

**79. Quinoxaline Derivatives. Part IV.\* Dihydro-oxo-1 : 4 : 5-triazanaphthalenecarboxyureides and Related spiroHydantoins.**

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The yellow compounds and their colourless isomers obtained by Rudy and Majer<sup>1</sup> from alloxan and 2 : 3-diaminopyridines are shown to be 3 : 4-dihydro-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxyureides and 1 : 2 : 3 : 4-tetrahydro-3-oxo-1 : 4 : 5-triazanaphthalene-2-*spiro*-5'-hydantoins respectively. The products from 2 : 3-diaminopyridines thus resemble those from *o*-phenylenediamines except that they cyclise faster and sometimes spontaneously.

CONDENSATION of alloxan with 2 : 3-diaminopyridine and with 2-alkylamino-3-aminopyridines in acid solution leads to analogues of alloxazine or *isalloxazine*<sup>2</sup> (*e.g.*, I; R = Me or Pr<sup>n</sup>), but in the absence of mineral acid the reaction yields yellow products which are readily converted into colourless isomers.<sup>1</sup> Rudy and Majer<sup>1</sup> formulated the latter as carboxyureides (II; R = H, Me, Pr<sup>n</sup>, Ph) and the yellow compounds, by analogy with products from *o*-phenylenediamines, as alloxan anils (III; R = H, Me, Pr<sup>n</sup>, Ph). The so-called "alloxan anils" of the *o*-phenylenediamine series are in fact 3 : 4-dihydro-3-oxoquinoxaline-2-carboxyureides<sup>3</sup> (*e.g.*, IV; R = H, Me, Ph), and it is now shown that Rudy and Majer's yellow compounds are 3 : 4-dihydro-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxyureides (II; R = H, Me, Pr<sup>n</sup>, Ph), although the unsubstituted compound is accompanied by its isomer (V; R = H). The colourless isomers are *spiro*hydantoins (VIII; R = H, Me, Pr<sup>n</sup>, Ph) formed by cyclisation of the ureides and are discussed below. The apparent anomaly noted by Rudy and Majer that 3-amino-2-dimethylaminopyridine failed to yield an "anil" with alloxan is explained by the inability of the dimethylamine to form a carboxyureide.

The pale yellow colour of the carboxyureides (II; R = H, Me, Pr<sup>n</sup>) is in marked

\* Part III, preceding paper.

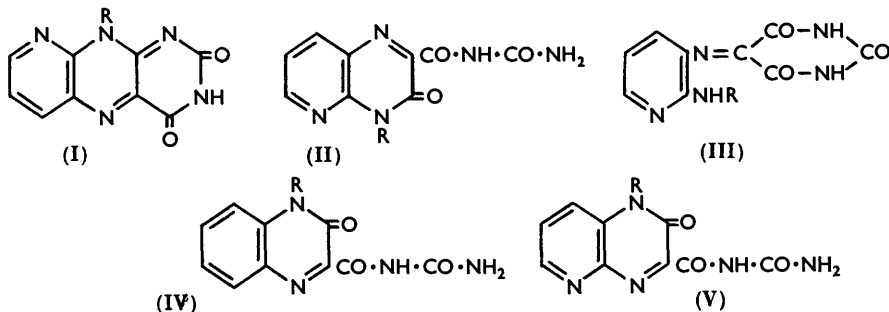
<sup>1</sup> Rudy and Majer, *Ber.*, 1938, **71**, 1323; 1939, **72**, 940.

<sup>2</sup> *Idem*, *Ber.*, 1938, **71**, 1243; see also Ziegler, *J. Amer. Chem. Soc.*, 1949, **71**, 1891.

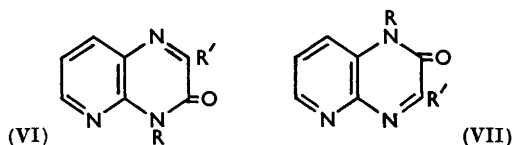
<sup>3</sup> King and Clark-Lewis, *J.*, 1951, 3379; *J.*, 1953, 172.

contrast to the intense colour of alloxan anils<sup>4,5</sup> comparable with (III), and moreover, failure of attempts<sup>1</sup> to effect cyclisation<sup>1,5,6</sup> to the alloxazine or *isalloxazine* analogues (I; R = H, Me) is understandable.

The ureides (II; R = H, Me) and (V; R = Me) were obtained in high yields from alloxan and the appropriate diaminopyridine. Alkaline hydrolysis of the ureides (II; R = H, Me) gave the acids (VI; R = H, Me; R' = CO<sub>2</sub>H) which by decarboxylation above the m. p. gave the two 3:4-dihydro-3-oxo-1:4:5-triazanaphthalenes (VI; R = H, Me, R' = H). Heating the triazanaphthalene-2-carboxyureide (II; R = Me) with acetic anhydride led to the *N*-acetylamide (VI; R = Me, R' = CO·NHAc), and in all the above reactions the triazanaphthalenecarboxyureides resemble their quinoxaline analogues.<sup>3</sup>



The products obtained by the above degradations were compared with authentic compounds prepared from the esters (VI; R = H, Me, R' = CO<sub>2</sub>Et) and (VII; R = Me, R' = CO<sub>2</sub>Et) which were synthesised from diethyl mesoxalate and the appropriate diaminopyridine. Thus 3-amino-2-methylaminopyridine and diethyl mesoxalate gave ethyl 3:4-dihydro-4-methyl-3-oxo-1:4:5-triazanaphthalene-2-carboxylate (VI; R = Me, R' = CO<sub>2</sub>Et) which, by ammonolysis and acetylation gave the *N*-acetylamide (VI; R = Me, R' = CO·NHAc). Hydrolysis of the ester (VI; R = Me, R' = CO<sub>2</sub>Et) and pyrolysis of the acid gave 3:4-dihydro-4-methyl-3-oxo-1:4:5-triazanaphthalene (VI; R = Me, R' = H) identical with that obtained from the ureide (II; R = Me). Reaction of alloxan or diethyl mesoxalate with 3-amino-2-methylaminopyridine and with 2-amino-3-methylaminopyridine gives products of known orientation. Similar condensations with 2:3-diaminopyridine however give mixtures (VI and VII; R = H) in which the former type (VI; R = H) predominate (over 90%), as expected from reaction of the alloxan (or diethyl



mesoxalate) carbonyl group with the more basic 3-amino-group. The two esters (VI and VII; R = H, R' = CO<sub>2</sub>Et) were separated by fractional crystallisation, but the ureide (II; R = H) is less easily separated from the isomeric contaminant (V; R = H) owing to the sparing solubilities and to a tendency to cyclise to *spirohydantoins* (discussed below). The products (II; R = H) and (VI; R = H, R' = CO<sub>2</sub>Et) from 2:3-diaminopyridine were orientated by conversion into 3-hydroxy-1:4:5-triazanaphthalene (VI; R = R' = H) which with diazomethane gave 3:4-dihydro-4-methyl-3-oxo-1:4:5-triazanaphthalene

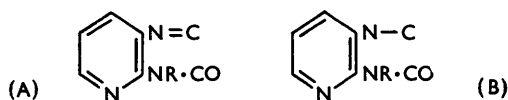
<sup>4</sup> Piloty and Finckh, *Annalen*, 1904, **333**, 37; King and Clark-Lewis, *J.*, 1951, 3080.

<sup>5</sup> Sachs and Meyerheim, *Ber.*, 1908, **41**, 3957; Hepner, Kerner, Simonberg, and Kaltmann, *Compt. rend. 17me congrès de chimie indust.*, 1937, **17**, 228; Wieland, Tartter, and Purrmann, *Annalen*, 1940, **545**, 209; Taylor, Cain, and Loux, *J. Amer. Chem. Soc.*, 1954, **76**, 1874; Brederick and Pfeiderer, *Chem. Ber.*, 1954, **87**, 1268.

<sup>6</sup> Pfeiderer, *ibid.*, 1955, **88**, 1625.

(VI; R = Me, R' = H) identical with a specimen obtained from 3-amino-2-methylamino-pyridine. The methylation gave a low yield of *N*-methyl compound, presumably owing to simultaneous formation of 3-methoxy-1 : 4 : 5-triazanaphthalene (not isolated), and no trace was found of the isomeric 1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene (VII; R = Me, R' = H), an authentic sample of which was prepared for reference. Orientation of 1 : 4 : 5-triazanaphthalene derivatives unsymmetrically substituted in the 2 : 3-positions<sup>7</sup> formed from 2 : 3-diaminopyridine has not previously been achieved, the orientation of substituents usually resting on analogy<sup>8,9</sup> with results obtained in the pteridine field. Chemical proof of such orientations can be obtained in the numerous cases where either the 2- or the 3-substituent is a hydroxyl group by conversion into the *N*-methyl derivative, and synthesis of the latter.

The triazanaphthalenecarboxyureide structure having been established for the yellow products formed from alloxan and diaminopyridines, attention was directed to the structures of the colourless isomers obtained from them by treatment with bases or with acids. The light-absorption characteristics of the colourless isomers are of simple aromatic type due to change from the carboxyureide chromophore (A) to the reduced system (B), and



this change is most simply accounted for by cyclisation of the ureides (*e.g.*, II; R = H, Me) to 1 : 2 : 3 : 4-tetrahydro-3-oxo-1 : 4 : 5-triazanaphthalene-2-*spiro*-5'-hydantoin (VIII; R = H, Me). Support for the structure of these *spiro*-hydantoin was obtained from the conversion of the analogous quinoxaline-2-carboxyureides (IV; R = H, Me, Ph) into the previously unknown tetrahydroquinoxaline-2-*spiro*-5'-hydantoin by cyclisation,<sup>10</sup> which is accompanied by changes in ultraviolet spectra similar to those observed with triazanaphthalenes. The *spiro*hydantoin (VIII; R = Me) and the two ureides (II; R = H, Me) with diazomethane each gave 1 : 2 : 3 : 4-tetrahydro-4 : 3'-dimethyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-*spiro*-5'-hydantoin (X; R = H), which illustrates the ready cyclisation of triazanaphthalene-carboxyureides and confirms the orientation of the ureide (II; R = H). More prolonged treatment of the hydantoin (X; R = H) with an excess of diazomethane gave the fully methylated spiran (X; R = Me), and similar methylations of the ureide (V; R = Me) and of the spiran (IX) gave successively the 3'-methyl (XI; R = H) and the 1 : 1' : 3'-trimethyl compound (XI; R = Me). The failure of the last compound to yield a nitroso-derivative with nitrous acid is possibly due to resonance stabilisation of the amidinium ion (conjugate acid of XI; R = Me) as the isomeric secondary amine (X; R = Me) readily formed a nitroso-compound (XII). Alkaline hydrolysis of this nitroso-amine (XII) gave 3 : 4-dihydro-4-methyl-2-methylamino-3-oxo-1 : 4 : 5-triazanaphthalene (VI; R = Me, R' = NHMe) in a reaction similar to that described<sup>10</sup> for the analogous quinoxaline compound.

The triazanaphthalene-carboxyureides and -*spiro*hydantoin are generally similar in properties to their quinoxaline analogues, although cyclisation of the ureides occurs more easily in the triazanaphthalene series. Boiling dilute hydrochloric acid converts the triazanaphthalenecarboxyureides into acid-stable *spiro*hydantoin whereas it hydrolyses the quinoxalinecarboxyureides. The ureides and hydantoin of both series are rapidly hydrolysed by aqueous sodium hydroxide to the carboxylic acids. 1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylic acid (VII; R = Me, R' = CO<sub>2</sub>H) differed from the corresponding quinoxaline acid in that thermal decarboxylation gave,

<sup>7</sup> For unequivocal syntheses from 2 : 6-diamino-3-nitrosopyridine, and for leading references, see Osdene and Timmis, *J.*, 1955, 2032.

<sup>8</sup> Korte, *Chem. Ber.*, 1952, **85**, 1012.

<sup>9</sup> Leese and Rydon, *J.*, 1955, 303.

<sup>10</sup> Preceding paper.



with water and with methanol (Found: C, 46.6; H, 3.3; N, 29.7.  $C_9H_7O_3N_5$  requires C, 46.3; H, 3.0; N, 30.0%). Rudy and Majer<sup>1</sup> record m. p. 280—285° and Ziegler<sup>2</sup> m. p. 277°.

3 : 4-Dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxyureide (II; R = Me).—3-Amino-2-methylaminopyridine<sup>12</sup> (2.4 g.) in water (25 c.c.) was added to alloxan monohydrate (5 g.) in water (50 c.c.). The bright yellow needles of 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxyureide (4.4 g., 91%), m. p. 232° (decomp.), were collected after 1 hr. and washed with water and with ethanol (Found: C, 48.4; H, 3.8; N, 28.4; N-Me, 5.2.  $C_{10}H_9O_3N_5$  requires C, 48.6; H, 3.7; N, 28.3; N-Me, 6.1%). Light absorption: max. 228 ( $\epsilon$  21,600), 278—279 ( $\epsilon$  4300), and 361  $m\mu$  ( $\epsilon$  7500); min. 269 (4100) and 303  $m\mu$  ( $\epsilon$  2500). Rudy and Majer<sup>1</sup> record m. p. 235—236° (decomp.). The ureide dissolves in aqueous alkali to give a yellow solution, but is sparingly soluble in other solvents.

1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxyureide (V; R = Me).—2-Amino-3-methylaminopyridine<sup>11</sup> (1.2 g.) in water (12 c.c.) added to alloxan monohydrate (2.5 g.) in water (25 c.c.) similarly gave a hemihydrate (2.2 g., 91%), m. p. 193° (decomp.) (Found: C, 46.6; H, 3.95.  $C_{10}H_9O_3N_5 \cdot \frac{1}{2}H_2O$  requires C, 46.9; H, 3.9%), which lost water slowly at 100° and gave anhydrous 1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxyureide, m. p. 284° (decomp.), when dried at 150°/1 mm. (Found: C, 48.1; H, 3.7.  $C_{10}H_9O_3N_5$  requires C, 48.6; H, 3.7%). The ureide is slightly soluble in boiling acetic acid, which causes cyclisation to the spirohydantoin, and gives yellow solutions in aqueous alkali.

1 : 2 : 3 : 4-Tetrahydro-3-oxo-1 : 4 : 5-triazanaphthalene-2-spiro-5'-hydantoin (VIII; R = H).—The above ureide (II; R = H) (0.9 g.) was suspended in boiling water (70 c.c.) and dissolved by addition of 2N-potassium hydroxide (3 c.c.). The dark yellow solution was immediately neutralised with 2N-hydrochloric acid, and boiling was continued for several minutes. The precipitated hydantoin (0.7 g., 78%), m. p. 277—278°, was collected from the cold solution, and recrystallisation of the solid from methanol (by Soxhlet extraction) gave a colourless powder, m. p. 280° (decomp.) (Found: C, 45.9; H, 3.35.  $C_9H_7O_3N_5$  requires C, 46.3; H, 3.0). Rudy and Majer<sup>1</sup> record m. p. 306° (decomp., rapid heating). The compound is sparingly soluble in most solvents but dissolves readily in aqueous alkali to a colourless solution. A blue fluorescence was observed in an ethanol solution under ultraviolet light. The spirohydantoin (80%) was also obtained by boiling the ureide with N-hydrochloric acid for 1 hr. before neutralisation.

1 : 2 : 3 : 4-Tetrahydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-spiro-5'-hydantoin (VIII; R = Me).—The ureide (II; R = Me) was converted into the hydantoin (80%) by 2N-hydrochloric acid on a steam-bath in 30 min. Cyclisation (85%) was also effected as for the analogue (VIII; R = H), but more readily. This spiran crystallised in needles, m. p. 240° (decomp.), which dissolved to colourless solutions in aqueous alkali, and showed a blue fluorescence in ethanol (Found: C, 48.9; H, 3.8; N-Me, 5.2.  $C_{10}H_9O_3N_5$  requires C, 48.6; H, 3.7; N-Me, 6.1%). Rudy and Majer<sup>1</sup> record m. p. 239° (decomp.). Light absorption: max. 312  $m\mu$  ( $\epsilon$  8100); min. 268—269  $m\mu$  ( $\epsilon$  2100). The hydantoin (0.5 g.) dissolved during 2 hr. when boiled with acetic anhydride (30 c.c.) and acetyl chloride (10 c.c.), and the solution was boiled for a further hour. Evaporation under reduced pressure followed by re-evaporation after the addition of methanol gave crystalline 1-acetyl-1 : 2 : 3 : 4-tetrahydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-spiro-5'-hydantoin, which crystallised from water containing a little ethanol (charcoal) in needles (0.28 g., 46%), m. p. 263—264° (decomp.) (Found: C, 47.2; H, 4.3; N, 23.0.  $C_{12}H_{11}O_4N_5 \cdot H_2O$  requires C, 46.9; H, 4.3; N, 22.8%).

1 : 2 : 3 : 4-Tetrahydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-spiro-5'-hydantoin (IX).—Cyclisation of the ureide (V; R = Me) by successive treatment with 2N-alkali and 2N-acid as described above gave 1 : 2 : 3 : 4-tetrahydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-spiro-5'-hydantoin (90%) in needles, m. p. 284—287° (decomp.) (Found: C, 48.1; H, 3.9; N, 28.2.  $C_{10}H_9O_3N_5$  requires C, 48.6; H, 3.7; N, 28.3%). The compound dissolved in aqueous alkali to a colourless solution, and ethanolic solutions showed a blue fluorescence. Light absorption: max. 308  $m\mu$  ( $\epsilon$  10,100); min. at 267  $m\mu$  ( $\epsilon$  2200). The hydantoin (1 g.) was boiled with acetic anhydride (50 c.c.) and when it had completely dissolved (20 min.) acetyl chloride (20 c.c.) was added and the solution was boiled for 30 min. Evaporation under reduced pressure left a residue which crystallised (0.68 g.; m. p. 195—200°) when treated with methanol (20 c.c.). The 4 : 1'-diacetyl derivative (0.32 g.) crystallised from ethanol in prisms, m. p. 204° with resolidification and remelting at 268° (decomp.) (Found: C, 50.8; H, 4.2; N, 20.9.  $C_{14}H_{13}O_5N_5$  requires C, 50.8; H, 4.0; N, 21.1%). The diacetyl compound was also obtained by the action

<sup>12</sup> Shick, Binz, and Schulz, *Ber.*, 1936, **69**, 2602.

of acetic anhydride on both the hydantoin and the corresponding ureide but in these cases was less easily purified.

*Ethyl 3-Hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylate* (VI; R = H, R' = CO<sub>2</sub>Et) and *Ethyl 2-Hydroxy-1 : 4 : 5-triazanaphthalene-3-carboxylate* (VII; R = H, R' = CO<sub>2</sub>Et).—A solution of 2 : 3-diaminopyridine (4 g.) and diethyl mesoxalate (10 c.c.) in ethanol (80 c.c.) and water (60 c.c.) was boiled for 2 hr., and material which crystallised from the cold solution was collected. Recrystallisation from ethanol gave a mixture (5 g., 62%), which was separated by fractional crystallisation from ethanol into *ethyl 3-hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylate* (2.5 g.), pale yellow, flat needles, m. p. 213—214° (Found : C, 55.1; H, 4.4; N, 19.2. C<sub>10</sub>H<sub>9</sub>O<sub>3</sub>N<sub>3</sub> requires C, 54.8; H, 4.1; N, 19.2%), and *ethyl 2-hydroxy-1 : 4 : 5-triazanaphthalene-3-carboxylate* (0.09 g.), pale yellow plates, m. p. 247—254° (decomp.) (Found : C, 54.8; H, 4.1%).

*Ethyl 3 : 4-Dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylate* (VI; R = Me, R' = CO<sub>2</sub>Et).—3-Amino-2-methylaminopyridine (1.7 g.) in ethanol (20 c.c.) was boiled for 20 min. with diethyl mesoxalate (2.6 g.) and the solution was then diluted with water (60 c.c.). Crystallisation gave *ethyl 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylate* in yellow plates (2.1 g., 65%), m. p. 115—118° raised by recrystallisation from aqueous ethanol to m. p. 119.5—120° (Found : C, 57.0; H, 4.8. C<sub>11</sub>H<sub>11</sub>O<sub>3</sub>N<sub>3</sub> requires C, 56.6; H, 4.8%). Light absorption : max. 225—226 (ε 23,900) and 345—346 mμ (ε 8700); inf. 264—274 mμ (ε 2600); min. 291 mμ (ε 1400).

*Ethyl 1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylate* (VII; R = Me; R' = CO<sub>2</sub>Et).—A solution of 2-amino-3-methylaminopyridine (1 g.) and ethyl mesoxalate (1.5 g.) in ethanol (10 c.c.) was boiled for 30 min., and when cold deposited *ethyl 1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylate* in pale yellow plates (0.97 g., 51%), m. p. 157—158° raised by recrystallisation from ethanol to m. p. 161—162° (Found : N, 17.9. C<sub>11</sub>H<sub>11</sub>O<sub>3</sub>N<sub>3</sub> requires N, 18.0%).

*3-Hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylic Acid* (VI; R = H, R' = CO<sub>2</sub>H).—(a) The above-mentioned ethyl ester (VI; R = H, R' = CO<sub>2</sub>Et) (2.9 g.) in 2N-potassium hydroxide (100 c.c.) was boiled for 2 min., and 30 min. later the solution was neutralised with 2N-hydrochloric acid which precipitated the acid as a light yellow powder (1.92 g., 76%), m. p. 230° raised to m. p. 232° (decomp.) by reprecipitation from aqueous ammonia (charcoal) (Found : C, 50.4; H, 2.8; N, 21.3. Calc. for C<sub>8</sub>H<sub>5</sub>O<sub>3</sub>N<sub>3</sub> : C, 50.3; H, 2.6; N, 22.0%). Rudy and Majer<sup>1</sup> record m. p. 235°.

(b) *3-Hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxyureide* (0.5 g.) in aqueous 2N-potassium hydroxide (10 c.c.) was heated on a steam-bath for 1½ hr. Acidification (pH ca. 2.0) gave an immediate precipitate of the acid (0.13 g., 32%), m. p. 234° alone and when mixed with the acid obtained by method (a). By boiling the filtrate, and by boiling the above acid or its ethyl ester with 2N-hydrochloric acid, a small quantity of red compound was obtained in needles, m. p. above 360° (decomp.). The red compound is apparently analogous to the di(triazanaphthylidene) (XIII) described below.

*3 : 4-Dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylic Acid* (VI; R = Me, R' = CO<sub>2</sub>H).—(a) *3 : 4-Dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxyureide* (0.5 g.) in 2N-potassium hydroxide (10 c.c.) was heated on a steam-bath for 1½ hr. and the acidified solution was extracted with chloroform (3 × 20 c.c.). The dried chloroform solution (MgSO<sub>4</sub>) was evaporated and crystallisation of the residue (0.2 g.) from benzene gave the acid in yellow prisms (0.08 g., 20%), m. p. 186° (decomp.) (Found : N, 21.0. C<sub>9</sub>H<sub>7</sub>O<sub>3</sub>N<sub>3</sub> requires N, 20.5%). Light absorption : max. 223 (ε 17,500), 324—326 mμ (ε 9600); inf. 264—276 mμ (ε 2500); min. 283—284 mμ (ε 2300).

(b) *3 : 4-Dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-spiro-5'-hydantoin* (1.0 g.) was hydrolysed as above for 3 hr. and gave the preceding acid which crystallised from benzene in prisms (0.35 g., 42%), m. p. and mixed m. p. 186° (decomp.).

(c) Alkaline hydrolysis of ethyl *3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylate* similarly gave the acid, m. p. 186° (decomp.) alone and when mixed with specimens obtained by methods (a) and (b).

*1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylic Acid* (VII; R = Me, R' = CO<sub>2</sub>H).—(a) A solution of ethyl *1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylate* (0.75 g.) in 2N-hydrochloric acid (15 c.c.) was heated on a steam-bath for 30 min. before neutralisation with 2N-potassium hydroxide and filtration from a red by-product (0.03 g.). The acid (0.43 g., 63%), m. p. 143° (decomp.), crystallised from the aqueous filtrate saturated

with chloroform (*i.e.*, after extraction with chloroform), and was sparingly soluble in chloroform, acetone, ether, ethanol, or benzene. 1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylic acid crystallised from water as a hydrate in thick rectangular plates, m. p. 146—148° (decomp.) after drying at 80°/1 mm., which became red on exposure to air (Found : C, 46.5; 46.8; H, 4.3, 4.6.  $C_9H_7O_3N_3 \cdot 1\frac{1}{2}H_2O$  requires C, 46.6; H, 4.3%). The monohydrate, m. p. 163° (decomp.), was obtained after drying the acid at 120°/1 mm. (Found : C, 48.7; H, 4.0; loss, 4.2.  $C_9H_7O_3N_3 \cdot H_2O$  requires C, 48.4; H, 4.1; loss 3.9%). Alkaline hydrolysis of the ester occurred readily with 2N-potassium hydroxide and neutralisation gave the acid described above.

(b) 1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylic acid hydrate, m. p. and mixed m. p. 146—148° (decomp.), was obtained together with a red basic by-product (XIII) (see below) by alkaline hydrolysis of the corresponding ureide.

*Di*-(1 : 2 : 3 : 4-tetrahydro-1-methyl-2-oxo-1 : 4 : 5-triaza-3-naphthylidene) (XIII).—Ethyl 1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylate (0.5 g.) was boiled with 2N-hydrochloric acid (30 c.c.) for 3 hr. before basification with aqueous ammonia, and the red precipitate was collected. The *di*(triazanaphthylidene) was obtained in dark red needles (0.12 g., 35%), m. p. >360° (decomp.), by gradually adding aqueous ammonia to its boiling solution in dilute hydrochloric acid (Found : C, 59.6; H, 4.4; N, 25.7.  $C_{16}H_{14}O_2N_6$  requires C, 59.6; H, 4.4; N, 26.1%). Solutions in dilute hydrochloric acid showed an orange-red fluorescence under ultraviolet light, and the colourless solution obtained by reduction with zinc dust showed an intense blue fluorescence.

*Di*-(1 : 2 : 3 : 4-tetrahydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphth-2-ylidene).—Ethyl 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylate (0.5 g.), treated as above, gave the *di*(triazanaphthylidene) (0.1 g., 30%), red needles, m. p. 303—304° (decomp.) (Found : C, 59.6; H, 4.4; N, 25.6%), slightly soluble in dilute hydrochloric acid to a deep magenta solution which exhibited an orange-red fluorescence in ultraviolet light. The colour of the acid solution was discharged by the addition of zinc dust and the solution then showed an intense blue fluorescence in ultraviolet light. The colour of solutions of the compound in dilute hydrochloric acid faded slowly on standing, and more quickly in sunlight, and the colourless solution showed a yellowish-green fluorescence under ultraviolet light.

3-Hydroxy-1 : 4 : 5-triazanaphthalene (as VI; R = R' = H).—3-Hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylic acid (1.9 g.) was heated under nitrogen at 250° until effervescence ceased (2—3 min.), and the residue was sublimed at 230°/2 mm. Crystallisation of the sublimate (0.76 g.) from boiling water (30 c.c.) gave 3-hydroxy-1 : 4 : 5-triazanaphthalene in pale yellow needles (0.56 g., 38%), m. p. 239—240° (Found : C, 57.3; H, 3.7; N, 28.6.  $C_7H_5ON_3$  requires C, 57.2; H, 3.4; N, 28.5%). A higher yield (60%) was obtained by decarboxylation of the acid (0.2 g.) at 240° under the sublimation conditions.

3 : 4-Dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene (VI; R = Me, R' = H).—(a) Pyrolysis of 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylic acid (0.5 g.) at 190° under nitrogen (2—3 minutes) and sublimation of the residue under reduced pressure gave crystalline 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene (0.22 g., 56%), m. p. 115—117°, which crystallised from hexane in colourless needles, m. p. 117°, and coloured in air (Found : C, 60.1; H, 4.45; N, 26.0.  $C_8H_7ON_3$  requires C, 59.6; H, 4.4; N, 26.1%). Light absorption : max. 221 ( $\epsilon$  27,100) and 329—330 m $\mu$  ( $\epsilon$  8800); min. 279 m $\mu$  ( $\epsilon$  1000).

(b) Diazomethane (*ca.* 0.16 g.) in ether (10 c.c.) was added to a solution of 3-hydroxy-1 : 4 : 5-triazanaphthalene (0.3 g.) in chloroform (50 c.c.) and methanol (10 c.c.) at 5°; after 4 hr. the excess of diazomethane was destroyed by addition of acetic acid and solvents were then removed from the solution by distillation. Crystallisation of the oily residue from hexane followed by recrystallisation gave 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene (0.05 g., 15%), m. p. and mixed m. p. 117°.

1 : 2-Dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene (VII; R = Me, R' = H).—Decarboxylation and sublimation of 1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene-3-carboxylic acid (0.43 g.) at 210°/15 mm. gave a white solid (0.12 g., 35%, after resublimation). Crystallisation of the sublimate from benzene gave 1 : 2-dihydro-1-methyl-2-oxo-1 : 4 : 5-triazanaphthalene in long needles, m. p. 223—224° (Found : C, 60.2; H, 4.5%). The compound is more stable in air and much less soluble in organic solvents than the isomer described above. The residue remaining after sublimation of the triazanaphthalene dissolved in dilute hydrochloric acid, and basification of the hot solution with aqueous ammonia gave red needles (0.1 g.,

30%) of di-(1 : 2 : 3 : 4-tetrahydro-1-methyl-2-oxo-1 : 4 : 5-triaza-3-naphthylidene) m. p.  $>360^\circ$  (decomp.) (cf. above).

3-*Hydroxy*-1 : 4 : 5-*triazanaphthalene*-2-*carboxyamide* (VI; R = H, R' = CO·NH<sub>2</sub>).—A solution of ethyl 3-hydroxy-1 : 4 : 5-triazanaphthalene-2-carboxylate (0.3 g.) in aqueous ammonia (*d* 0.88; 5 c.c.) rapidly deposited the amide. Next day the thick suspension was diluted with water, whereupon the solid dissolved, and after evaporation of the solution under reduced pressure the crystalline residue (needles) was collected with the aid of dilute acetic acid, washed with methanol, and dried. The *amide* (0.24 g., 92%) was thus obtained in the form of yellow needles which did not melt below  $360^\circ$  but gradually decomposed above  $300^\circ$ , and these properties were unchanged by recrystallisation of the compound from dimethylformamide (25 c.c.) (Found: C, 50.0; H, 3.5; N, 29.2. C<sub>8</sub>H<sub>8</sub>O<sub>2</sub>N<sub>4</sub> requires C, 50.5; H, 3.2; N, 29.5%). Light absorption: max. 226—227 ( $\epsilon$  20,200) and 358—359 m $\mu$  ( $\epsilon$  7900); inf. 264—272 m $\mu$  ( $\epsilon$  4000); min. 296 m $\mu$  ( $\epsilon$  1850).

3 : 4-*Dihydro*-4-*methyl*-3-*oxo*-1 : 4 : 5-*triazanaphthalene*-2-*carboxyamide* (VI; R = Me; R' = CO·NH<sub>2</sub>).—Addition of saturated methanolic ammonia (20 c.c.) to a methanol solution (10 c.c.) of ethyl 3 : 4-dihydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-carboxylate (0.5 g.) caused rapid separation of the sparingly soluble *amide* (0.44 g., ca. 100%), m. p.  $280^\circ$ , which recrystallised in yellow prisms, m. p.  $284$ — $285^\circ$  (decomp.), from ethanol (Soxhlet) (Found: N, 27.9. C<sub>9</sub>H<sub>8</sub>O<sub>2</sub>N<sub>4</sub> requires N, 27.5%). Light absorption: max. 226 ( $\epsilon$  25,200), 275 ( $\epsilon$  4000), and 350—360 m $\mu$  ( $\epsilon$  9500); min. 263—264 ( $\epsilon$  3700) and 296 m $\mu$  ( $\epsilon$  2300).

1 : 2-*Dihydro*-1-*methyl*-2-*oxo*-1 : 4 : 5-*triazanaphthalene*-3-*carboxyamide* (VII; R = Me; R' = CO·NH<sub>2</sub>).—The ethyl ester (0.5 g.) of the corresponding acid was dissolved in ethanol (25 c.c.) and treated with aqueous ammonia (20 c.c.), and the warm solution was kept for 1 hr. before evaporation to dryness under reduced pressure. Crystallisation of the residue from water (25 c.c.; charcoal) gave the *amide* in yellow needles (0.17 g., 39%), m. p.  $261$ — $262^\circ$  raised by recrystallisation to m. p.  $264$ — $265^\circ$  (decomp.). The yellow colour was rapidly discharged by drying the amide at  $100^\circ$ , after which it remained colourless (Found: C, 52.9; H, 4.0. C<sub>9</sub>H<sub>8</sub>O<sub>2</sub>N<sub>4</sub> requires C, 52.9; H, 4.0%). Light absorption: max. 229 ( $\epsilon$  22,800) and 357 m $\mu$  ( $\epsilon$  8500); min. 291 m $\mu$  ( $\epsilon$  3000).

2-*Acetylcarbamoyl*-3 : 4-*dihydro*-4-*methyl*-3-*oxo*-1 : 4 : 5-*triazanaphthalene* (VI; R = Me, R' = CO·NHAc).—(a) The *N*-*acetylamide* was prepared by boiling the amide (0.2 g.) with acetic anhydride (10 c.c.) and crystallised from the concentrated solution (3 c.c.) in yellow prisms (0.18 g., 74%), m. p.  $198^\circ$ . It crystallised from benzene or aqueous ethanol as colourless prisms or as bright yellow needles, both melting at  $204$ — $205^\circ$  (Found: N, 23.1. C<sub>11</sub>H<sub>10</sub>O<sub>3</sub>N<sub>4</sub> requires N, 22.8%). Light absorption: max. 339—340 m $\mu$  ( $\epsilon$  9400); min. 288 m $\mu$  ( $\epsilon$  2100).

(b) 3 : 4-*Dihydro*-4-*methyl*-3-*oxo*-1 : 4 : 5-*triazanaphthalene*-2-*carboxyureide* (1 g.) was boiled with acetic anhydride (30 c.c.) for 7 hr. and isolation of the product as described under (a) gave the same *N*-*acetylamide* (0.6 g., 60%), m. p. and mixed m. p.  $204$ — $205^\circ$  (Found: C, 54.2; H, 4.2; N, 22.7; Ac, 16.3. Calc. for C<sub>11</sub>H<sub>10</sub>O<sub>3</sub>N<sub>4</sub>: C, 53.7; H, 4.1; N, 22.8; Ac, 17.5%). The *spirohydantoin* (0.5 g.) corresponding to the ureide gave the *N*-*acetylamide* (0.27 g., 54%), m. p. and mixed m. p.  $204$ — $205^\circ$ , when similarly treated with acetic anhydride (15 c.c.) for 2 hr.

3-*Acetylcarbamoyl*-1 : 2-*dihydro*-1-*methyl*-2-*oxo*-1 : 4 : 5-*triazanaphthalene* (VII; R = Me, R' = CO·NHAc).—The *N*-*acetylamide* was prepared by boiling the amide (0.14 g.) with acetic anhydride (25 c.c.) for 1 hr. and evaporating the solution. The brown, viscous residue was dissolved in boiling benzene (50 c.c.; charcoal) and after concentration the cold solution (20 c.c.) gave needles (0.09 g., 53%), m. p.  $194$ — $195^\circ$  raised to  $195$ — $196^\circ$  by recrystallisation (Found: C, 53.8; H, 4.1; N, 22.9. C<sub>11</sub>H<sub>10</sub>O<sub>3</sub>N<sub>4</sub> requires C, 53.7; H, 4.1; N, 22.8%). The compound is dichromatic and may be obtained in colourless or bright yellow needles from benzene. Light absorption: max. 224—225 ( $\epsilon$  22,400) and 347 m $\mu$  ( $\epsilon$  9250); min. at 287 m $\mu$  ( $\epsilon$  1600).

1 : 2 : 3 : 4-*Tetrahydro*-4 : 3'-*dimethyl*-3-*oxo*-1 : 4 : 5-*triazanaphthalene*-2-*spiro*-5'-*hydantoin* (X; R = H).—(a) A stirred suspension of 1 : 2 : 3 : 4-tetrahydro-4-methyl-3-oxo-1 : 4 : 5-triazanaphthalene-2-*spiro*-5'-*hydantoin* (1.0 g.) in methanol (100 c.c.) was treated with ethereal diazomethane (180 c.c.) prepared from *N*-methyl-*N*-nitrosotoluene-*p*-sulphonamide (9 g.). The solid dissolved within 2 hr.; the solution was then evaporated to dryness, and crystallisation of the residue from water (80 c.c.; charcoal) gave the 4 : 3'-*dimethyl compound* (0.64 g., 60%) in plates, m. p.  $254$ — $255^\circ$  (Found: C, 50.8; H, 4.2; N, 26.8; *N*-Me, 9.3. C<sub>11</sub>H<sub>11</sub>O<sub>3</sub>N<sub>4</sub> requires



C, 50.6; H, 4.2; N, 26.8; *N*-Me, 11.5%). Light absorption: max. 310—311  $\mu$  ( $\epsilon$  8800), min. 267—268  $\mu$  ( $\epsilon$  2000). It is readily soluble in methanol or ethanol, and less soluble in benzene or water. The methylhydantoin dissolved in 2*N*-potassium hydroxide and hydrolysis gave 3:4-dihydro-4-methyl-3-oxo-1:4:5-triazanaphthalene-2-carboxylic acid, m. p. and mixed m. p. 186° (decomp.), but the methylhydantoin was recovered (70%) after being boiled with acetic anhydride for 30 min.

(b) A suspension of 3:4-dihydro-4-methyl-3-oxo-1:4:5-triazanaphthalene-2-carboxyureide (1.0 g.) was treated with ethereal diazomethane at 0° and after 3 hr. the solution was filtered from undissolved material (0.1 g.). The 4:3'-dimethyl derivative (0.49 g., 44%), m. p. and mixed m. p. 254—255°, was isolated from the filtrate as described under (a).

1:2:3:4-Tetrahydro-4:1':3'-trimethyl-3-oxo-1:4:5-triazanaphthalene-2-spiro-5'-hydantoin (X; R = Me).—A solution of the hydantoin (VIII; R = Me) (4 g.) in methanol (500 c.c.) was treated at room temperature with ethereal diazomethane from methylnitrosourea (30 g.). After 3 hr. the solvents were removed and the residue was dissolved in boiling water (80 c.c.; charcoal) and filtered when cold from the 4:3'-dimethyl compound (0.65 g.), m. p. 251—253°. Refrigeration of the concentrated filtrate gave a crystalline mixture from which the trimethyl compound was extracted with hot benzene, leaving an insoluble residue (0.8 g.) of the foregoing 3'-methylhydantoin. The 4:1':3'-trimethyl derivative crystallised from the cold benzene in rods (0.56 g.), m. p. 173—174° raised to 174—175° by recrystallisation (Found: C, 52.8; H, 5.0; N, 25.8; *N*-Me, 12.2.  $C_{12}H_{13}O_3N_5$  requires C, 52.4; H, 4.8; N, 25.5; *N*-Me, 16.4%). A further quantity of the 1':3'-dimethylhydantoin (0.52 g., 62%) was isolated as described above after treatment of the 3'-methylhydantoin (0.8 g.) with diazomethane (1.6 g.) in ether (150 c.c.) for 24 hr. at 20°.

1:2:3:4-Tetrahydro-1:3'-dimethyl-2-oxo-1:4:5-triazanaphthalene-3-spiro-5'-hydantoin (XI; R = H).—A solution of 1:2:3:4-tetrahydro-1-methyl-2-oxo-1:4:5-triazanaphthalene-2-spiro-5'-hydantoin (0.6 g.) in methanol (600 c.c.) was treated at room temperature with diazomethane (1 g.) in ether (100 c.c.) for a short time and the solution was then distilled under reduced pressure. Crystallisation of the residue from aqueous methanol gave the 1:3'-dimethyl compound in small prisms (0.23 g., 36%), m. p. 282—284° raised to m. p. 287° by recrystallisation (Found: C, 50.6; H, 4.2; N, 26.5; *N*-Me, 10.1.  $C_{11}H_{11}O_3N_5$  requires C, 50.6; H, 4.2; N, 26.8; *N*-Me, 11.5%). When treated with ethereal diazomethane as described above the corresponding ureide underwent cyclisation and methylation to the 3'-methylhydantoin, m. p. and mixed m. p. 287°.

1:2:3:4-Tetrahydro-1:1':3'-trimethyl-2-oxo-1:4:5-triazanaphthalene-3-spiro-5'-hydantoin (XI; R = Me).—A solution of 1:2:3:4-tetrahydro-1-methyl-2-oxo-1:4:5-triazanaphthalene-3-spiro-5'-hydantoin (1.1 g.) in methanol (1 l.) was treated with ethereal diazomethane prepared from nitrosomethylurea (20 g.) and the mixture was concentrated to 200 c.c. The solution (200 c.c.) was treated with further diazomethane (from methylnitrosourea, 30 g.) and, after 24 hr. at room temperature, was evaporated. Crystallisation of the residue from aqueous methanol gave 1:2:3:4-tetrahydro-1:1':3'-trimethyl-2-oxo-1:4:5-triazanaphthalene-3-spiro-5'-hydantoin in small rods (0.4 g., 33%), m. p. 209° raised by recrystallisation from benzene or from water to m. p. 218—219° (Found: C, 52.5; H, 4.7; N, 25.6; *N*-Me, 13.9.  $C_{12}H_{13}O_3N_5$  requires C, 52.4; H, 4.8; N, 25.5; *N*-Me, 16.4%). Light absorption: max. 307  $\mu$  ( $\epsilon$  9300); min. 265—266  $\mu$  ( $\epsilon$  1900). The compound did not yield a nitroso-derivative.

1:2:3:4-Tetrahydro-4:1':3'-trimethyl-1-nitroso-3-oxo-1:4:5-triazanaphthalene-2-spiro-5'-hydantoin (XII).—Sodium nitrite (0.4 g.) in water was added to a solution of 1:2:3:4-tetrahydro-4:1':3'-trimethyl-3-oxo-1:4:5-triazanaphthalene-2-spiro-5'-hydantoin (0.6 g.) in water (50 c.c.) and acetic acid (4 c.c.) at 0°. The nitroso-derivative rapidly crystallised as bright yellow needles (0.59 g., 89%), decomp. 154—155°. It recrystallised from aqueous methanol in orange prisms, decomp. 155—220° (Found: N, 27.4.  $C_{12}H_{12}O_4N_6$  requires N, 27.6%).

3:4-Dihydro-4-methyl-2-methylamino-3-oxo-1:4:5-triazanaphthalene (VI; R = Me, R' = NHMe).—Boiling the above nitroso-amine (0.6 g.) with 2.5*N*-sodium hydroxide (60 c.c.) for 10 min. caused the evolution of methylamine and a precipitate (0.13 g., 35%) which was collected (needles) by filtration of the cold suspension. The filtrate was boiled for 30 min., but the solution remained clear and an ether extract of the cooled solution left a negligible residue on evaporation. Crystallisation of the solid (0.13 g.) from water (80 c.c.) gave 3:4-dihydro-4-methyl-2-methylamino-3-oxo-1:4:5-triazanaphthalene in long thin needles, m. p. 211—212°

(Found : C, 57.0; H, 5.3; N, 29.8.  $C_9H_{10}ON_4$  requires C, 56.8; H, 5.3; N, 29.5%). (For an analogous reaction see preceding paper.) The amine dissolved readily in ethanol, but was sparingly soluble in boiling water and less soluble in aqueous alkali.

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