## 247. *Hydropyrimidines. Part IV.*[1] *Catalytic Reduction of Substituted Pyrimidines.*

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1,4,5,6-Tetrahydro-derivatives were obtained by catalytic reduction in acid solution of 2,4,6-trimethyl-, 2-hydroxy-, 2-methoxy-, and 5-methoxypyrimidines. 5-Hydroxypyrimidine gave 1,4,5,6-tetrahydro-5,5-dihydroxypyrimidine hydrochloride whilst 5-acetamidopyrimidine afforded 5-acetamido-1,3-diacetyl-1,2,3,4-tetrahydropyrimidine after reduction in hot acetic anhydride. Evidence is presented to show that reduction of 4-hydroxy- and 4-acetamido-pyrimidines involves the 1,2-positions.

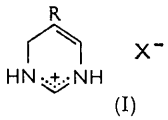
The basic and spectral properties of some of the derivatives are discussed.

Continuing the study of hydropyrimidines,[1-3] the reduction of 2,4,6-trimethyl-, hydroxy-, methoxy-, and acetamido-pyrimidines was investigated. In acidic solution, 2,4,6-trimethylpyrimidine absorbed two moles of hydrogen over palladised charcoal to give DL-*trans*-1,4,5,6-tetrahydro-2,4,6-trimethylpyrimidine, identified by conversion into the known nitrate [4] and by alkaline hydrolysis to DL-2,4-diaminopentane. Although heavily substituted, the rate of reduction of the trimethylpyrimidine was comparable to that of the

[1] Part III, Evans, *J.*, 1964, 2450.
[2] Brown and Evans, *J.*, 1962, 527.
[3] Brown and Evans, *J.*, 1962, 4039.
[4] Harries and Haga, *Ber.*, 1899, **32**, 1198.

parent compound,[2] because the substituents were symmetrically distributed.[5a] The isolation of a *trans* reduction product suggested that isomerisation followed the *cis*-reduction postulated by current theories of catalytic reduction.[5b]

1,4,5,6-Tetrahydro-derivatives were obtained by reduction of 2-hydroxy- and 2-methoxy pyrimidine in acidic media. The lability of the methoxy-group in aqueous acid rendered necessary the introduction of methanolic acetic acid as a reduction medium. Alkaline hydrolysis of 1,4,5,6-tetrahydro-2-methoxypyrimidine hydrochloride afforded trimethylenediamine; the picrate, however, yielded ammonia, presumably by dehydrogenation of the trimethylenediamine, followed by hydrolysis.


(I)

Although unstable to strong acids,[6] 5-hydroxypyrimidine could be reduced at pH 2 with the absorption of only one mole of hydrogen. The initial product (I; R = OH, X = Cl) tautomerised and hydrated to give 1,4,5,6-tetrahydro-5,5-dihydroxypyrimidine hydrochloride. 5-Methoxypyrimidine, on the other hand, underwent smooth reduction in dilute mineral acid to its 1,4,5,6-tetrahydro-derivative, which was also obtained by reduction of 4-chloro-5-methoxypyrimidine in aqueous medium. Alkaline hydrolysis of the tetrahydro-derivative gave 2-methoxypropane-1,3-diamine.

Attempts to obtain tetrahydro-derivatives of 5-hydroxypyrimidine were unsuccessful. Demethylation of 1,4,5,6-tetrahydro-5-methoxypyrimidine hydrobromide and the reaction of acetamidine hydrochloride with 1,3-diaminopropan-2-ol gave mixtures of weakly basic substances.

1,4,5,6-Tetrahydro-5,5-dihydroxypyrimidine hydrochloride was first produced [1] by the reduction of 5-aminopyrimidine in acid solution, and this involved hydrolysis of the intermediate (I; R = $NH_2$). 5-Acetamidopyrimidine in hot (100°) acetic anhydride, used as solvent to avoid hydrolysis, absorbed two moles of hydrogen and the major product was 5-acetamido-1,3-diacetyl-1,2,3,4-tetrahydropyrimidine. On acid hydrolysis it yielded formaldehyde, while the presence of C=C rather than of C=N unsaturation was indicated by its immediate decolorisation of a chloroform solution of bromine. The tetrahydro-compound was further reduced in the presence of platinum oxide, affording a hexahydro-derivative which, on acidic hydrolysis, gave formaldehyde and propane-1,2,3-triamine.

Acid treatment of the ill-defined products obtained by reduction of 4-acetamido- and 4-hydroxy-pyrimidines afforded formaldehyde, indicating that reduction involving the 1,2-positions had occurred.

*Ionisation and Spectra.*—1,4,5,6-Tetrahydropyrimidine is highly basic [2] ($pK_a$ 13·0) as befits its amidine structure. The introduction of a 5-methoxy-group, at a distance of two carbon atoms from the basic centre, lowered the $pK_a$ value by 1·8 units (cf. the drop of 2·2 units when a 2-methoxy-group was inserted).

Infrared spectra (KBr discs) ($cm.^{-1}$) of substituted 1,4,5,6-tetrahydropyrimidine salts.

| Substituent | Acid in salt | $\nu(\overset{+}{N{=}C{=}N})$ | $\delta$(N–H) | $\nu$(N–H) |
|---|---|---|---|---|
| 2,4,6-$(Me)_3$ | HCl | 1650 | 1625 | 3160, 3020 |
| | $HHgCl_3$ | 1648 | 1618 | 3290 |
| | $HHg_2Cl_5$ | 1645 | 1615 | 3330 |
| | $HNO_3$ | 1656 | | 3180, 3060 |
| 2-OMe | HCl | 1690, 1675 | 1613 | 3240, 3080 |
| | $\frac{1}{2}(H_2Hg_3Cl_8)$ | 1660 | 1616 | 3310 |
| 5-OMe | HBr | 1673—1690 | | 3240, 3080 |
| | $HHgCl_3$ | 1692 | 1580 | 3310 |

The infrared spectra (see Table) of the 1,4,5,6-tetrahydropyrimidine salts exhibit a prominent band in the upper part of the 1600—1700 $cm.^{-1}$ region which is assigned to the asymmetric $(N{=}C{=}N)^+$ stretching vibration. The value of its frequency varies slightly

[5] Smith, " Catalysis," ed. Emmett, Reinhold, New York, 1957, (*a*) p. 197, (*b*) p. 182.
[6] Chesterfield, McOmie, and Tute, *J.*, 1960, 4590.

with the anion present in the salt, in contrast with that for N–H stretching, which is very sensitive to hydrogen bonding. Diminution of hydrogen bonding in a salt, resulting from a change of anion from chloride, bromide, or nitrate to chloromercurate, is accompanied by a shift of ν(N–H) to higher frequencies.[7] The amide I band [8] due to the 5-acetamido-group is prominent at 1708 cm.$^{-1}$ in the spectrum of 5-acetamidopyrimidine. This moves to 1690 cm.$^{-1}$ in the 1,3-diacetyl-1,2,3,4-tetrahydro-derivative (II). The latter compound had considerable absorption in the ultraviolet region, due to the auxochromic effect of the substituted amino-groups at positions 1 and 5 on the ethylenic bond. This arose from the interaction of the unshared pairs of electrons on the nitrogen atoms with the π-electrons of the double bond.[9]

The nuclear magnetic resonance spectrum showed signals at 7·90 (singlet; 3 protons) 7·83 (singlet; 3 protons), and 7·77 τ (singlet; 3 protons) assigned to the three acetyl methyl groups. Signals at 5·77 (doublet, $J$ = 1·4 c./sec., 2 protons) and 2·24 τ (triplet, $J$ = 1·4 c./sec., 1 proton) were assigned to the allylic methylene group and the olefinic proton, respectively. The coupling constant was of the order expected for this system [10] and irradiation of one signal at the chemical shift difference (212 c./sec.) while scanning the other signal led to collapse of the multiplet structure, confirming the assignments The signal at 4·77 τ (singlet, 2 protons) was assigned to the methylene group between the two nitrogen atoms, and the signal at 1·62 τ (broad singlet, 1 proton) to the amide NH.

The nuclear magnetic resonance spectrum of 1,2,3-triacetamidoprop-1-ene, which was also isolated from the reduction of 5-acetamidopyrimidine in hot acetic anhydride, showed signals at 7·97 (singlet, 3 protons), 7·93 (singlet, 3 protons), and 7·88 τ (singlet, 3 protons) assigned to the three acetyl methyl groups. The signal at 5·95 τ (doublet, $J$ = 6·6 c./sec., 2 protons) was assigned to the allylic methylene group coupled to the 3-amido-proton, which appeared as a broad, partially resolved triplet at 2·75 τ ($J$ ~7 c./sec., 1 proton). Allylic coupling to the olefinic proton could not be resolved. The signal at 3·20 τ (doublet, $J$ = 9·4 c./sec., 1 proton) was assigned to the olefinic proton, coupled to the 1-amido-proton, which appeared as a broad, well-resolved doublet at 0·05 τ ($J$ = 9·5 c./sec., 1 proton). The signal at 1·2 τ (broad singlet; 1 proton) was assigned to the other amide NH. In general, corresponding signals in the cyclic compound appeared at lower field than those of the acyclic compound, probably reflecting increased deshielding by the acetyl carbonyl groups and the double bond in the more rigid cyclic structure.

The mass spectrum of 5-acetamido-1,3-diacetyl-1,2,3,4-tetrahydropyrimidine (II) had peaks at $m/e$ = 225 (226), 183 (184), 140 (141), 124 (124, 125), 98 (99), 82 (82, 83), 60 (61), thus establishing the molecular weight as 225. The peak values in brackets were those obtained after the compound had been exchanged with deuterium oxide within the inlet system of the mass spectrometer.[11] These data, when considered with the following observed metastable transitions:

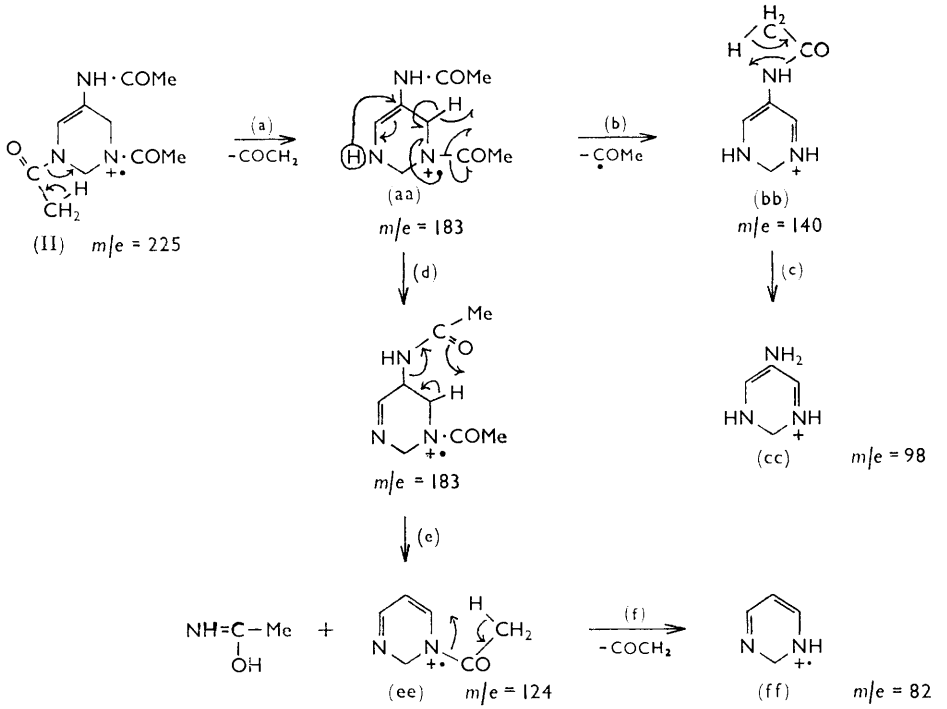
$$225^{\cdot+} \longrightarrow 183^{\cdot+} + 42$$
$$183^{\cdot+} \longrightarrow 140^{+} + 43$$
$$183^{\cdot+} \longrightarrow 124^{\cdot+} + 59$$
$$124^{\cdot+} \longrightarrow 82^{\cdot+} + 42$$

led to the formulation of the ion reactions shown in the Scheme, thus adding support to structure (II).

The loss of ketene [reactions (a), (c), and (f)] is a characteristic ion reaction of amides,[12,13] whilst reaction (b) has as a driving force the resonance stabilisation of the ion product (bb.)

[7] Evans, *J.*, 1962, 4259.
[8] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1960, p. 222.
[9] Matsen, " Chemical Applications of Spectroscopy," Vol. IX, Interscience, New York, 1956, p. 649.
[10] Collins, Hobbs, and Sternhell, *Austral. J. Chem.*, 1963, **16**, 1030.
[11] Shannon, *Austral. J. Chem.*, 1962, **15**, 265.
[12] Gilpin, *Analyt. Chem.*, 1959, **31**, 935.
[13] Petah, Kielzewski, Wilson, Ohashi, Budzikiewicz, and Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 470.

The elimination of acetamide, reaction (e), by way of a six-membered cyclic transition state is considered analogous to the elimination of acetic acid from cyclohexyl acetate.[14] On the other hand, the mass spectrum of *N*-acetylcyclohexylamine [13] shows only a very




weak peak at $M = 59$. Presumably the reaction is favoured in the present case because of the possibility of formation of the resonance-stabilised ion product (ee). The peak at $m/e = 60$ is probably due to the 1-hydroxyethylideneammonium ion, which is also produced by double hydrogen transfer from *N*-acetylcyclohexylamine.[13]

## Experimental

Microanalyses were by Dr. J. E. Fildes and her staff. Substances were examined chromatographically on Whatman paper No. 1 (method A) or No. 4 (method B) in butan-1-ol–5N-aqueous acetic acid (70 : 30 v/v) by the ascending technique. Papers were viewed (i) under a mercury lamp emitting radiation of 254 mμ or (ii) after exposure to iodine vapour, which rendered visible spots due to compounds which did not absorb in the ultraviolet region. "Catalyst" refers to 10% palladised charcoal [15] and light petroleum to the fraction b. p. 60—80°. Formaldehyde was either detected by the violet colour generated with chromotropic acid [16] or isolated as the dimedone derivative.[17] Ammonium chloride, trimethylenediamine dihydrochloride and propane-1,2,3-triamine trihydrochloride monohydrate were identified by comparison of their infrared spectra (KBr discs) with those of authentic specimens. The preparation of 5-methoxypyrimidine from 4-hydroxy-5-methoxypyrimidine [6] was improved by reduction of the intermediate 4-chloro-5-methoxypyrimidine *in situ*.

Descriptions of methods for ultraviolet and infrared spectra and for ionisation constants at 20° have been given earlier.[1] Nuclear magnetic resonance spectra were determined as 7% solutions in deuterochloroform (1,2,3-triacetamidoprop-1-ene) or in carbon tetrachloride–deuterochloroform (1 : 1, v/v) (5-acetamido-1,3-diacetyl-1,2,3,4-tetrahydropyrimidine) with a

[14] Macdonald, Shannon, and Sugowdz, *Tetrahedron Letters*, 1963, 807.
[15] *Org. Synth.*, Coll. Vol. III, 687.
[16] West and Sen, *Z. analyt. Chem.*, 1956, 153, 177.
[17] Veibel, "The Identification of Organic Compounds," Gad, Copenhagen, 1961, p. 142.

Varian D.P. 60 Spectrometer. Spectra were calibrated by the side-band technique with a Muirhead–Wigan D-890-A oscillator and double-irradiation experiments were made using side-bands from the integrator field modulation.[18] Chemical shifts were accurate ±0·01 p.p.m. and coupling constants to ±0·1 c./sec. The mass spectra were recorded on an Atlas CH4 mass spectrometer.

*General Procedure.*—The pyrimidine compound (*x* g.) in precisely one equivalent of acidic solvent was shaken with catalyst (*x* g. for 4- and 5-hydroxypyrimidines; 0·5*x* g. for 2,4,6-trimethyl- and 2- and 5-methoxy-pyrimidines; 0·33*x* g. for 2-hydroxy- and 4- and 5-acetamidopyrimidines) and hydrogen under laboratory conditions until hydrogen uptake ceased. The mixture was filtered, the filtrate evaporated at 50—60°/20 mm., and the residue crystallised from an alcohol.

1,4,5,6-*Tetrahydro*-2,4,6-*trimethylpyrimidine Salts.*—2,4,6-Trimethylpyrimidine dihydrate [19] in 0·334N-hydrochloric acid absorbed 1·8 mol. of hydrogen after 6 hr., and afforded (DL)-trans-1,4,5,6-*tetrahydro*-2,4,6-*trimethylpyrimidine hydrochloride* (1·9 g., 100%), m. p. 211—213° (from propan-2-ol–light petroleum) (Found: C, 52·0; H, 9·4; N, 17·5. $C_7H_{15}ClN_2$ requires C, 51·7; H, 9·3; N, 17·2%). The *picrate* had m. p. 188—190° (from propan-2-ol) (Found: C, 44·0; H, 4·75; N, 20·0. $C_{13}H_{17}N_5O_7$ requires C, 43·9; H, 4·8; N, 19·7%). The *trichloromercurate* had m. p. 119—122·5° (from propan-2-ol) (Found: C, 19·4; H, 3·4; N, 6·4. $C_7H_{15}Cl_3HgN_2$ requires C, 19·4; H, 3·5; N, 6·45%). The *pentachlorodimercurate* had m. p. 137—139° (from propan-2-ol) (Found: C, 12·1; H, 2·4; N, 3·9. $C_7H_{15}Cl_5Hg_2N_2$ requires C, 11·9; H, 2·1; N, 4·0%). The nitrate, obtained from the hydrochloride and silver nitrate, had m. p. 257—260° (from propan-2-ol–light petroleum) (lit.,[4] 250—251°) (Found: C, 44·4; H, 8·0. Calc. for $C_7H_{15}N_3O_3$: C, 44·4; H, 8·0%).

*Reduction of* 2-*Hydroxypyrimidine.*—The hydrochloride [20] (0·82 g.) in water (20 ml.) absorbed 1·6 mol. hydrogen after 9 hr. Removal of catalyst and solvent afforded 1,4,5,6-tetrahydro-2-hydroxypyrimidine hydrochloride, isolated and identified as the picrate.[21]

*Reduction of* 2-*Methoxypyrimidine.*—The compound [22] (1·5 g.), in 0·115N-acetic acid and redistilled methanol, absorbed 1·8 mol. hydrogen after 11 hr. Removal of catalyst gave a filtrate which afforded one spot, $R_F$ 0·45 [method B(ii)]. Removal of solvent gave a residue which deposited 1,4,5,6-tetrahydro-2-hydroxypyrimidine (0·17 g.) from propan-2-ol, identified by m. p. and mixed m. p.[21] The propan-2-ol was removed from the filtrate at 100°/20 mm. and the residue in water (120 ml.) was passed through anion exchange resin IRA-400 ($Cl^-$ form). Evaporation of the eluate at 100°/20 mm. gave a residue which, in propan-2-ol–light petroleum, deposited first 1,4,5,6-tetrahydro-2-hydroxypyrimidine (0·25 g.) and then deliquescent needles of 1,4,5,6-*tetrahydro*-2-*methoxypyrimidine hydrochloride* (0·3 g.) which decrepitated around 200° and finally melted between 263° and 269° (Found: C, 40·3; H, 7·4; N, 18·5. $C_5H_{11}ClN_2O$ requires C, 39·9; H, 7·4; N, 18·6%). The *octachlorotrimercurate* had m. p. 87—90° (from propan-2-ol) (Found: C, 11·0; H, 2·1; N, 5·05. $C_{10}H_{22}Cl_8Hg_3N_4O_2$ requires C, 10·8; H, 2·0; N, 5·0%). The *picrate* had m. p. 144—146° (from ethanol) (Found: C, 38·3; H, 3·9; N, 20·4. $C_{11}H_{13}N_5O_8$ requires C, 38·3; H, 3·8; N, 20·4%), $pK_a$ (potentiometric) 10·79 ± 0·05.

Catalytic reduction of 2-methoxypyrimidine in 1 equivalent of 0·07N-hydrobromic acid afforded mainly 1,4,5,6-tetrahydro-2-hydroxypyrimidine. A little of the 1,4,5,6-tetrahydro-2-methoxypyrimidine was isolated as the picrate.

1,4,5,6-*Tetrahydro*-5-*methoxypyrimidine Salts.*—(*a*) 4-Chloro-5-methoxypyrimidine [6] (0·7 g.) in water (10 ml.) absorbed 2·9 mol. of hydrogen after 5¼ hr. reduction in the presence of catalyst (0·35 g.). 1,4,5,6-Tetrahydro-5-methoxypyrimidine hydrochloride (0·53 g.) was obtained as an oil which was characterised as the *picrate*, m. p. 130—133° (from propan-2-ol) (Found: C, 38·6; H, 3·8; N, 20·4. $C_{11}H_{13}N_5O_8$ requires C, 38·5; H, 3·8; N, 20·4%) and as the *trichloromercurate*, m. p. 129—130° (from methanol) (Found: C, 14·5; H, 2·7; N, 6·6. $C_5H_{11}Cl_3HgN_2O$ requires C, 14·2; H, 2·6; N, 6·6%).

(*b*) 4-Hydroxy-5-methoxypyrimidine [6] (6·5 g.) and phosphoryl chloride (50 ml.) were refluxed for 1½ hr. and then evaporated at 20 mm./50—60° (water-bath). The residue was cautiously decomposed with ice–water and neutralised with 5N-sodium hydroxide. The mixture,

[18] Bhacca, Wolff, and Kowk, *J. Amer. Chem. Soc.*, 1962, **84**, 2976.
[19] Sullivan and Caldwell, *J. Amer. Chem. Soc.*, 1955, **77**, 1559.
[20] Hunt, McOmie, and Sayer, *J.*, 1959, 525.
[21] McKay, Buchanan, and Grant, *J. Amer. Chem. Soc.*, 1949, **71**, 766.
[22] Boarland and McOmie, *J.*, 1952, 3716.

on shaking with catalyst (1·5 g.), magnesium oxide (23 g.), and hydrogen for 8 hr., absorbed 0·8 mol. After filtration, the solution was mixed with saturated aqueous sodium hydrogen carbonate solution, saturated with sodium chloride, and continuously extracted with ether for 24 hr. The dried ($Na_2SO_4$) ether extract was distilled on a steam-bath and then under reduced pressure, affording 5-methoxypyrimidine (2·3 g., 41%), m. p. 39—43°, b. p. 109—110°/30 mm. (lit.,[6] m. p. 43—47°, b. p. 70—72°/16 mm.; 17% yield on a two-stage process).

5-Methoxypyrimidine (0·93 g.), after 3½ hr. reduction in 0·07158N-hydrobromic acid (1·95 mol. absorbed), yielded deliquescent 1,4,5 6-*tetrahydro-5-methoxypyrimidine hydrobromide* (1·5 g., 90%), m. p. 108—112° (from propan-2-ol) (Found: C, 30·9; H, 5·8; Br, 41·15; N, 14·45. $C_5H_{11}BrN_2O$ requires C, 30·8; H, 5·7; Br, 41·0; N, 14·4%), p$K_a$ (potentiometric) 11·72 ± 0·07.

Demethylation of the methoxy-hydrobromide (0·1 g.), $R_F$ 0·31 [method B(ii)], was effected by 8 hr. refluxing with concentrated hydrobromic acid (2 ml.). Evaporation of the mixture gave an oil containing at least two components, $R_F$ 0·26 and 0·62, respectively, which did not crystallise or form a picrate.

1,4,5,6-Tetrahydro-5,5-dihydroxypyrimidine hydrochloride, obtained by catalytic reduction of 5-hydroxypyrimidine [6] (52·8 mg.) in 0·01N-hydrochloric acid for 4½ hr., was identified by comparison of its infrared spectrum (KBr disc) with an authentic specimen.

*Reaction of Acetamidine Hydrochloride with* 1,3-*Diaminopropan-2-ol.*—The diamine dihydrochloride [23] was obtained by hydrolysis of 1,3-diphthalimidopropan-2-ol with hydrazine.[24] The *tetrachloromercurate* had m. p. 245—250° (decomp.) (from aqueous methanol) (Found: C, 8·1; H, 2·6; N, 6·3. $C_3H_{12}Cl_4HgN_2O$ requires C, 8·3; H, 2·8; N, 6·45%). The hydrochloride (1·65 g.) in water (65 ml.) and ethanol (7 ml.) was mixed with a solution from sodium (0·46 g.) and ethanol (10 ml.), and sodium chloride (0·95 g., 82%) was filtered off. The filtrate, mixed with acetamidine hydrochloride (1·0 g.) and ethanol (11·5 ml.), was refluxed for 3 hr. while a stream of nitrogen swept evolved gases into 2N-hydrochloric acid (50 ml.). Evaporation of the acid gave ammonium chloride (0·86 g., 80%). The mixture contained several components [method A(ii)] but no solid derivative could be isolated on treatment with picric acid, mercuric chloride, or hexachloroantimonic acid.

*Hydrolyses.*—The substituted 1,4,5,6-tetrahydropyrimidine salt (0·1 g.) was refluxed with N-sodium hydroxide for 0·5—2 hr. and evaporated at 100°/0·2 mm. The distillate was titrated with the appropriate acid and evaporated, and the residue crystallised. The hydrochloride of the 2,4,6-trimethyl derivative yielded β-2,4-diaminopentane dinitrate (from ethanol) identified by m. p. and mixed m. p.[1] The hydrobromide of the 2-methoxy-substituted compound yielded trimethylenediamine dihydrochloride (from propan-2-ol–light petroleum). Its picrate yielded ammonium chloride (from propan-2-ol); ammonia was detected (Nessler) during the alkaline hydrolysis of trimethylenediamine dipicrate. 1,4,5,6-Tetrahydro-5-methoxypyrimidine hydrochloride was converted into 2-*methoxypropane*-1,3-*diamine bistrichloromercurate*, m. p. 208—211° (from methanol–ethanol) (Found: C, 6·8; H, 1·9; Cl, 24·4; N, 3·9. $C_4H_{14}Cl_6Hg_2N_2O$ C, 6·7; H, 2·0; Cl, 24·6; N, 3·9%).

5-*Acetamido*-1,3-*diacetyl*-1,2,3,4-*tetrahydropyrimidine.*—*Preparation.* 5-Acetamidopyrimidine, obtained by reaction of 5-aminopyrimidine [25] with acetic anhydride in boiling benzene, had, at pH 7 (phosphate), $\lambda_{max.}$ 237 mμ (log ε 4·09), $\nu_{max.}$ (KBr) 1708 cm.$^{-1}$ (C:O). The *ethiodide* had m. p. 165° (decomp.) (from propan-2-ol) (Found: C, 32·8; H, 4·1; N, 14·0. $C_8H_{12}IN_3O$ requires C, 32·8; H, 4·1; N, 14·3%), $\nu_{max.}$ (KBr) 1705 cm.$^{-1}$ (C:O). The acetamido-compound (0·86 g.) in acetic anhydride (10 ml.) absorbed 1·8 mol. when shaken with catalyst and hydrogen at 100° for 5 hr. Removal of catalyst and solvent furnished an oil which, upon repeated crystallisations from acetone–light petroleum, was separated into 5-*acetamido*-1,3-*diacetyl*-1,2,3,4-*tetrahydropyrimidine* (0·48 g.), m. p. 157—160° (Found: C, 53·6; H, 6·5; N, 18·9. $C_{10}H_{15}N_3O_2$ requires C, 53·3; H, 6·7; N, 18·65%), $\lambda_{max.}$ 253 mμ (log ε 4·11) (pH 7); $\nu_{max.}$ (KBr) 1690, 1660, 1644 cm.$^{-1}$; and 1,2,3-*triacetamidoprop*-1-*ene* (0·09 g.), m. p. 175—176° (from acetone) (Found: C, 50·3; H, 7·3; N, 19·6. $C_9H_{15}N_3O_3$ requires C, 50·7; H, 7·1; N, 19·7%), $\lambda_{max.}$ 245 mμ (log ε 4·13), $\nu_{max.}$ (KBr) 1643 cm.$^{-1}$ (C:O). The former decolourised a chloroform solution of bromine immediately, but the bromo-compound decomposed on working up.

*Hydrolysis.* The compound (0·1 g.) in 1N-hydrochloric acid was refluxed for 15 min. in an apparatus closed with a water-seal. The mixture was evaporated and the distillate, mixed with

[23] Goedeckemeyer, *Ber.*, 1888, **21**, 2684.
[24] Ing and Manske, *J.*, 1926, 2348.
[25] Whittaker, *J.*, 1951, 1565.

the water from the seal, was treated with acetic acid and ethanolic dimedone, affording the dimedone derivative of formaldehyde (22·6 mg., 18%), identified by m. p. and mixed m. p.

*Reduction.* The compound (0·1 g.), $R_F$ 0·79 [method A(i)], in propan-1-ol (5 ml.), was shaken with platinum oxide (0·1 g.) and hydrogen under laboratory conditions for 2½ hr. Removal of catalyst and solvent gave an oil, $R_F$ 0·64 [method A(ii)], which was boiled with ethanol (2 ml.) and 20% hydrochloric acid (5 ml.) for 2 hr. and evaporated. Formaldehyde was detected in the distillate. The residue gave needles (43·7 mg., 45%) (from ethanol at −15°) of propane-1,2,3-triamine trihydrochloride monohydrate.

1,2,3-Triacetamidoprop-1-ene was reduced in ethanol solution with hydrogen and platinum oxide under laboratory conditions to 1,2,3-triacetamidopropane, identified by infrared spectrum.[26]

*Other Reductions.*—4-Acetamidopyrimidine [27] was reduced under conditions similar to those for the 5-isomer to an involatile oil which slowly reduced hot ammoniacal silver nitrate. On treatment with aqueous acid both formaldehyde and ammonia (Nessler) were detectable. Formaldehyde was isolated as its dimedone derivative from the reduction of 4-hydroxypyrimidine [27] in 0·19N-acetic acid. 4-Methoxypyrimidine was not reduced in methanolic acetic acid.

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[26] Mann and Pope, *Proc. Roy. Soc.*, 1925, *A*, **107**, 86.
[27] Brown and Short, *J.*, 1953, 331.