888. *Pyrimidines. Part XI.* Synthesis of 5-Hydroxypyrimidine and Related Compounds.*

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The synthesis of the hitherto unknown 5-hydroxypyrimidine and of its 2-phenyl and 4,6-dimethyl derivatives is described.

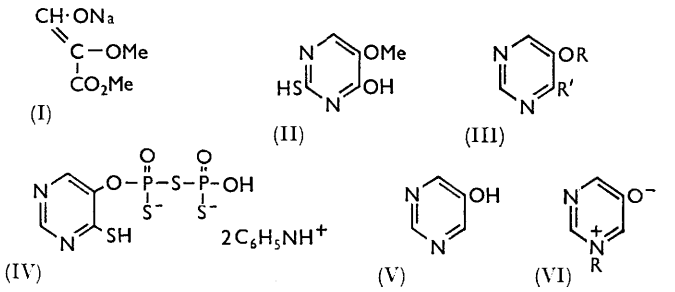
Early work on the synthesis of derivatives of 5-hydroxypyrimidine has been summarised by Hull [1] and by Davoll and Laney.[2] Hull prepared several 5-hydroxy-compounds by persulphate oxidation of pyrimidines containing at least one electron-releasing group. Davoll and Laney used a more versatile method in which the potential 5-hydroxy-group was protected during the ring synthesis as its tetrahydropyranyl (or in one example benzyl) ether. More recently Henze and Kahlenberg [3] have prepared a number of 5-hydroxy-2-thiouracils and 5-hydroxyuracils from alkyl $\alpha\gamma$-dialkoxyacetoacetates. All of the 5-hydroxypyrimidines so far prepared have contained at least one extra hydroxy-, amino-, or substituted amino-group, and hence the properties of the 5-hydroxyl group have been to some extent obscured. The present work was undertaken in order to study some 5-hydroxypyrimidines which did not contain another potentially tautomeric group; part of the work has been outlined in a preliminary publication.[4]

Methyl methoxyacetate was formylated and the crude ester (I) was treated with

* Part X, *J.*, 1959, 525.

[1] Hull, *J.*, 1956, 2033.
[2] Davoll and Laney, *J.*, 1956, 2124.
[3] Henze and Kahlenberg, *J. Amer. Chem. Soc.*, 1958, **80**, 1664.
[4] McOmie and Chesterfield, *Chem. and Ind.*, 1956, 1453.

thiourea, giving 4-hydroxy-2-mercapto-5-methoxypyrimidine (II). Desulphurisation of the latter with Raney nickel yielded 4-hydroxy-5-methoxypyrimidine (III; R = Me,



R′ = OH), which was converted into the 4-chloro-compound (III; R = Me, R′ = Cl) and thence, by reaction with thiourea,[5] into 4-mercapto-5-methoxypyrimidine (III; R = Me, R′ = SH). The direct replacement of the 4-hydroxyl by the 4-mercapto-group by treatment with phosphorus pentasulphide in pyridine was less satisfactory: the yield of the desired mercapto-compound was variable, the major product of the reaction often being the dipyridine salt of a trithiopyrophosphate ester which is thought to have structure (IV) or one of its tautomeric forms. This pyridine salt was boiled with Raney nickel in ethanol and in a few experiments 5-hydroxypyrimidine (V) was obtained in traces. Kenner and Williams [6] have recently shown that reduction of aryl diethyl phosphates proceeds mainly by aryl–oxygen cleavage and a similar fission probably occurs with compound (IV). In addition it was found later that 5-hydroxypyrimidine is gradually destroyed when boiled with Raney nickel and this method is of no preparative use. Desulphurisation of 4-mercapto-5-methoxypyrimidine gave only a 32% yield of 5-methoxypyrimidine (III; R = Me, R′ = H), demethylation of which proved difficult. The use of hydrobromic, hydrochloric, or sulphuric acid, of aluminium chloride, or of pyridine hydrochloride gave black amorphous material, indicating that 5-hydroxypyrimidine is very unstable towards strong acids. However, hydrolysis with potassium hydroxide in ethylene glycol gave 5-hydroxypyrimidine (V) in 25% yield. Attempts to prepare 5-methoxypyrimidine from its 2,4-dichloro-derivative by zinc dust and water or by catalytic reduction gave only 2-chloro-5-methoxypyrimidine which did not react with thiourea. 4-Hydrazino-5-methoxypyrimidine, made from the 4-chloro-compound, gave a low yield of 5-methoxypyrimidine when oxidised by aqueous copper sulphate. Bredereck *et al.*[7] have recently made 5-methoxypyrimidine by the action of sodium methoxide on 5-bromopyrimidine.

A parallel series of reactions was carried out with benzyl in place of methyl as the protective group. However, the overall yield of 5-benzyloxypyrimidine was much less than that of the 5-methoxy-compound and this route was not further explored.

5-Hydroxy-2-phenylpyrimidine was made by a four-stage synthesis. Benzamidine was condensed with methyl sodio-β-hydroxy-α-methoxyacrylate (I), and the resulting 4-hydroxy-5-methoxy-2-phenylpyrimidine was converted *via* the corresponding 4-mercapto-compound into 5-methoxy-2-phenylpyrimidine. Finally alkaline hydrolysis of the latter compound gave 5-hydroxy-2-phenylpyrimidine. The preparation of 5-hydroxy-4,6-dimethylpyrimidine started from 3-acetoxypentane-2,4-dione, which with thiourea gave 5-hydroxy-2-mercapto-4,6-dimethylpyrimidine directly. Desulphurisation of this mercapto-compound gave 5-hydroxy-4,6-dimethylpyrimidine; hydrolysis of the same mercapto-compound gave 2,5-dihydroxy-4,6-dimethylpyrimidine which had previously been prepared [1] by persulphate oxidation of 2-hydroxy-4,6-dimethylpyrimidine.

Ultraviolet and infrared spectroscopy has established that 2- and 4-hydroxypyrimidine

[5] Ochiai and Naito, *J. Pharm. Soc. Japan*, 1943, **63**, 317; Boarland and McOmie, *J.*, 1951, 1218.
[6] Kenner and Williams, *J.*, 1955, 522.
[7] Bredereck, Gompper, and Herlinger, *Chem. Ber.*, 1958, **91**, 2832.

exist predominantly in the lactam forms. Although the neutral form (V) of 5-hydroxypyrimidine could not tautomerise to a lactam form it could exist as a zwitterion (VI; R = H). However, ultraviolet studies [8] show that 5-hydroxypyrimidine in neutral solution exists almost entirely as neutral molecules. In contrast to this, neutral solutions of 3-hydroxypyridine contain about 54% of the zwitterion form.[9] Attempts to prepare the *N*-methyl derivative (VI; R = Me), which must exist in a dipolar form, were unsuccessful. As would be expected, 5-hydroxypyrimidine shows phenolic properties. It has pK_a 6·78,[8] compared with 8·26 for the neutral form of 3-hydroxypyridine [9] and 9·9 for phenol. The compound and its 2-phenyl derivative give an orange-red colour with aqueous ferric chloride (3-hydroxypyridine gives a red colour [10]) whereas the 4,6-dimethyl derivative gives a brown-orange colour. Towards substitution 5-hydroxypyrimidine is less reactive than 3-hydroxypyridine which in turn is less reactive than phenol. Thus in the Gibbs test [11] for phenols with a free *para*-position 3-hydroxypyridine,[10] like phenol, gives an immediate blue colour, whereas 5-hydroxypyrimidine reacts slowly and gives a weak purplish-black colour; the 4,6-dimethyl derivative, however, is more reactive and gives an immediate blue colour. 3-Hydroxypyridine couples with diazonium salts,[10] but the three 5-hydroxypyrimidines described in this paper failed to couple with diazotised *p*-nitroaniline.

Experimental

4-Hydroxy-2-mercapto-5-methoxypyrimidine (II).—A mixture of methyl methoxyacetate [12] (104 g.) and ethyl formate (74 g.) was added dropwise to a stirred suspension of sodium (23 g.) in toluene (300 ml.), the temperature being kept below 30°. Next day the toluene layer was decanted and to the crude, viscous methyl sodio-β-hydroxy-α-methoxyacrylate were added ethanol (150 ml.) and thiourea (76 g.). The mixture was stirred for 1 hr. at room temperature, then boiled under reflux for 5 hr. After cooling, the solid was collected and dissolved in water (500 ml.), and the solution was neutralised with 6N-hydrochloric aicd. The precipitated pyrimidine (84 g., 52%) was collected and dried at 100°; it was pure enough to be used directly in the next stage. A portion was recrystallised from water, giving *4-hydroxy-2-mercapto-5-methoxypyrimidine* as needles, m. p. 280—281° (decomp.) (Found: C, 38·2; H, 3·7; N, 17·4. $C_5H_6N_2O_2S$ requires C, 38·0; H, 3·8; N, 17·7%).

4-Hydroxy-5-methoxypyrimidine (III; R = Me, R′ = OH).—Raney nickel sludge [13] (160 g.) was added to a hot solution of 4-hydroxy-2-mercapto-5-methoxypyrimidine (30 g.) in water (300 ml.) and ammonia (30 ml.; *d* 0·88). After being boiled under reflux with vigorous stirring for 4 hr. the mixture was filtered and the combined filtrate and washings were evaporated to dryness on a water-bath. The residue recrystallised from ethanol (charcoal), giving *4-hydroxy-5-methoxypyrimidine* (16·5 g., 69%) as needles, m. p. 210—211° (Found: C, 47·8; H, 5·0; N, 22·5. $C_5H_6N_2O_2$ requires C, 47·6; H, 4·8; N, 22·2%).

4-Chloro-5-methoxypyrimidine (III; R = Me, R′ = Cl).—4-Hydroxy-5-methoxypyrimidine (6·5 g.) and phosphoryl chloride (50 ml.) were boiled under reflux for 1·5 hr. Excess of phosphoryl chloride was removed under reduced pressure and the solution remaining was poured on ice. The mixture was neutralised with 2N-sodium hydroxide, and the crude chloropyrimidine (5·6 g., 75%) collected in ether (6 × 150 ml.). The compound was sublimed at 80—85°/15 mm., giving *4-chloro-5-methoxypyrimidine*, m. p. 63—64°, which became yellow when kept (Found: C, 41·7; H, 3·3; N, 19·3. $C_5H_5ClN_2O$ requires C, 41·5; H, 3·5; N, 19·4%).

4-Mercapto-5-methoxypyrimidine (III; R = Me, R′ = SH).—A mixture of 4-chloro-5-methoxypyrimidine (4·2 g.), thiourea (2·5 g.), and ethanol was boiled under reflux for 5 hr. The solution was concentrated under reduced pressure and, after cooling, it yielded a yellow solid which was dissolved in water. The solution was neutralised with sodium carbonate. Concentration then gave *4-mercapto-5-methoxypyrimidine* (2·2 g., 54%) as yellow, hexagonal plates, m. p. 209—211° (Found: N, 19·5; OMe, 21·7. $C_5H_6N_2OS$ requires N, 19·7; OMe, 21·8%).

[8] Mason, *J.*, 1957, 5010; 1958, 674.
[9] Metzler and Snell, *J. Amer. Chem. Soc.*, 1955, **77**, 2431.
[10] Stiller, Keresztesy, and Stevens, *J. Amer. Chem. Soc.*, 1939, **61**, 1237.
[11] Gibbs, *J. Biol. Chem.*, 1927, **72**, 649.
[12] Schreiner, *Annalen*, 1879, **197**, 8.
[13] Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.

With methyl sulphate and sodium hydrogen carbonate it gave *5-methoxy-4-methylthiopyrimidine*, m. p. 75° (Found: C, 46·3; H, 5·1; N, 18·4. $C_6H_8N_2OS$ requires C, 46·2; H, 5·1; N, 18·0%).

Action of Phosphorus Pentasulphide on 4-Hydroxy-5-methoxypyrimidine.—(*a*) A mixture of 4-hydroxy-5-methoxypyrimidine (5·1 g.) and phosphorus pentasulphide (9·9 g.) in pyridine (70 ml.) was boiled under reflux for 1 hr. After being cooled, the mixture was added to water (300 ml.), and the solution was concentrated to about 75 ml. on the water-bath. On cooling, a brown solid separated and was recrystallised from water (charcoal), giving 4-mercapto-5-methoxypyrimidine (3·1 g., 54%), m. p. 209—211°, identical with that obtained as above.

(*b*) A similar experiment in which the hydroxypyrimidine (10 g.), phosphorus pentasulphide (36 g.), and pyridine (200 ml.) were boiled for 1·5 hr. and worked up as before gave a *compound* (IV) which, after crystallisation from water, formed yellow prisms (11·8 g.), m. p. 205—209° (decomp.) (Found: C, 36·8; H, 3·2; N, 11·9; S, 25·7; P, 14·0. $C_4H_6N_2O_4P_2S_4,2C_5H_5N$ requires C, 34·0; H, 3·2; N, 11·3; S, 25·9; P, 12·6%).

The compound gave a positive molybdate test for phosphate, and pyridine was liberated when it was boiled with alkali and then steam-distilled. The pyridine was identified by conversion into the mercuric chloride adduct, m. p. 179—180° alone or mixed with an authentic specimen. The bright yellow colour of an aqueous solution of the compound was almost completely discharged on addition of sodium hydroxide, and was restored on acidification. This behaviour is typical of 4-mercaptopyrimidines.

5-Methoxypyrimidine.—4-Mercapto-5-methoxypyrimidine (2·0 g.) in water (30 ml.) was boiled under reflux with Raney nickel sludge (15 g.) which had been deactivated previously by boiling in acetone for 2 hr. and then washed with water. After cooling, the nickel was removed by filtration and washed with hot water (10 ml.), then the combined filtrate and washings were saturated with sodium chloride. Extraction with ether, followed by distillation, gave *5-methoxypyrimidine* (0·5 g., 32%), b. p. 70—72°/16 mm., m. p. 46—47° (Found: N, 25·7; OMe, 27·2. $C_5H_6N_2O$ requires N, 25·5; OMe, 28·2%), $\lambda_{max.}$ 2745 Å (ε 4027 in EtOH). The *mercuric chloride adduct*, recrystallised from ethanol, formed needles, m. p. 232—234° (decomp.) (Found: C, 9·3; H, 0·8; N, 4·3. $C_5H_6N_2O,2HgCl_2$ requires C, 9·2; H, 0·9; N, 4·3%). The *picrate*, crystallised from ethanol, formed yellow needles, m. p. 126—127° (Found: C, 38·6; H, 2·7; N, 20·2. $C_5H_6N_2O,C_6H_3N_3O_7$ requires C, 38·9; H, 2·7; N, 20·6%).

5-Hydroxypyrimidine.—5-Methoxypyrimidine (1 g.) and dry, powdered potassium hydroxide (2·5 g.) in ethylene glycol (15 ml.) were boiled under reflux for 3 hr. The excess of glycol was removed at 120—130°/20 mm. and the residue was neutralised with acetic acid and boiled with dioxan (10 ml.). After filtration, the residue was extracted four more times with boiling dioxan (10 ml. each time). The united extracts were concentrated *in vacuo* to *ca.* 50 ml. and cooled in a refrigerator. After 2 hr. the needles were collected and washed with a little cold dioxan, then purified by sublimation at 140—150°/16 mm., giving pure *5-hydroxypyrimidine* (0·19 g., 25%), m. p. 211—212° (decomp.) (Found: C, 50·0; H, 4·2; N, 28·9. $C_4H_4N_2O$ requires C, 50·0; H, 4·2; N, 29·2%), $\lambda_{max.}$ 2760 Å (ε 5360 in EtOH). 5-Hydroxypyrimidine is very soluble in water, but sparingly soluble in ether. It gives an orange-red colour with aqueous ferric chloride.

2,4-Dihydroxy-5-methoxypyrimidine.—(*a*) 4-Hydroxy-2-mercapto-5-methoxypyrimidine (15 g.) and chloroacetic acid (15 g.) in water (375 ml.) were boiled under reflux for 2 hr., then concentrated hydrochloric acid (60 ml.) was added and the boiling continued for 7 hr. After cooling, the *dihydroxypyrimidine* (12·4 g., 92%) was collected and washed. A sample, recrystallised from hot water, had m. p. 341—345° (decomp.) (Found: C, 42·4; H, 4·6; N, 19·9. $C_5H_6N_2O_3$ requires C, 42·3; H, 4·2; N, 19·7%).

(*b*) A suspension of urea (30 g.) in ethanol (200 ml.) was added to crude methyl sodio-β-hydroxy-α-methoxyacrylate (prepared from 52 g. of methyl methoxyacetate as described previously), and the mixture boiled under reflux for 5 hr., then was cooled, diluted with water (200 ml.), and acidified with acetic acid. The precipitated dihydroxypyrimidine (19 g., 21%), m. p. 328—333° (decomp.), was collected and washed with water and ethanol.

2,4-Dichloro-5-methoxypyrimidine.—2,4-Dihydroxy-5-methoxypyrimidine (6 g.), phosphoryl chloride (30 ml.), and dimethylaniline (6 ml.) were boiled under reflux for 2 hr. The mixture was poured on crushed ice (80 g.), and the product collected in ether. Recrystallisation from light petroleum (b. p. 40—60°) gave *2,4-dichloro-5-methoxypyrimidine* (4·6 g., 61%) as needles, m. p. 66—68° (Found: C, 33·9; H, 2·3. $C_5H_4Cl_2N_2O$ requires C, 33·5; H, 2·2%).

4-Amino-2-chloro-5-methoxypyrimidine.—Sodium was added to 2,4-dichloro-5-methoxypyrimidine (4·4 g.) in ether (10 ml.) and liquid ammonia (200 ml.) until there was no further sign of reaction. After the ammonia had been allowed to evaporate, the residue was dissolved in dilute hydrochloric acid and treated with charcoal. The filtered solution was neutralised with sodium carbonate, and the precipitate collected in ether. The product was crystallised from light petroleum (b. p. 60—80°), then twice from ethanol, thereby giving the *aminopyrimidine* (0·3 g.), m. p. 181—182° (decomp.) (Found: N, 26·4. $C_5H_6ClON_3$ requires N, 26·3%).

2-Chloro-4-hydrazino-5-methoxypyrimidine.—2,4-Dichloro-5-methoxypyrimidine (1 g.) and 64% w/w hydrazine hydrate (1 ml.) in ethanol (10 ml.) were boiled for 1 hr. After cooling, the *hydrazinopyrimidine* (0·95 g.), m. p. 148—150°, was collected (Found: C, 34·8; H, 4·3; N, 31·9. $C_5H_7ClN_4O$ requires C, 34·5; H, 4·1; N, 32·1%).

2-Chloro-5-methoxypyrimidine.—2,4-Dichloro-5-methoxypyrimidine (4 g.), zinc dust (8 g.), ethanol (20 ml.), and water (20 ml.) were boiled under reflux for 4 hr. The hot mixture was filtered and the ethanol was removed under reduced pressure. After cooling, the product was collected in ether. Recrystallisation from light petroleum (b. p. 40—60°) gave *2-chloro-5-methoxypyrimidine* (1·3 g., 41%), m. p. 75—77° (Found: C, 41·7; H, 3·5. $C_5H_5ClN_2O$ requires C, 41·5; H, 3·5%).

4-Hydrazino-5-methoxypyrimidine.—4-Chloro-5-methoxypyrimidine (0·5 g.), 64% w/w hydrazine hydrate (2 ml.), and ethanol (10 ml.) were boiled under reflux for ½ hr., then cooled and the product was collected by filtration. Recrystallisation from water gave *4-hydrazino-5-methoxypyrimidine* (0·3 g.), m. p. 184—185° (Found: C, 43·2; H, 5·7; OMe, 21·9. $C_5H_8N_4O$ requires C, 42·9; H, 5·7; OMe, 22·1%).

Oxidation of 4-Hydrazino-5-methoxypyrimidine.—10% Copper sulphate solution (8 ml.) was added dropwise to the hydrazino-compound (0·3 g.) in boiling water (10 ml.). After being boiled for ½ hr. more the mixture was filtered, made alkaline, refiltered, and distilled. The distillate yielded with mercuric chloride a small amount of the 5-methoxypyrimidine adduct, m. p. and mixed m. p. 225—232°.

Benzyl Benzyloxyacetate (with Dr. E. R. Sayer).—Ethyl chloroacetate (245 g.) was added slowly to a stirred solution of sodium (47 g.) in benzyl alcohol (800 ml.). The mixture was heated on the water-bath for 8 hr. and, after cooling, ether (2 l.) was added, and the solution filtered. The filtrate was decolorised with charcoal and distilled; the fraction (66 g., 17%), b. p. 140—145°/15 mm., was redistilled, giving ethyl benzyloxyacetate, b. p. 155°/21 mm. (lit.,[14] b. p. 142°/13 mm.). The fraction, b. p. 170—172°/0·6 mm., consisted of *benzyl benzyloxyacetate* (126 g., 25%) (Found: C, 74·8; H, 6·4. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·2%).

5-Benzyloxy-4-hydroxy-2-mercaptopyrimidine (with Dr. E. R. Sayer).—This was obtained in 50% yield from benzyl benzyloxyacetate by the method described above for the corresponding 5-methoxypyrimidine. *5-Benzyloxy-4-hydroxy-2-mercaptopyrimidine* formed needles, m. p. 230—232° (decomp.) (Found: C, 56·2; H, 4·2; N, 11·8. $C_{11}H_{10}N_2O_2S$ requires C, 56·4; H, 4·3; N, 12·0%).

5-Benzyloxy-4-hydroxypyrimidine (with Dr. E. R. Sayer).—5-Benzyloxy-4-hydroxy-2-mercaptopyrimidine (19 g.) and dectivated Raney nickel (45 g.) in water (150 ml.) and ammonia (30 ml.; *d* 0·88) were boiled under reflux for 2½ hr. with stirring. The solution was filtered and the filtrate and washings were acidified to pH 5 with hydrochloric acid. The solution, concentrated to 150 ml., was cooled and the solid which separated was recrystallised from water, giving *5-benzyloxy-4-hydroxypyrimidine monohydrate* (11·0 g., 62%), m. p. 87—90° (Found: C, 60·5; H, 5·5; N, 13·2. $C_{11}H_{10}N_2O_2,H_2O$ requires C, 60·0; H, 5·5; N, 12·7%).

5-Benzyloxy-4-chloropyrimidine.—The preceding hydroxypyrimidine (0·5 g.) and phosphoryl chloride (4 ml.) were boiled under reflux for 20 min., then cooled and poured on ice. The yellow precipitate (0·32 g.) was collected in ether. A portion was sublimed at 95—100°/21 mm., giving the very unstable *chloropyrimidine* as needles, m. p. 126—128° (Found: C, 57·7; H, 4·4; N, 13·4. $C_{11}H_9ClN_2O$ requires C, 59·8; H, 4·1; N, 12·7%).

5-Benzyloxy-4-mercaptopyrimidine.—(*a*) The above, crude chloropyrimidine (0·22 g.) was boiled for 45 min. with thiourea (0·08 g.) in ethanol (3 ml.). The product which separated on cooling was recrystallised from ethanol, giving *S-(5-benzyloxy-4-pyrimidyl)thiouronium chloride* (0·08 g.), m. p. 188—190° (decomp.) (Found: N, 18·7. $C_{12}H_{13}ClN_4OS$ requires N, 18·9%). The thiouronium salt (0·075 g.) was boiled in N-sodium hydroxide for ½ hr. After being cooled, the solution was neutralised with acetic acid, and the precipitate was recrystallised from water,

[14] Rothstein, *Bull. Soc. chim. France*, 1932, **51**, 691.

giving yellow needles (0·02 g., 36%) of 5-benzyloxy-4-mercaptopyrimidine, m. p. 156—158°, not depressed when mixed with authentic material (see below).

(*b*) A stirred mixture of 5-benzyloxy-4-hydroxypyrimidine monohydrate (3 g.), purified phosphorus pentasulphide (3 g.), and pyridine (50 ml.) was boiled under reflux for 1 hr., then cooled and poured into water (75 ml.). The mixture was evaporated to *ca.* 60 ml. on the steam-bath and then allowed to cool. The crude product was collected and recrystallised twice from water (charcoal), giving the *mercaptopyrimidine* as pale yellow needles, m. p. 157—159° (Found: C, 60·2; H, 4·8; N, 12·7. $C_{11}H_{10}N_2OS$ requires C, 60·5; H, 4·6; N, 12·8%). The yield varied from 0 to 32%.

5-Benzyloxypyrimidine.—5-Benzyloxy-4-mercaptopyrimidine (0·5 g.) was boiled for 70 min. in ethanol (25 ml.) with Raney nickel (3 g.) which had been saturated with hydrogen at room temperature and pressure. After being filtered, the solution was distilled, giving 5-benzyloxypyrimidine as an oil (0·18 g.) (Found: C, 70·7; H, 5·4; N, 14·7. $C_{11}H_{10}N_2O$ requires C, 71·0; H, 5·4; N, 15·1%). The *picrate*, recrystallised from ethanol, formed yellow prisms, m. p. 125—127° (Found: C, 49·5; H, 3·4; N, 16·9. $C_{11}H_{10}N_2O,C_6H_3N_3O_7$ requires C, 49·2; H, 3·1; N, 16·9%).

4-Hydroxy-5-methoxy-2-phenylpyrimidine.—Benzamidine hydrochloride (40 g.) in ethanol (200 ml.) was added to methyl sodio-β-hydroxy-α-methoxyacrylate (prepared from 40 g. of methyl methoxyacetate as described above for 4-hydroxy-2-mercapto-5-methoxypyrimidine), then sodium (5 g.) in ethanol (50 ml.) was added. The stirred mixture was boiled for 4½ hr., then poured into water (200 ml.) and acidified with hydrochloric acid. After being concentrated to half its volume the solution was adjusted to pH 5 and the resulting precipitate was collected. It was recrystallised from ethanol–aqueous ammonia (charcoal), giving the *phenylpyrimidine* (31 g., 60%) as needles, m. p. 206—208° (Found: C, 65·1; H, 4·9. $C_{11}H_{10}N_2O_2$ requires C, 65·4; H, 4·95%).

4-Mercapto-5-methoxy-2-phenylpyrimidine.—A stirred mixture of 4-hydroxy-5-methoxy-2-phenylpyrimidine (20·8 g.), phosphorus pentasulphide (23 g.), and pyridine (340 ml.) was boiled under reflux for 70 min., then poured, while hot, into water (400 ml.). The resulting solution, after being concentrated to *ca.* 200 ml., deposited the *mercaptopyrimidine* (12·5 g., 56%) as yellow needles, m. p. 193—196° (decomp.). A sample was recrystallised from benzene then sublimed under reduced pressure, the m. p. rising to 198—199° (decomp.) (Found: N, 12·7. $C_{11}H_{10}ON_2S$ requires N, 12·85%).

5-Methoxy-2-phenylpyrimidine.—A suspension of 4-mercapto-5-methoxy-2-phenylpyrimidine (12·5 g.) in hot benzene (200 ml.) was added to Raney nickel sludge (85 g.) in ethanol (300 ml.), and the mixture boiled under reflux for 3 hr. The hot solution was filtered and concentrated to *ca.* 20 ml., thereby yielding *5-methoxy-2-phenylpyrimidine* (5 g., 47%) as plates, m. p. 55—58° raised to 57—58° on sublimation under reduced pressure (Found: C, 71·7; H, 5·3; N, 14·7. $C_{11}H_{10}N_2O$ requires C, 71·0; H, 5·4; N, 15·05%), $\lambda_{max.}$ 2630 Å (ε 24,210 in EtOH).

5-Hydroxy-2-phenylpyrimidine.—A mixture of 5-methoxy-2-phenylpyrimidine (0·5 g.) and potassium hydroxide (1 g.) in ethylene glycol (10 ml.) was boiled gently under reflux for 10 hr. The cooled solution was added to water (10 ml.) and acidified with glacial acetic acid, then extracted six times with ether, thereby yielding *5-hydroxy-2-phenylpyrimidine* as needles which were collected and washed with a little cold water, then dried and sublimed. The product (yield 0·28 g., 61%) had m. p. 148—151° and $\lambda_{max.}$ 2630 Å (ε 22,080 in EtOH) (Found: C, 69·5; H, 4·5; N, 16·1. $C_{10}H_8N_2O$ requires C, 69·8; H, 4·7; N, 16·3%); it gave an orange-red colour with aqueous ferric chloride.

5-Hydroxy-2-mercapto-4,6-dimethylpyrimidine.—3-Acetoxypentane-2,4-dione [15] (1·6 g.), thiourea (0·7 g.), concentrated hydrochloric acid (1 ml.), and ethanol (20 ml.) were boiled for 5 hr., then the mixture was evaporated to about 5 ml. and cooled, giving yellow needles (0·83 g., 47%) of the hydrochloride of 5-hydroxy-2-mercapto-4,6-dimethylpyrimidine. This compound, dissolved in the minimum volume of water, was neutralised with sodium hydrogen carbonate, giving the free *hydroxypyrimidine* as yellow needles, m. p. >230° (decomp.) (Found: C, 46·1; H, 5·4; N, 18·0. $C_6H_8N_2OS$ requires C, 46·1; H, 5·1; N, 17·9%). The compound gave a transient dark colour with aqueous ferric chloride.

5-Hydroxy-4,6-dimethylpyrimidine.—Raney nickel sludge (2 g.) was added to the preceding compound (0·5 g.) in hot water (15 ml.), and the mixture was boiled for 40 min., then cooled, filtered, and extracted with ether. The crude product was sublimed at 100—110°/12 mm.,

[15] Cavill and Solomon, *J.*, 1955, 4426.

giving *5-hydroxy-4,6-dimethylpyrimidine* as very hygroscopic needles (0·1 g., 25%), m. p. 138—139° (Found: C, 58·3; H, 6·9; N, 23·0. $C_6H_8N_2O$ requires C, 58·1; H, 6·5; N, 22·6%). The *mercuric chloride adduct*, recrystallised from water, formed needles, m. p. 192° (decomp.) [Found: C, 27·4; H, 3·0; N, 10·6. $(C_6H_8N_2O)_2,HgCl_2$ requires C, 27·7; H, 3·1; N, 10·8%].

2,5-Dihydroxy-4,6-dimethylpyrimidine.—3-Acetoxypentane-2,4-dione (1·6 g.), urea (0·6 g.), concentrated hydrochloric acid (2·5 ml.), and ethanol (15 ml.) were boiled for 2 hr., then concentrated to *ca.* 5 ml. and cooled, giving 2,5-dihydroxy-4,6-dimethylpyrimidine hydrochloride (0·5 g., 28%). Neutralisation of a solution of the hydrochloride gave the free dihydroxypyrimidine which, on recrystallisation from water, formed needles, m. p. >300° (Found: C, 51·6; H, 5·9; N, 19·7. Calc. for $C_6H_8N_2O_2$: C, 51·4; H, 5·7; N, 20·0%). An aqueous solution of the compound gave an intense violet-red colour with ferric chloride.

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