Polyazanaphthalenes. Part I. Some Derivatives of 1 : 4 : 5-*Triazanaphthalene and Quinoxaline.*

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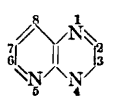
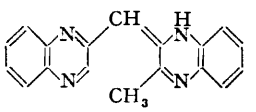
Numerous derivatives of 1 : 4 : 5-triazanaphthalene have been prepared by condensation of 2 : 3-diaminopyridines with α-diketones, ethyl oxaloacetate and ethyl pyruvate, and by condensation of 2 : 6-diamino-3-nitrosopyridine with deoxybenzoin, ethyl acetoacetate, and ethyl malonate. Two analogues of pteroic acid containing the quinoxaline ring system have been synthesised. An orange compound similar to methylpteridine-red has been obtained by the action of acid on 2-methylquinoxaline.

THE work described in this paper had as its objective the synthesis of analogues of pteroic acid based on the 1 : 4 : 5-triazanaphthalene (I) and the quinoxaline ring system. The chemistry of 1 : 4 : 5-triazanaphthalene is little known; a number of symmetrically 2 : 3-disubstituted derivatives have been prepared by condensing 2 : 3-diaminopyridines with α-diketones (Tschitschibabin and Kirsanow, *Ber.*, 1927, **60**, 766; Petrow and Saper, *J.*, 1948, 1389; Bernstein, Stearns, Shaw, and Lott, *J. Amer. Chem. Soc.*, 1947, **69**, 1151; Lappin and Slezak, *ibid.*, 1950, **72**, 2806; Albert and Hampton, *J.*, 1952, 4985) and a few unsymmetrically 2 : 3-disubstituted derivatives from 2 : 3-diaminopyridines and alloxan (Rudy and Majer, *Ber.*, 1938, **71**, 1323; 1939, **72**, 940).

Petrow and Saper (*loc. cit.*) obtained 1 : 4 : 5-triazanaphthalene itself (I) in poor yield by condensation of 2 : 3-diaminopyridine with glyoxal; we have obtained a greatly improved yield by this method and have also obtained this compound by hydrogenolysis of the 7-bromo-derivative. We have also prepared 7-chloro-, 7-chloro-2 : 3-dimethyl-, and 7-chloro-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene by condensing 2 : 3-diamino-5-chloropyridine with the appropriate α-dicarbonyl compound.

(I) 

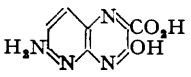
 (II)

Attempts to prepare 2- or 3-methyl-1 : 4 : 5-triazanaphthalene by condensing 2 : 3-diaminopyridine with pyruvic aldehyde or hydroxyiminoacetone yielded intractable red pigments. This is surprising since *o*-phenylenediamine condenses readily with pyruvic aldehyde (Jones, Kornfeld, and McLaughlin, *J. Amer. Chem. Soc.*, 1950, **72**, 3539) and hydroxyiminoacetone (Böttcher, *Ber.*, 1913, **46**, 3084; Bennett and Willis, *J.*, 1928, 1960; Borsche and Doeller, *Annalen*, 1939, **537**, 39) to yield 2-methylquinoxaline and with dimethylglyoxime to yield 2 : 3-dimethylquinoxaline. An orange pigment, " 2-methylquinoxaline-orange," is formed as a by-product in the condensation of *o*-phenylenediamine with hydroxyiminoacetone in aqueous hydrochloric acid and is also produced by the action

of aqueous hydrochloric acid on 2-methylquinoxaline; this compound we formulate as (II), by analogy with " methylpteridine-red " (Karrer, Schwyzer, and Nicolaus, *Helv. Chim. Acta*, 1950, **33**, 557, 1233). The red compounds produced from 2 : 3-diaminopyridine no doubt have similar structures. Attempts to condense 2 : 3-diaminopyridine, or its 5-chloro- or 5-bromo-derivative with pyruvic aldehyde di-*n*-butyl acetal, αα′-dichloroacetone, ethyl αβ-dibromopropionate, dihydroxyacetone, and hexoses likewise failed, as did attempted condensation of 2 : 3-diaminopyridine with αβ-dibromopropaldehyde and *p*-aminobenzoic acid (cf. the synthesis of pteroic acid; Waller *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 19).

Timmis (*Nature*, 1949, **164**, 139) prepared pteridines by condensing 4-amino-5-nitrosopyrimidines with suitably activated carbonyl compounds. Under the acid conditions employed by him, this reaction failed with 2 : 6-diamino-3-nitrosopyridine, yielding only black amorphous products; satisfactory results were, however, obtained on using ethanolic sodium ethoxide as the condensing agent. Thus, 2 : 6-diamino-3-nitrosopyridine and deoxybenzoin yielded 6-amino-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene, which was smoothly deaminated by nitrous acid to the corresponding 6-hydroxy-compound. Condensation of 2 : 6-diamino-3-nitrosopyridine with ethyl acetoacetate and ethyl malonate proceeded equally smoothly, affording 2-acetyl-6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene and 6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylic acid (III), respectively.

When heated, the acid (III) was smoothly decarboxylated to 6-amino-3-hydroxy-1 : 4 : 5-triazanaphthalene; this was readily methylated by methyl sulphate in alkaline solution to a compound formulated, by analogy with the quinoxaline series (for references see Simpson, " Condensed Pyridazine and Pyrazine Rings," Interscience Publ., New York, 1953, p. 241), as the *N*-methyl derivative (IV; R = NH_2), which yielded the corresponding 6-hydroxy-compound (IV; R = OH) on deamination.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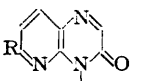
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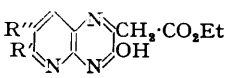
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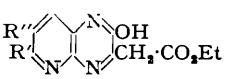
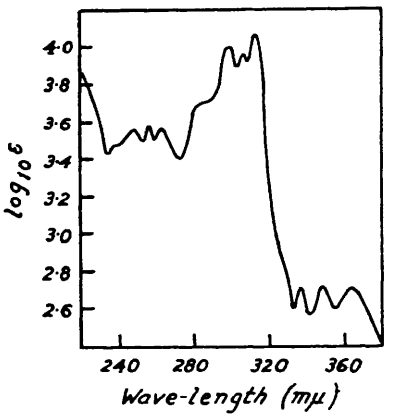

(VI)

We next investigated the applicability to the 1 : 4 : 5-triazanaphthalene series of the convenient procedure of Tschesche, Köhncke, and Korta (*Z. Naturforsch.*, 1950, **5**b, 132) for the synthesis of 7-hydroxypteridines. 2 : 3-Diamino-5-bromopyridine condensed smoothly with ethyl oxaloacetate in acetic acid to give the ester (V; R′ = H, R″ = Br), which was readily hydrolysed and decarboxylated to 7-bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene, also obtained by condensation of 2 : 3-diamino-5-bromopyridine with ethyl pyruvate in benzene; hydrogenolysis yielded 3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene, likewise also obtained by condensing 2 : 3-diaminopyridine with ethyl pyruvate. A similar series of reactions with 2 : 3 : 6-triaminopyridine yielded the ester (V; R′ = NH_2, R″ = H) and 6-amino-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene. Substitution of 2N-sulphuric acid for acetic acid in the condensation of 2 : 3-diamino-5-bromopyridine with ethyl oxaloacetate led, after hydrolysis, decarboxylation, and hydrogenolysis to 2-hydroxy-3-methyl-1 : 4 : 5-triazanaphthalene, isomeric with the compound obtained by using acetic acid; the assignment of structure (V) to the condensation product formed in acetic acid and structure (VI) to that formed in sulphuric acid is based on similar findings in the pteridine field (cf. Elion, Hitchings, and Russell, *J. Amer. Chem. Soc.*, 1950, **72**, 78); an attempt to establish the structure of the ester (V; R′ = NH_2, R″ = H) by oxidising the derived amino-hydroxy-methyltriazanaphthalene to (III) with permanganate failed owing to breakdown of the ring-system with liberation of ammonia. Numerous attempts were made to brominate 3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene in the side-chain, but no homogeneous bromomethyl compound could be obtained; condensation of the crude bromination product with *p*-aminobenzoic acid gave none of the required pteroic acid analogue.

In general, derivatives of 1 : 4 : 5-triazanaphthalene appear to be less stable than their

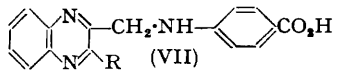
quinoxaline and pteridine analogues being, in many cases, very sensitive to both acid and alkali; as in the acridine (Albert, " The Acridines," Ed. Arnold, London, 1951, p. 152) and pteridine (Albert, Brown, and Cheeseman, *J.*, 1951, 474) series, and no doubt for the same reasons, the introduction of amino- or hydroxy-groups causes a marked lowering in solubility and increase in melting point.

The light absorption of 1 : 4 : 5-triazanaphthalene is shown in the Figure, while the rounded maxima for the two main peaks are compared with those for naphthalene and a series of azanaphthalenes in the Table. It will be seen that, except for quinoxaline, the successive replacement of methine by aza-groups leads to a progressive shortening of the wave-length of the maxima, the effect being greatest with the band of shorter wave-length; the reason for the irregularity with quinoxaline is obscure. Light-absorption data for the other 1 : 4 : 5-triazanaphthalene and quinoxaline derivatives prepared are recorded in the Experimental section.



Light absorption of 1 : 4 : 5-*triazanaphthalene in ethanol.*

In the quinoxaline series we were able to prepare two analogues of pteroic acid. Quinoxaline-2-aldehyde, prepared by an improved method from 2-D-*arabo*-tetrahydroxybutylquinoxaline, condensed readily with *p*-toluidine and *p*-aminobenzoic acid to yield Schiff's bases; that from *p*-aminobenzoic acid gave, on hydrogenation, the pteroic acid analogue (VII; R = H). 3-Hydroxy-2-methylquinoxaline was readily prepared from *o*-phenylenediamine and ethyl pyruvate, a method which is much superior to the older one employing pyruvic acid (Hinsberg, *Annalen*, 1896, **292**, 249); bromination afforded the 2-bromomethyl compound which with ethyl *p*-aminobenzoate gave a product which was readily hydrolysed to the pteroic acid analogue (VII; R = OH).



(VII)

Main absorption bands of naphthalene and some azanaphthalenes.

Compound	Solvent	$\lambda_{max.}$ (mμ)	$\log_{10}\varepsilon$	$\lambda_{max.}$ (mμ)	$\log_{10}\varepsilon$	Ref.
Naphthalene	EtOH	275	3·75	314	2·50	1
Quinoline	EtOH	276	3·59	313	3·41	2
Quinoxaline	MeOH	233	4·41	315	3·79	3
1 : 8-Naphthyridine	H_2O	260	3·62	305	3·81	4
1 : 4 : 7-Triazanaphthalene	EtOH	256	3·58	306	4·07	5
Pteridine	H_2O	234	3·50	304	3·87	4

1, Braude, *Ann. Reports*, 1945, **42**, 123. 2, Miller, Knight, and Roe, *J. Amer. Chem. Soc.*, 1950, **72**, 1629. 3, Bohlmann, *Chem. Ber.*, 1951, **84**, 860; Albert *et al.* (ref. 4) obtained almost identical results in water. 4, Albert, Brown, and Cheeseman, *J.*, 1951, 474. 5, This paper.

Experimental

Figures for light absorption are wave-lengths in mμ for maxima or inflections (in italics) and are followed by $\log_{10}\varepsilon$ in parentheses.

1 : 4 : 5-*Triazanaphthalene derivatives.*

1 : 4 : 5-*Triazanaphthalene.*—(*a*) 2 : 3-Diaminopyridine (0·5 g.) and glyoxal sodium bisulphite (1·33 g.) were refluxed in 50% aqueous ethanol (7 ml.) for 1 hr. The cooled mixture was made strongly alkaline with 5N-sodium hydroxide and continuously extracted with light petroleum (b. p. 40—60°) for 4 hr. The extract, after treatment with charcoal and filtration, deposited the base (0·3 g., 51%) as needles, m. p. 146° (Petrow and Saper, *loc. cit.*, give m. p. 147—148°); light absorption in EtOH, *238* (3·47), 249 (3·57), 256 (3·58), 263 (3·57), *286* (3·71), 299 (4·01), 306 (3·96), 313 (4·07), 337 (2·72), 348 (2·72), 364 (2·72).

(*b*) 7-Bromo-1 : 4 : 5-triazanaphthalene (2 g.; Petrow and Saper, *loc. cit.*) was suspended in 0·5N-sodium hydroxide and hydrogenated over 5% palladised strontium carbonate. After the theoretical amount of hydrogen had been absorbed, the solution was made more strongly

alkaline and continuously extracted with light petroleum (b. p. 60—80°) for 12 hr. The extract, after treatment with charcoal and filtration, deposited the base (0·51 g., 41%), m. p. 146°.

7-*Chloro*-1 : 4 : 5-*triazanaphthalene*.—2 : 3-Diamino-5-chloropyridine (1·43 g.) and glyoxal sodium bisulphite (2·6 g.) were heated in 25% aqueous ethanol (40 ml.) at 100° for 1 hr. Basification of the cooled solution with 5N-sodium hydroxide yielded the *base* (1·0 g., 60%) which crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 161° (Found : C, 50·6; H, 2·6; N, 25·6. $C_7H_4N_3Cl$ requires C, 50·8; H, 2·4; N, 25·4%); light absorption in EtOH, 258 (3·30), 265 (3·32), 310 (3·93), 316 (3·93), 324 (4·08).

7-*Chloro*-2 : 3-*dimethyl*-1 : 4 : 5-*triazanaphthalene*.—2 : 3-Diamino-5-chloropyridine (1·43 g.) and diacetyl (1 g.) were refluxed in ethanol (40 ml.) for 90 min. Evaporation to dryness, followed by recrystallisation from light petroleum (b. p. 80—100°), afforded the *base* (1·8 g., 93%) in needles, m. p. 155—156° (Found : C, 55·4; H, 4·2; N, 21·5. $C_9H_8N_3Cl$ requires C, 55·8; H, 4·1; N, 21·7%); light absorption in EtOH, 255 (3·43), 265 (3·32), 319 (4·09), 329 (4·16).

7-*Chloro*-2 : 3-*diphenyl*-1 : 4 : 5-*triazanaphthalene*.—2 : 3-Diamino-5-chloropyridine (1·43 g.) and benzil (2·1 g.) were refluxed in benzene (40 ml.) for 90 min. Evaporation to dryness, followed by recrystallisation from light petroleum (b. p. 80—100°), afforded the *base* (2·1 g., 66%) in fine needles or stout rods, m. p. 136—137° (Found : C, 71·5; H, 4·05; N, 13·1. $C_{17}H_{12}N_3Cl$ requires C, 71·8; H, 3·8; N, 13·2%); light absorption in EtOH, 228 (4·55), 236 (4·55), 364 (4·17).

6-*Hydroxy*-2 : 3-*diphenyl*-1 : 4 : 5-*triazanaphthalene*.—2 : 6-Diamino-3-nitrosopyridine (5 g.), deoxybenzoin (6·5 g.) and ethanolic sodium ethoxide (from sodium, 0·8 g., and ethanol, 150 ml.) were refluxed together for 24 hr. Recrystallisation, from ethanol, of the solid (6·5 g.) which separated from the cooled, filtered product yielded 6-amino-2 : 3-diphenyl-1 : 4 : 5-triazanaphthalene (4·1 g., 38%) as bright yellow needles, m. p. 271°, not depressed on admixture with a specimen prepared by Petrow and Saper's method (*loc. cit.*); light absorption in EtOH, 237 (4·64), 281 (4·13), 291 (4·13), 390 (4·38).

This amine (1·47 g.) was dissolved in warm 7N-sulphuric acid (50 ml.), and the solution cooled in ice; a solution of sodium nitrite (5 g.) in water (20 ml.) was added dropwise, with stirring, during 5 min. and the mixture then warmed at 100° for 15 min. The solid deposited on cooling was recrystallised from ethanol; the *hydroxy-compound* (1·0 g., 68%) had m. p. 273—274° (Found : C, 75·7; H, 4·5; N, 13·7. $C_{19}H_{13}ON_3$ requires C, 76·3; H, 4·3; N, 14·0%) and light absorption in EtOH, 280 (4·04), 290 (4·04), 376 (4·35).

2-*Acetyl*-6-*amino*-3-*hydroxy*-1 : 4 : 5-*triazanaphthalene*.—2 : 6-Diamino-3-nitrosopyridine (1·38 g.) was refluxed for 24 hr. with ethanolic ethyl sodioacetoacetate [from sodium, (0·23 g.), ethanol (50 ml.), and ethyl acetoacetate (1·3 g.)]. The brown solid which separated on cooling was collected, washed and dissolved in 0·01N-sodium hydroxide (50 ml.). After being heated with charcoal and filtered, the hot solution was acidified with 2N-hydrochloric acid. The *compound* (0·65 g., 32%) was a bright yellow granular solid, m. p. >360° (Found : C, 52·35; H, 4·1; N, 27·7. $C_9H_8O_2N_4$ requires C, 52·9; H, 3·9; N, 27·5%); light absorption in 0·01N-NaOH, 229 (4·40), 281 (3·73), 291 (3·80), 402 (416).

6-*Amino*-3-*hydroxy*-1 : 4 : 5-*triazanaphthalene*.—2 : 6-Diamino-3-nitrosopyridine (10 g.) was refluxed for 24 hr. with ethanolic ethyl sodiomalonate [from sodium (1·7 g.), ethanol (400 ml.), and ethyl malonate (12 g.)]. The mixture was then evaporated under reduced pressure and the residue dissolved in 0·2N-sodium hydroxide, heated with charcoal, filtered, and acidified while still hot with 2N-hydrochloric acid. 6-*Amino*-3-*hydroxy*-1 : 4 : 5-*triazanaphthalene*-2-*carboxylic acid* (III) (6·0 g., 40%) was precipitated as a bright yellow, granular powder, m. p. >360° (Found : C, 45·95; H, 3·4; N, 26·6. $C_8H_6O_3N_4$ requires C, 46·6; H, 2·9; N, 27·2%); light absorption in 0·01N-NaOH, 280 (3·46), 371 (4·05), *360* (3·98).

This acid (2 g.) was heated to above 300° in a nitrogen atmosphere at 20 mm. pressure. Resublimation of the sublimate afforded 6-*amino*-3-*hydroxy*-1 : 4 : 5-*triazanaphthalene* (1 g., 63%) as fine yellow needles, m. p. >360° (Found : C, 51·9; H, 3·9; N, 35·1. $C_7H_6ON_4$ requires C, 51·8; H, 3·7; N, 34·6%); light absorption in 0·01N-NaOH, 280 (3·49), 352 (4·35), 367 (4·37). Methylation (methyl sulphate in N-sodium hydroxide), followed by recrystallisation from methanol, gave 6-*amino*-3 : 4-*dihydro*-4-*methyl*-3-*oxo*-1 : 4 : 5-*triazanaphthalene* (IV; R = NH_2) (74%), m. p. 287—288° (Found : C, 55·1; H, 4·7; N, 31·2. $C_8H_8ON_4$ requires C, 54·5; H, 4·5; N, 31·8%); light absorption in EtOH, 369 (4·28). Sodium nitrite (0·26 g.) in water (5 ml.) was added dropwise to a stirred, ice-cooled solution of this *N*-methyl-compound (0·26 g.) in 2N-hydrochloric acid (50 ml.); the light brown precipitate was washed, dried, and recrystallised from *n*-butanol–light petroleum (b. p. 80—100°), affording 3 : 4-*dihydro*-6-*hydroxy*-4-*methyl*-3-*oxo*-1 : 4 : 5-*triazanaphthalene* (IV; R = OH) (0·5 g., 83%), m. p. 297° (Found : C, 54·4; H, 4·3; N, 24·1. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·9; N, 23·7%); light absorption in

EtOH, 227 (4·23), 347 (4·23), *354* (4·12); this compound resisted further methylation with methyl sulphate and aqueous sodium hydroxide.

7-Bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene.—(*a*) 2 : 3-Diamino-5-bromopyridine (6·0 g.) in acetic acid (25 ml.) was mixed with ethyl sodio-oxaloacetate (8·75 g.) in acetic acid (50 ml.), and the mixture heated at 100° for 1 hr. The crystalline solid which separated (7·38 g., 74%), was washed, dried, and recrystallised from pyridine, affording *ethyl 7-bromo-3-hydroxy-1 : 4 : 5-triaza-2-naphthylacetate* (V; R′ = H, R″ = Br) in needles, decomp. 260° (Found : C, 41·9; H, 3·3; N, 12·8. $C_{11}H_{10}O_3N_3Br$ requires C, 42·3; H, 3·2; N, 13·5%); light absorption in EtOH, 281 (4·02), 290 (3·96), 360 (4·38). This ester (6·41 g.) was warmed with 2N-sodium hydroxide (25 ml.) for 30 min. The pH was brought to 8·5 with acetic acid, and the solution heated with charcoal and filtered; the pH of the filtrate was then brought to 4 with more acetic acid, carbon dioxide being copiously evolved. The precipitate was collected and recrystallised from ethanol, yielding *7-bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene* (3·04 g., 62%), decomp. 240° (Found : C, 40·3; H, 2·6; N, 18·5. $C_8H_6ON_3Br$ requires C, 40·0; H, 2·5; N, 17·5%); light absorption in 0·01N-NaOH, 228 (4·52), 234 (4·44), 264 (3·92), *333* (4·10), 348 (4·14), *358* (4·10).

(*b*) The same compound was prepared by refluxing 2 : 3-diamino-5-bromopyridine (1·88 g.) and ethyl pyruvate (2·32 g.) in benzene (75 ml.) for 12 hr.; the pale brown precipitate was purified by acidification of its alkaline solution (yield, 1·22 g., 51%) (Found : C, 40·5; H, 2·7; N, 17·3%); light absorption in 0·01N-NaOH, 228 (4·53), 236 (4·45), 257 (3·89), 353 (4·13).

3-Hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene.—(*a*) 7-Bromo-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene (0·7 g.) was hydrogenated over 5% palladised strontium carbonate in 0·5N-sodium hydroxide (7 ml.). When absorption of hydrogen was complete, the solution was heated with charcoal, filtered, and acidified; vacuum-sublimation or crystallisation from ethanol yielded the *hydroxy-methyl-compound* (0·4 g., 85%) as needles, decomp. 240° (Found : C, 59·9; H, 4·6; N, 26·2. $C_8H_7ON_3$ requires C, 59·6; H, 4·3; N, 26·1%); light absorption in 0·01N-NaOH, 227 (4·44), 342 (4·10).

(*b*) The same compound was prepared by refluxing 2 : 3-diaminopyridine (0·7 g.) and ethyl pyruvate (0·8 g.) in benzene (25 ml.) for 1 hr. Vacuum-sublimation of the precipitate gave needles (0·6 g., 58%), decomp. 240° (Found : C, 59·9; H, 4·5%); light absorption in 0·01N-NaOH, 227 (4·32), 345 (4·12).

6-Amino-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene.—2 : 6-Diamino-3-nitrosopyridine (2·64 g.) was suspended in acetic acid (25 ml.) and hydrogenated over Adams catalyst. When the theoretical amount of hydrogen had been absorbed, ethyl sodio-oxaloacetate (5 g.) was added and the mixture heated on the steam-bath under nitrogen for 90 min. The crystalline precipitate was collected, washed with ethanol and ether, and recrystallised from pyridine, affording *ethyl 6-amino-3-hydroxy-1 : 4 : 5-triaza-2-naphthylacetate* (V; R′ = NH_2, R″ = H) (3·1 g., 66%), in yellow crystals, m. p. >360° (Found: C, 53·6; H, 4·9; N, 22·2. $C_{11}H_{12}O_3N_4$ requires C, 53·2; H, 4·8; N, 22·6%); light absorption in 0·01N-NaOH, 268 (3·38), 280 (3·40), 354 (4·36), 365 (4·36).

This ester (10 g.) was dissolved in 0·25N-sodium hydroxide (400 ml.), and the solution heated at 90° for 15 min. Acidification of the hot solution with acetic acid gave a gelatinous precipitate, which was collected by filtration, washed, dried, and sublimed in a high vacuum, yielding *6-amino-3-hydroxy-2-methyl-1 : 4 : 5-triazanaphthalene* (6 g., 85%) as colourless crystals, m. p. >360° (Found : C, 54·5; H, 4·7; N, 32·5. $C_8H_8ON_4$ requires C, 54·5; H, 4·5; N, 31·8%); light absorption in 0·01N-NaOH, 353 (4·33), 264 (4·33). Methylation (methyl sulphate in N-sodium hydroxide), followed by recrystallisation from aqueous methanol, afforded *6-amino-3 : 4-dihydro-2 : 4-dimethyl-3-oxo-1 : 4 : 5-triazanaphthalene* (74%), m. p. 296—297° (Found : C, 56·5; H, 5·4; N, 29·6. $C_9H_{10}ON_4$ requires C, 56·9; H, 5·3; N, 29·5%); light absorption in EtOH, 227 (4·30), 346 (4·22). This *N*-methyl-compound (0·4 g.) was dissolved in 4N-hydrochloric acid (15 ml.), and the solution cooled to 0° and treated dropwise with sodium nitrite (0·15 g.) in water (5 ml.); after 15 min. the crystalline precipitate was recrystallised from ethanol, affording *3 : 4-dihydro-6-hydroxy-2 : 4-dimethyl-3-oxo-1 : 4 : 5-triazanaphthalene* (0·2 g. 50%), m. p. 266—268° (Found : C, 56·1; H, 4·7; N, 21·8. $C_9H_9O_2N_3$ requires C, 56·6; H, 4·7; N, 22·0%); light absorption in EtOH, 342 (4·25).

2-Hydroxy-3-methyl-1 : 4 : 5-triazanaphthalene.—2 : 3-Diamino-5-bromopyridine (1·88 g.) and ethyl sodio-oxaloacetate (2·3 g.) were heated on the steam-bath in 2N-sulphuric acid (70 ml.) for 2 hr. The crystalline product was purified by acidification of its solution in dilute sodium hydroxide; this ester had light absorption in 0·01N-NaOH, 238 (4·38), 348 (4·16), *356* (4·10). Without further purification the ester (0·7 g.) was dissolved in N-sodium hydroxide (20 ml.) and

hydrogenated over 5% palladised strontium carbonate. Removal of the catalyst and acidification of the filtrate afforded the *hydroxy-methyl-compound*, decomp. 270° (Found: C, 59·9; H, 4·6; N, 26·2. $C_8H_7ON_3$ requires C, 59·6; N, 4·3; N, 26·1%); light absorption in 0·01N-NaOH, 343 (4·18).

Quinoxaline derivatives.

2-Methylquinoxaline and 2-Methylquinoxaline-orange.—*o*-Phenylenediamine (10 g.) and hydroxyiminoacetone (9 g.), in 2N-hydrochloric acid (50 ml.), were heated on the steam-bath for 20 min.; a deep red colour developed after 2 min. The solution was basified with sodium hydroxide, and the red amorphous precipitate removed by filtration and recrystallised from ethyl acetate; "*2-methylquinoxaline-orange*" (II) (0·8 g., 6%) formed orange needles, m. p. 255° (Found: C, 75·9; H, 4·6; N, 19·5. $C_{18}H_{14}N_4$ requires C, 75·5; H, 4·9; N, 19·6%); light absorption in EtOH, *225* (4·61), 271 (4·71), 278 (4·71), 369 (4·24), 382 (4·24), 455 (3·76), 484 (3·80). Extraction of the filtrate with ether, followed by distillation of the dried extract, yielded 2-methylquinoxaline (10·1 g., 76%), b. p. 110—111°/15 mm.

2 : 3-*Dimethylquinoxaline.*—*o*-Phenylenediamine (2 g.) and dimethylglyoxime (2 g.) in 2N-hydrochloric acid (25 ml.) were heated on the steam-bath for 1 hr. The product was treated with charcoal, filtered, and basified. Recrystallisation from hot water yielded 2 : 3-dimethylquinoxaline (2·6 g., 89%), m. p. 104—105°.

Quinoxaline-2-aldehyde and its Derivatives.—2-D-*arabo*-Tetrahydroxybutylquinoxaline (5 g.; Ohle and Hielscher, *Ber.*, 1941, **74**, 13) and sodium metaperiodate (13 g.) were suspended in water (300 ml.), containing acetic acid (10 ml.). After 16 hr. at room temperature with occasional shaking, the mixture was filtered and the filtrate continuously extracted with ether for 4 hr. Evaporation of the dried extract afforded the aldehyde (2 g., 63%), pale yellow needles (from light petroleum), m. p. 107—108° (lit., m. p. 108°); light absorption in EtOH, 235 (4·49), *304* (3·79), 314 (3·85).

The aldehyde (0·25 g.), in ethanol (5 ml.) was added to a boiling solution of *p*-toluidine (0·5 g.) in water (30 ml.), containing acetic acid (2 ml.), sodium acetate (1 g.), and sodium hydrogen carbonate (0·05 g.). After 5 minutes' heating, the mixture was diluted with water (20 ml.) and cooled. Recrystallisation of the precipitate from aqueous ethanol or from methanol yielded N-*2'-quinoxalinylmethylene*-p-*toluidine* (0·37 g., 95%), as orange prisms or needles, m. p. 120—121° (Found: C, 77·8; H, 5·3; N, 17·5. $C_{16}H_{13}N_3$ requires C, 77·7; H, 5·3; N, 17·0%); light absorption in EtOH, 227 (4·32), *247* (4·40), 251 (4·44), *256* (4·40), *333* (4·24), 348 (4·27).

The aldehyde (1 g.) in ethanol (10 ml.), was condensed similarly with *p*-aminobenzoic acid (2·6 g.), in acetic acid (5 ml.) and water (200 ml.), containing sodium acetate (10 g.) and sodium hydrogen carbonate (0·5 g.). Crystallisation of the solid product from ethanol–pyridine yielded N-*2'-quinoxalinylmethylene*-p-*aminobenzoic acid* (1·6 g., 91%), as pale yellow needles, m. p. 288° (Found: C, 69·9; H, 4·6; N, 15·4. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%); light absorption in EtOH, 227 (4·50), 286 (4·50), 290 (4·50). This Schiff's base (1·0 g.) was hydrogenated over Adams catalyst (0·01 g.) in ethanol (250 ml.). When hydrogen-uptake ceased, the deep red solution was boiled with charcoal, filtered, concentrated under reduced pressure to 30 ml., and diluted with water (100 ml.). The light brown precipitate which was slowly formed was purified by precipitation with acetic acid from its solution in dilute aqueous ammonia; N-*2'-quinoxalinylmethyl*-p-*aminobenzoic acid* (VII; R = H) was so obtained as a pale brown amorphous solid melting indefinitely between 160° and 190° (Found: C, 69·0; H, 5·0; N, 15·1. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%); light absorption in EtOH, 237 (4·42), 251 (4·16), 257 (4·16), 268 (4·24), 291 (4·16), 314 (3·90).

3-Hydroxy-2-methylquinoxaline and its Derivatives.—*o*-Phenylenediamine (20 g.) in benzene (200 ml.) was treated with ethyl pyruvate (20 g.); after the vigorous reaction, which necessitated cooling, had abated, the crude 3-hydroxy-2-methylquinoxaline was collected and recrystallised from aqueous ethanol (yield, 24 g., 76%; m. p. 245—246°; lit., m. p. 245°); light absorption in 0·01N-NaOH, 237 (4·42), 343 (3·85). This compound (6·4 g.) and anhydrous sodium acetate (2·8 g.) were dissolved in warm acetic acid (120 ml.); a solution of bromine (6·2 g.) in acetic acid (20 ml.) was added gradually, with stirring, and the mixture heated on the steam-bath for 15 min. The crystals, which separated on cooling, were collected by filtration (7·1 g., 75%); sublimation at 4×10^{-5} mm. yielded *2-bromomethyl-3-hydroxyquinoxaline*, decomp. 225° (Found: C, 45·3; H, 3·5; Br, 33·35. $C_9H_7ON_2Br$ requires C, 45·3; H, 2·95; Br, 33·4%), characterised as the quaternary *pyridinium bromide*, needles (from ethanol), m. p. 244—245° (Found: C, 52·6; H, 4·05; Br, 24·6. $C_{14}H_{12}ON_3Br$ requires C, 52·85; N, 3·8; Br, 25·1%).

The bromomethyl compound (1 g.), ethyl *p*-aminobenzoate (0·7 g.) and calcium carbonate (0·45 g.) were refluxed in ethanol (100 ml.) for 4 hr. The filtered solution was diluted with water (200 ml.), and the pale brown precipitate which slowly formed was reprecipitated from its solution in dilute sodium hydroxide solution by acidification with acetic acid. The resulting N-(3-*hydroxy*-2-*quinoxalinylmethyl*)-p-*aminobenzoic acid* (VII; R = OH) was a light brown solid, decomp. 200° (Found: C, 64·2; H, 4·35; N, 14·7. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%); light absorption in 0·01N-NaOH, 227 (4·46), 236 (4·46), 328 (3·93), 348 (4·05), 358 (4·00).

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