 : 6-*Dihydro*-1-*methyl*-6-*oxo*-2-*styrylpyrimidine* (VI; R = CH:CHPh, R′ = H).—1 : 6-Dihydro-1 : 2-dimethyl-6-oxopyrimidine (3·72 g.), benzaldehyde (3·6 c.c.), and anhydrous zinc chloride (0·8 g.) were heated together in a sealed tube for 3 hr. at 110—120°. The *styryl compound*, which separated on cooling, had m. p. 136° after crystallisation first from benzene–light petroleum (b. p. 60—80°), then from alcohol (yield, 1·25 g.) (Found : C, 73·1; H, 5·35; N, 13·2. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7; N, 13·0%).

1 : 6-*Dihydro*-1-*methyl*-6-*oxopyrimidine* (VI; R = R′ = H).—(*a*) 1 : 6-Dihydro-1-methyl-2-methylthio-6-oxopyrimidine (0·8 g.), methanol (25 c.c.), and Raney nickel (10 g.) were stirred under reflux for 2 hr. The nickel was removed and the filtrate evaporated to dryness in a vacuum. 1 : 6-Dihydro-1-methyl-6-oxopyrimidine thus obtained was converted into the *picrate* which crystallised first from 2-ethoxyethanol and then from water as rectangular prisms, m. p. 176—178° (Found : C, 38·7; H, 2·75; N, 20·5. $C_5H_6ON_2,C_6H_3O_7N_3$ requires C, 38·3; H, 2·6; N, 20·65%).

(*b*) 1 : 6-Dihydro-1-methyl-6-oxo-2-stryrylpyrimidine (2·7 g.) was dissolved in acetone (150 c.c., dried over P_2O_5), and excess of potassium permanganate (8·3 g.) added. The mixture was filtered, the residue extracted with boiling water (200 c.c.), and the extract neutralised with hydrochloric acid and evaporated to dryness in a vacuum. The residue was sublimed in a vacuum and the sublimate converted into the picrate, m. p. and mixed m. p. 176—178° (from water).

(*c*) 4-Hydroxypyrimidine (Wheeler, *loc. cit.*) (2·88 g.) was dissolved in a solution of potassium hydroxide (1·68 g.) in alcohol (25 c.c.) and heated under reflux with methyl iodide (2·06 c.c.) until the mixture was no longer alkaline. The precipitated solid was filtered off, the filtrate evaporated to dryness in a vacuum, and the residue sublimed in a high vacuum. The sublimate was 1 : 6-*dihydro*-1-*methyl*-6-*oxopyrimidine* (Found : C, 54·9; H, 5·4. $C_5H_6ON_2$ requires C, 54·5; H, 5·4%). It formed a picrate, m. p. and mixed m. p. 176—178° (from 2-ethoxyethanol).

4-*Amino*-1 : 2-*dimethyl*-6-6′-*quinolylaminopyrimidinium Iodide* (VIII).—4-Amino-6-chloro-1 : 2-dimethylpyrimidinium iodide (2·85 g.), 6-aminoquinoline (2·88 g.), and water (10 c.c.) were heated together under reflux for 3 hr. The *pyrimidinium iodide*, which separated on cooling,

was collected and dissolved in water. The aqueous solution was filtered from a little insoluble material and the filtrate salted with sodium iodide. The *iodide* crystallised from 50% ethanol as flat prisms, m. p. 268—270° (Found : C, 43·65; H, 4·4; I, 31·1. $C_{15}H_{16}N_5I,H_2O$ requires C, 43·8; H, 4·4; I, 30·9%).

1 : 6-*Dihydro*-1 : 4-*dimethyl*-6-*oxopyrimidine* (VI; R = H, R′ = Me).—(*a*) 6-Hydroxy-4-methylpyrimidine hydriodide (Gabriel and Colman, *loc. cit.*) (14·28 g.), potassium hydroxide (6·72 g.), alcohol (50 c.c.), and methyl iodide (4·13 c.c.) were heated under reflux for 2 hr. After cooling, the mixture was filtered and the filtrate evaporated to dryness in a vacuum. The residue was sublimed in a high vacuum (bath-temp. 100°). The sublimate of 1 : 6-dihydro-1 : 4-dimethyl-6-oxopyrimidine was hygroscopic. It formed a *picrate*, m. p. 188—190° (from 2-ethoxyethanol) (Found : C, 40·55; H, 3·05; N, 19·6. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1; N, 19·8%).

(*b*) 1 : 6-Dihydro-1 : 4-dimethyl-2-methylthio-6-oxopyrimidine (Wheeler and McFarland, *loc. cit.*) (1·0 g.) was heated under reflux with Raney nickel (10·0 g.) in methanol (100 c.c.) for 2 hr. The nickel was removed and the filtrate evaporated to dryness in a vacuum. The residue formed a picrate, yellow prisms (from 2-ethoxyethanol), m. p. and mixed m. p. 188—190°.

4-*Amino*-1 : 2-*dihydro*-1 : 6-*dimethyl*-2-*thiopyrimidine*.—Sodium (0·92 g.) was dissolved in alcohol (50 c.c.) and hydrogen sulphide passed in until the gain in weight was 1·3 g. This solution was added to a suspension of 4-amino-1 : 6-dimethyl-2-methylthiopyrimidinium iodide (previous paper) (5·66 g.) in alcohol (50 c.c.), and the mixture heated under reflux for 1 hr., hydrogen sulphide being passed through the solution. After cooling, the *dihydropyrimidine* was collected and crystallised from water : it had m. p. 322° (decomp.) (yield, 2·5 g.) (Found : C, 45·6; H, 6·0; N, 26·65; S, 21·15. $C_6H_9N_3S$ requires C, 46·5; H, 5·8; N, 27·1; S, 20·6%).

4-*Amino*-1 : 6-*dimethylpyrimidinium Iodide* (IV; R = H, R′ = Me).—(*a*) 4-Amino-2-chloro-1 : 6-dimethylpyrimidinium iodide (2·0 g.) and hydriodic acid (25 c.c.; *d* 1·7) were warmed together on the steam-bath for 0·25 hr. After dilution with water (25 c.c.) the mixture was neutralised with potassium carbonate. The *pyrimidinium iodide* was collected, washed with acetone, and purified by crystallisation from alcohol; it formed prisms, m. p. 262—264° (Found : C, 28·65; H, 3·9; N, 16·6. $C_6H_{10}N_3I$ requires C, 28·7; H, 4·0; N, 16·6%).

(*b*) 4-Amino-6-methylpyrimidine (Gabriel and Colman, *loc. cit.*) (11·0 g.), methyl iodide (14 c.c.), and 2-ethoxyethanol (25 c.c.) were heated under reflux on the steam-bath for 2·5 hr. The product, crystallised from 75% aqueous alcohol (70 c.c.), had m. p. and mixed m. p. 262—264° (yield, 15·7 g.).

(*c*) 4-Amino-1 : 2-dihydro-1 : 6-dimethyl-2-thiopyrimidine (2·1 g.) was stirred under reflux with Raney nickel (20 g.) in methanol (100 c.c.) for 3 hr. After filtration, the solution was made acid with hydriodic acid and evaporated to small bulk. The material which crystallised had m. p. and mixed m. p. 260—262°.

1 : 4-*Dihydro*-1 : 6-*dimethyl*-4-*oxopyrimidine* (V; R = H, R′ = Me).—4-Amino-1 : 6-dimethylpyrimidinium iodide (2·5 g.), potassium hydroxide (0·56 g.), and water (20 c.c.) were boiled together for 1 hr. The solution was evaporated to dryness in a vacuum and the residue extracted with dry acetone. The crude material remaining after evaporation of the acetone formed a *picrate*, m. p. 174—176° (from 2-ethoxyethanol) (Found : C, 41·25; H, 3·2; N, 19·75. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1; N, 19·8%).

1 : 4-*Dihydro*-1 : 3 : 6-*trimethyl*-4-*oxopyrimidinium Iodide* (VII; R = H, R′ = Me).—1 : 6-Dihydro-1 : 4-dimethyl-6-oxopyrimidine (2·4 g.) and methyl iodide (2·0 c.c.) were heated together in a sealed tube at 100° for 6 hr. The *pyrimidinium iodide* crystallised from alcohol as plates, m. p. 268—270° (Found : C, 31·95; H, 4·45; N, 10·05; I, 48·25. $C_7H_{11}ON_2I$ requires C, 32·1; H, 4·25; N, 10·5; I, 47·7%). The same compound was obtained from 1 : 4-dihydro-1 : 6-dimethyl-4-oxopyrimidine and methyl iodide under pressure for 15 hr. at 100°.

4-*Amino*-1-*methylpyrimidinium Iodide* (IV; R = R′ = H).—4-Aminopyrimidine (Büttner, also Wheeler and Johnson, *locc. cit.*) (2·15 g.), 2-ethoxyethanol (10 c.c.), and methyl iodide (5 c.c.) were heated under reflux for 5 hr. The *pyrimidinium iodide* which separated (4·2 g.) crystallised from alcohol–ethyl acetate as prisms, m. p. 204—206° (Found : C, 25·9; H, 3·5; I, 53·1. $C_5H_8N_3I$ requires C, 25·3; H, 3·4; I, 53·6%).

1 : 4-*Dihydro*-1-*methyl*-4-*oxopyrimidine* (V; R = R′ = H).—4-Amino-1-methylpyrimidinium iodide (2·37 g.), potassium hydroxide (0·56 g.), and water (20 c.c.) were heated under reflux for 1 hr. The solution was evaporated to dryness in a vacuum and the residue extracted with hot acetone. The crude product remaining after evaporation of the solvent formed a *picrate*, m. p. 164—166° (from 2-ethoxyethanol) (Found : C, 38·25; H, 2·9; N, 20·15. $C_5H_6ON_2,C_6H_3O_7N_3$ requires C, 38·3; H, 2·6; N, 20·65%).

1 : 4-*Dihydro*-1 : 3-*dimethyl*-4-*oxopyrimidinium Iodide* (VII; R = R′ = H).—1 : 6-Dihydro-1-methyl-6-oxopyrimidine (0·7 g.) and methyl iodide (0·5 c.c.) were heated in a sealed tube for 6 hr. at 100°. The *pyrimidinium iodide* crystallised from alcohol as flat needles, m. p. 204—206° (Found : C, 29·0; H, 4·0; N, 11·1; I, 50·6. $C_6H_9ON_2I$ requires C, 28·5; H, 3·1; N, 11·1; I, 50·4%). The same compound was obtained from 1 : 4-dihydro-1-methyl-4-oxopyrimidine and methyl iodide.

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[*Received, February 18th*, 1955.]