109. *Pyrimidines. Part X.* Pyrimidine, 4 : 6-Dimethylpyrimidine, and their 1-Oxides.*

By R. R. Hunt, J. F. W. McOmie, and E. R. Sayer.

A convenient four-stage synthesis of pyrimidine is described which starts from acetylacetone and thiourea, and proceeds *via* 2-mercapto-4 : 6-dimethylpyrimidine, 4 : 6-dimethylpyrimidine, and pyrimidine-4 : 6-dicarboxylic acid.

Other syntheses of pyrimidine and of 4-methylpyrimidine have been explored. Pyrimidine and its 4 : 6-dimethyl derivative, when treated with hydrogen peroxide in acetic acid, give the corresponding 1-oxides, but these could only be made to undergo two of the many rearrangements typical of the pyridine 1-oxides.

As a prelude to studies of substitution in pyrimidine we have devised a convenient, four-stage synthesis of this compound in which the usual tedious isolation *via* the mercuric chloride complex has been avoided. Acetylacetone reacts with thiourea to give 2-mercapto-4 : 6-dimethylpyrimidine which is desulphurised to give 4 : 6-dimethylpyrimidine. Oxidation of the latter to pyrimidine-4 : 6-dicarboxylic acid followed by pyrolysis then gives pyrimidine. The sequence has not previously been used for the preparation of pyrimidine, yet each of the four reactions has been effected at various times, although no details of the last two stages have been published.

The condensation of acetylacetone with thiourea by Evans's method [1] gave a mixture of 2-mercapto-4 : 6-dimethylpyrimidine hydrochloride and a 1 : 1 molecular complex [2] of the pyrimidine with thiourea, but by modifying the conditions a 90% yield of the pyrimidine hydrochloride, free from thiourea, was obtained. Desulphurisation of the mercapto-compound by Raney nickel was first studied in neutral aqueous solution. At the end of the reaction the mixture was filtered and steam-distilled until the distillate no longer gave a turbidity with mercuric chloride. The distillate then contained 4 : 6-dimethylpyrimidine in 68—72% yield, but when attempts were made to oxidise the dimethylpyrimidine in this solution much more than the theoretical amount of potassium

* Part IX, *J.*, 1957, 1830.

[1] Evans, *J. prakt. Chem.*, 1893, **48**, 493.
[2] Boarland and McOmie, *J.*, 1952, 3722.

permanganate was consumed and the yield of pyrimidine-4 : 6-dicarboxylic acid was low. Presumably some di- or tetra-hydro-4 : 6-dimethylpyrimidine had been produced and complete oxidation of this would account for the large amount of potassium permanganate required. The desulphurisation was therefore carried out in ethanol, and the 4 : 6-dimethylpyrimidine (45—60% yield) isolated by distillation. The yield was not improved by converting the mercaptopyrimidine into 4 : 6-dimethyl-2-methylthiopyrimidine before desulphurisation.

Oxidation of 4 : 6-dimethylpyrimidine by alkaline potassium permanganate gave good but variable (43—72%) yields of pyrimidine-4 : 6-dicarboxylic acid. A less favourable conversion was effected by bromination of the dimethylpyrimidine followed by hydrolysis of the 4 : 6-bistribromomethylpyrimidine with silver nitrate in acetic acid. Similar conversions have been carried out by Brown *et al.*[3] in the pyrimidine and quinoline series and by Holland and Slack [4] for the preparation of 5-bromopyrimidine-2-carboxylic acid. The dicarboxylic acid could be decarboxylated on a very small scale by dry distillation,[5] but even on a one-gram scale the yield dropped so much that the method was useless. However, by heating the acid in diphenyl ether, it was possible to decarboxylate 38-gram batches in 60% yield. Thus pyrimidine is available in an overall yield of 10—23% based on acetylacetone.

The commercial availability of 1 : 1 : 3 : 3-tetraethoxypropane suggested the possibility of a two-stage synthesis of pyrimidine. Thiourea and the acetal in presence of hydrochloric acid readily gave 2-mercaptopyrimidine, but re-investigation of the desulphurisation of the latter [6] showed that the yield of pyrimidine was unsatisfactory, even if the 2-mercapto-compound was first converted into 2-methylthiopyrimidine or 2-(pyrimidylthio)acetic acid. Oxidative desulphurisation of 2-mercaptopyrimidine by the method of Evans *et al.*[7] was more promising but large-scale experiments were not carried out. 1 : 1 : 3 : 3-Tetraethoxypropane also condensed readily with urea to give 2-hydroxypyrimidine, but it could not be condensed with benzamidine. Bredereck, Gompper, and Morlock [8] recently showed that 1 : 1 : 3-triethoxy-3-methoxypropane and formamide gave pyrimidine in 65% yield, so that this method is the simplest so far devised. We have shown that 1 : 1 : 3 : 3-tetraethoxypropane also undergoes this reaction, but we obtained only a 30% yield of pyrimidine. A few experiments were made to utilise the commercially available 1-methoxybut-1-en-3-yne. Condensation with thiourea in presence of hydrochloric acid gave 2-mercapto-4-methylpyrimidine hydrochloride which on desulphurisation with Raney nickel gave a low yield of 4-methylpyrimidine.

Pyridine 1-oxide and related compounds undergo a variety of substitution and rearrangement reactions (for reviews see Ochiai [9] and Katritzky [10]). Ochiai [9,11] prepared the *N*-oxides of a few substituted pyrimidines and showed that with alkali-metal cyanides in the presence of benzoyl chloride they give cyanopyrimidines. After completion of our work, Wiley and Slaymaker [12] described the preparation of the *N*-oxides of pyrimidine and the monoethyl- and 2 : 4 : 6-trimethyl-pyrimidines. Employing the usual method of oxidation with hydrogen peroxide in acetic acid we found that 4 : 6-dimethylpyrimidine 1-oxide could be obtained easily but pyrimidine itself gave only a 9% yield of oxide (Wiley and Slaymaker [12] obtained an 11% yield under slightly different conditions). The following 4 : 6-dimethylpyrimidines gave no *N*-oxides, possibly because of steric hindrance: 2-benzyloxy-, 2-chloro-, 2-hydroxy-, and 2-phenyl-.

[3] Brown, Hammick, and Thewlis, *J.*, 1951, 1146.
[4] Holland and Slack, *Chem. and Ind.*, 1954, 1203.
[5] Angerstein, *Ber.*, 1901, **34**, 3956.
[6] Boarland, McOmie, and Timms, *J.*, 1952, 4691.
[7] Evans, Jones, Palmer, and Stephens, *J.*, 1956, 4106.
[8] Bredereck, Gompper, and Morlock, *Chem. Ber.*, 1957, **90**, 942.
[9] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[10] Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[11] Ochiai and Yamanaka, *Pharm. Bull.* (*Japan*), 1955, **3**, 175.
[12] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1957, **79**, 2233.

4 : 6-Dimethylpyrimidine 1-oxide and toluene-*p*-sulphonyl chloride gave a low yield of a very unstable chlorine-containing product, not identical with 2-chloro-4 : 6-dimethylpyrimidine. The product is considered to be 4-chloromethyl-6-methylpyrimidine since the other possible product, 5-chloro-4 : 6-dimethylpyrimidine, would be expected to be stable; moreover, 2-methylpyridine 1-oxide is known to give 2-chloromethylpyridine in this reaction.[13] When 4 : 6-dimethylpyrimidine 1-oxide was heated in acetic anhydride it gave what is thought to be 4-acetoxymethyl-6-methylpyrimidine—by analogy with the pyridine series,[14] and because the absorption spectrum ($\lambda_{max.}$ 248 mμ, $\log_{10}\varepsilon$ 3·48) of the product in ethanol closely resembles that of 4 : 6-dimethylpyrimidine (245·5 mμ, $\log_{10}\varepsilon$ 3·30).

Attempts to nitrate pyrimidine 1-oxide were unsuccessful and no useful products were obtained by the reaction of 4 : 6-dimethylpyrimidine 1-oxide under the conditions used in the pyridine and quinoline series with phenylmagnesium bromide,[15] benzoyl chloride–potassium hydroxide,[16] or benzoyl chloride–potassium cyanide.[16] It is clear that the pyrimidine 1-oxides are much less useful for synthetic purposes than the pyridine or quinoline oxides.

The ultraviolet absorption spectra of some of the compounds described in this paper have been measured. It is known[17] that the spectrum of pyrimidine ($\lambda_{max.}$ 243 mμ, $\log_{10}\varepsilon$ 3·38) and of 4 : 6-dimethylpyrimidine ($\lambda_{max.}$ 246 mμ, $\log_{10}\varepsilon$ 3·63) in water is scarcely altered when the bases are converted into their hydrochlorides. Like the latter the 1-oxides bear a positive charge on one of the nitrogen atoms, but the spectrum of pyrimidine 1-oxide ($\lambda_{max.}$ 258 mμ, $\log_{10}\varepsilon$ 4·00) and that of 4 : 6-dimethylpyrimidine 1-oxide ($\lambda_{max.}$ 257 mμ, $\log_{10}\varepsilon$ 4·02) show a bathochromic displacement. For comparison, the methiodides of pyrimidine and of 4 : 6-dimethylpyrimidine in water were also examined. They absorbed at 226, 293 mμ ($\log_{10}\varepsilon$ 4·21, 3·18) and 226, 247 (infl.) mμ ($\log_{10}\varepsilon$ 4·18, 3·86) respectively. The short-wavelength band is probably due to the iodide anion which absorbs at 226 mμ ($\log_{10}\varepsilon$ *ca.* 4) in water, the absorption being due to charge transfer from the ion to the solvent.[18] The long-wavelength band is probably due to charge transfer from the iodide ion to the 1-methylpyrimidinium cation, and is similar to that discussed by Kosower[19] for pyridine methiodide.

Experimental

2-Mercapto-4 : 6-dimethylpyrimidine.—Concentrated hydrochloric acid (250 ml.) was added to a suspension of finely powdered thiourea (76 g., 1 mole) in acetylacetone (120 g., 1·2 moles) and ethanol (2500 ml.), and the mixture boiled under reflux for 2 hr. After cooling, the yellow needles (140 g., 80%) of 2-mercapto-4 : 6-dimethylpyrimidine hydrochloride were collected. To the mother-liquor were added more powdered thiourea (76 g.), acetylacetone (110 g.), ethanol (100 ml.), and concentrated hydrochloric acid (150 ml.), and the mixture was boiled as before. Cooling and filtration then gave the hydrochloride (160 g., 90%). After three such preparations making use of the original mother-liquor, the final mother-liquor was discarded. The batches of hydrochloride gave a white precipitate with ammoniacal silver nitrate and were sufficiently pure to be used in the next stage. When the hydrochloride was contaminated with thiourea a brown precipitate was obtained.

4 : 6-Dimethylpyrimidine.—(*a*) Raney nickel[20] (180 g., ethanol-wet), followed by concentrated hydrochloric acid (30 ml.), was added to 2-mercapto-4 : 6-dimethylpyrimidine hydrochloride (90 g.) in ethanol (600 ml.) at *ca.* 50°. The mixture was boiled under reflux for 4 hr. while being stirred. The hot solution was filtered, the nickel was washed with hot ethanol (75 ml.), and the combined filtrates were concentrated to *ca.* 150 ml. This solution was mixed with ether (150 ml.) and then transferred to a large mortar. Powdered sodium hydroxide was

[13] Matsumura, *J. Chem. Soc. Japan*, 1953, **74**, 363.
[14] Boekelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.
[15] Colonna and Risaliti, *Gazzetta*, 1953, **83**, 58.
[16] Montanari and Pentimalli, *ibid.*, p. 273.
[17] Boarland and McOmie, *J.*, 1951, 1218.
[18] Smith and Symons, *Trans. Faraday Soc.*, 1958, **54**, 338.
[19] Kosower, *J. Amer. Chem. Soc.*, 1958, **80**, 3253.
[20] Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.

added in portions and ground into the sludge (much heat evolved) until the mixture was strongly alkaline. The liquid was decanted and the solid ground with more ether until about 500 ml. of extract had been obtained. After being filtered (sintered-glass funnel) and dried, the ethereal solution was distilled. The fraction of b. p. 45—110° was mainly ethanol and was used as part of the solvent for another desulphurisation, thereby raising the yield of dimethylpyrimidine by 5—8%. The fraction boiling above 110° was collected and redistilled through a short fractionating column, giving dimethylpyrimidine (25—30 g., 45—55%), b. p. 154°/758 mm., m. p. 24—26° (lit.,[21] 25°) [picrate, m. p. 143° (lit.,[21] 143°)]. The *methiodide* recrystallised from ethanol as needles, m. p. 220—222° (decomp.) (Found: C, 34·1; H, 4·3; N, 11·5. $C_7H_{11}N_2I$ requires C, 33·7; H, 4·4; N, 11·2%).

(*b*) The mercaptopyrimidine in aqueous sodium hydrogen carbonate was treated with methyl sulphate, yielding 4 : 6-dimethyl-2-methylthiopyrimidine as a light yellow oil (61%), b. p. 123—126°/15 mm., m. p. 21—24° (lit.,[22] b. p. 123—125°/14 mm., m. p. 23—24°). A mixture of the methylthio-compound (4·6 g.) and Raney nickel (22 g.) in water (38 ml.) and ethanol (12 ml.) was boiled under reflux for 2 hr. After being filtered, the solution was steam-distilled and a saturated aqueous solution of mercuric chloride added to the distillate, giving the adduct with 4 : 6-dimethylpyrimidine ($C_6H_8N_2$,2$HgCl_2$; 15 g., 77%).

Pyrimidine-4 : 6-dicarboxylic Acid.—A hot solution of potassium permanganate (90 g.) in water (550 ml.) was added during ~3 hr. to a stirred solution of 4 : 6-dimethylpyrimidine (15 g.) in water (50 ml.) containing sodium hydroxide (3·6 g.), at 70—80°. The hot solution was filtered and the manganese dioxide washed with hot water (50 ml.). The filtrate and washings were concentrated to *ca.* 100 ml., and concentrated hydrochloric acid was added until the pH was 2—3. After cooling, pyrimidine-4 : 6-dicarboxylic acid dihydrate, m. p. 210—211° (decomp.), was collected. In 25 oxidations the yield varied from 43 to 72% (average 60%).

Pyrimidine.—(*a*) Pyrimidine-4 : 6-dicarboxylic acid dihydrate (46 g.) was dried at 60° for one week to give the anhydrous acid (38 g.), m. p. 218° (decomp.) [lit.,[5] m. p. 220—222° decomp.)].

Anhydrous pyrimidine-4 : 6-dicarboxylic acid (38 g.) was added in portions to dry, redistilled diphenyl ether (50 g.) in a two-necked flask heated in an oil-bath at about 240° and fitted with a still-head, condenser, and receiver. Decarboxylation was rapid and, by maintaining the pressure in the system at a few mm. below atmospheric, the pyrimidine formed distilled over rapidly together with some diphenyl ether. When the decarboxylation was complete the distillate was redistilled through a short fractionating column, giving pyrimidine (10·7 g., 60%), b. p. 124—128°/760 mm.

(*b*) 2-Mercaptopyrimidine (0·5 g.) was desulphurised as previously described,[6] and the pyrimidine obtained was isolated as its complex with mercuric chloride (0·38 g., 25%), m. p. 230—232° (Found: C, 14·1; H, 1·3; N, 8·2. Calc. for $C_4H_4N_2$,$HgCl_2$: C, 13·7; H, 1·1; N, 8·0%).

(*c*) A mixture of 2-(pyrimidylthio)acetic acid (0·34 g.) (see below), sodium carbonate (0·15 g.), and ethanol-wet Raney nickel (1·6 g.) in ethanol (10 ml.) was boiled under reflux for 2 hr. After filtration the solution was distilled and a saturated ethanol solution of picric acid was then added to the distillate, giving pyrimidine picrate (0·086 g., 14%), m. p. 150—155°.

(*d*) 6% Hydrogen peroxide (15 ml.) was added dropwise during 1 hr. to an ice-cold solution of 2 mercaptopyrimidine (2 g.) in 2N-sodium hydroxide. After being stirred for 1·5 hr. more, the solution was made slightly acid by the addition of acetic acid. 2-Mercaptopyrimidine (0·3 g.) was removed and the filtrate was then concentrated to dryness under reduced pressure. Concentrated hydrochloric acid was added to the residue, whereupon sulphur dioxide was evolved. Sodium carbonate solution was added until the mixture was alkaline, then it was continuously extracted with ether for 2 hr. The ether reservoir contained picric acid, thus converting the extracted pyrimidine into its picrate which was collected (2·15 g., 39%; m. p. 152—155°).

4 : 6-*Bistribromomethylpyrimidine.*—Bromine (52 g.) in glacial acetic acid (48 ml.) was added dropwise during 2 hr. to a well-stirred mixture of anhydrous sodium acetate (30 g.) and 4 : 6-dimethylpyrimidine (5·4 g.) in acetic acid (48 ml.) and acetic anhydride (10 ml.) at 70—80°. After a further 5 hours' heating at 80—85° the acetic acid and excess of bromine were removed by distillation and the residue was poured into ice-water. The crude product (25 g.) was

[21] Gabriel and Colman, *Ber.*, 1899, **32**, 1536.
[22] Wheeler and Jamieson, *Amer. Chem. J.*, 1904, **32**, 342.

recrystallised from light petroleum (b. p. 60—80°), giving orange needles (12·5 g.), m. p. 118—121°. A second recrystallisation then gave 4 : 6 *bistribromomethylpyrimidine* as pale fawn needles (11·2 g., 39%), m. p. 125—126° (Found: C, 12·4; H, 0·2; N, 4·9; Br, 81·5. $C_6H_2N_2Br_6$ requires C, 12·4; H, 0·4; N, 4·8; Br, 82·4%), $\lambda_{max.}$ 267 mμ ($\log_{10}$ ε 3·89) in ethanol.

Hydrolysis of 4 : 6-*Bistribromomethylpyrimidine.*—4 : 6-Bistribromomethylpyrimidine (2·9 g.) was boiled under reflux for 3 hr. with silver nitrate (4·6 g.) in acetic acid (40 ml.). The hot mixture was filtered and, after cooling, the filtrate gave pyrimidine-4 : 6-dicarboxylic acid (0·2 g., 24%), m. p. and mixed m. p. 206° (decomp.).

Methyl Pyrimidine-4 : 6-*dicarboxylate.*—A solution of the hydrated dicarboxylic acid (1·3 g.) in methanol (150 ml.) containing concentrated hydrochloric acid (1 ml.) was boiled under reflux for 0·5 hr. The solvent was removed under reduced pressure, and the residue was recrystallised from light petroleum (b. p. 60—80°), giving needles (1·0 g., 80%), m. p. 77—79°, which after sublimation had m. p. 82—83° (Found: C, 49·1; H, 4·3; OMe, 30·7. $C_8H_8O_4N_2$ requires C, 49·0; H, 4·1; N, 14·3; OMe, 32·6%), $\lambda_{max.}$ 269, 320 mμ ($\log_{10}$ ε 3·80, 2·46) in ethanol.

2-*Mercaptopyrimidine.*—1 : 1 : 3 : 3-Tetraethoxypropane (11 g.) was added to a hot, stirred mixture of thiourea (3·8 g.), ethanol (30 ml.), and concentrated hydrochloric acid (9 ml.). After being boiled for 10 min., the mixture was cooled and the yellow 2-mercaptopyrimidine (3·0 g.) collected. Addition of ether to the filtrate gave a further quantity (0·8 g.; total, 66%). Recrystallisation from ethanol–water gave the pure compound, m. p. 229—230° (decomp.) [lit.,[17] m. p. 230° (decomp.)] (Found: C, 43·0; H, 3·9; N, 24·9. Calc. for $C_4H_4N_2S$: C, 42·9; H, 3·6; N, 25·0%).

2-(*Pyrimidylthio*)*acetic Acid.*—A mixture of 2-mercaptopyrimidine (2 g.) and chloroacetic acid (1·5 g.) in water (10 ml.) was boiled under reflux for 0·5 hr. On cooling, the solution yielded 2-(*pyrimidylthio*)*acetic acid* (1·8 g., 60%), m. p. 190—197° raised to 199—200° by recrystallisation from water (Found: C, 42·2; H, 3·8; N, 16·6. $C_6H_6O_2N_2S$ requires C, 42·4; H, 3·5; N, 16·5%).

2-*Hydroxypyrimidine.*—1 : 1 : 3 : 3-Tetraethoxypropane (5·5 g.) was added to a warm solution of urea (1·5 g.) in ethanol (10 ml.) and concentrated hydrochloric acid (5 ml.). After being stirred at 30—40° for 1 hr., the solution was cooled to 0° and the 2-hydroxypyrimidine hydrochloride (1·3 g.), m. p. 210°, was collected. Addition of ether to the mother-liquor gave a further crop (1·2 g.) of the hydrochloride. The combined product was dissolved in aqueous sodium carbonate, then acidified to pH 5 with 5N-sulphuric acid. The solution was evaporated to dryness and the residue, after being powdered, was extracted with boiling ethyl acetate (1500 ml.). The extract gave 2-hydroxypyrimidine (1·8 g., overall yield 73%) as needles, m. p. and mixed m. p. 179—181°.

2-*Mercapto*-4-*methylpyrimidine Hydrochloride.*—Concentrated hydrochloric acid (62 ml.) and 1-methoxybut-1-en-3-yne (29 g.) were added to a solution of thiourea (25·5 g.) in ethanol (275 ml.), and the mixture was boiled under reflux for 6 hr. Next day the yellow-brown precipitate (43·8 g.) of 2-mercapto-4-methylpyrimidine hydrochloride was collected. Concentration of the filtrate gave a further amount (2·8 g.) of the hydrochloride. In agreement with Burness,[23] attempts to recrystallise the compound resulted in an insoluble polymer.

The crude mercaptopyrimidine, dissolved in aqueous sodium hydrogen carbonate, was treated with methyl sulphate, giving 4-methyl-2-methylthiopyrimidine (60%), b. p. 116—119°/21 mm., which gave a picrate, m. p. 108—110° (lit.,[24] m. p. 106—108°).

4-*Methyl*-2-(*pyrimidylthio*)*acetic Acid.*—A mixture of 2-mercapto-4-methylpyrimidine hydrochloride (1·6 g.) and sodium hydroxide (1·2 g.) in water (10 ml.) was added to a solution of chloroacetic acid (1 g.) in water (3 ml.) previously neutralised with sodium carbonate. After 4 days the mixture was acidified with dilute hydrochloric acid. The pale brown powder obtained recrystallised from water, giving 4-*methyl*-2-(*pyrimidylthio*)*acetic acid* as plates (0·75 g., 41%), m. p. 191° (Found: N, 15·0. $C_7H_8O_2N_2S$ requires N, 15·2%).

4-*Methylpyrimidine.*—Water-wet Raney nickel (20 g.) was added to a solution of 2-mercapto-4-methylpyrimidine hydrochloride (8 g.) in water (75 ml.) which had been neutralised by adding sodium carbonate. The mixture was boiled under reflux, with stirring, for 3 hr., then filtered hot, and the filtrate distilled. Ether-extraction of the distillate gave 4-methylpyrimidine (0·9 g., 20%), b. p. 139—140°/763 mm. The adduct with mercuric chloride had m. p. 198—200° (lit.,[21] m. p. 198°), and the picrate had m. p. 130—131° (lit.,[21] 131—134°).

[23] Burness, *J. Org. Chem.*, 1956, **21**, 97.
[24] Marshall and Walker, *J.*, 1951, 1013.

4 : 6-*Dimethylpyrimidine* 1-*Oxide*.—A mixture of 4 : 6-dimethylpyrimidine (10·8 g.), acetic acid (60 ml.), and 30% hydrogen peroxide (10 ml.) was kept at 70—80° for 3 hr., then more hydrogen peroxide (8 ml.) was added and the mixture warmed for 9 hr. more. Most of the solvent was removed under reduced pressure, then a little water was added, and the mixture again distilled. Anhydrous potassium carbonate was added to the residue until it was strongly alkaline. The resulting pasty mass was extracted in a Soxhlet apparatus with chloroform (100 ml.) for 3 hr. The chloroform solution, after being dried, was concentrated to *ca.* 15 ml., and light petroleum (b. p. 40—60°) added, precipitating 4 : 6-*dimethylpyrimidine* 1-*oxide* (7·1 g., 57%), m. p. 100—102°. After two recrystallisations the compound was obtained as hygroscopic needles, m. p. 113—115° (Found: C, 58·2; H, 6·3; N, 22·2. $C_6H_8ON_2$ requires C, 58·0; H, 6·4; N, 22·6%). The oxide was without action on acidified starch–iodide paper. It gave a *picrate*, m. p. 86° (from ethanol) (Found: C, 41·0; H, 3·2; N, 20·1. $C_{12}H_{11}O_8N_5$ requires C, 40·9; H, 3·1; N, 19·8%). The *mercuric chloride adduct* had, after recrystallisation from water, m. p. 158° [Found: C, 13·7; H, 1·5; N, 5·6. $(C_6H_8ON_2)_2(HgCl_2)_3$ requires C, 13·5; H, 1·5; N, 5·3%].

4-*Chloromethyl*-6-*methylpyrimidine*.—A mixture of 4 : 6-dimethylpyrimidine 1-oxide (3·3 g.) and toluene-*p*-sulphonyl chloride (5·0 g.) in benzene (20 ml.) was kept at room temperature for 0·5 hr. The benzene was distilled off under reduced pressure and the residual oil heated on a water-bath for 1 hr. After being cooled, the oil was washed with ether, then aqueous sodium hydrogen carbonate was added and the mixture extracted with chloroform. The extract was distilled under a high vacuum and gave a very unstable chlorine-containing yellow oil which was immediately treated with picric acid in ethanol, giving 4-*chloromethyl*-6-*methylpyrimidine picrate*, m. p. 115° (Found: C 38·8; H, 2·7; N, 18·1. $C_{12}H_{10}O_7N_5Cl$ requires C, 38·8; H, 2·7; N, 18·8%).

4-*Acetoxymethyl*-6-*methylpyrimidine*.—Acetic anhydride (10 ml.) was added to 4 : 6-dimethylpyrimidine 1-oxide (2·5 g.) and after 10 min. the mixture was heated on the water-bath for 15 min. A vigorous exothermic reaction occurred and the liquid became almost black. The mixture was distilled and the pale yellow fraction (0·9 g.) of b. p. 130—150°/0·1 mm. was twice redistilled, giving 4-*acetoxymethyl*-6-*methylpyrimidine* as a colourless oil, b. p. 100—110° (bath temp.)/15 mm. (Found: C, 57·0; H, 6·0; N, 16·5. $C_8H_{10}O_2N_2$ requires C, 57·6; H, 6·0; N, 16·9%). This gave a *picrate* which after two recrystallisations from ethanol formed yellow needles, m. p. 135—136° (Found: C, 42·9; H, 3·2. $C_{14}H_{13}O_9N_5$ requires C, 42·7; H, 3·3%).

Pyrimidine 1-*Oxide*.—A mixture of pyrimidine (6 g.), glacial acetic acid (45 ml.), and 36% hydrogen peroxide (7·5 ml.) was kept at 70—80° for 3 hr., then more hydrogen peroxide (6 ml.) was added and the mixture warmed for 9 hr. more. Acetic acid was removed under reduced pressure and sodium carbonate was added to the residue until the mixture became alkaline; then it was continuously extracted with chloroform, yielding brown needles (1·1 g.) which were purified by sublimation followed by recrystallisation from light petroleum (b. p. 40—60°)–benzene. The oxide (0·6 g., 9%) formed very deliquescent white needles, m. p. 89—91° (lit.,[12] m. p. 85—88°) which became brown after a few days (Found: C, 50·0; H, 4·1; N, 29·4. Calc. for $C_4H_4ON_2$: C, 50·0; H, 4·2; N, 29·2%). The oxide formed a *picrate*, m. p. 84—85° (Found: C, 37·0; H, 2·3. $C_{10}H_7O_8N_5$ requires C, 37·0; H, 2·2%), and a mercuric chloride adduct, m. p. 161—162°.

2-*Benzyloxy*-4 : 6-*dimethylpyrimidine*. 2-Chloro-4 : 6-dimethylpyrimidine (15 g.) was added to a solution of sodium (2·5 g.) in benzyl alcohol (75 ml.), and the mixture boiled under reflux for 4 hr., cooled, and poured into water. The product was extracted with ether, giving an oil, b. p. 188—195°/20 mm., which was redistilled, giving 2-*benzyloxy*-4 : 6-*dimethylpyrimidine* (14·7 g.), b. p. 160—165°/2·5 mm. (Found: C, 72·8; H, 6·4; N, 13·1. $C_{13}H_{14}ON_2$ requires C, 73·0; H, 6·6; N, 13·2%).

The 2-benzyloxy-compound (2 g.) was easily debenzylated by boiling 20% hydrochloric acid (10 ml.) (20 min.). After cooling, the mixture was made neutral and extracted with chloroform, which on evaporation gave 2-hydroxy-4 : 6-dimethylpyrimidine dihydrate (0·9 g., 60%), m. p. 198°.

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