Synthesis and Some Properties of Dyes containing the Pyrano[2,3-*d*]-pyrimidine Nucleus

By **Joseph Bailey**, Research Division, Kodak Limited, Headstone Drive, Harrow, Middlesex*, HA1 4TY
John A. Elvidge, University of Surrey, Guildford, Surrey

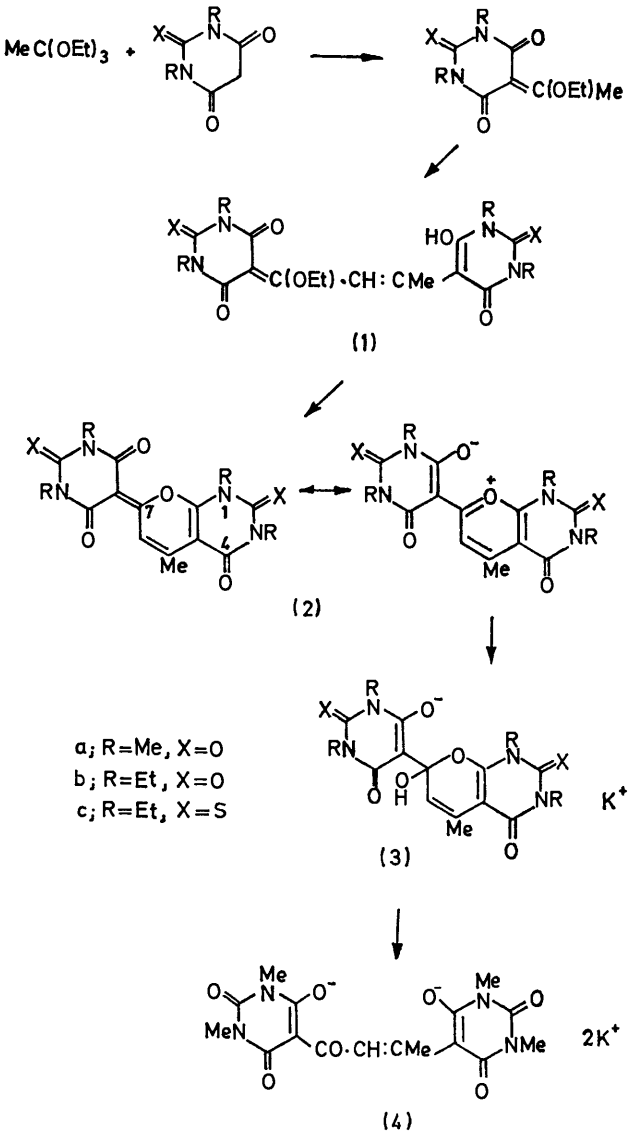
The condensation of 1,3-dialkylbarbituric acids with ethyl orthoacetate gives 7*H*-pyrano[2,3-*d*]pyrimidines. The structures of these dyes were confirmed by their reactions. The preparation and light absorptions of several non-ionic trinuclear dyes containing the pyrano[2,3-*d*]pyrimidine nucleus are discussed.

DERIVATIVES of pyrano[2,3-*d*]pyrimidine result from condensations of barbituric and 2-thiobarbituric acids and their 1,3-disubstituted derivatives with *o*-vanillin,[1] 2-hydroxy-1-naphthaldehyde,[2] malonyl chloride,[3] methylmalonic acid,[4] and β-keto-esters.[5,6] Other pyrano[2,3-*d*]pyrimidines can be obtained from 5-(3-phenylprop-2-ynyl)barbituric acid [7] and from dihydroxypyrimidines.[8] However, Δ^2-pyrazolin-5-ones [9] and rhodanines [10] condense with orthoesters to yield the corresponding 4- and 5-alkoxyalkylidene derivatives, respectively. Likewise, 1,3-diethyl-2-thiobarbituric acid condenses with ethyl orthoformate in acetic anhydride to give the 5-ethoxymethylene derivative [11] and an analogue is formed [12] from 1,3-dimethylbarbituric acid and boiling ethyl orthoformate. In contrast, barbituric acids condense with ethyl orthoformate in pyridine to yield the corresponding monomethineoxonol dyes.[13]

In this paper, condensations of 1,3-dialkylbarbituric acids with ethyl orthoacetate to give pyranopyrimidines are reported.

1,3-Diethylbarbituric acid and ethyl orthoacetate in acetic anhydride at 100° gave a 6% yield of a yellow dye. The same dye was obtained when the anhydride was omitted, and an improved yield of 27% resulted when the low-boiling products were slowly distilled off. Under similar conditions, 1,3-dimethylbarbituric acid and 1,3-diethyl-2-thiobarbituric acid gave analogous dyes. The course of the condensations of the orthoester with 1,3-diethyl- and -dimethyl-barbituric acids was not altered by addition of pyridine.

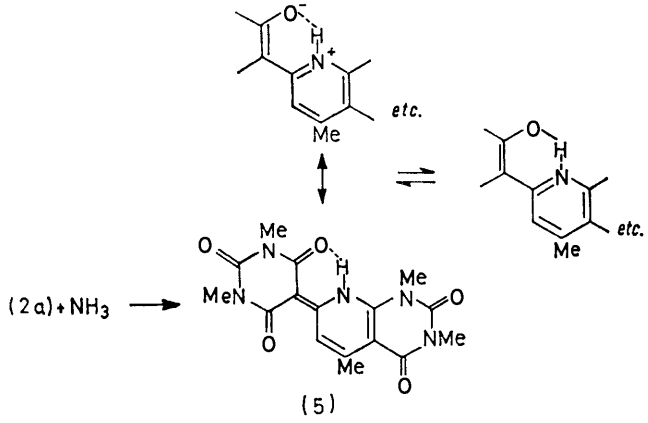
Because the products from the condensations in pyridine and in acetic anhydride were identical, it appeared that the new dyes were not oxonols. Oxonols would have been expected from pyridine as pyridinium salts. Furthermore, the new dyes were not readily soluble in aqueous alkali and electrophoresis showed that the dyes were uncharged. These facts, the molecular formulae, and the ^{1}H n.m.r. spectra pointed to the dyes being pyrano[2,3-*d*]pyrimidines (2). Further support for this constitution came from the chemical properties of the dyes. When 1,3-diethyl-2-thiobarbituric acid was heated with ethyl orthoacetate in boiling pyridine, an orange-red dye formed, the composition of which corresponded to the pyridinium salt of the 1-ethoxy-3-



methyltrimethineoxonol (1c). As this was hygroscopic and unstable, it was not investigated further.

[1] S. Akabori, *Chem. Ber.*, 1933, **66***B*, 139.
[2] M. Ridi and G. Aldo, *Gazzetta*, 1952, **82**, 13.
[3] H. Schulte, *Chem. Ber.*, 1954, **87**, 820.
[4] H. C. Scarborough, *J. Org. Chem.*, 1964, **29**, 219.
[5] M. Ridi and G. Feroci, *Gazzetta*, 1950, **80**, 121.
[6] M. Ridi and G. Aldo, *Gazzetta*, 1952, **82**, 23.
[7] K. E. Schulte, J. Reisch, A. Mock, and K. H. Kander, *Arch. Pharm.*, 1963, **296**, 235.
[8] H. Bredereck, G. Simchen, and A. A. Santos, *Chem. Ber.*, 1967, **100** (4), 1344.
[9] J. D. Kendall and D. J. Fry, B.P. 544,647/1940.
[10] E. B. Knott, *J. Chem. Soc.*, 1954, 1482.
[11] R. A. Jeffreys, *J. Chem. Soc.*, 1956, 2991.
[12] J. W. Clark-Lewis and M. J. Thompson, *J. Chem. Soc.*, 1959, 2401.
[13] L. G. S. Brooker, G. H. Keyes, R. H. Sprague, R. H. Van Dyke, E. Van Lare, G. Van Zandt, F. L. White, H. W. J. Cressman, and S. G. Dent, *J. Amer. Chem. Soc.*, 1951, **73**, 5332.

When methanolic solutions of the dyes (2a—c) were treated with cold aqueous potassium hydroxide, the colours were discharged, probably with formation of the carbinol bases (3), and from dye (2a) a dipotassium salt (4) was isolated. The dyes were recovered when the alkaline solutions were acidified. When the dye (2a) was heated with ammonia in methanol, a pale yellow product resulted, soluble in aqueous alkali and recoverable when the solution was neutralised. The elemental analysis, molecular weight, and ^{1}H n.m.r. spectrum indicated the pyrido[2,3-*d*]pyrimidine structure (5).



(5)

When the dye (2a) was treated with ethylamine in boiling ethanol, it decomposed with the formation of a colourless crystalline enamine (6a), the structure of which was confirmed by its hydrolysis with alkali to give ethylamine and the known 5-acetyl-1,3-dimethylbarbituric acid.[14] The yield of the enamine (6a) from the dye (2a) indicated that both pyrimidine nuclei in the dye had afforded this one product, which was strong confirmatory evidence for the structure (2) assigned to the dyes. Scheme 1 depicts the likely course of the interconversion.

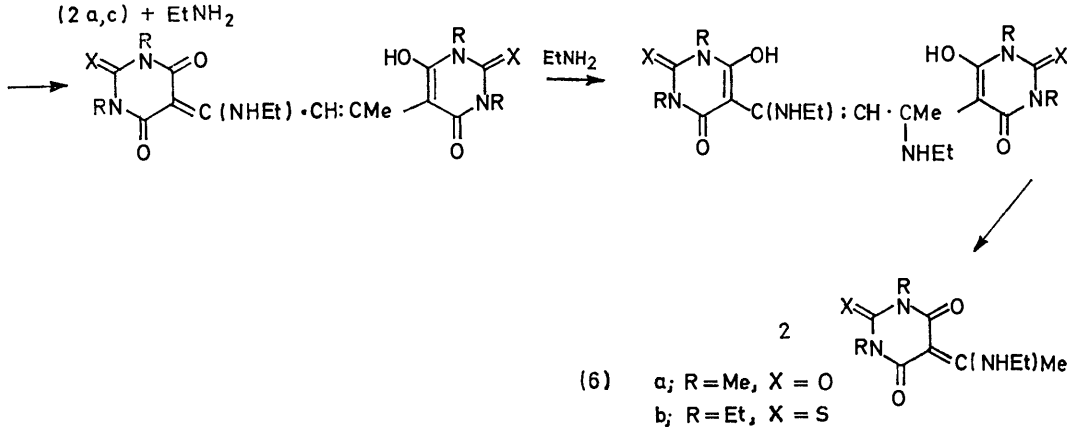
The dye (2c) behaved similarly to (2a) on treatment with ethylamine and gave, as a single product in high yield, the enamine (6b). Attempts to hydrolyse this with alkali to the corresponding ketone were unsuccessful. Hydrogen sulphide was evolved in the work-up, indicating decomposition of the thiobarbituric acid product.

Condensation of the dye (2b) with aniline in boiling ethanol afforded the anilino-ketone (7b), which was soluble in both base and acid and was recoverable in each case on neutralisation. The compound (7b) did not condense with 2,4-dinitrophenylhydrazine and was not acetylated by acetic anhydride, but normal ketonic and acylation reactions are suppressed[15] when there is hydrogen-bonding of the type shown in (7). The ^{1}H n.m.r. spectrum agreed with a hydrogen-bonded structure and showed the presence of the acetonyl residue. The mass spectrum of the compound (7b) and of its analogue (7a) showed loss of $CO{\cdot}CH_3$ from the molecular ion, as accurate mass measurements confirmed. How the compounds (7) may arise from interaction of the dyes (2) with aniline is indicated in Scheme 2.

Dyes (2b and c), separately dissolved in strong sulphuric acid and in perchloric acid, were recovered when the solutions were poured into water. No oxonium salt was obtained by passage of dry hydrogen chloride into benzene solutions of the dyes (2a and c).

Bromination of the dye (2a) in boiling chloroform with an excess of bromine gave only a dibromo-compound. That this had the structure (8) was shown by ^{1}H n.m.r. data. Whereas the dye (2a) gave a three-proton signal at τ 7·28 which could be assigned to a methyl group on the pyran ring, the product gave a one-proton signal at τ 2·89 (Br_2CH); that it appeared at lower field than expected (Tables[16] suggest τ 3·65) could be attributed to steric crowding by the bromine atoms and the adjacent carbonyl group. This crowding presumably explained why tribromination did not occur.

The treatment of dye (2a) in chloroform with bromine



(6) a; R = Me, X = O
b; R = Et, X = S

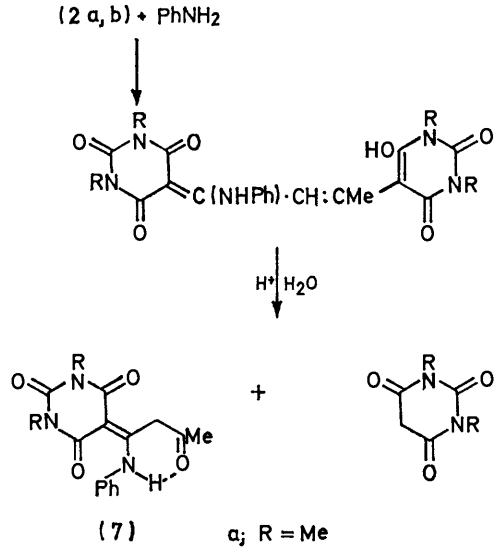
SCHEME 1

[14] W. Pfleiderer and G. Strauss, *Annalen*, 1958, **612**, 173.

[15] L. N. Ferguson, ' The Modern Structural Theory of Organic Chemistry,' Prentice-Hall, Englewood Cliffs, New Jersey, 1963, p. 153.

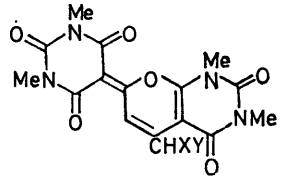
[16] J. A. Elvidge, in ' Interpretation of Organic Spectra,' ed. D. W. Mathieson, Academic Press, London and New York, 1965, p. 54.

sufficient to substitute only one hydrogen atom produced a monobrominated dye (9), the structure of which was confirmed by the ^1H n.m.r. spectrum. The dye (2a) also reacted with oleum to give a water-soluble, monosulphonated product (10); again the ^1H n.m.r. spectrum indicated the structure.



SCHEME 2

Complex dyes (13) containing the pyrano[2,3-*d*]-pyrimidine nucleus were then prepared. Thus, by treating the dye (2b) with 2-[2-(*N*-acetylanilino)vinyl]-3-ethylbenzoxazolium iodide in alcohol, in the presence

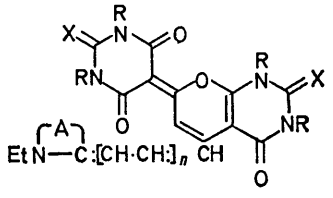


(8) X=Y = Br
(9) X=H, Y = Br
(10) X=H, Y = SO_3H
(11) XY = :CH·NHPh
(12) XY = :CH·NAcPh

of triethylamine, the complex dye (13a) was obtained. Its vinylogue (13b) resulted when the dye (2b) was condensed with 2-[4-(*N*-acetylanilino)butadienyl]-3-ethylbenzoxazolium iodide, under similar conditions. The complex dyes (13c and d) were obtained by condensing 3-ethyl-2-ethylthiobenzothiazolium iodide with dyes (2b) and (2c), respectively. Likewise, the dyes (13e and f) resulted from use of 1-ethyl-2-iodoquinolinium iodide. Finally, the dye (2a) was condensed with *N*-ethoxymethyleneaniline to give the aniline derivative (11). This was acetylated to give the acetanilide (12) and then heated with 3-ethyl-2-methylbenzoxazolium iodide to give the complex dye (13 g).

Light Absorption Properties.—The 7*H*-pyrano[2,3-*d*]-pyrimidines derived from the condensation of 1,3-dialkylbarbituric acids with ethyl orthoacetate, are yellow dyes having an absorption doublet in the blue region of the visible spectrum. The replacement of an oxygen atom in dye (2b) by sulphur as in dye (2c) results in a bathochromic shift of the absorption maximum and an increase in extinction, as expected:[17] evidently the two dyes have similar fine structures. The absorption maxima for the dyes (2b and c) vary only slightly on changing from the solvent methanol to the less polar solvents, chloroform and cyclohexane. The extinction values of the shorter wavelength band of each dye in these solvents remain roughly constant, but those of the longer wavelength band decrease with the decreasing polar character of the solvent. The comparative insensitivity of the light absorption of these pyrano[2,3-*d*]-pyrimidine dyes to solvent change is characteristic of a moderately polar merocyanine comprising a strongly acidic nucleus joined to a weakly basic nucleus.[13]

The trinuclear dyes containing the pyrano[2,3-*d*]-pyrimidine nucleus (13) have high extinction values,



(13)

	R	X	*n*	A ring completed as
a;	Et	O	1	Benzoxazoline
b;	Et	O	2	Benzoxazoline
c;	Et	O	0	Benzothiazoline
d;	Et	S	0	Benzothiazoline
e;	Et	O	0	Dihydroquinoline
f;	Et	S	0	Dihydroquinoline
g;	Me	O	1	Benzoxazoline

implying planar resonance systems, and there are two absorption bands in the visible spectra, the main band being that at longer wavelength. The peak absorptions of these complex dyes (13) are displaced bathochromically by decreasing the polar character of the solvent, and these displacements are accompanied by increases in extinction values. Therefore the dyes are appreciably mesomeric and probably exist predominantly in the charge-separated form.

Extension of the chain in dye (13a) by an extra dimethine link as in dye (13b) causes a bathochromic shift of 85 nm, behaviour typical of cyanines.

The absorption of the pyrido[2,3-*d*]pyrimidine (5), is hypsochromically displaced compared with that of the corresponding pyrano[2,3-*d*]pyrimidine (2a). This is presumably due to the greater basicity or electron-donating capacity of the nitrogen atom of the pyrido-[2,3-*d*]pyrimidine over that of the oxygen atom of the

[17] E. A. Braude, *Ann. Reports*, 1945, **42**, 105.

pyrano[2,3-*d*]pyrimidine. This case parallels that of Acridine Orange in comparison with Pyronine G.[18]

EXPERIMENTAL

The u.v.–visible spectroscopic measurements were made with a Unicam SP 800 instrument. The mass spectra were determined with an A.E.I. MS-902 instrument operating at 70 eV with a direct insertion probe. ^{1}H N.m.r. spectra were measured with a Varian HA100 instrument (tetramethylsilane as internal standard).

Dyes were subjected to electrophoresis on paper for 2 h at 320 V, with sodium phthalate (5 g) in methanol (5 ml) and water (90 ml) as electrolyte, and with the trimethineoxonol derived from 1,3-diethylbarbituric acid as a control.

Condensations of Barbituric Acids with Ethyl Orthoacetate.—(i) 1,3-Diethylbarbituric acid (*cf.* ref. 19) (4·6 g; m.p. 52°), ethyl orthoacetate (5 ml), and acetic anhydride (10 ml) were heated at 100° for 90 min. The mixture was then concentrated and the residual orange gum treated with light petroleum (b.p. 80—100°; 70 ml), and the solution was chilled for 48 h. From methanol, 7-(1,3-*diethylhexahydro*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,3-*diethyl*-1,7-*dihydro*-5-*methylpyrano*[2,3-d]*pyrimidine*-2,4-*dione* (2b) crystallised as hard yellow rods, m.p. 195° (Found: C, 57·6; H, 6·0; N, 13·4%; *m/e*, 416. $C_{20}H_{24}N_4O_6$ requires C, 57·7; H, 5·8; N, 13·5%; *M*, 416), $\lambda_{max.}$ (MeOH) 420 (ε 32,700) and 441 nm (38,000), $\lambda_{max.}$ ($CHCl_3$) 423 (ε 32,700) and 444 nm (33,500), $\lambda_{max.}$ (cyclohexane) 421 (ε 32,800) and 442 nm (28,400). The dye was highly fluorescent in u.v. light.

The same yellow dye (light absorption, mixed m.p.) resulted when (ii) 1,3-diethylbarbituric acid (4·6 g) and ethyl orthoacetate (5 ml) were heated together under reflux for 1 h (yield 0·3 g, 5·8%), (iii) 1,3-diethylbarbituric acid (23 g) and ethyl orthoacetate (25 ml) were heated under reflux for 1 h while the low-boiling products (b.p. 74—75°; 12 ml) were distilled off through a fractionating column (yield 7 g, 27%), and (iv) 1,3-diethylbarbituric acid (5 g), ethyl orthoacetate (5 ml), and pyridine (10 ml) were heated under reflux for 10 min (yield 0·7 g, 12%).

The dye (0·1 g), dissolved in concentrated sulphuric acid (2 ml), was recovered (mixed m.p.) when the solution was diluted with water (20 ml).

The dye (0·2 g) was stirred with methanol (3 ml) and aqueous potassium hydroxide (2 ml; 2%). When the colourless solution was acidified with acetic acid, the yellow dye was recovered (mixed m.p.).

The dye was immobile on electrophoresis.

(v) 1,3-Dimethylbarbituric acid [19] (46 g) and ethyl orthoacetate (120 ml) were heated under reflux for 30 min while low-boiling products were distilled off through a fractionating column. Chilling of the mixture afforded 7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3,5-*trimethylpyrano*[2,3-d]*pyrimidine*-2,4-*dione* (2a) (15 g, 27%) as short yellow needles, m.p. 277° (from benzene) (Found: C, 53·3; H, 4·6; N, 15·5%; *m/e*, 360. $C_{16}H_{16}N_4O_6$ requires C, 53·3; H, 4·4; N, 15·6%; *M*, 360), $\lambda_{max.}$ ($CHCl_3$) 424 (ε 31,800) and 442 nm (32,000), τ ($CDCl_3$) 1·58 (1H, q, *J* 0·9 Hz, 6-H), 6·09 (3H, s, 1-Me), 6·6 (3H, s, 3-Me), 6·67 (6H, s, 2 × Me in pyrimidine), and 7·28 (3H, d, *J* 0·9 Hz, 5-Me). The dye was highly fluorescent in u.v. light.

(vi) 1,3-Dimethylbarbituric acid (15·6 g), ethyl orthoacetate (20 ml), and pyridine (40 ml) were heated under reflux for 30 min. After cooling of the solution, golden yellow crystals were deposited (3 g, 15·8%), m.p. 277°, identical with the preceding dye (light absorption and mixed m.p.).

The dye (1·2 g) was stirred with potassium hydroxide (0·4 g) in methanol (25 ml), and the solution heated under reflux for 10 min. Evaporation of the methanol and crystallisation of the residue from methanol gave almost colourless needles of *dipotassium* 5,5′-(1-*methyl*-3-*oxoprop*-1-*ene*-1,3-*diyl*)*bis*-(1,2,3,6-*tetrahydro*-1,3-*dimethyl*-2,6-*dioxopyrimidin*-4-*olate* (4) (0·4 g) (Found: K, 16·9. $C_{16}H_{16}K_2N_4O_7$ requires K, 17·2%). By acidification of an aqueous solution with acetic acid, the starting dye was recovered, mixed m.p. 277°.

The dye (2a) did not move when subjected to electrophoresis.

(vii) 1,3-Diethyl-2-thiobarbituric acid [20] (20 g) and ethyl orthoacetate (25 ml) were heated under reflux for 45 min and the mixture was then chilled. From ethanol, 7-(1,3-*diethylhexahydro*-4,6-*dioxo*-2-*thioxopyrimidin*-5-*ylidene*)-1,3-*diethyl*-1,2,3,7-*tetrahydro*-5-*methyl*-2-*thioxopyrano*[2,3-d]-*pyrimidin*-4-*one* (2c) (4·5 g, 20%) crystallised as yellowish-brown needles, m.p. 200° (Found: C, 53·8; H, 5·5; N, 12·45; S, 14·2%; *m/e* 448. $C_{20}H_{24}N_4O_4S_2$ requires C, 53·6; H, 5·4; N, 12·5; S, 14·3%; *M*, 448), $\lambda_{max.}$ (MeOH) 450 (ε 42,500) and 475 nm (56,300), $\lambda_{max.}$ ($CHCl_3$) 454 (ε 45,400) and 482 nm (54,000), $\lambda_{max.}$ (cyclohexane) 452 (ε 44,200) and 482 nm (44,000), τ ($CDCl_3$) 1·5 (1H, q, *J* 0·8 Hz, 6-H), 4·82 (2H, q, *J* 6·9 Hz, 1-C*H*$_2$·CH$_3$), 5·4 (2H, q, *J* 6·9 Hz, 3-C*H*$_2$·CH$_3$), 5·42 (4H, q, *J* 7 Hz, 2 × C*H*$_2$·CH$_3$ in pyrimidine), 7·22 (3H, d, *J* 0·8 Hz, 5-Me), 8·6 (3H, t, *J* 6·9 Hz, 1-CH$_2$·C*H*$_3$), 8·67 (3H, t, *J* 6·9 Hz, 3-CH$_2$·C*H*$_3$), and 8·71 (6H, t, *J* 7 Hz, 2 × CH$_2$·C*H*$_3$ in pyrimidine). The dye was fluorescent in u.v. light.

A mixture of the dye (0·22 g), methanol (3 ml) and aqueous potassium hydroxide (2 ml; 2%) was stirred until the solid had dissolved. The starting dye was recovered (mixed m.p.) when the colourless solution was acidified with acetic acid.

The dye (0·1 g) was recovered (mixed m.p.) when a solution in concentrated perchloric acid (2 ml) was diluted with water (30 ml).

(viii) 1,3-Diethyl-2-thiobarbituric acid (4 g), ethyl orthoacetate (5 ml), and pyridine (10 ml) were heated under reflux for 5 min. The red solution was chilled, dye crystals were collected, and a further crop was obtained by adding ether (40 ml) to the filtrate (yield 1 g). From ethyl acetate, *pyridinium* 5-[3-(1,3-*diethylhexahydro*-4,6-*dioxo*-2-*thioxopyrimidin*-5-*ylidene*)-3-*ethoxy*-1-*methylprop*-1-*enyl*]1,3-*diethyl*-1,2,3,6-*tetrahydro*-6-*oxo*-2-*thioxopyrimidin*-4-*olate* crystallised as red needles, m.p. 154° (Found: C, 56·4; H, 6·5; N, 12·4; S, 10·9. $C_{27}H_{35}N_5O_5S_2$ requires C, 56·5; H, 6·1; N, 12·2; S, 11·2%), $\lambda_{max.}$ (EtOH) 494, $\lambda_{max.}$ (C_5H_5N) 504, $\lambda_{max.}$ (H_2O) 480 nm. The dye became sticky on storage and rapidly faded in aqueous solution.

Action of Ammonia on 7-(*Hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3,5-*trimethylpyrano*[2,3-d]*pyrimidine*-2,4-*dione*.—A mixture of com-

[18] S. F. Mason, in ' The Chemistry of Synthetic Dyes,' vol. 3, ed. K. Venkataraman, Academic Press, New York and London, 1970, p. 169.

[19] J. W. Clark-Lewis and M. J. Thompson, *J. Chem. Soc.*, 1959, 1628.

[20] L. G. S. Brooker, G. H. Keyes, R. H. Van Dyke, E. Van Lare, G. Van Zandt, and F. L. White, *J. Amer. Chem. Soc.*, 1951, **73**, 5326.

pound (2a) (0·5 g), methanol (40 ml), and ammonia (*d* 0·880; 20 ml) was stirred until the dye had dissolved. The solution was heated under reflux for 1 h and then the methanol and excess ammonia were removed by distillation to leave a pale yellow residue, recrystallisation of which from benzene gave 7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-7,8-*dihydro*-1,3,5-*trimethylpyrido*-[2,3-d]*pyrimidine*-2(1H),4-*dione* (5) (0·2 g, 40%), as pale yellow needles, m.p. >330° (Found: C, 53·4; H, 4·75; N, 19·9%; *m/e*, 359. $C_{16}H_{17}N_5O_5$ requires C, 53·5; H, 4·7; N, 19·5%; *M*, 359), $\lambda_{max.}$ ($CHCl_3$) 382sh (ε 35,900) and 394 nm (50,200), τ ($CDCl_3$) −8·5 (1H, s, 8-H or OH), 1·25 (1H, q, *J* 0·8 Hz, 6-H), 6·21 (3H, s, 1-Me), 6·58 (3H, s, 3-Me), 6·61 (3H, s, Me in pyrimidine), 6·63 (3H, s, Me in pyrimidine), and 7·15 (3H, d, *J* 0·8 Hz, 5-Me). The dye was highly fluorescent in u.v. light. It dissolved in aqueous alkali and was recovered on neutralisation.

Condensation of 7-(*Hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3,5-*trimethylpyrano*-[2,3-d]*pyrimidine*-2,4-*dione with Ethylamine*.—A mixture of compound (2a) (1 g), ethanol (30 ml), and a solution of ethylamine in ethanol (33%; 20 ml) was heated under reflux until all the dye had dissolved (*ca.* 3 h). Then the solvents and excess of ethylamine were evaporated off to provide 5-(1-*ethylaminoethylidene*)-1,3-*dimethylpyrimidine*-2,4,6-*trione* (6a) (1 g, 80%), as needles, m.p. 165° (from water) (Found: C, 53·6; H, 6·7; N, 18·7%; *m/e*, 225. $C_{10}H_{15}N_3O_3$ requires C, 53·3; H, 6·7; N, 18·7%; *M*, 225), $\lambda_{max.}$ (MeOH) 223 (ε 11,700), 246 (3150), and 302 nm (23,900), τ ($CDCl_3$) −2·5br (1H, NH), 6·53 (2H, dq, *J* 5 and 7 Hz, NH·CH_2·CH_3), 6·73 (6H, s, 1,3-Me_2), 7·33 (3H, s, CH_3·C=), and 8·66 (3H, t, *J* 7 Hz, NH·CH_2·CH_3).

Hydrolysis of 5-(1-*Ethylaminoethylidene*)-1,3-*dimethylpyrimidine*-2,4,6-*trione*.—A mixture of compound (6a) (1·1 g), water (10 ml), and sodium hydroxide solution (40%; 0·5 ml) was heated under reflux for 30 min, during which ethylamine was evolved. The solution was cooled and acidified (HCl). Crystallisation of the precipitate (0·91 g, 92%) (from methanol) gave 5-acetyl-1,3-dimethylbarbituric acid [14] as pale yellow needles, m.p. and mixed m.p. 97—98° (Found: C, 48·7; H, 5·1; N, 14·0%; *m/e*, 198. Calc. for $C_8H_{10}N_2O_4$: C, 48·5; H, 5·0; N, 14·1%; *M*, 198).

Action of Ethylamine on 7-(1,3-*Diethylhexahydro*-4,6-*dioxo*-2-*thioxopyrimidin*-5-*ylidene*)-1,3-*diethyl*-1,2,3,7-*tetrahydro*-5-*methyl*-2-*thioxopyrano*[2,3-d]*pyrimidine*-4-*one*.—A mixture of compound (2c) (1 g), ethanol (10 ml), and a solution of ethylamine in ethanol (33%; 15 ml) was heated under reflux for 3 h, concentrated under reduced pressure, and treated with water (50 ml). An oil separated, which rapidly solidified. Crystallisation of the solid from methanol gave 1,3-*diethyl*-5-(1-*ethylaminoethylidene*)-1,2-*dihydro*-2-*thioxopyrimidine*-4,6-*dione* (6b) (0·9 g, 78%) as needles, m.p. 113° (Found: C, 53·6; H, 7·2; N, 15·5; S, 11·9%; *m/e*, 269. $C_{12}H_{19}N_3O_2S$ requires C, 53·5; H, 7·1; N, 15·6; S, 11·9%; *M*, 269), $\lambda_{max.}$ (MeOH) 229 (ε 13,500), 267 (4,800), 326 sh (37,300), and 330 nm (41,000), τ ($CDCl_3$) −2·5br (1H, NH), 5·45 [4H, q, *J* 7 Hz, 1,3-(CH_2·CH_3)$_2$], 6·46 (2H, dq, *J* 5 and 7 Hz, NH·CH_2·CH_3), 7·3 (3H, s, CH_3·C=), 8·63 (3H, t, *J* 7 Hz, NH·CH_2·CH_3), and 8·72 [6H, t, *J* 7 Hz, 1,3-(CH_2·CH_3)$_2$]. When the dye was boiled with 10% sodium hydroxide in water and the solution cooled and acidified, hydrogen sulphide was evolved.

Action of Aniline on 7-(1,3-*Diethylhexahydro*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,3-*diethyl*-1,7-*dihydro*-5-*methylpyrano*-[2,3-d]*pyrimidine*-2,4-*dione*.—A mixture of compound (2b) (1 g), aniline (1·25 ml), and ethanol (180 ml) was heated under reflux for 2 h. The solution was cooled, diluted with water (500 ml), and set aside for 12 h. Recrystallisation of the colourless solid from methanol gave 5-(1-*anilino*-3-*oxobutylidene*)-1,3-*diethylpyrimidine*-2,4,6-*trione* (7b) (0·6 g, 73%), as needles, m.p. 124—125° (Found: C, 63·2; H, 6·2; N, 12·5%; *m/e*, 343·152412 and 300·135143. $C_{18}H_{21}N_3O_4$ requires C, 63·0; H, 6·1; N, 12·2%; *M*, 343·153200, *M* − CH_3CO, 300·134811), $\lambda_{max.}$ (MeOH) 224 (ε 18,700) and 312 nm (28,500), τ ($CDCl_3$) −4·3br (1H, NH), 2·68 (5H, m, aromatic), 5·93 (2H, s, CH_2·CO·CH_3), 6·03 [4H, q, *J* 7 Hz, 1,3-(CH_2·CH_3)$_2$], 7·71 (3H, s, CH_2·CO·CH_3), and 8·8 [6H, t, *J* 7 Hz, 1,3-(CH_2·CH_3)$_2$].

Action of Aniline on 7-(*Hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3,5-*trimethylpyrano*-[2,3-d]*pyrimidine*-2,4-*dione*.—Compound (2a) (1 g), aniline (1 ml), and ethanol (75 ml) were heated together under reflux for 3 h. The solution was cooled, diluted with water (80 ml), and acidified (dilute H_2SO_4), and the precipitate (0·8 g) recrystallised from methanol to give 5-(1-*anilino*-3-*oxobutylidene*-1,3-*dimethylpyrimidine*-2,4,6-*trione* (7a) as needles, m.p. 167—168° (Found: C, 61·1; H, 5·5; N, 13·3%; *m/e*, 315·120868 and 272·103142. $C_{16}H_{17}N_3O_4$ requires C, 61·0; H, 5·4; N, 13·3%; *M*, 315·121900, *M* − CH_3CO, 272·103511), $\lambda_{max.}$ (MeOH) 223 (ε 19,100) and 310 nm (28,000).

Substitution Reactions of 7-(*Hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3,5-*trimethylpyrano*-[2,3-d]*pyrimidine*-2,4-*dione*.—(a) *Bromination*. (i) Compound (2a) (0·9 g) in chloroform (35 ml) was treated with bromine (1·6 g) and the solution heated under reflux for 3 h. Hydrogen bromide was evolved. The solution was evaporated to dryness and the residue was recrystallised from benzene to give 5-*dibromomethyl*-7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3-*dimethylpyrano*[2,3-d]-*pyrimidine*-2,4-*dione* (8) (0·6 g, 48%) as orange needles, m.p. 260° (Found: C, 36·9; H, 2·8; Br, 30·7; N, 10·6%; *m/e*, 516. $C_{16}H_{14}Br_2N_4O_6$ requires C, 37·1; H, 2·7; Br, 30·9; N, 10·8%; *M*, 516), $\lambda_{max.}$ (pyridine) 444 nm (ε 10,000), τ ($CDCl_3$) 0·67 (1H, s, 6-H), 2·89 (1H, s, $CHBr_2$), 6·05 (3H, s, 1-Me), 6·54 (3H, s, 3-Me), 6·57 (3H, s, Me in pyrimidine), and 6·61 (3H, s, Me in pyrimidine).

(ii) Compound (2a) (0·9 g) in chloroform (30 ml) was treated with bromine (0·4 g) in chloroform (10 ml) and the solution heated under reflux for 3 h. Hydrogen bromide was evolved. Evaporation of the solution to dryness afforded 5-*bromomethyl*-7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3-*dimethylpyrano*-[2,3-d]*pyrimidine*-2,4-*dione* (9) (0·85 g, 77%) (from benzene) as orange leaflets, m.p. 240—241° (Found: C, 43·5; H, 3·3; Br, 18·0; N, 12·6%; *m/e*, 438. $C_{16}H_{15}BrN_4O_6$ requires C, 43·7; H, 3·4; Br, 18·2; N, 12·8%; *M*, 438), $\lambda_{max.}$ (MeOH) 440 nm (ε 12,200), τ ($CDCl_3$) 1·3 (1H, s, 6-H), 5·11 (2H, s, CH_2Br), 6·07 (3H, s, 1-Me), 6·54 (3H, s, 3-Me), and 6·62 (6H, s, 2 × Me in pyrimidine).

(b) *Sulphonation*. A solution of compound (2a) (3·6 g) in concentrated sulphuric acid (10 ml) and oleum (20%; 8 ml) was heated on a steam bath for 13 h, then cooled and poured into water (200 ml), and neutralised (Na_2CO_3). The precipitate was collected and dissolved in hot ethanol, and the solution was acidified with acetic acid. From ethanol, the 7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,2,3,4-*tetrahydro*-1,3-*dimethyl*-2,4-*dioxo*-7H-*pyrano*[2,3-d]*pyrimidin*-5-*ylmethanesulphonic acid* (10) (1·2 g, 27%) crystallised as yellow needles (Found: C, 43·3; H,

3·3; N, 12·5; S, 7·2. $C_{16}H_{16}N_4O_9S$ requires C, 43·7; H, 3·6; N, 12·7; S, 7·3%), $\lambda_{max.}$ (H_2O) 440 (ε 19,200) and 457 nm (21,000), τ (D_2O) 1·44 (1H, s, 6-H), 4·95 (2H, s, CH_2·SO_3H), 6·05 (3H, s, 1-Me), 6·41 (3H, s, 3-Me), and 6·61 (6H, s, 2 × Me in pyrimidine).

Preparation of Trinuclear Dyes containing the Pyrano[2,3-d]*pyrimidine Nucleus.*—(i) 1,3-*Diethyl*-5-[3-(3-*ethylbenzoxazolin*-2-*ylidene*)*prop*-1-*enyl*]-7-(1,3-*diethylhexahydro*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydropyrano*[2,3-d]-*pyrimidine*-2,4-*dione* (13a). Compound (2b) (0·2 g), 2-[2-(*N*-acetylanilino)vinyl]-3-ethylbenzoxazolium iodide [21] (0·22 g), ethanol (5 ml), and triethylamine (0·2 ml) were heated under reflux for 5 min and then the solution was chilled. The *product* (0·12 g, 43%) crystallised (pyridine–methanol) as dark green needles, m.p. 267° (Found: C, 63·7; H, 5·8; N, 11·8%; *m/e*, 587. $C_{31}H_{33}N_5O_7$ requires C, 63·4; H, 5·6; N, 11·9%; *M*, 587), $\lambda_{max.}$ (acetone) 442 (ε 37,600) and 612 nm (143,000), $\lambda_{max.}$ (C_5H_5N) 448 (ε 35,200) and 622 nm (140,000).

(ii) 1,3-*Diethyl*-5-[5-(3-*ethylbenzoxazolin*-2-*ylidene*)*penta*-1,3-*dienyl*]-7-(1,3-*diethylhexahydro*-2,3,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydropyrano*[2,3-d]*pyrimidine*-2,4-*dione* (13b). Similarly, compound (2b) (0·4 g), 2-[4-(*N*-acetylanilino)-butadienyl]-3-ethylbenzoxazolium iodide [22] (0·46 g), ethanol (30 ml), and triethylamine (0·5 ml) were heated under reflux for 10 min to give the *product* (0·28 g, 47%) as green needles with a bronze reflex, m.p. 173° (from pyridine–ethanol) (Found: C, 64·8; H, 5·8; N, 11·2%; *m/e*, 613. $C_{33}H_{35}N_5O_7$ requires C, 64·6; H, 5·7; N, 11·4%; *M*, 613), $\lambda_{max.}$ ($CHCl_3$) 475 (ε 28,200) and 700 nm (140,000), $\lambda_{max.}$ (C_5H_5N) 480 (ε 23,300) and 707 nm (139,000).

(iii) 1,3-*Diethyl*-5-(3-*ethylbenzothiazolin*-2-*ylidenemethyl*)-7-(1,3-*diethylhexahydro*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydropyrano*[2,3-d]*pyrimidine*-2,4-*dione* (13c). Compound (2b) (0·2 g) 3-ethyl-2-ethylthiobenzothiazolium toluene-*p*-sulphonate [23] (0·2 g), ethanol (20 ml), and triethylamine (0·2 ml) were heated under reflux for 15 min; ethanethiol was evolved. The mixture was then chilled. Recrystallisation of the solid (0·25 g, 90%) from pyridine gave the *product* as bright orange needles, m.p. 319° (Found: C, 59·8; H, 5·6; N, 12·3; S, 5·4. $C_{29}H_{31}N_5O_6S$ requires C, 60·3; H, 5·4; N, 12·1; S, 5·5%), $\lambda_{max.}$ (acetone) 401 (ε 33,800) and 523 nm (71,700), $\lambda_{max.}$ (C_5H_5N) 404 (ε 32,300) and 530 nm (81,500).

(iv) 1,3-*Diethyl*-5-(3-*ethylbenzothiazolin*-2-*ylidenemethyl*)-7-(1,3-*diethylhexahydro*-4,6-*dioxo*-2-*thioxopyrimidin*-5-*ylidene*)-1,2,3,7-*tetrahydro*-2-*thioxopyrano*[2,3-d]*pyrimidin*-4-*one* (13d). Compound (2c) (0·34 g), 3-ethyl-2-ethylthiobenzothiazolium toluene-*p*-sulphonate [23] (0·2 g), ethanol (30 ml), and triethylamine (0·2 ml) were heated under reflux for 15 min. The mixture was chilled, and the precipitate recrystallised from pyridine, then suspended in boiling methanol (50 ml,) and finally washed with methanol to give the *dye* (0·12 g, 26%) as red needles, m.p. 333° (Found: C, 57·5; H, 5·3; N, 11·3; S, 15·6. $C_{29}H_{31}N_5O_4S_3$ requires C, 57·1; H, 5·1; N, 11·5; S, 15·8%), $\lambda_{max.}$ (acetone) 420 and 538 nm, $\lambda_{max.}$ (C_5H_5N) 426 (ε 49,800) and 548 nm (90,000).

(v) 1,3-*Diethyl*-5-(1-*ethyl*-1,2-*dihydroquinolin*-2-*ylidenemethyl*)-7-(1,3-*diethylhexahydro*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydropyrano*[2,3-d]*pyrimidine*-2,4-*dione* (13e). Compound (2b) (0·4 g), 1-ethyl-2-iodoquinolinium iodide [24] (0·4 g), ethanol (50 ml), and triethylamine (0·3 ml) were heated under reflux for 15 min and the mixture was then chilled. The *product* (0·35 g, 64%) formed dark red fluffy needles, m.p. 263° (from ethanol) (Found: C, 64·9; H, 5·9; N, 12·5%; *m/e*, 571. $C_{31}H_{33}N_5O_6$ requires C, 65·2; H, 5·8; N, 12·3%; *M*, 571), $\lambda_{max.}$ (EtOH) 403 (ε 17,100) and 550 nm (38,800), $\lambda_{max.}$ (C_5H_5N) 420 (ε 22,800) and 585 nm (59,300).

(vi) 1,3-*Diethyl*-5-(1-*ethyl*-1,2-*dihydroquinolin*-2-*ylidenemethyl*)-7-(1,3-*diethylhexahydro*-4,6-*dioxo*-2-*thioxopyrimidin*-5-*ylidene*)-1,2,3,7-*tetrahydro*-2-*thioxopyrano*[2,3-d]*pyrimidin*-4-*one* (13f). Compound (2c) (0·45 g), 1-ethyl-2-iodoquinolinium iodide [24] (0·4 g), ethanol (50 ml), and triethylamine (0·3 ml) were heated under reflux for 15 min. Chilling of the mixture afforded the *dye* (0·26 g, 43%) as purple needles, m.p. 277° (from pyridine) (Found: C, 61·9; H, 5·7; N, 11·2; S, 10·8. $C_{31}H_{33}N_5O_4S_2$ requires C, 61·7; H, 5·5; N, 11·6; S, 10·6%), $\lambda_{max.}$ (C_5H_5N) 432 (ε 32,600) and 590 nm (60,300).

5-(2-*Anilinovinyl*)-7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3-*dimethylpyrano*[2,3-d]-*pyrimidine*-2,4-*dione* (11).—Compound (2a) (0·8 g) and *N*-ethoxymethyleneaniline [25] (1·5 ml) were stirred together and heated under reflux until the solid material had dissolved (*ca.* 3 min). A red solid separated from the hot mixture, which was then diluted with ethanol (20 ml). From ethanol, the *product* (0·85 g, 83%) crystallised as red needles, m.p. 296—297° (Found: C, 59·3; H, 4·7; N, 14·9%; *m/e*, 463. $C_{23}H_{21}N_5O_6$ requires C, 59·6; H, 4·5; N, 15·1%; *M*, 463, $\lambda_{max.}$ (C_5H_5N) 408 (ε 30,800) and 531 nm (42,800).

5-[2-(N-*Acetylanilino*)*vinyl*]-7-(*hexahydro*-1,3-*dimethyl*-2,4,6-*trioxopyrimidin*-5-*ylidene*)-1,7-*dihydro*-1,3-*dimethyl*-*pyrano*[2,3-d]*pyrimidine*-2,4-*dione* (12).—Compound (11) (0·8 g), pyridine (10 ml), and acetic anhydride (1 ml) were heated under reflux for 5 min, the reaction mixture was then cooled, and the red solid was treated with boiling methanol (50 ml). The *product* (0·7 g, 81%) formed red needles, m.p. 330° (Found: C, 59·2; H, 4·7; N, 13·7. $C_{25}H_{23}N_5O_7$ requires C, 59·4; H, 4·6; N, 13·9%), $\lambda_{max.}$ (C_5H_5N) 370 (ε 31,700) and 490 nm (34,400).

Heating this product (0·12 g) and 3-ethyl-2-methylbenzoxazolium iodide (0·1 g) in pyridine (5 ml) containing triethylamine (0·1 ml) afforded a blue dye (13 g), $\lambda_{max.}$ 622 and 447 nm.

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