100. *Hydropyrimidines. Part I.* 1,4,5,6-*Tetrahydropyrimidine and its Derivatives.*

By D. J. Brown and R. F. Evans.

Methods for the preparation of 1,4,5,6-tetrahydropyrimidine and its salts have been investigated. The properties of this base discussed include basic strength, stability in aqueous solution, behaviour on methylation, and dehydrogenation. Significant differences have been observed between the infrared spectra of its simple hydrohalides and the complex metallochlorides. On the basis of infrared and nuclear magnetic resonance spectra, it is concluded that carbon tetrachloride solutions of 1,3,5-triazine contain less than 10% of an open-chain form.

1,4,5,6-Tetrahydropyrimidine was first prepared by Skinner and Wunz [1] who condensed trimethylenediamine with ethyl formate and pyrolysed the monoformylated derivative. Grundmann and Kreutzberger [2] allowed trimethylenediamine to react with 1,3,5-triazine and claimed the isolation of another tetrahydropyrimidine with physical properties different from those of the first product. In view of biochemical interest in hydropyrimidines we repeated both syntheses and found that the same substance resulted from both methods. Identity was established by infrared spectra, and by mixed melting points of the picrates and of the mercurichlorides.

A tetrahydropyrimidine hydrochloride of unproved orientation has also been made by catalytic reduction,[3] either of pyrimidine in hydrochloric acid, or of 2,4-dichloropyrimidine in water. The former method is preferred because 1,4,5,6-tetrahydro-2-hydroxypyrimidine was also formed in the latter. The product has now been shown to be 1,4,5,6-tetrahydropyrimidine hydrochloride since it gave the same mercurichloride as that produced from authentic base and hydrogen chloride, followed by mercuric chloride. From the hydrochloride the original base could be recovered. During the latter process, however, a considerable amount of monoformylated trimethylenediamine was produced, but this was also rapidly formed even when free tetrahydropyrimidine was dissolved in water. The easy ring opening of the tetrahydropyrimidine ring was again exemplified in its reaction with α-naphthyl isocyanate, when 1,3-di-1′-naphthylureidopropane was formed.

1,4,5,6-Tetrahydropyrimidine acetate has now been synthesized by condensation of trimethylenediamine with formamidine acetate, a rapid and convenient reaction which seems [4] to be of general application. Its structure was confirmed by conversion of the acetate into a picrate identical with that obtained from the previous specimen of 1,4,5,6-tetrahydropyrimidine.

Methylation of the tetrahydropyrimidine occurred readily with methyl iodide, giving 1,4,5,6-tetrahydropyrimidine hydriodide (isolated as the mercurichloride), 1,4,5,6-tetrahydro-1-methylpyrimidine hydriodide (isolated as the picrate), and 1,4,5,6-tetrahydropyrimidine-1,3-dimethylpyrimidinium iodide. The presence of the last was inferred from the formation of 1,3-bismethylaminopropane on hydrolysis of a portion of the reaction mixture. Ammonia was also produced during this hydrolysis. The monomethyl compound (II), formed initially, must lose hydrogen iodide to unchanged tetrahydropyrimidine (I) and the resulting base (III) must then react further with methyl iodide to give the dimethyl derivative (IV).

Diazomethane has been used [5] to liberate 1,3,5-triazine from its hydrochloride, but similar treatment of 1,4,5,6-tetrahydropyrimidine hydrochloride left most of it unaltered.

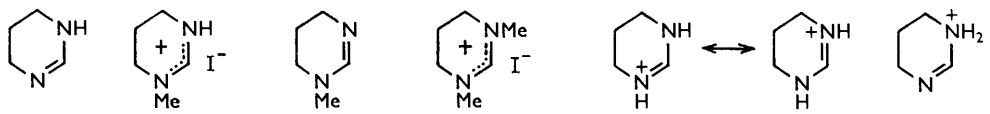
[1] Skinner and Wunz, *J. Amer. Chem. Soc.*, 1951, **73**, 3814.
[2] Grundmann and Kreutzberger, *J. Amer. Chem. Soc.*, 1955, **77**, 6559.
[3] Smith and Christensen, *J. Org. Chem.*, 1955, **20**, 829.
[4] Evans, unpublished results.
[5] Grundmann and Kober, *J. Org. Chem.*, 1956, **21**, 641.

The remainder afforded an ether-soluble base whose picrate, on alkaline hydrolysis, yielded ammonia.

The salts of 1,4,5,6-tetrahydropyrimidine, unlike the free base, were not decomposed by water. In acid solution, 1,4,5,6-tetrahydropyrimidine was more stable towards potassium permanganate or dichromate than was pyrimidine itself. An attempt (by use of palladised charcoal) to convert the tetrahydropyrimidine into pyrimidine gave only bi-(1,4,5,6-tetrahydropyrimidin-2-yl), whose structure was confirmed by alkaline hydrolysis to trimethylenediamine and oxalic acid (isolated as calcium salt).

1,4,5,6-Tetrahydropyrimidine reacted with sulphur, to give 1,4,5,6-tetrahydro-2-mercaptopyrimidine.

pK_a *Determination.*—Since the neutral molecule of 1,4,5,6-tetrahydropyrimidine was so rapidly attacked by water, a pK_a value could be obtained only from pH measurements



(I) (II) (III) (IV) (V) (VI)

rapidly made on mixed aqueous solutions of 1,4,5,6-tetrahydropyrimidine hydrochloride and alkali. Concentrated solutions were required to furnish the high pH's necessary, which were measured potentiometrically with a hydrogen electrode. The value obtained (13·0 at 20°) was approximate, since large activity corrections had to be applied in the calculations, but it sufficed to show that 1,4,5,6-tetrahydropyrimidine was highly basic, as befitted its amidine structure. A proton can add to the tetrahydropyrimidine molecule in two ways, affording either the cation (V) (which will be stabilised by resonance between two equivalent structures), or the cation (VI). The C=N group is base-weakening, so that if the cation were (VI), a pK_a value less than that of piperidine [6] (11·2 at 25°) would be expected.

Infrared Spectra.—(1) 1,3,5-*Triazine.* The specimen of 1,3,5-triazine used in this work was conveniently prepared by heating a mixture of sodiodiformamide and formamidine acetate (rather than the deliquescent hydrochloride [7]). On the other hand, while pyrolysis of formamidine hydrochloride alone yielded triazine, similar treatment of the acetate or mercurichloride gave but little triazine. Our specimen showed the same infrared spectrum (10% solution in carbon tetrachloride) as a specimen presented to this Department by Dr. C. Grundmann. However, by using in a double-beam spectrometer a path-length 8 times as great as that previously used in a single-beam instrument, a series of well-defined peaks in the 1660—3100 cm.$^{-1}$ region was made visible. Some of these (see Experimental section) occurred in the region associated with the stretching of triply bonded CN groups, suggesting that, in carbon tetrachloride solutions, a small quantity of open-chain compound might be in tautomeric equilibrium with the cyclic structure of 1,3,5-triazine. Nuclear magnetic resonance measurements, however, indicated that the proportion of open-chain compounds, if present, must be less than 10%.

(2) 1,4,5,6-*Tetrahydropyrimidine derivatives.* Prominent bands of the infrared spectra of 1,4,5,6-tetrahydropyrimidine and its derivatives are given in the Table.

In the 2800—3500 cm.$^{-1}$ region tetrahydropyrimidine exhibited two C–H stretching bands (2920 and 2840 cm.$^{-1}$) and a broad N–H stretching band (3180 cm.$^{-1}$), the low frequency of the last being due to hydrogen bonding. On protonation, two broad and intense N–H stretching bands appear, one of which masked the C–H stretching bands. On deuteration of the hydrobromide, the bands at 3120 and 2980 cm.$^{-1}$ moved to 2430 and 2350 cm.$^{-1}$, respectively [ν(NH)/ν(ND) = 1·28 and 1·27, respectively]. In the complex metallochlorides, however, only one sharp and intense N–H stretching band at much

[6] Searles, Tamres, Block, and Quarterman, *J. Amer. Chem. Soc.*, 1956, **78**, 4917.
[7] Grundmann, *Chem. Ber.*, 1954, **87**, 1867.

Infrared spectra (cm.$^{-1}$) of 1,4,5,6-tetrahydropyrimidine and its salts.

Substance	ν (as N–C–N)	ν (NH)	δ (NH)
1,4,5,6-Tetrahydropyrimidine	1632	3180	1535
Hydrochloride	1675	3170, 2970	1587
Hydrobromide	1675	3120, 2980	1585
Hydriodide	1685	3200, 2990	1573
Chloromercurate	1684	3300	1569
Chloroaurate	1690	3340	1575
Chloroplatinate	1693	3310	1575

higher frequencies (3300—3340 cm.$^{-1}$) is observed because hydrogen bonding is here strongly diminished. This shift of N–H stretching bands to higher frequencies as the halide ion in an amine hydrohalide was replaced by a complex ion was previously observed for amine tetrachloroborates,[8] chloromercurates,[9] and tetrafluoroborates.[10] Nuttall *et al.*[10] concluded that in a large complex anion MX_n^-, the negative charge would be shared by several X's so that the contribution of the electrostatic component N–H · · · X$^-$, which is the major contributing structure to the hydrogen bond in ammonium salts,[11] would be greatly diminished.

For all substances examined, the most intense band of the whole spectrum falls within the range 1600—1700 cm.$^{-1}$, in which the C=N stretching frequency of a number of open-chain amidines is known to occur.[12] In 1,4,5,6-tetrahydropyrimidine, this band is found at 1632 cm.$^{-1}$. On protonation the band, which is now strictly an asymmetric $\overset{+}{\overbrace{N \cdots C \cdots N}}$ stretching band, moves to higher frequencies, by 33—53 cm.$^{-1}$ for the hydrohalides and by 53—61 cm.$^{-1}$ for the complex halides. Deuteration decreases slightly the frequency of this band in the hydrobromide (from 1675 to 1672 cm.$^{-1}$).

A prominent band in the 1500—1600 cm.$^{-1}$ region is an N–H deformation vibration, whose frequency is raised in going from the free base to the hydrohalides. This frequency is lower for the complex halides than for the hydrohalides owing to the weakness of the hydrogen bonding in the former (N–H stretching and N–H bending frequencies are known to be oppositely affected by this).

Experimental

Analyses are by Dr. J. E. Fildes and her staff.

1,4,5,6-*Tetrahydropyrimidine*.—(*a*) Ethyl formate (41 ml.) was cautiously added during 10 min. to trimethylenediamine (51 ml.) in an apparatus guarded against entry of moisture and carbon dioxide. The mixture was refluxed for 15 hr. and volatile material was removed at 100°/20 mm. A sample of the residue formed 3-*formamidopropylamine picrate*, m. p. 137·5—139° (from ethanol) (Found: C, 36·6; H, 4·0; N, 21·1. $C_{10}H_{13}N_5O_8$ requires C, 36·3; H, 4·0; N, 21·2%). The bulk was heated at 150° ± 5°/20 mm. in a slow stream of nitrogen for 90 min. and distilled (50%). Redistillation (80—82°/0·5 mm.) gave the tetrahydropyrimidine, n_D^{20} 1·5166, $n_D^{23·5}$ 1·5154, n_D^{25} 1·5149 (Found: C, 58·0; H, 9·7; N, 32·9. Calc. for $C_4H_8N_2$: C, 57·1; H, 9·6; N, 33·3%). Skinner and Wunz [1] give b. p. 88—89°/1 mm., $n_D^{23·5}$ 1·5143. With it, in ether, α-naphthyl isocyanate formed 1,3-*di*-1′-*naphthylureidopropane*, m. p. 236—237° (decomp.) (from acetone) (Found: C, 72·3; H, 5·9; N, 13·4. $C_{25}H_{24}N_4O_2$ requires C, 72·8; H, 5·9; N, 13·6%). Prepared from either the free base and ethanolic hydrogen chloride or ice-cold N-hydrochloric acid, 1,4,5,6-tetrahydropyrimidine hydrochloride formed deliquescent needles which recrystallised from methanol–ethyl acetate had m. p. 189—190° (lit.,[3] m. p. 119—122°) (Found: C, 39·5; H, 7·3; N, 22·9. Calc. for $C_4H_9ClN_2$: C, 39·8; H, 7·5; N, 23·2%). The *hydrobromide*, prepared from titration of the base in propan-2-ol at 0° with 48% hydrobromic acid, formed deliquescent needles (from propan-2-ol), m. p. 163—164·5° (Found: C, 29·1; H, 5·4; Br, 48·9; N, 16·8. $C_4H_9BrN_2$ requires C, 29·1; H, 5·5; Br, 48·4; N, 17·0%). The *hydriodide*, prepared and recrystallised similarly, had m. p. 315° (decomp.) (Found: C, 22·6;

[8] Kynaston, Larcombe, and Turner, *J.*, 1960, 1772.
[9] Evans and Kynaston, unpublished results.
[10] Nuttall, Sharp, and Waddington, *J.*, 1960, 4965.
[11] Chenon and Sandorfy, *Canad. J. Chem.*, 1958, **36**, 1181.
[12] Grivas and Taurins, *Canad. J. Chem.*, 1960, **37**, 795, 1260.

H, 4·1; N, 13·0; I, 58·9. $C_4H_9IN_2$ requires C, 22·7; H, 4·3; N, 13·2; I, 59·8%). The picrate formed in ethanol had m. p. 109—110° (lit.,[2] m. p. 279—280°) (Found: C, 38·4; H, 3·5; N, 22·3. $C_{10}H_{11}N_5O_7$ requires C, 38·3; H, 3·5; N, 22·4%). The *trichloromercurate* (from equivalent quantities of the hydrochloride and mercuric chloride in methanol) formed needles, m. p. 164—165·5° (Found: C, 12·2; H, 2·5; Hg, 50·9; N, 7·1. $C_4H_9Cl_3HgN_2$ requires C, 12·3; H, 2·3; Hg, 51·2; N, 7·2%). From water it crystallised as an *adduct hydrate*, m. p. 177·5—179° (Found: C, 7·3; H, 1·5; N, 4·1. $C_4H_{11}Cl_5Hg_2N_2O$ requires C, 7·1; H, 1·6; N, 4·1%). The *tetrachloroaurate*, from the hydrochloride and auric chloride in methanol, formed yellow plates, m. p. 266—267° (decomp.) (Found: C, 11·3; H, 2·2; Au, 46·2; Cl, 33·1; N, 6·5. $C_4H_9AuCl_4N_2$ requires C, 11·3; H, 2·1; Au, 46·5; Cl, 33·4; N, 6·6%). The *hexachloroplatinate*, obtained from the hydrochloride and hydrogen chloroplatinate in methanol, had m. p. 230—231° (decomp.) (Found: C, 16·6; H, 3·1; Cl, 36·8; N, 9·5; Pt. 33·6. $C_8H_{18}Cl_6N_4Pt$ requires C, 16·6; H, 3·1; Cl, 36·8; N, 9·7; Pt, 33·8%).

(*b*) Trimethylenediamine (1·5 ml.) was cautiously pipetted on to 1,3,5-triazine (0·46 g.; resublimed *in vacuo*) in a distillation apparatus guarded as above. The vigorous reaction, accompanied by the evolution of ammonia, was controlled by cooling. After 1 hr. at 20°, the mixture was refluxed on the steam bath for 2 hr., and distillation under reduced pressure then afforded a liquid (61%), b. p. 64°/0·35 mm. It had the same infrared spectrum as the 1,4,5,6-tetrahydropyrimidine prepared as above and gave the same picrate and mercurichloride. The picrate, m. p. 279—280°, isolated by Grundmann and Kreutzberger [2] may have been ammonium picrate which has the correct nitrogen content.

The required 1,3,5-triazine was prepared by heating an intimate mixture of formamidine acetate [13] (11·5 g.) and sodiodiformamide [14] (10·1 g.) at 130°/1 mm. for 1 hr. in a distillation apparatus, the receiver of which was cooled in acetone–carbon dioxide. The distillate (1·6 g., 17%) was resublimed *in vacuo* and had m. p. 76—79° (lit.,[15] 80—81°).

Pyrolysis of formamidine acetate alone at 170—180°/20 mm. for 1¼ hr. in the above apparatus furnished triazine (8%), but most of the acetate sublimed unchanged. Equivalent quantities of methanolic mercuric chloride and formamidine hydrochloride (prepared from the acetate [13]) gave *formamidine trichloromercurate–mercuric chloride adduct*, m. p. 210—213° (from ethanol) (Found: C, 2·0; H, 0·85; Hg, 64·5; N, 4·4. $CH_5Cl_5Hg_2N_2$ requires C, 1·9; H, 0·8; Hg, 64·4; N, 4·5%). Pyrolysis of this salt at 180°/1 mm. for 1 hr. afforded triazine (6%). Mercuric chloride sublimed out of the reaction mixture, leaving a residue containing mainly unchanged formamidine mercurichloride.

(*c*) Pyrimidine (1·5 g.), 0·7N-hydrochloric acid (52 ml.), and 10% palladised charcoal (0·2 g.) were shaken with hydrogen under laboratory conditions for 4 hr. The hydrochloride obtained by evaporation of the filtrate was mixed with mercuric chloride (5·1 g.) in concentrated methanol solution to give 1,4,5,6-tetrahydropyrimidine mercurichloride, m. p. 164—165·5°, undepressed on admixture with authentic material.

(*d*) Shaking 2,4-dichloropyrimidine (7·44 g.) under water (100 ml.) with 10% palladised charcoal (0·6 g.) and hydrogen for 9 hr. furnished a mixture rich in 1,4,5,6-tetrahydropyrimidine hydrochloride (8 g.). In another experiment, the reaction mixture was made alkaline and extracted with ether. Addition of oxalic acid to the extract gave 1,4,5,6-tetrahydropyrimidine oxalate, m. p. 146—148° [lit.,[16] 151·5° (decomp.)]. The mother liquor was neutralised and continuously extracted with ether for 3 days. Evaporation of the extract and recrystallisation of the residue from propan-2-ol gave a solid, m. p. 254—256°, identical (mixed m. p.) with 1,4,5,6-tetrahydro-2-hydroxypyrimidine obtained from trimethylenediamine and diethyl carbonate.[17]

(*e*) Formamidine acetate (5·18 g.) was cautiously added during 20 min. to trimethylenediamine (3·69 g.). When the vigorous evolution of ammonia ceased, the mixture was heated on the steam bath for 1 hr. The resulting oil (7·2 g.) was crystallised from propanol-2-ol–ethyl acetate at −15° to give deliquescent prisms of 1,4,5,6-*tetrahydropyrimidine acetate*, m. p. 62—66° (Found: C, 49·8; H, 8·3; N, 19·2. $C_6H_{12}N_2O_2$ requires C, 50·0; H, 8·4; N, 19·4%).

Hydrolysis of 1,4,5,6-*Tetrahydropyrimidine.*—When a solution of tetrahydropyrimidine

[13] Taylor and Ehrhart, *J. Amer. Chem. Soc.*, 1960, **82**, 3138.
[14] Rakshit, *J.*, 1913, **103**, 1557.
[15] Schaefer, Hechenbleikner, Peters, and Wystrach, *J. Amer. Chem. Soc.*, 1959, **81**, 1466.
[16] Lythgoe and Rayner, *J.*, 1951, 2323.
[17] Fischer and Koch, *Annalen*, 1886, **232**, 224.

(0·08 g.) in water (1·1 ml.) had been kept at room temperature for 2 min., 72% of the tetrahydropyrimidine was recovered as its picrate. Tetrahydropyrimidine (0·33 g.) in water (1·0 ml.) was mixed after 15 min. with picric acid (0·9 g.) in ethanol and cooled to 0°. The precipitate (1·0 g.), after crystallisation from methanol, had m. p. 137·5—139° undepressed on admixture with 3-formamidopropylamine picrate.

1,4,5,6-Tetrahydropyrimidine hydrochloride (5 g.) in water (2 ml.) under ether (20 ml.) was treated at 0° with potassium hydroxide (4 g.) in water (2 ml.). The ethereal layer was dried (Na_2SO_4), and the residue from evaporation was distilled at 0·5 mm., affording a little liquid with infrared spectrum identical with that of 1,4,5,6-tetrahydropyrimidine. The aqueous layer was treated with picric acid, to yield trimethylenediamine and 3-formamidopropylamine as their picrates.

When 1,4,5,6-tetrahydropyrimidine hydrobromide (0·25 g.) in water (5 ml.) was refluxed for 4 hr., not only did its chromatography on paper in acetic acid–butanol remain unchanged, but picric acid precipitated 1,4,5,6-tetrahydropyrimidine picrate.

Methylation of 1,4,5,6-*Tetrahydropyrimidine.*—(*a*) Tetrahydropyrimidine (1·3 g.) and methyl iodide (2·2 g.) in ether at room temperature immediately developed a white opalescence. After 1 hr., the ether-insoluble oil (2·95 g.) was separated and from propan-2-ol–ethyl acetate at −15° gave a solid (1·4 g.) and a mother liquor (A). Recrystallisation of the solid from methanol–ethyl acetate afforded a mother liquor (B) and crystals, m. p. 317—322° (decomp.), which yielded an unidentified *picrate*, m. p. 115—117° (Found: C, 38·3; H, 3·5; N, 21·9. $C_{10}H_{11}N_5O_7$ requires C, 38·3; H, 3·5; N, 22·4%). Evaporation of mother liquor (A) furnished an oil (0·6 g.) which was mixed with picric acid (0·9 g.) in methanol. The resultant oil, after 3 extractions with hot light petroleum (b. p. 60—80°), was induced to crystallise from propan-2-ol. Three recrystallisations from ethanol afforded yellow crystals of 1,4,5,6-*tetrahydro*-1-*methylpyrimidine picrate*, m. p. 104—106° (Found: N, 21·6. $C_{11}H_{13}N_5O_7$ requires N, 21·4%), which on alkaline hydrolysis yielded 3-methylaminopropylamine identified as the chloromercurate by m. p., mixed m. p., and infrared spectrum. The combined mother liquors from the above (containing picric acid) were evaporated to dryness and the residue was refluxed with N-potassium hydroxide (100 ml.) for 20 min. The mixture was distilled, the distillate (50 ml.) was mixed with picric acid (3·3 g.) in methanol, and the whole was evaporated to dryness. Extraction of the residue with benzene removed picric acid, and the residue was fractionally crystallised from ethanol–propan-2-ol, giving ammonium picrate (0·22 g.), m. p. 277—282° (decomp.) and 1,3-bismethylaminopropane picrate (0·01 g.), m. p. 193—195° (lit.,[18] 193—194°). Mother liquor (B) was evaporated to dryness and the residue (1·1 g.) was treated with hot aqueous mercuric chloride (0·7 g.) to precipitate mercuric iodide. The filtrate was evaporated to dryness at 100°/20 mm. and the residue was dissolved in methanol (15 ml.) containing mercuric chloride (0·7 g.). 1,4,5,6-Tetrahydropyrimidine mercurichloride (0·6 g.) was precipitated. The mother liquor was steam distilled for 1 hr. with 2N-potassium hydroxide (140 ml.). The distillate was treated with picric acid (2 g.) and worked up as above, affording 1,3-bismethylaminopropane picrate (0·03 g.) and ammonium picrate (0·08 g.).

(*b*) Tetrahydropyrimidine hydrochloride (0·85 g.) was set aside for 3 days in dry ethereal diazomethane.[19] The ether layer, which gave an alkaline reaction, was evaporated on the steam bath. Since the residue (0·05 g.) did not give a crystalline derivative with either hydrochloric acid–mercuric chloride or picric acid, the oil was refluxed with N-sodium hydroxide (18 ml.) for 1 hr., water (50 ml.) was added, and the mixture was distilled. The distillate was acidified with picric acid and evaporated to dryness. The residue crystallised from ethanol to give ammonium picrate (0·03 g.). Treatment of the ether-insoluble residue with methanolic mercuric chloride precipitated only 1,4,5,6-tetrahydropyrimidine mercurichloride.

Oxidation of 1,4,5,6-*Tetrahydropyrimidine.*—(*a*) Two drops of tetrahydropyrimidine were added to ice-cold 0·1N-sulphuric acid followed by dilute aqueous potassium permanganate. No diminution in colour was observed at 20° during 20 min. and heating on the steam bath for 10 min. was required to discharge the colour. With pyrimidine under similar conditions, the colour was discharged in 5 min. at 20°.

(*b*) Tetrahydropyrimidine (0·2 g.) was mixed with 2N-sulphuric acid (5 ml.) and *N*-phenylanthranilic acid indicator solution (0·05 ml.) at 0°, and 0·1N-potassium dichromate (5 ml.) was

[18] Gibson, Harley-Mason, Litherland, and Mann, *J.*, 1942, 163.

[19] Hickinbottom in " Reactions of Organic Compounds," Longmans, Green and Co., London, 1957, p. 478.

added. At 20°, the solution did not change colour during several days. With pyrimidine, however, a colour change was observed within 42 hr.

Dehydrogenation of 1,4,5,6-*Tetrahydropyrimidine.*—Tetrahydropyrimidine (5 g.) and 10% palladised charcoal (1 g.) were rapidly heated to 190° in a slow current of nitrogen. The temperature was then raised to 260° during the next 55 min. The cooled mixture was extracted first with ether and then with propan-2-ol. The ether extract furnished a solid, which on crystallisation from propan-2-ol formed *bi*-(1,4,5,6-*tetrahydropyrimidin-2-yl*) (0·1 g.) melting between 160° and 170° [Found: C, 57·5; H, 8·7%; *M* (ebullioscopic in benzene), 179. $C_8H_{14}N_4$ requires C, 57·8; H, 8·5%; *M*, 166]. The presence of a conjugated system of double bonds in the solid was indicated [by $\lambda_{max.}$ 235 mμ (log ε 3·8 in hexane)]. The most intense band in the infrared spectrum (potassium bromide disc), at 1610 cm.$^{-1}$, was assigned to the antisymmetric stretching of the N=C–C=N system. NH groups gave rise to bands at 3210 (stretching) and 1500 cm.$^{-1}$ (deformation).

The propanol extract on evaporation gave a gum, by sublimation of which at 200°/0·5 mm. was obtained impure bi-(1,4,5,6-tetrahydropyrimidin-2-yl) (0·85 g.).

The *chloroplatinate* was precipitated from methanol–propan-2-ol as an orange solid, decomp. 332—340° (Found: C, 16·5; H, 2·8; Cl, 37·4; N, 9·8; Pt, 34·5. $C_8H_{16}Cl_6N_4Pt$ requires C, 16·7; H, 2·8; Cl, 36·9; N, 9·7; Pt, 33·9%), $\nu_{max.}$ (silver chloride disc) 1679, 3250 (N–H stretching), and 1587 cm.$^{-1}$ (N–H deformation).

The dehydrogenation product (0·013 g.) was refluxed with 0·25N-sodium hydroxide (11 ml.) for 2 hr. and evaporated to dryness. The distillate, on treatment with picric acid and evaporation, afforded trimethylenediamine picrate (0·04 g.), identified by m. p. and mixed m. p. The residue was acidified with concentrated hydrochloric acid, evaporated, and redissolved in water. Addition of calcium chloride precipitated calcium oxalate, identified by its infrared spectrum.

Reaction of Sulphur with 1,4,5,6-*Tetrahydropyrimidine.*—A mixture of sulphur (1·32 g.) and tetrahydropyrimidine (1·73 g.) was heated at 200° ± 10° for 1 hr. The mixture was extracted with hot methanol, and the extract was evaporated. The residue (1·2 g., 40%), on sublimation at 180°/0·1 mm. and crystallisation from ethanol, furnished needles, m. p. 209—211°, identical (mixed m. p.) with 1,4,5,6-tetrahydro-2-mercaptopyrimidine obtained from trimethylenediamine and carbon disulphide.[20]

pK_a *Determination.*—1·463M-1,4,5,6-Tetrahydropyrimidine hydrochloride (5·0 ml.) was rapidly added to 0·998M-potassium hydroxide (4·0 ml.) into which dipped a hydrogen and a calomel electrode. The initial change in E.M.F. indicated a drop in pH from 14·05 to 13·09 [the potential fell steadily (*ca.* 3 mv/min.) because of hydrolysis of the free tetrahydropyrimidine, and extrapolation of E.M.F.–time plot was necessary in obtaining the latter value]. The pK_a was calculated as described by Schwarzenbach and Lutz,[21] with the arbitrary assumption that 1,4,5,6-tetrahydropyrimidine hydrochloride and potassium chloride had the same activity coefficients. A pK_a value of 13·0 was obtained.

Infrared Spectra.—Infrared spectra were determined with a Perkin-Elmer 21 double-beam spectrophotometer fitted with a sodium chloride prism. 1,4,5,6-Tetrahydropyrimidine was examined as the pure liquid, and its salts in potassium bromide discs, except for the chloroplatinate which was examined in a silver chloride disc. (In the attempted preparation of a potassium bromide disc, double decomposition with formation of potassium chloroplatinate occurred and the spectrum observed was that of 1,4,5,6-tetrahydropyrimidine hydrobromide.)

The hydrobromide was deuterated by three consecutive dissolutions in, and evaporations from, heavy water. The deuterated derivative was examined as a silver chloride disc.

The infrared spectrum of 1,3,5-triazine was measured as a 10% solution in carbon tetrachloride (cell thickness 1 mm.). The spectrum was identical with that of the specimen of triazine prepared by Grundmann. In addition to two very strong bands at 1410 and 1560 cm.$^{-1}$, noted by previous workers,[22] the following bands were observed in the 1600—3100 cm.$^{-1}$ region: 1666, 1688, 1713, 1745, 1775, 1800, 1842, 1888, 1941, 2040, 2090, 2190, 2270, 2335, 2390, 2495, 2530, 2565, 2670, 2900, 2940, 3040, 3100 cm.$^{-1}$. Depending upon the nature of the other groups in the molecule, C≡N stretching vibrations give rise to bands in the 2120—

[20] McKay and Hatton, *J. Amer. Chem. Soc.*, 1956, **78**, 1618.
[21] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1162.
[22] Goubeau, Jahn, Kreutzberger, and Grundmann, *J. Phys. Chem.*, 1954, **58**, 1078.

2260 cm.$^{-1}$ range.[23] Nuclear magnetic resonance measurements on the carbon tetrachloride solution of triazine (tetramethylsilane internal standard) were carried out for us by Dr. W. F. Forbes, C.S.I.R.O., Melbourne. The spectrum consisted of one signal only, assigned to the three identical ·CH: groups of the ring form of the triazine molecule. Limitations of the instrument were such that the upper limit of the concentration of open-chain form, if present, was 9—10%.

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[23] Cross, "Introduction to Practical Infra-Red Spectroscopy," Butterworths Scientific Publns., London, 1960, p. 68.