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Vat Dyes from Three New Heterocyclic Ring Systems

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SUMMARY

*The syntheses of a new angular azaphenoxazine and of two new angular azaphenothiazine ring systems are described and the dyeing properties of their derivatives studied. Thiocyanation of 2-amino-6-picoline (***8***) followed by hydrolysis and condensation with 2,3-dichloro-1,4-naphthoquinone (***11***) gave the purple-coloured 6-chloro-10-methylbenzo*[a]*-11-azaphenothiazin-5-one (***12***) in excellent yields. Similarly, from 4,6-diaminopyrimidine (***15***) and 2-amino-3-pyridinol (***22***), the compounds, 8-amino-6-chlorobenzo*[a]*-9,11-diazaphenothiazin-5-one (***18***) and 6-chlorobenzo*[a]*-11-azaphenoxazin-5-one (***23***), were obtained as bluish-purple and orange colourants, respectively. Elemental analysis, infrared, ultraviolet, NMR and mass spectroscopy agree with the assigned tetracyclic structures. Reduction with* $Na_2S_2O_4$ *and the ease of air oxidation of the reduced forms to the quinoid coloured materials make them applicable as vat dyes. Fastness to washing, light, acids and bases was also investigated, and also their toxicity in laboratory animals.*

1. INTRODUCTION

Studies of the chemistry of phenothiazine and phenoxazine derivatives has continued because of the wide range of applications[1–3] of the derivatives of these heterocycles. Several modifications[4–8] of the basic structures have

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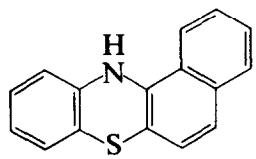
been undertaken, not only to improve their usefulness but also to open new areas of application.

One of the earliest and least developed modifications is the introduction of a benzo group at the 1,2-bond of phenothiazine and phenoxazine resulting in benzo[*a*]phenothiazine (**1**) and benzo[*a*]phenoxazine (**2**). Such systems are also referred to as angular phenothiazines[9] and phenoxazines[10] because of the angular nature of the tetracyclic structure.



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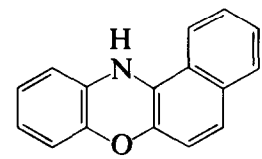
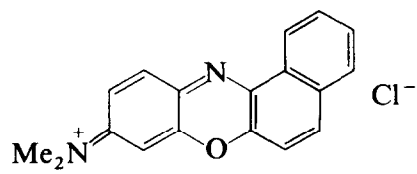


2

Although benzo[*a*]phenothiazine (**1**), the prototype of the angular phenothiazines, was first prepared[11] in 1890, seven years after Bernthsen's synthesis of the parent ring,[12] its chemistry remains largely undeveloped. Meldola Blue (**3**),[13] a derivative of the angular phenoxazine **2**, was commercially available as a blue dye long before the parent phenoxazine and phenothiazine were discovered.



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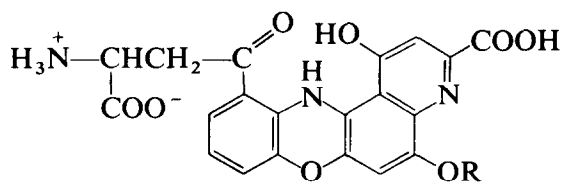
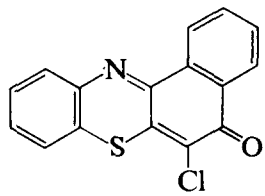


4, R = β-glucose
5, R = SO_3H

In spite of these early reports, little is known about the chemistry of the angular systems. Whereas no naturally occurring phenothiazine derivative has been isolated, phenoxazine[3,14–17] and angular phenoxazine derivatives[18] are widely distributed in nature. The angular phenoxazines are mainly distributed as pigments in arthropods and are responsible for the coloration in the eyes, wings and cuticle of insects. Typical examples of these natural pigments, known as ommochromes,[19] are rhodommatin (**4**)[20]

and ommatin D (**5**)[21] which are isolated from the wings of different arthropods.

More recently, interest in these angular systems has been focused on the 5-oxo derivatives in view of their potential as good colouring matters. 6-Chloro-5*H*-benzo[*a*]phenothiazin-5-one (**6**) and its 7-oxygen analogue (**7**) have been recently reported by Agarwal[22] and Schafer.[23]



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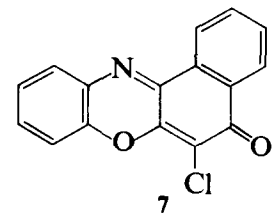


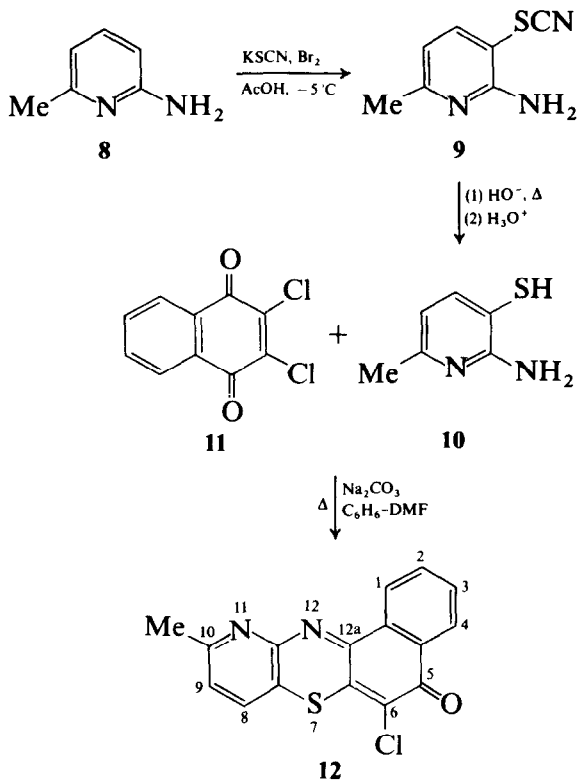
7

Whereas four monoaza-, ten diaza-, four triaza-[24,25] and nine tetra-aza-isomeric phenothiazine ring systems[26] have been prepared and characterized, only two monoaza-[27,28] and one diaza-[28] angular phenothiazine ring systems have been reported. In the phenoxazine series, only one angular azaphenoxazine[19,29] and one angular oxaphenoxazine[30] are known out of several possible isomeric forms. We have now successfully synthesized three new heterocyclic ring systems in these series. These compounds were further examined for applicability as dyes and pigments for the textile and varnish industries.

2. RESULTS AND DISCUSSION

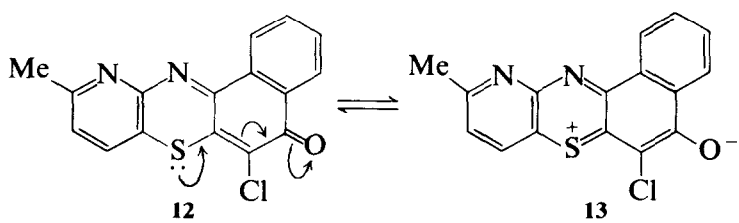
2-Amino-6-picoline (**8**) was converted to the 3-thiocyanato[31] derivative (**9**) by the action of potassium thiocyanate and bromine in glacial acetic acid at −5 to 0°C. Refluxing in 15% sodium hydroxide for 8 h followed by acidification gave 2-amino-6-methylpyridine-3-thiol (**10**) in good yields.[32] The action of 2,3-dichloro-1,4-naphthoquinone (**11**) on an equimolar amount of the thiol **10** in dry benzene–*N*,*N*-dimethylformamide (DMF) mixture (10:1) in the presence of anhydrous sodium carbonate led to the formation of a high melting brown solid (melting above 300°C), which was isolated in 81% yield.

Microanalysis and ultraviolet, infrared and mass spectroscopy were in agreement with the tetracyclic structure **12**. The nuclear magnetic resonance spectrum showed a six-proton multiplet at δ7·32 due to the aromatic protons and a three-proton singlet at δ1·50 which was assigned to the methyl protons. Thus, the product of this reaction is 6-chloro-10-methylbenzo[*a*]-11-azaphenothiazin-5-one (**12**), the first known compound with the 11-azaphenothiazine structural framework.



8 9 11 10 12

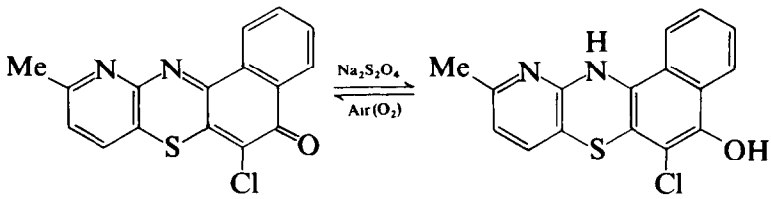
Further condensation of this product with another mole of dichloronaphthoquinone (**11**) under similar conditions was unsuccessful, starting compounds being recovered. This indicates that after removal of the first chlorine atom the second halogen in the naphthoquinone moiety tends to lose its reactivity, suggesting the existence of the ionic structure **13**.



12 13

Evidence for the existence of this equilibrium is provided by the infrared spectrum in which the carbonyl absorption band of **12** was shifted from the expected 1680 to 1640 cm^{-1} due to resonance stabilization by structure **13**. Structure **13** will increase the carbonyl bond length of structure **12** leading to an increase in the wavelength of carbonyl absorption or a decrease in the frequency of absorption, as was observed.

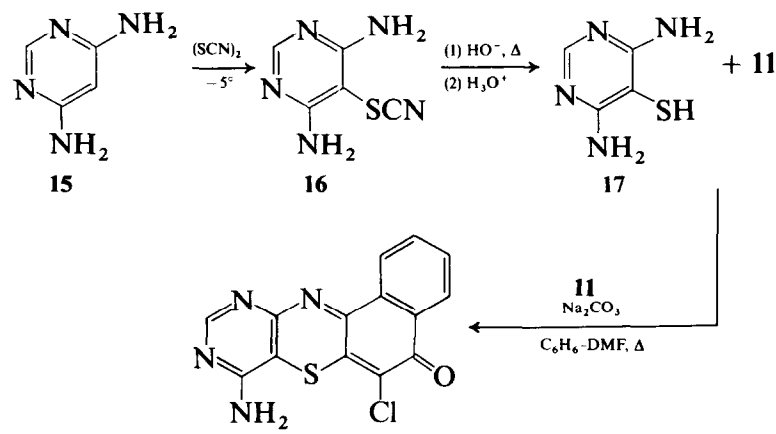
Product **12** is a purple solid, the intense colouration being attributed to the extended conjugation from the naphthalene to the pyridine rings through the iminoquinoid system. The colour was, however, discharged by refluxing with such reducing agents as sodium hydrosulphite due to the formation of the reduced form, **14**, in which the extended conjugation is lost.



12 **14**

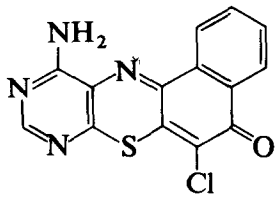
Compound **14** is a yellow unstable solid; it reverted readily to the starting angular monoazaphenothiazinone **12** on exposure to air. Conversion of **14** to **12** proceeded much faster in dilute hydrogen peroxide. The ease of air oxidation of the reduced form, **14**, to the purple compound, **12**, in the presence or absence of any other oxidizing agent makes the phenothiazinone **12** suitable for consideration as a vat dye.

Thiocyanation of 4,6-diaminopyrimidine (**15**) in place of 2-amino-6-picoline (**8**) gave 4,6-diamino-5-thiocyanatopyrimidine (**16**)[33] which, on alkaline hydrolysis and acidification, led to good yields of 4,6-diaminopyrimidine-5-thiol (**17**). The base-catalysed reaction of compound **17** with 2,3-dichloro-1,4-naphthoquinone (**11**) led to 98% yields of the bluish-purple 8-amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one (**18**), a novel angular diazaphenothiazine which is isomeric with compound **19**, which has been previously reported.[29]

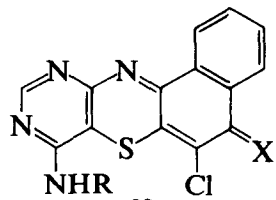


15 **16** **17**

18 (bluish-purple)



19 (magenta)



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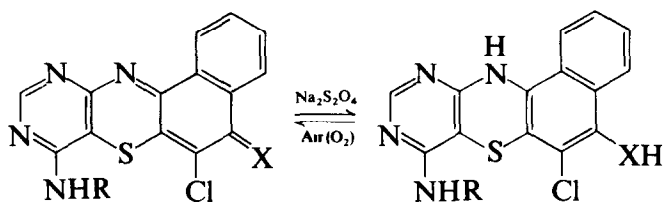
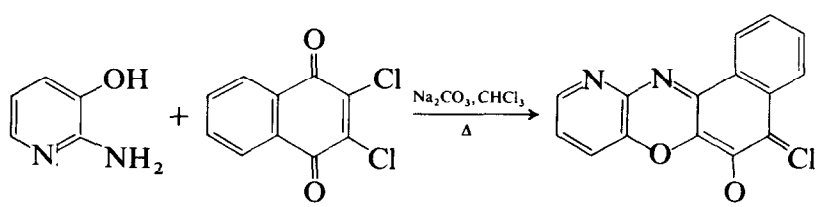
Microanalysis and spectroscopic data were in agreement with the assigned structure **18**. 8-Acetylation was achieved by reaction with acetic anhydride, whilst the hydrazone was obtained by condensation with 2,4-dinitrophenylhydrazine. The isomers, **18** and **19**,[28] are both intensely coloured compounds due to extended conjugation. Product **18** and its acetyl derivative **20** (R = Ac, X = 0) were reduced with sodium hydrosulphite to the angular diazaphenothiazinol, **21**, which reverted in atmospheric oxygen to the starting quinoid forms. The reduced form, **21** (R = H, X = 0), is discoloured because of the loss of extended conjugation in the system.



18, R = H
20, R = Ac

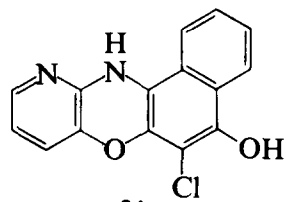
21

Further variation of these angular azaphenothiazines was achieved by the replacement of the ring sulphur with oxygen leading to angular azaphenoxazine. 2-Amino-3-pyridinol (**22**) was therefore treated with a stoichiometric amount of 2,3-dichloro-1,4-naphthoquinone (**11**) in chloroform in the presence of anhydrous sodium carbonate or sodium acetate. The product, obtained in 97% yield, was an orange solid, m.p. 232–3°C. Microanalysis and spectroscopy show that the compound is 6-chlorobenzo[*a*]-11-azaphenoxazin-5-one (**23**).



22 **11** **23**

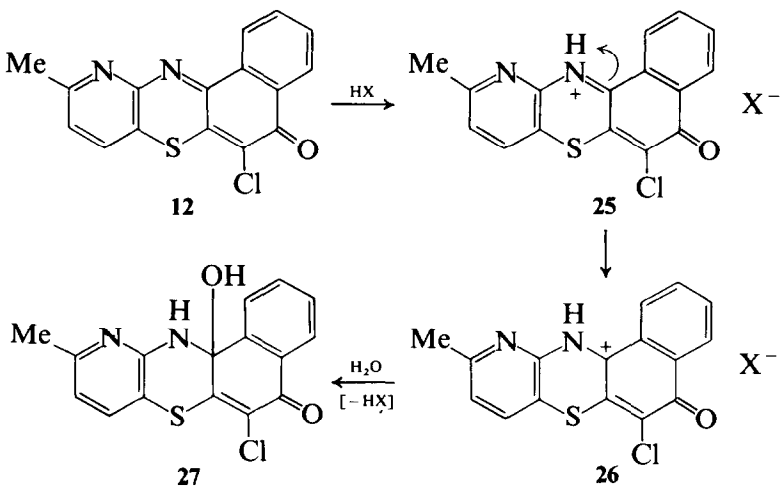
As for its phenothiazinone counterpart, the orange colour of product **23** is discharged on refluxing with sodium hydrosulphite due to destruction of the extended conjugation. However, the resulting angular azaphenoxazinol **24** reverted to the starting quinoid form **23** on exposure to air.



24

Due to their ease of formation, these angular azaphenoxazines and azaphenothiazines are good colourants which are applicable as vat dyes. Cotton and polyester fabrics dyed with them showed good fastness properties to washing, ironing, sunlight and alkalis. Because of the ease of $Na_2S_2O_4$ reduction of these angular azaphenothiazines and azaphenoxazines and their ready autoxidation in atmospheric oxygen to the intensely coloured dyes, vat dyeing appears to be a good method of application. It was found, however, that the colour of the dyed fabric was lighter than that obtained by direct dyeing methods. Nevertheless, the colour was intensified by the addition of dilute hydrogen peroxide which helped to accelerate and complete the oxidation process.

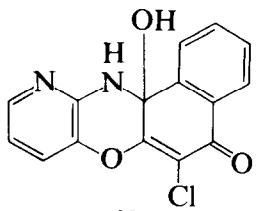
When a drop of 10% hydrochloric acid was added to the dyed material, the colour was discharged, implying that the dye is not acid-fast. This is probably due to the destruction of the extended conjugation in these angular systems as exemplified with compound **12**. The original colour is not regenerated on addition of concentrated ammonia, in support of the



12 **25** **27** **26**

assigned structure. The observed discoloration in dilute acid is probably due to the formation of compound **27** via protonation of the more basic tertiary ring nitrogen (position 12) followed by the formation of the carbonium ion, **26**, that is attacked by water at C-12a leading to the formation of 6-chloro-12a-hydroxy-10-methyl-11-azaphenothiazin-5-one (**27**). The formation of compound **27**, which lacks an extended conjugative system, is probably responsible for the discoloration.

Similarly, application of dilute hydrochloric acid to dyeings of compound **23** led to a colour change from orange to light yellow which was not reversed by ammonia. This suggests loss of the extended conjugation reminiscent of the yellowish starting naphthoquinone. Thus the probable structure of the yellow compound is **28**. In the same way, structure **29** is probably responsible for the discoloration of product **18**.



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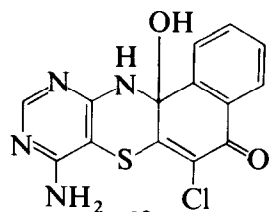
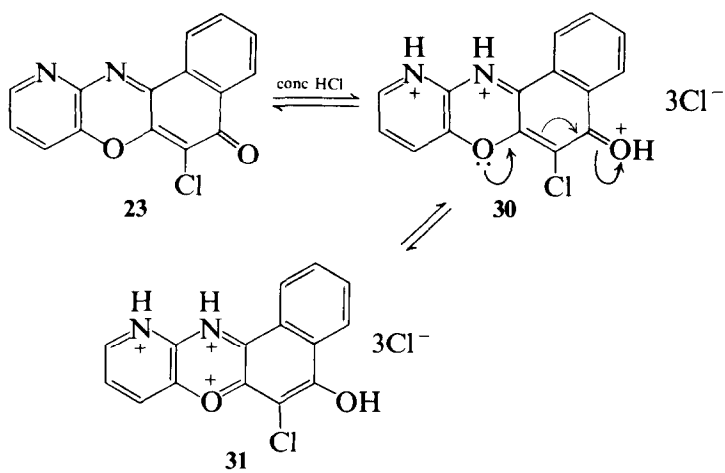


29

Application of concentrated hydrochloric acid to dyeings of compound **23** gave a red colour which was reconverted to the original orange colour on addition of ammonia, implying that the red colouration is probably due to the protonation of all basic points (structure **31**).



23 **30** **31**

Varnishes for wood, shoe and leather were also compounded using these dyes (**12**, **18** and **23**) as the colouring agents producing coloured shiny surfaces.

In view of the good potential of these compounds as dyes, it was thought desirable to carry out some toxicity tests on them to assess their possible hazards when used as dyes. The observed LD_{50} values of the dyes **12** and **18** were 39·81 and 107·2 mg/kg, respectively.

A dye can be absorbed into the body through the skin during perspiration. During perspiration the skin oil and saline solution excreted by the body on the skin surface may dissolve dye present in clothing material. In this way, the dye may then be absorbed into the body system through the pores on the skin. Compounds **12** and **18** are generally insoluble even in dimethyl sulphoxide and this low solubility, coupled with the high LD_{50} values, indicates that the dyes are unlikely to be hazardous.

3. EXPERIMENTAL

3.1. General

Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Ultraviolet and visible spectra were recorded on a Pye–Unicam SP 8000 spectrophotometer using matched 1-cm quartz cells. The solvent was methanol and absorption maxima are given in nanometres (nm); the figures in parentheses are ε values. Infrared spectra were obtained on a Perkin–Elmer Model 137 spectrophotometer using potassium bromide discs unless otherwise stated. ^{1}H-NMR spectra were determined on a Varian Associates T-60 instrument. Chemical shifts are reported on the δ scale relative to Me_4Si used as an internal standard. The letters br, s, d and m are used to indicate broad, singlet, doublet and multiplet, respectively. The mass spectra were determined on an AE1 MS-9 double-focusing mass spectrometer at 70 eV.

3.2. 2-Amino-6-methylpyridine-3-thiol, 10

2-Amino-6-picoline (**8**) was converted to 2-amino-6-methyl-3-thiocyanatopyridine (**9**), followed by refluxing with 20% sodium hydroxide for 8 h instead of 4 h as previously described. The resulting crude 2-amino-6-methylpyridine-3-thiol (**10**) was collected and recrystallized from aqueous methanol–DMF mixture (Norit); m.p. 244–5°C (dec.).

3.3. 6-Chloro-10-methylbenzo[*a*]-11-azaphenothiazin-5-one, 12

2-Amino-6-methylpyridine-3-thiol (**10**; 1·40 g, 10 mmol) was added to a mixture of 2·12 g (20 mmol) anhydrous sodium carbonate in 55 ml of

benzene–DMF (10:1) mixture. The mixture was warmed for 15 min while stirring.

2,3-Dichloro-1,4-naphthoquinone (**11**; 2·50 g, 11 mmol) was then added and the mixture refluxed for 3 h. As reaction proceeded, the yellowish slurry gradually turned to a purple colour which became more intense with time. At the end of the reflux period, the solvent was removed by evaporation to near-dryness on a steam bath. Water (500 ml) was added to remove the inorganic salts, and the mixture was stirred and filtered. The aqueous filtrate was discarded.

The dark purple residue was crystallized from acetone after treatment with activated charcoal. Brown crystals of 6-chloro-10-methylbenzo[*a*]-11-azaphenothiazin-5-one (**12**; 2·52 g, 81% yield) were isolated; m.p. >300°C (dec.); λ_{max} 502 (1019), 391 (2038), 310 (8152), 279 (21 060), 244 nm (18 478); ν_{max} 1640 (strong, C=O), 820 (strong, 2,3,6-trisubstituted pyridine), 740 cm^{-1} (medium, 1,2-disubstituted benzene); δ 7·32 (m, 6H, aromatic protons) and 1·50 (s, 3H, 10-CH_3); *m/e* 312 (M^+, 100%), 314 (M + 2, 34%). $C_{16}H_9N_2ClOS$ requires: C, 61·44; H, 2·88; N, 8·96; Cl, 11·36; S, 10·24%.

3.4. 6-Chloro-10-methyl-12*H*-benzo[*a*]-11-azaphenothiazin-5-ol, 14

A mixture of 6-chloro-10-methylbenzo[*a*]-11-azaphenothiazin-5-one (**12**; 1·563 g, 5 mmol) and 2·61 g (15 mmol) sodium hydrosulphite in 55 ml of acetone–water (10:1) mixture was refluxed for 2 h. Colour change was observed from purple to yellow. The mixture was poured into 1 litre of chilled water containing 5 g sodium hydrosulphite. The reduced yellow product **14** could not be isolated by filtration since it was oxidized by atmospheric oxygen during filtration to the purple quinoid starting compound **12**.

3.5. 8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one, 18

4,6-Diaminopyrimidine (**15**) was converted to the 5-thiocyanato derivative (**16**) by reaction with sodium thiocyanate and bromine in glacial acetic acid at −5°C. The resulting product was hydrolysed in 15–20% sodium hydroxide. The 4,6-diaminopyrimidine-5-thiol (**17**; 0·71 g, 0·005 mol) thus formed was taken up in 100 ml of benzene containing 10 ml of *N,N*-dimethylformamide. Anhydrous sodium carbonate was added and the mixture warmed for 20 min on a water bath with stirring.

To this slurry was added 2,3-dichloro-1,4-naphthoquinone (**11**) (1·25 g, 5·5 mmol) and the mixture refluxed for 4 h while stirring, during which time a colour change from yellow to dark purple was observed. Benzene was removed by distillation and water (500 ml) was then added to the near-solid

product to remove inorganic materials. On filtering, the aqueous filtrate was discarded and the dark purple residue was crystallized from a large quantity of acetone after treatment with decolourizing carbon. 8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one (**18**; 1·54 g, 98% yield) was obtained as a bluish-purple powder, m.p. >300°C (dec.); λ_{max} 506 (4462), 321 nm (10 759); ν_{max} 3360 (8-NH_2), 1643 (C=O), 897 (10-CH in the pyrimidine moiety), 782 cm^{-1} (four adjacent hydrogen atoms in the naphthalene moiety); *m/e* 314 [M^+, 100%], 316 [M + 2, 38]. (Found: C, 53·19; H, 2·38; N, 18·00; Cl, 11·25; S, 10·02. $C_{14}H_7N_4ClOS$ requires: C, 53·42; H, 2·22; N, 17·81; Cl, 11·29; S, 10·17%.)

3.6. 8-Acetamido-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one, 20 (R = Ac, X = 0)

8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one (**18**; 0·63 g, 2 mmol) was added to 25 ml acetyl chloride containing 1 ml pyridine. The mixture was refluxed for 4 h while stirring. Removal of the excess acetyl chloride by distillation gave a solid residue which was washed with water and recrystallized from acetone after treatment with activated charcoal to give 8-acetamido-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one (**20**; 0·66 g, 93% yield) as a brown solid; m.p. >300°C; λ_{max} 261 (12 300), 306 (12 880), 349 (6457), 488 nm (4169); ν_{max} 3500 (8-NHAc), 1700 cm^{-1} (C=O). (Found: C, 53·61; H, 2·59; N, 15·88; Cl, 10·12; S, 9·12. $C_{16}H_9N_4ClOS$ requires: C, 53·86; H, 2·52; N, 15·71; Cl, 9·96; S, 8·98%.)

3.7. 8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-ol, 21 (R = H, X = 0)

8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one, **18**, was reduced with sodium hydrosulphite, as described for 6-chloro-10-methyl-12*H*-benzo[*a*]-11-azaphenothiazin-5-ol (**14**). The yellow product could not be isolated as it was readily oxidized by atmospheric oxygen to the starting bluish-purple diazaphenothiazinone, **18**.

3.8. 6-Chlorobenzo[*a*]-11-azaphenoxazin-5-one, 23

To a mixture of 2-aminopyridin-3-ol (1·10 g, 10 mmol) and 2,3-dichloro-1,4-naphthoquinone (**11**; 2·27 g, 10 mmol) was added anhydrous sodium carbonate (3·18 g, 30 mmol) and 90 ml chloroform and the slurry refluxed with stirring for 3 h. Solvent was removed and water (600 ml) added to remove inorganic materials. The filtrate was discarded and the residue was recrystallized from aqueous DMF after treatment with activated charcoal.

Orange crystals of 6-chlorobenzo[*a*]-11-azaphenoxazin-5-one (**23**) (2·74 g, 97% yield) were obtained, m.p. 232–3°C (dec.); λ_{max} 438 (25 168), 349 (24 141), 262 (31 075), 257 (31 332), 24 nm (34 927); ν_{max} 3088 (aromatic protons), 1680 (C=O), 1207 (Ar—O—Ar), 770 cm^{-1} (four adjacent hydrogen atoms); δ 8·67 (m, 1H, 4H), 8·55 (m, 1H, 10H), 7·50–8·26 (m, 5H, 1H, 2H, 3H, 8H, 9H); *m/e* 284 [M + 2, 34%], 282 [M^-, 100%], 254 (M − CO, 29%), 219 (M − CO − Cl, 9%). (Found: C, 63·82; 2·49; N, 9.86; Cl, 12·51. $C_{15}H_7N_2ClO$ requires: C, 63·72; H, 2·48; N, 9·91; Cl, 12·56%.)

3.9. 8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-(2,4-dinitrophenyl)hydrazone, 20 (R = H, X = 2,4-dinitrophenylhydrazyl)

8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one (0·3 g, 0·95 mmol) was mixed with 2,4-dinitrophenylhydrazine (0·19 g, 0·095 mmol). Dimethyl sulphoxide (5 ml) was added and the mixture refluxed for 1 h. The resulting dark brown solution was cooled and diluted with 10 ml of ice-cold water and chilled. On filtration, a dark brown residue was collected and recrystallized from aqueous methanol. 8-Amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-(2,4-dinitrophenyl)hydrazone (0·3 g, 64% yield) was collected as a purple-red powder, m.p. >300°C; λ_{max} 250 (14 450), 316 (23 440), 352 (17 780), 500 nm (8511); ν_{max} 3340 (8-NH_2), 1330 cm^{-1} (NO_2); *m/e* 494 [69%, M^+], 496 [23%, M + 2].

4. CONCLUSION

The three compounds 6-chloro-10-methylbenzo[*a*]-11-azaphenothiazin-5-one (**12**), 8-amino-6-chlorobenzo[*a*]-9,11-diazaphenothiazin-5-one (**18**) and 6-chlorobenzo[*a*]-11-azaphenoxazin-5-one (**23**) are respectively new brown, bluish-purple and orange colourants applicable as vat and direct dyes to textile materials. Ease of production and good fastness to washing, light and basic solutions make them suitable for commercial application. However, they are not fast to dilute acids and the observed discoloration is not reversed by the addition of a base. Shoe polish and leather varnishes have been compounded using these dyes as the colourants.

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REFERENCES

1. S. P. Massie, *Chem. Rev.*, **54**, 797 (1954).
2. C. Bodea and I. Silberg, in *Advances in heterocyclic chemistry*, Vol. 9, ed. A. R. Katritzky and A. J. Boulton, pp. 321–460. New York, Academic Press (1968).
3. M. Ionescu and H. Mantsch, in *Advances in heterocyclic chemistry*, Vol. 8, ed. A. R. Katritzky and A. J. Boulton, pp. 83–113. New York, Academic Press (1967).
4. C. O. Okafor, *Int. J. Sulfur Chem., B*, **6**, 237 (1971).
5. C. O. Okafor, *Int. J. Sulfur Chem., B*, **7**, 109 (1972).
6. C. O. Okafor, *Phosphorus and Sulfur*, **4**, 79 (1978).
7. C. O. Okafor, M. L. Steenberg and J. P. Buckley, *Chem. Pharm. Bull. (Japan)*, **30**, 302 (1982).
8. C. O. Okafor, M. L. Steenberg and J. P. Buckley, *Eur. J. Med. Chem.*, **12**, 249 (1977).
9. C. O. Okafor, *Dyes and Pigments*, **7**, 249 (1986).
10. C. O. Okafor, *Dyes and Pigments*, **7**, 103 (1986).
11. O. Kym, *Ber. Deut. Chem. Ges.*, **23**, 2458 (1890).
12. A. Bernthsen, *Ber. Deut. Chem. Ges.*, **16**, 2896 (1883).
13. R. Meldola, *Ber. Deut. Chem. Ges.*, **12**, 2065 (1879).
14. G. W. K. Cavill, P. S. Clezy, J. R. Tetaz and R. L. Werner, *Tetrahedron*, **5**, 275 (1959).
15. G. W. K. Cavill, P. S. Clezy and F. B. Whitfield, *Tetrahedron*, **12**, 139 (1961).
16. H. Brockmann, in *The chemistry of natural products*, pp. 405–24. IUPAC, Section of Organic Chemistry. London, Butterworths (1961).
17. C. Hackmann, *Z. Krebsforsch.*, **58**, 607 (1952).
18. C. O. Okafor, *Int. J. Sulfur Chem., B*, **6**, 345 (1971).
19. A. Butenandt, U. Schiedt, E. Biekert and P. Kornmann, *Justus Liebigs Ann. Chem.*, **586**, 217 (1954).
20. A. Butenandt, E. Biekert, H. Kuebler, B. Linzen and P. Traub, *Hoppe-Seylers Z. Physiol. Chem.*, **334**, 71 (1963).
21. A. Butenandt and R. Beckmann, *Hoppe-Seylers Z. Physiol. Chem.*, **301**, 115 (1955).
22. N. L. Agarwal and R. L. Mital, *J. Chem. Eng. Data*, **20**, 199 (1975).
23. N. L. Agarwal and W. Schafer, *J. Org. Chem.*, **45**, 2155, 5144 (1980).
24. C. O. Okafor, I. O. Uche and L. E. S. Akpanisi, *J. Heterocyclic Chem.*, **18**, 1589 (1981).
25. C. O. Okafor, *J. Org. Chem.*, **47**, 592 (1982).
26. C. O. Okafor, R. N. Castle and D. S. Wise Jr, *J. Heterocyclic Chem.*, **20**, 1047 (1983).
27. A. N. Gritsenko, Z. I. Ermakova, T. Ya. Mozhaeva, V. S. Troitskaya and S. V. Zhuravlev, *Khim. Geterotsikl. Soedin.*, (1)50 (1975); *Chem. Abstr.*, **83**, 9942e (1975).

28. C. O. Okafor, *Tetrahedron*, **42**(10), 2771 (1986).
29. E. Noelting, *Chimie et Industrie*, **8**, 758 (1922); *Chem. Abstr.*, **17**, 473 (1923).
30. M. S. Newman and C. Y. Perry, *J. Org. Chem.*, **28**, 116 (1963).
31. C. O. Okafor, *J. Org. Chem.*, **38**, 5383 (1973).
32. C. O. Okafor, *J. Org. Chem.*, **40**, 2753 (1975).
33. C. O. Okafor, *J. Heterocyclic Chem.*, **17**, 1587 (1980).