

988. Triazanaphthalenes. Part II.¹ Covalent Hydration in 1,4,6-Triazanaphthalenes.

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Syntheses of new 1,4,6-triazanaphthalenes are described. The substance previously considered (by others) to be 2-hydroxy-3-methyl-1,4,6-triazanaphthalene is shown to be the 3-hydroxy-2-methyl derivative, and *vice versa*.

Ionization constants and ultraviolet spectra are presented for the various ionic species. The cation of 3-hydroxy-1,4,6-triazanaphthalene, like that of the parent compound, binds water strongly at the 1,2-bond. These water adducts are stabilized by a 4-aminopyridinium type of resonance.

Two hypotheses seem to cover all known examples of covalent hydration, *e.g.*, (I) \rightleftharpoons (II), across a C=N bond of heteroaromatic substances: (A) Hydration is apt to occur at a double bond if sufficient electron-attracting centres are present so that this double bond no longer participates greatly in aromatic conjugation. (B) Formation of the water adduct is greatly favoured if this species is stabilized by resonance.² In most cases the electron-attracting centres referred to in (A) have usually been doubly bound ring-nitrogen atoms, and the stabilizing resonances in (B) have usually been of the type $\text{HN}-\text{CR}=\overset{+}{\text{N}}\text{H} \longleftrightarrow \overset{+}{\text{H}}\text{N}=\text{CR}-\text{NH}$, *e.g.*, amidinium-, guanidinium-, and urea-type resonances in quinazoline cations,³ the 2-aminopteridine cation,⁴ and 2-hydroxypteridine,⁵ respectively. The 1,3,*x*-triazanaphthalene cations, discussed in Part I,¹ also show amidinium-type stabilization of hydration.

On the other hand, 4-aminopyridinium-type stabilization (III) has been postulated⁶ for the cation of 6-hydroxypteridine (IV). So we examined the cations of some 1,4,6-triazanaphthalenes for covalent hydration in the hope of finding undoubted examples of this type of resonance stabilization, because (in contrast to the pteridines) no amidinium

¹ Part I, Armarego, *J.*, 1962, 4094.

² Albert, Proc. Third Internat. Pteridine Symposium, Stuttgart, 1962, Pergamon, Oxford, 1963.

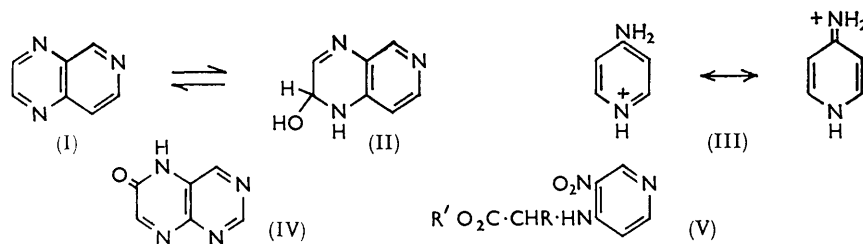
³ Albert, Armarego, and Spinner, *J.*, 1961, 2689, 5267.

⁴ Albert, Howell, and Spinner, *J.*, 1962, 2595.

⁵ Albert and Howell, *J.*, 1962, 1591.

⁶ Albert and Reich, *J.*, 1961, 127.

resonance is possible in the non-pyrazine ring. These triazanaphthalenes differ from pteridines only by lacking N-1, and the structural formulæ, *e.g.*, (I), are drawn to bring out this relation.



Preparations.—The preparation, from 4-hydroxypyridine, of the two intermediates most often required, namely, 4-chloro-3-nitro- and 3,4-diamino-pyridine, is described in the Experimental section because published methods^{7,8} omit some essential details. 1,4,6-Triazanaphthalene was made as before⁹ from 3,4-diaminopyridine and glyoxal.

3-Hydroxy-1,4,6-triazanaphthalene (6-hydroxy-1-deazapteridine) was first prepared by an unequivocal route: 4-chloro-3-nitropyridine was condensed with ethyl aminoacetate; to give ethyl 3-nitro-4-pyridylaminoacetate (V; R = H, R' = Et), which was hydrogenated to 1,2-dihydro-3-hydroxy-1,4,6-triazanaphthalene. Iodine oxidized this, in poor yield, to 3-hydroxy-1,4,6-triazanaphthalene, which was more conveniently prepared by the action of ethyl glyoxylate hemiacetal on 3,4-diaminopyridine under acidic conditions. The two specimens had identical R_F values and ultraviolet and infrared spectra; moreover, the one made from ethyl glyoxylate was reduced by potassium borohydride, in good yield, to the above 1,2-dihydro-derivative.

In the pteridine series, ethyl glyoxylate hemiacetal with 4,5-diaminopyrimidine gives 6-hydroxypteridine under acid conditions,¹⁰ and a mixture of 6- and 7-hydroxypteridine under neutral conditions.¹¹ Here too, acidic conditions gave only the 3-hydroxy- and neutral conditions a mixture of 2- and 3-hydroxy-1,4,6-triazanaphthalene. The less basic 2-isomer was separated by a pH-adjustment suggested by the relevant ionization constants.

The 2 (but not the 3)-isomer, when spotted on paper, gives a photo-reaction also shown by 7 (but not by 6)-hydroxypteridine. The dark (absorption) spot seen in light of 254 $m\mu$ changes, after irradiation for a minute at that wavelength, to a violet fluorescence (suitably detected in light of 365 $m\mu$). This type of change is known to be a photoreduction in the pteridine series¹² and can be correlated well with structure.

Oxidation, more vigorous than that mentioned above, of 1,2-dihydro-3-hydroxy-1,4,6-triazanaphthalene with iodine or potassium ferricyanide, and of 3-hydroxy-1,4,6-triazanaphthalene with the latter, gave 2,3-dihydroxy-1,4,6-triazanaphthalene. This substance was more conveniently made by ring-closure of 4-amino-3-carboxyformamidopyridine (from 3,4-diaminopyridine and dimethyl oxalate). The identity of the products was shown by R_F values and infrared spectra.

Attempts to prepare 3-chloro- and 3-mercapto-1,4,6-triazanaphthalene failed, *e.g.*, by refluxing with phosphorus halides, or with phosphorus pentasulphide in boiling benzene, xylene, or pyridine (a solvent series of increasing efficacy¹³).

When it was found that 1,4,6-triazanaphthalene and its 3-hydroxy-derivative had strongly hydrated cations (see below), it was decided to prepare the 2-methyl derivatives

⁷ Crowe, *J.*, 1925, 2028.

⁸ Bishop, Cavell, and Chapman, *J.*, 1952, 437.

⁹ Albert and Pedersen, *J.*, 1956, 4683.

¹⁰ Albert, *J.*, 1955, 2690.

¹¹ Albert, Brown, and Cheeseman, *J.*, 1952, 1620.

¹² Albert, *Nature*, 1956, 178, 1672.

¹³ Albert and Barlin, *J.*, 1959, 2384; 1962, 3129.

to see if hydration was lessened in analogy with the insertion of a 7-methyl-group into 6-hydroxypteridine (IV).⁶

Only one methyl-1,4,6-triazanaphthalene was obtained on reaction between pyruv-aldehyde and 3,4-diaminopyridine (at various pH values and in various solvents as in ref. 14). This substance is considered to be the 3-methyl isomer from evidence of hydration (see below). Attempts to confirm this structure by oxidation to a known hydroxy-methyltriazanaphthalene with potassium permanganate or hydrogen peroxide failed because of extensive decomposition. We have been unable to prepare the 2-methyl derivative.

Next we attempted the simultaneous preparation of 2-hydroxy-3-methyl- and 3-hydroxy-2-methyl-1,4,6-triazanaphthalene from ethyl pyruvate and 3,4-diaminopyridine, by a recently published method.¹⁵ It soon occurred to us that these authors had accidentally transposed the melting points of these isomers. Thus the isomer of m. p. 265° gave the characteristic photo-decomposition described above for 2-hydroxy-1,4,6-triazanaphthalene, and hence we considered it likely to be the 2-hydroxy-3-methyl derivative, and not the 3-hydroxy-2-methyl derivative as stated.¹⁵ If this assignment is correct, the other isomer (m. p. 280°), which is photo-stable, must be the 3-hydroxy-3-methyl isomer.

These new assignments were confirmed by reducing the isomer of m. p. 280° to 1,2-dihydro-3-hydroxy-2-methyl-1,4,6-triazanaphthalene. The latter was unequivocally synthesized from 4-chloro-3-nitropyridine by condensation with alanine methyl ester to methyl α -(3-nitro-4-pyridylamino)propionate (V; R = R' = Me), followed by catalytic reduction and ring closure.

Although it has been claimed¹⁵ that reaction of these two hydroxy-methyltriazanaphthalenes with diazomethane gave *N*-methyl derivatives, we found that no methylation took place with this reagent (or with methyl sulphate or iodide) under a great variety of conditions. Hence we repeated these authors more direct syntheses¹⁵ of these derivatives from ethyl pyruvate and 3-amino-4-methylamino- and 4-amino-3-methylaminopyridine,⁸ respectively. The products gave good elemental analytical figures (C₉H₉N₃O) and their ultraviolet spectra closely resembled those of the corresponding -NH-analogues. Also the expected photo-reaction (see above) was elicited from the 2-oxo (and not from the 3-oxo)-derivative. Our melting points differed greatly from those published,¹⁵ viz., 1,2-dihydro-1,3-dimethyl-2-oxo-(141—142°; lit., 276—277°), and 3,4-dihydro-2,4-dimethyl-3-oxo-1,4,6-triazanaphthalene [114—115°; lit., 228—230° (decomp.)]. These lower figures (which Dr. J. W. Clark-Lewis tells us he has confirmed on specimens that he has recently made) are reasonable for a triazanaphthalene which has no bondable hydrogen atom (cf. 3,4-dihydro-4-methyl-3-oxo-1,4,5-triazanaphthalene¹⁶ which melts at 117°).

Synthesis of 7-amino-1,4,6-triazanaphthalene (the 1-deaza-analogue of 2-aminopteridine the cation of which is hydrated readily⁴) was attempted from ethyl 4,6-dihydroxy-pyridine-3-carboxylate.¹⁷ This ester was prepared from diethyl acetonedicarboxylate and converted (through ethyl 4,6-dichloropyridine-3-carboxylate) into 4,6-dichloropyridine-3-carboxylic acid. This acid was investigated further as it is said¹⁷ to exist as a hydrate, m. p. 155°, and an "anhydrous" form, m. p. 152—153°, obtained from the former by the consecutive action of phosphorus halides and ammonia. The "anhydrous" form proved to be 4,6-dichloropyridine-3-carboxamide, and the erroneous earlier assignment¹⁷ is partly explained by the omission of elemental analysis for nitrogen.

We converted this amide, by Hofmann degradation, into 5-amino-2,4-dichloropyridine. This failed to react with ammonia, even at 180°, but readily condensed with hydrazine hydrate to give 5-amino-2-chloro-4-hydrazinopyridine. The latter, reduced with zinc and

¹⁴ Albert, Brown, and Wood, *J.*, 1954, 3832.

¹⁵ Clark-Lewis and Singh, *J.*, 1962, 3162.

¹⁶ Clark-Lewis and Thompson, *J.*, 1957, 430.

¹⁷ den Hertog, Schogt, de Bruyn, and de Klerk, *Rec. Trav. chim.*, 1950, **69**, 673.

acid, gave 2-chloro-4,5-diaminopyridine, previously known only as a by-product in the consecutive amination, nitration, and reduction of 2,4-dichloropyridine.¹⁸

Condensation of this diamine with glyoxal gave 7-chloro-1,4,6-triazanaphthalene which was quite different from the substance given this name by early workers;¹⁹ the latter is now known to be the 5-chloro-isomer.¹⁵ Our chloro-compound gave the required 7-amino-1,4,6-triazanaphthalene with ammonia (incidentally, it could not be converted into the 7-hydroxy-analogue by boiling aqueous acid, alkali, or sodium acetate, or into the 7-methoxy-analogue with sodium methoxide).

Measurements of the ionization constants and ultraviolet spectra of these triazanaphthalenes are reported in the Table.

Covalent Hydration.—It was found in 1956 that the cation of 1,4,6-triazanaphthalene slowly changes into that of a stronger base during titration with acid, and that alkali regenerates the original substance.⁹ Three pK_a values, 3.05, 4.60, and 8.50, were found, and ring-opening was suspected. Later work,²⁰ in which rapid reaction techniques^{21,22} were used, showed that the lowest pK_a was that of the starting material, 8.50 was that of the (solitary) product, and 4.60 was that of the equilibrium mixture of initial and final substances. The evidence was compatible equally with ring-opening or hydration of a double bond in the cation.²⁰ That ring-opening does not occur was shown⁴ by a negative result in the sensitive *p*-nitrophenylhydrazine test for aldehydes, at pH 2.

In the present work, 1,4,6-triazanaphthalene, when oxidized with cold potassium

Physical properties.

| Substance | Species | Ionization (H ₂ O; 20°) | | | λ. w. 1 | Spectroscopy in water ^j | | pH |
|-------------------------|---------------------|------------------------------------|------------------|------------------|---------|---|-------------------------------|------|
| | | ^a pK_a | Spread (±) | Concn. (M) | | ^b λ_{max} . (m μ) | log ϵ | |
| 1,4,6-Triazanaphthalene | | | | | | | | |
| Unsubst. | ○ A ^c | — | — | — | — | 230, 306, 314 | 4.38, 3.58, 3.57 | 9.6 |
| | ○ H | — | — | — | — | 217, 254, 296 | 4.38, 3.65, 3.70 | 9.6 |
| | + A | 2.62 | 0.02 | 10 ⁻³ | 328 | 228, 301, 312 | 4.33, 3.64, 3.59 | 1.6 |
| | + Eq ^d | 4.60 | } ^e | — | — | 211, 232, 264, 305 | 4.15, 4.37, 3.34, 3.89 | 1.0 |
| | + H ^c | 8.50 | | | | | | |
| 3-Me | ○ A ^c | — | — | — | — | 232, 303, 309 | 4.40, 3.65, 3.65 | 7.0 |
| | ○ H | — | — | — | — | 299 | 3.69 | 11.2 |
| | + A | 2.87 | 0.04 | 10 ⁻⁴ | 315 | 229, 271, 298, 307 ^f | 4.42, 3.64, 3.67, 3.62 | 1.7 |
| | + Eq | 3.83 | 0.02 | 0.004 | — | 230, 300, 307 | 4.37, 3.77, 3.77 | 1.0 |
| | + H ^c | ~9.2 | — | 0.004 | — | — | — | — |
| 2,3-Me ₂ | ○ A ^c | — | — | — | — | 233, 305, 312 | 4.41, 3.67, 3.69 | 7.0 |
| | + A ^c | 3.33 | 0.03 | 10 ⁻⁴ | 320 | 230, 268, 301, 311 | 4.41, 3.66, 3.69, 3.64 | 1.0 |
| 2-OH | ○ A | — | — | — | — | 232, 309 | 4.37, 3.79 | 5.8 |
| | + A | 3.80 | 0.03 | 10 ⁻⁴ | 271 | 214, 235, 261 + 270, 297 | 4.09, 4.45, 3.74 + 3.74, 3.77 | 1.0 |
| | — A | 7.86 | 0.05 | 10 ⁻⁴ | 350 | 241, 328 | 4.52, 3.81 | 12.0 |
| 3-OH | ○ A ^c | — | — | — | — | 224, 248, 344 | 4.32, 4.15, 3.43 | 5.6 |
| | ○ H | — | — | — | — | <225, 265, 280 > | 4.43, 3.78, 3.77 | 9.0 |
| | + A | (4) | — | — | — | — | — | — |
| | + Eq | 6.79 | 0.02 | 0.001 | — | — | — | — |
| | + H ^c | 7.21 | 0.05 | 0.001 | — | 214, 232, 288 | 4.38, 4.42, 4.04 | 2.0 |
| | — A ^c | 7.32 | 0.02 | 0.001 | — | 235, 250, 357 | 4.33, 4.18, 3.71 | 12.0 |
| | — Eq | 7.48 | 0.02 | 0.001 | — | — | — | — |
| — H | (10.8) ^g | — | 10 ⁻⁴ | 300 | — | — | — | |

¹⁸ Talik and Plazek, *Roczniki Chem.*, 1956, **30**, 1139.

¹⁹ Koenigs, Bueren, and Jung, *Ber.*, 1936, **69**, 2690.

²⁰ Perrin and Inoue, *Proc. Chem. Soc.*, 1960, 342.

²¹ Perrin, *J.*, 1960, 3189.

²² Perrin, *J.*, 1962, 645.

TABLE (Continued.)

| Substance | Species ^a | Ionization (H ₂ O; 20°) | | | A.w. l ^b | Spectroscopy in water ^j | | |
|--|----------------------|------------------------------------|------------------|------------------|---------------------|------------------------------------|---------------------------------|------|
| | | pK _a | Spread (±) | Concn. (M) | | λ _{max.} (mμ) | log ε | pH |
| 1,2-H ₂ -3-OH | ○ | — | — | — | — | 226, 287 | 4.45, 3.73 | 10.0 |
| | + | 7.96 | 0.04 | 10 ⁻⁴ | 309 | 213, 233, 290 | 4.40, 4.36, 3.96 | 1.0 |
| | — | 12.15 | 0.05 | 10 ⁻⁴ | 309 | 233, 299 | 4.55, 3.88 | 14.2 |
| 3-OH-2-Me | ○ Eq ^h | — | — | — | — | 223, 223, 250, 272, 335 | 4.28, 4.24, 4.13, 3.68, 3.64 | 6.5 |
| | ○ H | — | — | — | — | 275—279 | 3.79 | 9.85 |
| | + Eq | 4.61 | 0.03 | 10 ⁻⁴ | 254 | 213, 232, 289 | 4.39, 4.40, 4.03 | 2.0 |
| | + H ^c | 7.17 | 0.03 | 10 ⁻⁴ | 299 | — ⁱ | — ⁱ | — |
| — A | 8.29 | 0.04 | 10 ⁻⁴ | 237 | 235, 267, 348 | 4.35, 3.90, 3.79 | 12.0 | |
| 1,2-H ₂ -3-OH-2-Me | ○ | — | — | — | — | 226, 286 | 4.46, 3.74 | 10.0 |
| | + | 7.89 | 0.05 | 10 ⁻⁴ | 310 | 213, 235 + 243, 297 | 4.12, 4.35 + 4.27, 3.99 | 5.0 |
| | — | 12.24 | 0.05 | 10 ⁻⁴ | 310 | 233, 299 | 4.53, 3.90 | 14.2 |
| 3,4-H ₂ -2,4-Me ₂ -3-oxo | ○ A ^c | — | — | — | — | 225, 229, 248, 270, 337 | 4.29, 4.27, 4.08, 3.63, 3.64 | 7.0 |
| | + Eq | 4.38 | 0.02 | 10 ⁻⁴ | 290 | 219, 232, 290 | 4.38, 4.40, 4.01 | 1.0 |
| 2-OH-3-Me | ○ | — | — | — | — | 232, 247, 302 | 4.34, 4.03, 3.89 | 6.3 |
| | + | 4.15 | 0.03 | 10 ⁻⁴ | 240 | 215, 236, 261, 291 | 4.30, 4.47, 3.75, 3.94 | 1.0 |
| | — | 8.63 | 0.05 | 10 ⁻⁴ | 240 | 210, 240, 322 | 4.26, 4.47, 3.92 | 11.0 |
| 1,2-H ₂ -1,3-Me ₂ -2-oxo | ○ | — | — | — | — | 235, 249, 305 | 4.40, 4.09, 3.86 | 7.0 |
| | + | 4.00 | 0.02 | 10 ⁻⁴ | 330 | 217, 238, 276, 292 | 4.28, 4.53, 3.84, 3.92 | 2.0 |
| 2,3-(OH) ₂ | ○ | — | — | — | — | 235, 251, 300 | 3.99, 4.00, 3.99 | 6.15 |
| | + | 4.10 | 0.02 | 10 ⁻⁴ | 225 | 219, 246, 254, 302 | 4.43, 4.14, 4.11, 4.06 | 1.0 |
| | — | 8.19 | 0.01 | 10 ⁻⁴ | 330 | 217, 241, 304, 316, 329 | 4.49, 4.08, 4.05, 4.11, 3.88 | 9.9 |
| | — — | 11.50 | 0.05 | 10 ⁻⁴ | 249 | 227, 247, 308, 319, 333 | 4.58, 4.24, 4.05, 4.19, 4.05 | 14.2 |
| 7-Cl | ○ | — | — | — | — | 235, 321 | 4.46, 3.54 | 7.0 |
| | + | 1.22 | 0.03 | 10 ⁻⁴ | 300 | 241, 310 | 4.49, 3.84 | -1.1 |
| 7-NH ₂ | ○ A ^c | — | — | — | — | 244, 286, 395 | 4.47, 3.73, 4.46 | 7.0 |
| | ○ H | — | — | — | — | 239, 300 | 4.38, 3.64 | 9.0 |
| | + H | 3.18 | 0.04 | 10 ⁻⁵ | 254 | 240, 266, 301, 405 | 4.49, 3.92, 3.54, 2.82 | 1.0 |
| <i>Pyridine</i> | | | | | | | | |
| 4-NH ₂ -3-NH-CO-CO ₂ H | ± | — | — | — | — | 212, 265 | 4.22, 4.40 | 5.0 |
| | + | 1.37 | 0.05 | 10 ⁻⁴ | 240 | 212, 264 | 4.18, 4.16 | -1.1 |
| | — | 8.04 | 0.05 | 10 ⁻⁴ | 266 | 238, 281 | 4.07, 3.35 | 10.5 |

^a ○ Neutral species, + cation, — anion, — — dianion, ± zwitterion; A anhydrous (or substantially so), H hydrated, Eq equilibrium of anhydrous and hydrated species. ^b Analytical wavelength (mμ) for spectroscopic determinations of pK_a; when there is no entry in this column, the determination was potentiometric. ^c This is the more stable hydration form of this ionic species. ^d About 99% hydrated. ^e Perrin and Inoue, *Proc. Chem. Soc.*, 1960, 342. ^f Contains ~7% of neutral molecule. ^g Obtained by continuous-flow spectrometry; the very small amount of hydrated anion present at equilibrium, and the rapidity of the hydration reaction at pH 12 (time for half-conversion is 1 sec.), make this figure only a lower limit. ^h Almost anhydrous. ⁱ Almost identical with line above. ^j Shoulders and inflections in italics.

permanganate (a reagent successfully used to locate the position of hydration in hydroxypteridines²³), gave 2-hydroxy-1,4,6-triazanaphthalene. This result permits the following summary of equilibria and species. 1,4,6-Triazanaphthalene (neutral species) is stable and substantially anhydrous.²⁰ The lowest pK_a (now refined to 2.62) relates this species and the unstable anhydrous cation. Hydration occurs in the 1,2-position, *i.e.*, the only position where the addition of water to a C=N bond could be stabilized by resonance [actually a resonance of the 4-aminopyridinium type (III) which favours the cation]. The pK_a 8.50 relates the (stable) hydrated cation and the (unstable) hydrated neutral

²³ Brown and Mason, *J.*, 1956, 3443.

species. [The spectrum of this neutral species (see Table) was obtained by the stopped-flow method: the extinction was found for a given wavelength instantly after basification of an acidic solution and this process was repeated.] The ratio (K_1) of hydrated to anhydrous cations, at equilibrium, is 95 calculated from the expression²⁰ $K_1 = (K_a^A - K_a^{Eq})/K_a^{Eq}$, where pK_a^A is 2.62, and pK_a^{Eq} is 4.60. The ratio of hydrated to anhydrous neutral species was calculated²⁰ to be 0.0001 : 1.

The α -methyl-1,4,6-triazanaphthalene obtained from pyruvaldehyde and 3,4-diaminopyridine may be the 2- or the 3-methyl derivative. If the former (nucleophilic attack by a water molecule), this group should strongly inhibit hydration by a (largely) steric effect. Thus the ratios of hydrated to anhydrous species, at equilibrium, in quinazoline cation,³ and 2-hydroxy-,²⁰ and 6-hydroxy-pteridine²⁶ (neutral species) are decreased by a methyl group in the 4-, 4-, and 7-position by factors of 400, 53, and 100, respectively. But if the methyl group is in the 3-position, where a $+M$ effect, as found in 7-methylpteridine²² and 7-methoxyquinazoline,²⁴ cannot be exerted, a relatively smaller (inductive) effect can be expected. The expected hydration-depressing effect of a 2-methyl group is clearly seen in the cation of 2,3-dimethyl-1,4,6-triazanaphthalene²⁵ in which no hydration would be detected. In the monomethyl derivative, the ratio of hydrated to anhydrous cation (calculated from the pK_a values in the Table) at equilibrium is 9. Hence it is concluded that the methyl group is in the 3-position.

2-Hydroxy-1,4,6-triazanaphthalene, like the structural analogue 7-hydroxypteridine, gave no evidence of hydration.

3-Hydroxy-1,4,6-triazanaphthalene was hydrated strongly as the cation. Thus, the spectrum of the cation was found strongly to resemble that of 1,2-dihydro-3-hydroxy-1,4,6-triazanaphthalene, just as that of 6-hydroxypteridine cation (its structural analogue) strongly resembles that of 7,8-dihydro-6-hydroxypteridine.²³ This indication that 3-hydroxy-1,4,6-triazanaphthalene is hydrated in the 1,2-position was confirmed by oxidation to 2,3-dihydroxy-1,4,6-triazanaphthalene. As with the parent substance, hydration has occurred in the only position where the hydrate could be stabilized by resonance, and this again is of the 4-aminopyridinium type (III). When a solution of the hydrated cation was made suddenly alkaline, the very large shift in the long-wavelength peak (from 288 to 357 $m\mu$) gave evidence that the anion is anhydrous. Because the pK_a of the (stable) hydrated cation is almost the same as that of the (stable) anhydrous cation (7.21 and 7.32, respectively), it is not possible to obtain the spectrum of the equilibrium neutral molecule. However, by rapid adjustment to pH 9.0 of an acidic solution of the (hydrated) cation, the spectrum of the hydrated neutral species was obtained (see Table). Similarly, by rapid adjustment to pH 5.6 of an alkaline solution of the (anhydrous) anion, the spectrum of the anhydrous neutral molecule was found.

In 3-hydroxy-2-methyl-1,4,6-triazanaphthalene, the pK_a values of the stable species lie further apart, and a purer spectrum of the anhydrous neutral species was obtained. The similarity of the spectrum of the cation, at equilibrium, to that of the cation of 1,2-dihydro-3-hydroxy-2-methyl-1,4,6-triazanaphthalene indicates that the former is largely hydrated. However, the low pK_a^{Eq} (4.61, to be compared with 6.79 for 3-hydroxy-1,4,6-triazanaphthalene) provides evidence of the blocking effect expected from a methyl group at the position of hydration (this is because, as the degree of hydration decreases, the pK_a^{Eq} value moves towards that of the anhydrous species). The small change in λ_{max} in passing from the hydrated cation to the hydrated neutral species is as expected; so also is the large bathochromic change when this species is dehydrated, and the increase of 13 $m\mu$ when the (anhydrous) anion is formed. *N*-Methylation (to 3,4-dihydro-2,4-dimethyl-3-oxo-1,4,6-triazanaphthalene) alters the pK_a^{Eq} and the spectrum of the cation very little (this compound gives no anion).

²⁴ Armarego, J., 1962, 561.

²⁵ De Selms and Mosher, *J. Amer. Chem. Soc.*, 1960, **82**, 3767.

²⁶ Inoue and Perrin, *J.*, 1963, 4803.

Further study of the hydration at 20° of 3-methyl-1,4,6-triazanaphthalene cation (half-conversion time = 17 sec. at pH 1.7) and of the dehydration of the neutral molecule of 3-hydroxy-2-methyl-1,4,6-triazanaphthalene ($t_{0.5} = 11$ sec. at pH 9.85) revealed strict first-order kinetics. The processes were catalysed by both H^+ and OH^- ; the minimum effect was observed at about pH 8.0 for the 3-hydroxy-compound.

When an acid solution of 7-amino-1,4,6-triazanaphthalene was neutralized, the $\log \epsilon$ value of the long-wavelength band increased during 4 minutes ($t_{0.5} = 150$ sec. at pH 8.2) from 2.87 to 4.46. First-order kinetics and catalysis by both H^+ and OH^- were observed. These results are consistent with covalent hydration in the cation and the formation of a neutral species that is more stable when anhydrous. This behaviour is similar to that of 2-aminopteridine⁴ but has not yet been examined so closely.

EXPERIMENTAL

Microanalyses were by Dr. J. E. Fildes and her staff. Solids for analysis were dried at 110° unless otherwise stated. M. p.s were taken in soda-glass capillaries.

Yields refer to material which gave only one spot on paper chromatography (ascending) which was carried out on Whatman No. 1 paper with (a) 3% aqueous ammonium chloride, and (b) butan-1-ol-5*N*-acetic acid (7 : 3) as solvent.

Ionization constants were determined (several of them by Mr. H. Satrapa) by the methods developed in this Department.²⁷ Ultraviolet spectra were measured first on a Shimadzu model RS 27 recording spectrophotometer and then the λ_{max} and ϵ values were checked on a Hilger "Uvispek" manual instrument (by Mr. D. Light and Mr. C. Arandjelovic). Infrared spectra were taken with a Perkin-Elmer 21 spectrophotometer, potassium bromide discs being used.

The rapid-reaction methods, which Dr. D. D. Perrin has developed,^{21,22} were kindly applied by him (assisted sometimes by Mr. Y. Inoue, sometimes by one of us) to all substances likely to give evidence of covalent hydration. These tests were (a) a three-minute self-recording potentiometric titration,²¹ and (b) the "stopped flow" technique (for faster reactions) in which the change in extinction coefficient with time (at a chosen set of wavelengths) is observed on solutions submitted to a sudden pH change and is then extrapolated to zero time.²²

4-Hydroxy-3-nitropyridine.—4-Hydroxypyridine (18 g.) was added slowly, with stirring, to a cooled mixture of sulphuric acid (30 ml.; d 1.84) and nitric acid (50 ml.; d 1.5). The mixture was then heated under reflux on a steam-bath for 24 hr. (4 days gave no improvement) and poured on ice (about 500 g.). The mixture was slowly adjusted to pH 2.5 with aqueous sodium hydroxide and re-chilled. The product was filtered off and, recrystallized once from boiling water, gave 4-hydroxy-3-nitropyridine (61%), m. p. 275—277° (lit.,²⁸ 280—281°). A further 1.55 g. were obtained by evaporating the filtrate to dryness, extracting the residue with boiling ethanol, and recrystallizing the dried extracted material from water. This nitration avoids the use of oleum.^{28,29} Quantities of reagents and yields were not given by earlier users of these conditions.^{7,8}

4-Chloro-3-nitropyridine was prepared essentially as before²⁹ but at a higher temperature (bath at 150°, 2 hr.). The product, purified as before,⁸ and redistilled, had b. p. 76°/0.7 mm. (lit.,⁸ 68—70°/0.5 mm.). It proved unstable on storage.

4-Amino-3-nitropyridine Hydrochloride.—(i) 4-Hydroxy-3-nitropyridine was prepared as described previously.³⁰ 4-Amino-3-nitropyridine, prepared from this hydrochloride and aqueous ammonia,³⁰ had m. p. 200—202° (lit.,³⁰ 204°).

3,4-Diaminopyridine.—4-Amino-3-nitropyridine (10 g.) and methanol (750 ml.) were hydrogenated over 5% palladium-charcoal (2.5 g.) at 20°/710 mm. The catalyst was filtered off and the solvent evaporated. The product, crystallized once from water, gave 3,4-diaminopyridine (85%) m. p. 215° (lit.,³¹ 218—219°).

Ethyl 3-Nitro-4-pyridylaminoacetate (V; R = H, R' = Et).—To a stirred and cooled suspension of ethyl aminoacetate hydrochloride (12 g.), water (7 ml.), and benzene (27 ml.), was added 10*N*-sodium hydroxide (11 ml.) during 3 min. The mixture was stirred for a further

²⁷ Albert and Serjeant, "Ionization Constants," Methuen, London, 1962.

²⁸ Koenigs and Fulde, *Ber.*, 1927, **60**, 2108.

²⁹ Kruger and Mann, *J.*, 1955, 2755.

³⁰ Clark-Lewis and Singh, *J.*, 1962, 2379.

³¹ Weidenhagen, Train, Wegner, and Nordström, *Ber.*, 1942, **75**, 1936.

15 min., potassium carbonate was added to form a paste, and the benzene was decanted. The paste was repeatedly shaken with benzene. The combined benzene extracts (70 ml.) were dried (K_2CO_3). 4-Chloro-3-nitropyridine (3.5 g., 0.023 mole) was added to this solution, with cooling and stirring. The mixture was set aside at 20° overnight, then filtered from ethyl aminoacetate hydrochloride (m. p. 142°) and evaporated. The residue, crystallized from dilute alcohol, gave *ethyl 3-nitro-4-pyridylaminoacetate* (85%), m. p. 81° (Found, for material dried at 20°: C, 48.1; H, 5.05; N, 18.4. $C_9H_{11}N_3O_4$ requires C, 48.0; H, 4.9; N, 18.7%).

1,2-Dihydro-3-hydroxy-1,4,6-triazanaphthalene.—The preceding ester (2 g.) in ethanol (160 ml.) was hydrogenated over Raney nickel at room temperature and pressure. The catalyst was filtered off and extracted with boiling water (3 × 50 ml.). The combined filtrates were evaporated to dryness under reduced pressure, to give *1,2-dihydro-3-hydroxy-1,4,6-triazanaphthalene* (57%) which crystallized from boiling water (35 parts) as needles, m. p. >250° (decomp.) (Found: C, 56.2; H, 4.6; N, 28.2. $C_7H_7N_3O$ requires C, 56.4; H, 4.7; N, 28.2%), ν_{max} , 2970 (NH stretching) and 1675 cm^{-1} (C=O stretching).

To this substance (0.075 g.), dissolved in boiling water (3 ml.) and cooled to 55°, 0.5N-iodine (1 ml.) was added. The dark suspension was rapidly heated, and 2N-potassium hydroxide was added until the pH became 7.2. On refrigeration, the mixture deposited 3-hydroxy-1,4,6-triazanaphthalene (0.02 g.), identical with that described below.

3-Hydroxy-1,4,6-triazanaphthalene.—3,4-Diaminopyridine (0.55 g., 0.005 mole), ethyl glyoxylate hemiacetal³² (1 g., 1.3 equiv.), and 2N-sulphuric acid (9 ml.) were set aside at ~25° for a week. Sodium citrate (0.5 g.) was added, and the solution adjusted to pH 7.2 with 10N-sodium hydroxide (~2 ml.) and chilled overnight. The crystals of *3-hydroxy-1,4,6-triazanaphthalene* (78%) were recrystallized from 33 parts of water (Found, for material dried at 110°/0.001 mm.: C, 55.9; H, 3.8; N, 27.6. $C_7H_5N_3O \cdot 0.25H_2O$ requires C, 55.5; H, 3.7; N, 27.7%). At 280° it becomes deep orange without melting. Unlike 6-hydroxypteridine, which is rapidly disproportionated in 0.1N-sodium hydroxide at 20°, this substance was unchanged after a week.

2-Hydroxy-1,4,6-triazanaphthalene.—3,4-Diaminopyridine (1.1 g.), water (10 ml.), and ethyl glyoxylate hemiacetal (2.2 ml.) were refluxed for 35 min. The initial pH was 7.0, the final pH 5.8. The crystals of *2-hydroxy-1,4,6-triazanaphthalene* (56%) which were deposited on chilling overnight were recrystallized from 90 parts of boiling water (carbon) (Found, for material dried at 20°: C, 57.2; H, 3.4; N, 28.2. $C_7H_5N_3O$ requires C, 57.1; H, 3.4; N, 28.6%), ν_{max} , 2850 (NH stretching), 1660 cm^{-1} (C=O stretching). It became orange at 240° without melting. The hydrochloride crystallized from N-hydrochloric acid.

The filtrate, adjusted to pH 7.2 with sodium phosphate and hydroxide, deposited the 3-hydroxy-isomer as quartahydrate, in 35% yield (Found: C, 55.8; H, 3.9; N, 27.5%).

Paper chromatography (see above) gave R_F 0.70 and 0.75 in ammonium chloride, and 0.65 and 0.35—0.55 in butanol-acetic acid, for the 2- and the 3-hydroxy-isomer, respectively.

Reduction of 3-Hydroxy-1,4,6-triazanaphthalene.—To this substance (0.45 g.) in 0.5N-potassium hydroxide (6.6 ml., 1.1 equiv.) was added potassium borohydride (0.07 g.) at 20°. The next day the pH was adjusted from >13 to 9.5. *1,2-Dihydro-3-hydroxy-1,4,6-triazanaphthalene* (75%) was recrystallized from water (Found, for material dried at 20°: C, 56.3; H, 4.9; N, 28.0%).

Oxidation of 1,2-Dihydro-3-hydroxy-1,4,6-triazanaphthalene.—To this substance (0.1 g., 0.0007 mole) in boiling water (4 ml.) was added iodine (0.2 g., 0.0008 mole) dissolved in water (3 ml.) with potassium iodide. The mixture was heated on a steam-bath for 40 min., then adjusted to pH 7 with sodium carbonate. The *2,3-dihydroxy-1,4,6-triazanaphthalene* (0.045 g.) that separated was recrystallized from water, then having m. p. >320° (Found: C, 51.25; H, 3.1. $C_7H_5N_3O_2$ requires C, 51.5; H, 3.1%), ν_{max} , 3235 and 2700 (NH stretching) and 1701 cm^{-1} (C=O stretching).

4-Amino-3-carboxyformamidopyridine.—3,4-Diaminopyridine (0.55 g.) in N-hydrochloric acid (4 ml.) was refluxed with dimethyl oxalate (1.1 g., 2 equiv.) for 1 hr. The solution (pH <2.5), adjusted to pH 5.0 and chilled, deposited *4-amino-3-carboxyformamidopyridine* (90%), which recrystallized from 140 parts of boiling water (Found, for material dried at 110°/0.001 mm. with P_2O_5 : C, 46.6; H, 4.0; N, 23.0. $C_7H_7N_3O_3$ requires C, 46.4; H, 3.9; N, 23.2%). This acid (0.055 g.), heated at 230° for 1.5 hr., gave *2,3-dihydroxy-1,4,6-triazanaphthalene* (0.030 g.) (Found: C, 51.4; H, 3.25; N, 25.3%. $C_7H_5N_3O$ requires C, 51.5; H, 3.1; N, 25.8%).

³² Rigby, J., 1950, 1912.

Oxidation of 3-Hydroxy-1,4,6-triazanaphthalene.—This substance (0.1 g.) in 2.5N-potassium hydroxide was added to potassium ferricyanide (1.6 g.), dissolved in a little water at 20°. Next day the pH was adjusted to 7, and the precipitated 2,3-dihydroxy-1,4,6-triazanaphthalene (0.09 g.) was recrystallized from water (Found: C, 51.7; H, 3.3; N, 25.65%).

3-Methyl-1,4,6-triazanaphthalene.—Commercial 30% aqueous pyruvaldehyde (9 ml.) was refluxed with a suspension of 3,4-diaminopyridine (2.7 g.) in benzene (50 ml.) for 3 hr. (under nitrogen), while water was removed by azeotropic distillation. The residual benzene was removed under reduced pressure, and the residue extracted by refluxing light petroleum (b. p. 60–80°) (5 ml.) for 15 min. Sublimation of the extracted material at 50°/0.001 mm. gave colourless crystals (0.5 g.) of a *product*, m. p. 78–79° (Found: C, 66.45; H, 5.0; N, 28.9. $C_8H_7N_3$ requires C, 66.2; H, 4.9; N, 28.95%).

2-Hydroxy-3-methyl- and 3-Hydroxy-2-methyl-1,4,6-triazanaphthalene.—Ethyl pyruvate³³ (4 g.) (freshly prepared from pyruvic acid³⁴ and fractionated; b. p. 144–148°/710 mm.), 3,4-diaminopyridine (2.8 g.), and ethanol were refluxed for 1 hr. and chilled overnight. The white solid (A) (2.5 g.) was filtered off. The filtrate, taken to dryness, gave a solid (B) (3.0 g.). Solid A was extracted (Soxhlet) with benzene. The extract, taken to dryness, gave a residue which recrystallized from ethanol to give *3-hydroxy-2-methyl-1,4,6-triazanaphthalene* (1.3 g.), m. p. 280° (decomp.) (Found: C, 59.9; H, 4.4; N, 26.2. $C_8H_7N_3O$ requires C, 59.6; H, 4.4; N, 26.1%), ν_{\max} 2680 (NH stretching) and 1679 cm^{-1} (C=O stretching). Solid B was chromatographed in ethanol over alumina. The earlier fractions of the eluate were evaporated to dryness, and the residue recrystallized from water gave *2-hydroxy-3-methyl-1,4,6-triazanaphthalene* (0.37 g.), m. p. 265° (Found: C, 59.85; H, 4.4; N, 26.3%), ν_{\max} 2860 (NH stretching) and 1688 cm^{-1} (C=O stretching). Paper chromatography in butanol–acetic acid, as above, gave R_F 0.70 and 0.60 for the 2- and the 3-hydroxy-isomer, respectively (see Introduction for photolytic differentiation).

Methyl α -(3-Nitro-4-pyridyl)aminopropionate (V; R = R' = Me).—10N-Sodium hydroxide (30 ml.) was added during 5 min. to a stirred suspension of methyl α -aminopropionate hydrochloride (32 g.), water (16 ml.), and benzene (75 ml.). After 15 minutes' further stirring, sufficient potassium carbonate was added to form a paste. The benzene was decanted and the residue extracted with benzene (3 \times 50 ml.). The combined extracts were dried (K_2CO_3), cooled, and stirred, and 4-chloro-3-nitropyridine (9 g.), in a little benzene, was added. The mixture was set aside overnight at 20° and for some hours at 5°. Unused methyl aminopropionate hydrochloride was filtered off; the filtrate, after concentration, deposited yellow needles of *methyl α -(3-nitro-4-pyridyl)aminopropionate* (5 g.), m. p. 96–97° (from alcohol) (Found: C, 47.9; H, 4.8; N, 18.2. $C_9H_{11}N_3O_4$ requires C, 48.0; H, 4.9; N, 18.7%).

1,2-Dihydro-3-hydroxy-2-methyl-1,4,6-triazanaphthalene.—(a) The above nitro-ester (0.72 g.) in ethanol (70 ml.) was shaken with hydrogen over Raney nickel at 20°/710 mm. The catalyst was filtered off and washed with boiling ethanol. The combined filtrates, when evaporated, gave a residue that was extracted with boiling water (0.1 g. of insoluble material discarded). The extract, after concentration, gave *1,2-dihydro-3-hydroxy-2-methyl-1,4,6-triazanaphthalene* (0.1 g.), m. p. 261–263° (Found: C, 58.7; H, 5.5; N, 25.5. $C_8H_9N_3O$ requires C, 58.9; H, 5.6; N, 25.75%), ν_{\max} 2980 (NH stretching) and 1680 cm^{-1} (C=O stretching).

(b) Potassium borohydride (0.02 g.) was added to 3-hydroxy-2-methyl-1,4,6-triazanaphthalene (0.15 g.; m. p. 280°) in 0.5N-potassium hydroxide (2 ml.), and the mixture was set aside at 20° overnight. On each of the next two days, potassium borohydride (0.04 g.) was added. After two more days at 20°, the suspension was adjusted to pH 9.0 with 10N-hydrochloric acid. The colourless precipitate (0.135 g.) was filtered off and recrystallized from water, to give *1,2-dihydro-3-hydroxy-2-methyl-1,4,6-triazanaphthalene*, m. p. 265°, identical in R_F and infrared spectrum with the above material (Found: C, 58.7; H, 5.4; N, 26.0%). This substance resisted oxidation by either iodine or potassium ferricyanide.

1,2-Dihydro-1,3-dimethyl-2-oxo-1,4,6-triazanaphthalene.—3-Amino-4-methylaminopyridine³⁰ (0.5 g.), ethyl pyruvate (0.7 g.), and ethanol (25 ml.) were refluxed for 1.5 hr. The solvent was evaporated; the residue, crystallized from cyclohexane, gave *1,2-dihydro-1,3-dimethyl-2-oxo-1,4,6-triazanaphthalene* (0.35 g.), m. p. 141–142° (Found, for sample sublimed at 130°/0.1 mm.; C, 61.5; H, 5.2; N, 24.0. $C_9H_9N_3O$ requires C, 61.7; H, 5.2; N, 24.0%), ν_{\max} 1665 cm^{-1} (C=O stretching). After chromatography on paper, this compound (but not its isomer) gives

³³ Archer and Pratt, *J. Amer. Chem. Soc.*, 1944, **66**, 1656.

³⁴ Howard and Fraser, *Org. Synth.*, Coll. Vol. I, 1948, p. 475.

the photo-change described above for 2-hydroxy- and 2-hydroxy-3-methyl-1,4,6-triazanaphthalene.

3,4-Dihydro-2,4-dimethyl-3-oxo-1,4,6-triazanaphthalene.—4-Amino-3-methylaminopyridine³⁰ (0.2 g.), ethyl pyruvate (0.25 g.), and benzene (12 ml.) were refluxed, under nitrogen, for 4 hr. Water was removed by azeotropic distillation and refluxing continued for 4 hr., followed by evaporation to dryness. The residue, when chromatographed in chloroform over alumina and recrystallized from light petroleum (b. p. 60–80°), gave 3,4-dihydro-2,4-dimethyl-3-oxo-1,4,6-triazanaphthalene (0.14 g.), m. p. 114–115° (Found: C, 61.7; H, 5.2; N, 24.0%), ν_{\max} , 1670 cm^{-1} (C=O stretching).

4,6-Dichloropyridine-3-carboxylic Acid and its Amide.—Ethyl 4,6-dihydroxypyridine-3-carboxylate (12 g.) and phosphorus oxychloride (120 ml.) were refluxed at 120° for 1.5 hr. (this is preferable to heating in sealed tubes¹⁷). The excess of reagent was removed under reduced pressure. The residue, poured on ice (100 g.), gave the low-melting ethyl 4,6-dichloropyridine-3-carboxylate (13 g.). Alkaline hydrolysis gave 4,6-dichloropyridine-3-carboxylic acid monohydrate, m. p. 154–156° (lit.,¹⁷ 155°). This acid (7 g.), phosphorus oxychloride (10 ml.), and phosphorus pentachloride (21 g.) were refluxed at 140° for 30 min. The excess of oxychloride was removed under reduced pressure and the residue shaken with benzene. Ammonia was passed into the filtered solution. The ensuing white precipitate gave 4,6-dichloropyridine-3-carboxamide (5 g.) m. p. 151–152° (from water), identical with a specimen of the “anhydrous 2,4-dichloropyridine-5-carboxylic acid” prepared as described¹⁷ by den Hertog *et al.* (m. p. 152–153°) (Found: C, 38.0; H, 2.4; N, 14.6. $\text{C}_6\text{H}_4\text{Cl}_2\text{N}_2\text{O}$ requires C, 37.7; H, 2.1; N, 14.7%). The same amide (m. p. 153–154°) was produced by similarly treating 4,6-dihydroxypyridine-3-carboxylic acid³⁵ with phosphorus halides followed by ammonia.

5-Amino-2,4-dichloropyridine.—Bromine (5 ml.) was slowly stirred into cooled 7% aqueous potassium hydroxide (500 ml.). 4,6-Dichloropyridine-3-carboxamide (5 g.) was added. The mixture was set aside at 20° for 1.5 hr., then at 70° for 4 hr., cooled, and acidified with acetic acid. After an hour, the solution was made alkaline with potassium hydroxide and extracted with chloroform. The residue obtained by evaporating the chloroform and crystallized from light petroleum (b. p. 60–80°) gave 5-amino-2,4-dichloropyridine (1.8 g.), m. p. 84–85° (Found, for a sublimed sample: C, 36.65; H, 2.7; Cl, 43.15; N, 17.2. Calc. for $\text{C}_5\text{H}_4\text{Cl}_2\text{N}_2$: C, 36.8; H, 2.5; Cl, 43.5; N, 17.2%). Earlier workers¹⁷ gave m. p. 80–81° for 5-amino-2,4-dichloropyridine prepared from 2,4-dichloro-5-cyanopyridine and potassium hypobromite, a method which we found unsatisfactory.

2-Chloro-4,5-diaminopyridine.—5-Amino-2,4-dichloropyridine (0.5 g.) and 98% hydrazine hydrate (10 ml.) were refluxed for 5 hr. The volatile components were removed under reduced pressure. The residue, evaporated twice with ethanol and recrystallized from water, gave 5-amino-2-chloro-4-hydrazinopyridine (0.43 g.), m. p. 167–169° (Found: C, 37.8; H, 4.4; Cl, 22.3; N, 35.1. $\text{C}_5\text{H}_7\text{ClN}_4$ requires C, 37.9; H, 4.45; Cl, 22.4; N, 35.3%). This hydrazine (4.6 g.) was refluxed with zinc dust (2.7 g.) in *n*-sulphuric acid (540 ml.) for 3 hr. The cooled solution was made strongly alkaline with 10*N*-sodium hydroxide and repeatedly extracted with chloroform. The extracts were dried (Na_2SO_4) and evaporated. The residue, recrystallized from benzene, gave 2-chloro-4,5-diaminopyridine (3.3 g.) m. p. 146° (lit.,¹⁸ m. p. 145°).

7-Chloro-1,4,6-triazanaphthalene.—4,5-Diamino-2-chloropyridine (2.1 g.), polymeric glyoxal monohydrate (1.47 g.; British Drug Houses), and ethanol (105 ml.) were refluxed for 2 hr. The mixture was evaporated to dryness. The residue, crystallized from light petroleum (b. p. 60–80°), gave 7-chloro-1,4,6-triazanaphthalene (1.93 g.), m. p. 114–115° (Found: C, 51.1; H, 2.6; Cl, 21.7; N, 25.3. $\text{C}_7\text{H}_4\text{ClN}_3$ requires C, 50.8; H, 2.4; Cl, 21.4; N, 25.4%). Refluxing this with hydrazine hydrate gave 2-chloro-4,5-diaminopyridine.

7-Amino-1,4,6-triazanaphthalene.—7-Chloro-1,4,6-triazanaphthalene (1.5 g.), freshly precipitated copper (0.7 g.), and liquid ammonia (80 ml.) were heated in a stirred autoclave at 110–120° for 24 hr. When the vessel had cooled, the ammonia was allowed to evaporate and the residue extracted with boiling ethanol. The alcohol was evaporated, and the residue chromatographed in chloroform over alumina. The main yellow band (the second band) was collected, and the solvent evaporated. The residue, crystallized from benzene and sublimed at 180°/0.01 mm., gave 7-amino-1,4,6-triazanaphthalene (175 mg.), m. p. 210–212° (Found: C, 58.1; H, 4.15; N, 37.9. $\text{C}_7\text{H}_6\text{N}_4$ requires C, 57.5; H, 4.1; N, 38.3%).

Oxidation of 1,4,6-Triazanaphthalene.—A mixture of 0.3*M*-potassium permanganate (5 ml.)

³⁵ Errera, *Ber.*, 1898, **31**, 1632.

and 1,4,6-triazanaphthalene (0.18 g.) in 0.1N-sodium hydroxide (18 ml.) was set aside overnight at 20°, filtered over kieselguhr, and evaporated to dryness. The residue, recrystallized from water, gave 3-hydroxy-1,4,6-triazanaphthalene (65 mg.), identical in infrared spectrum with that described above.

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