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Synthesis of 6-Acetamido-2-substituted Quinoxaline Derivatives and Their Use as Fluorescent Whiteners for Polyester Fibres

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SUMMARY

6-Nitro-2-chloroquinoxaline (**3**), *obtained from quinoxalin-2-one* (**1**) *by nitration and subsequent treatment with phosphorus oxychloride, was condensed with amines, alcohols and phenols to give 6-nitro-2-substituted quinoxalines* (**5a–5d**, **8a–8b** *and* **11a–11b**). *The nitro compounds were reduced to the corresponding amino compounds* (**6a–6d**, **9a–9b** *and* **12a–12b**) *and then acetylated to yield 6-acetamido-2-substituted quinoxalines* (**7a–7d**, **10a–10b** *and* **13a–13b**). *6-Nitro-2-substituted amino quinoxalines* (**5a–5d**) *and 6-acetamido-2-substituted quinoxalines* (**7a–7d**, **10a–10b** *and* **13a–13b**) *were evaluated as disperse dyes and fluorescent whiteners respectively on polyester fibres.*

1. INTRODUCTION

A wide variety of heterocyclic compounds have been reported to be useful as fluorescent whiteners and in this context we have reported[1] the use of 1,3,4-oxadiazole derivatives.

In the present work, quinoxaline derivatives have been synthesised and evaluated as disperse dyes and fluorescent whiteners for polyester fibres. Although quinoxaline derivatives have been reported to be useful as cyanine dyes,[2],[3] reactive dyes[4] and azopyrazoloquinoxaline disperse

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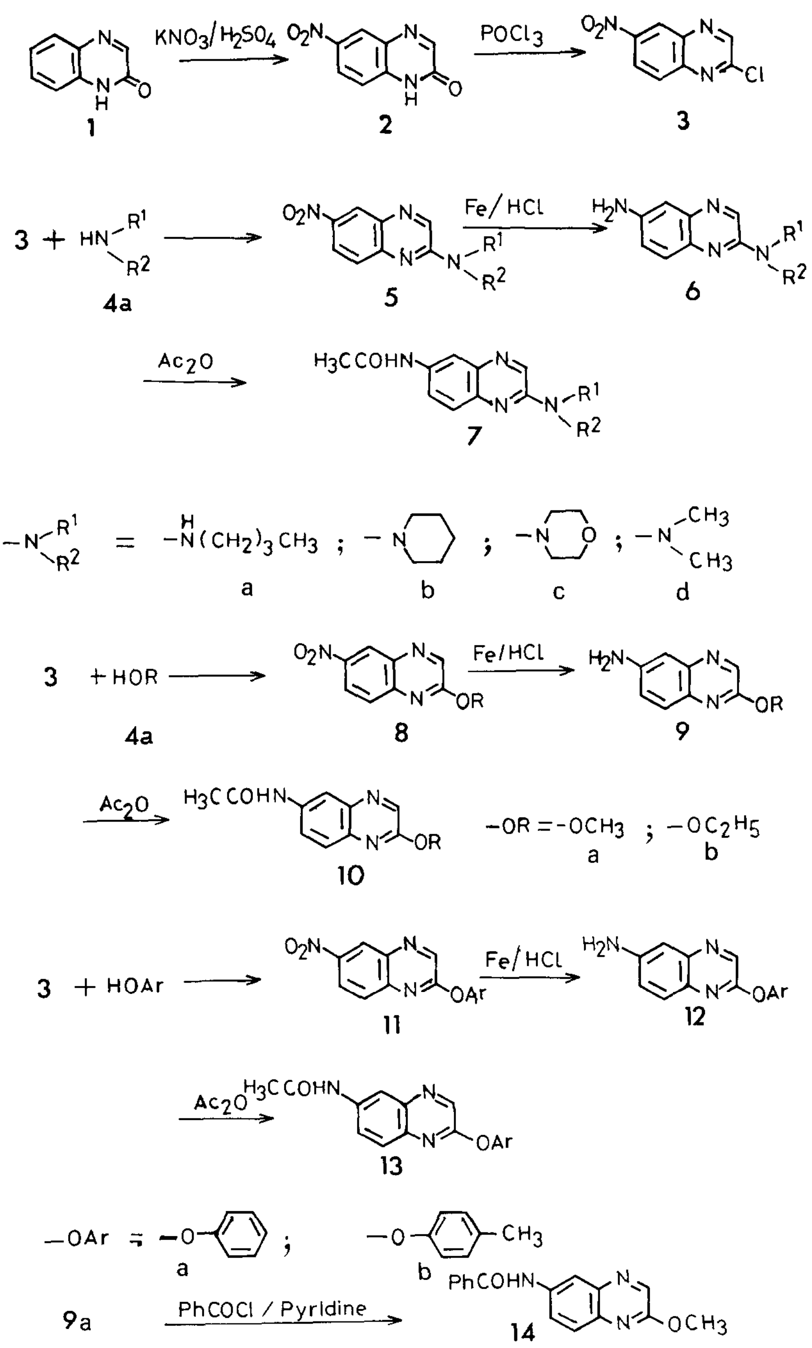
dyes,[5] the quinoxaline moiety has not been exploited much in the field of dyes and fluorescent whiteners. In studies of the synthesis of heterocyclic compounds with appropriate substitutions useful as fluorophoric systems, it was found that quinoxaline derivatives suitably substituted in 2- and 6-positions fluoresce in the blue region in daylight. We report here the synthesis of some 6-acetamido-2-substituted quinoxaline derivatives (**7a–7d**, **10a–10b** and **13a–13b**) and their use as fluorescent whiteners for polyester fibres. 6-Nitro-2-substituted aminoquinoxalines (**5a–5d**), the bright yellow intermediate compounds in the synthesis of the above, were also applied as disperse dyes to polyester fibres.

2. RESULTS AND DISCUSSION

Various 6-acetamido-2-substituted aminoquinoxalines (**7a–7d**), 6-acetamido-2-alkoxyquinoxalines (**10a–10b**) and 6-acetamido-2-aryloxyquinoxalines (**13a–13b**) were synthesised from 6-nitro-2-chloroquinoxaline (**3**) as a common starting material. The chlorine atom in **3** is highly reactive with nucleophiles, being conjugated both to the nitro group in the 6-position and to a nitrogen atom in the heterocyclic system. Compound **3**, on reaction with substituted amines, alcohols and phenols afforded the corresponding amino, alkoxy and aryloxy derivatives. The resulting 6-nitro-2-substituted quinoxalines (**5a–5d**, **8a–8b** and **11a–11b**) were reduced with iron and hydrochloric acid to give the 6-amino-2-substituted quinoxalines (**6a–6d**, **9a–9b** and **12a–12b**) which were subsequently acetylated with acetic anhydride to yield the 6-acetamido-2-substituted quinoxalines (**7a–7d**, **10a–10b** and **13a–13b**).

To compare the effect of a benzamido group at the 6-position in place of the acetamido group, 6-benzamido-2-methoxyquinoxaline (**14**) was also synthesised and its properties compared with the compounds containing the acetamido group.

The PMR spectrum of 6-nitro-2-dimethylaminoquinoxaline (**5d**) in trifluoroacetic acid showed a singlet centered at 3·7 (6H, aliphatic) corresponding to two methyl groups, a finely split doublet ($J_{7-8} = 10$ Hz) centered at 8·0 (1H, aromatic) corresponding to C-8, two finely split doublets ($J_{7-8} = 10$ Hz, $J_{5-7} = 2$ Hz) centered at 8·66 (1H, aromatic) corresponding to C-7, a finely split doublet ($J_{5-7} = 2$ Hz) centered at 9·0 (1H, aromatic) corresponding to C-5 and a sharp singlet at 9·2 (1H,


KNO3/H2SO4
POCl3
1
2
3
3 + HN R1 R2
4a
5
Fe/HCl
6
Ac2O
7
−N(CH2)3CH3
a
b
c
d
3 + HOR
4a
8
Fe/HCl
9
Ac2O
10
−OR = −OCH3 ; −OC2H5
a
b
3 + HOAr
11
Fe/HCl
12
Ac2O
13
−OAr =
a
b
9a
PhCOCl / Pyridine
14

aromatic) corresponding to C-3. The PMR spectrum of 6-amino-2-morpholinoquinoxaline (**6c**) in DMSO-d_6 showed a multiplet centered between 3·5 to 4·0 corresponding to eight protons of the morpholine residue and two D_2O-exchangeable protons corresponding to the amino group, a multiplet centered between 6·8 and 7·5 corresponding to three aromatic protons at C-5, C-7 and C-8, and a sharp singlet centered at 8·6 corresponding to the aromatic proton at C-3.

The IR spectrum of compound **5a** showed a peak at 3280 cm^{-1} corresponding to the —NH— group and the spectra of compounds **6a–6d**, **9a–9b** and **12a–12b** (recorded in Nujol mull) showed peaks at 3220 cm^{-1} and 3320 cm^{-1} corresponding to the amino group. The IR spectra of compounds **7a–7d**, **10a–10b**, **13a–13b** and **14** (recorded in Nujol mull) showed a peak at 3300 cm^{-1} corresponding to the —NH— group and a peak at 1720 cm^{-1} corresponding to the —C=O group.

Absorption maxima and fluorescence emission maxima are given in Table 1. The 6-nitro-2-substituted quinoxalines (**5a–5d**, **8a–8b** and **11a–11b**) did not give fluorescence emission maxima, indicating that these compounds do not fluoresce in daylight. The 6-amino-2-substituted quinoxalines (**6a–6d**, **9a–9b** and **12a–12b**) showed emission maxima in the greenish-blue to green region and are thus not suitable for use as fluorescent whiteners. The 6-acetamido-2-substituted quinoxalines (**7a–7d**, **10a–10b**, **13a–13b**) and 6-benzamido-2-methoxyquinoxaline (**14**) showed fluorescence emission maxima in the region close to blue (410–470 nm) and the spectral properties of these compounds may thus be considered satisfactory in accord with standard fluorescent whitener requirements. The quantity of compounds (Q) dissolved in 100 ml of solvent required for 100 units of intensity indicated that for the 6-acetamido-2-substituted quinoxalines (**7a–7d**, **10a–10b** and **13a–13b**) and 6-benzamido-2-substituted quinoxaline (**14**) the quantity required was comparable with that for a standard fluorescent whitener (e.g. 7-*N*,*N*-diethylamino-4-methylcoumarin requires $Q = 1{\cdot}52$ mg).

The 6-acetamido-2-substituted quinoxalines **7a–7d**, **10a–10b** and **13a–13b** and 6-benzamido-2-methoxyquinoxaline **14** were applied to polyester fibres as fluorescent whiteners and in general showed only a moderate whitening effect of the fibre. The 6-nitro-2-substituted aminoquinoxalines **5a–5d** were applied to polyester fibres as disperse dyes and had a generally low pick-up, moderate light fastness and excellent sublimation fastness.

TABLE 1

Absorption and Fluorescence Emission Spectra of Quinoxaline Derivatives

Compound	*Absorption max (nm)*	*Fluorescence emission max (nm)*	*log e*	*Q (mg)*
5a	385	—	4·18	—
5b	400	—	4·15	—
5c	393	—	4·24	—
5d	397	—	3·92	—
6a	413	505	3·75	3·13
6b	421	512	3·72	3·45
6c	416	520	3·68	3·41
6d	403	503	3·72	3·90
7a	361	419	4·13	1·71
7b	384	464	4·12	1·73
7c	389	470	4·20	1·79
7d	385	410	4·05	1·82
8a	327	—	4·05	—
8b	328	—	4·15	—
9a	393	499	3·80	3·13
9b	384	483	3·95	3·12
10a	338	424	3·81	1·76
10b	355	424	3·80	1·68
11a	330	—	4·04	—
11b	330	—	4·17	—
12a	403	511	3·91	3·81
12b	404	510	3·93	3·92
13a	362	457	4·00	1·83
13b	360	442	4·07	1·97
14	354	438	4·11	1·97

3. EXPERIMENTAL

All the melting points are uncorrected and are in °C. Absorption and fluorescence emission spectra in DMF solutions were recorded on a Beckman Model 25 spectrophotometer and an Aminco Bowman spectrophotofluorimeter respectively. Infrared spectra were recorded on a Perkin-Elmer Model 397 spectrometer. The PMR spectra were recorded on a Varian 60 MHz instrument EM-360-L using TMS as internal standard; the chemical shifts are given on the δ (ppm) scale.

3.1. Preparation of starting materials

Commercially available quinoxalin-2-one (**1**) was used. 6-Nitroquinoxalin-2-one (**2**)[6] and 6-nitro-2-chloroquinoxaline (**3**)[6] were prepared by known methods.

3.2. 6-Nitro-2-(*n*-butylamino)quinoxaline (5a)

To well-cooled *n*-butylamine (10 ml) was added 6-nitro-2-chloroquinoxaline (**3**) (2·1 g, 0·01 mol) very slowly with stirring. A yellow solid separated and after the addition was complete, the reaction mixture was refluxed for 2 h. The resultant reaction mixture was cooled to room temperature and then added slowly to ice water. The yellow solid which separated was filtered, washed with water and dried. It was recrystallised from benzene to give **5a** as yellow needles (94%), m.p. 178°. Calculated for $C_{12}H_{14}N_4O_2$: C, 58·5; H, 5·7; N, 22·7. Found: C, 58·4; H, 5·5; N, 22·6%.

The synthesis of other 6-nitro-2-substituted aminoquinoxalines (**5b–5d**) was carried out in a similar way using the typical procedure described above.

3.3. 6-Nitro-2-piperidinoquinoxaline (5b)

Crystallised from benzene as yellow crystals (93%), m.p. 150°. Calculated for $C_{13}H_{14}N_4O_2$: C, 60·5; H, 5·4; N, 21·7. Found: C, 60·5; H, 5·2; N, 21·4%.

3.4. 6-Nitro-2-morpholinoquinoxaline (5c)

Crystallised from benzene as yellow needles (95%), m.p. 208°. Calculated for $C_{12}H_{12}N_4O_3$: C, 55·4; H, 4·6; N, 21·5. Found: C, 55·2; H, 4·4; N, 21·3%.

3.5. 6-Nitro-2-dimethylaminoquinoxaline (5d)

Crystallised from benzene as yellow crystals (94%), m.p. 238°. Calculated for $C_{10}H_{10}N_4O_2$: C, 55·0; H, 4·6; N, 25·6. Found: C, 49·8; H, 4·4; N, 25·5%.

3.6. 6-Nitro-2-methoxyquinoxaline (8a)

Sodium (0·23 g, 0·01 mol) was slowly added to absolute methanol (200 ml) with stirring and to the resultant solution was added 6-nitro-2-chloroquinoxaline (**3**) (2·1 g, 0·01 mol). The reaction mixture was refluxed for 5 h then cooled to room temperature and slowly added to ice water. The pale yellow solid which separated was filtered, washed with water and dried. It was recrystallised from benzene to give **8a** as pale yellow crystals (89%), m.p. 171°. Calculated for $C_9H_7N_3O_3$: C, 52·7; H, 3·4; N, 20·5. Found: C, 52·5; H, 3·1; N, 20·3%.

3.7. 6-Nitro-2-ethoxyquinoxaline (8b)

The compound **8b** was synthesised similarly using the typical procedure described in Section 3.6. Crystallised from benzene as pale yellow crystals (85%), m.p. 148°. Calculated for $C_{10}H_9N_3O_3$: C, 54·8; H, 4·1; N, 19·2. Found: C, 54·4; H, 4·1; N, 19·0%.

3.8. 6-Nitro-2-phenoxyquinoxaline (11a)

A mixture of 6-nitro-2-chloroquinoxaline (**3**) (2·1 g, 0·01 mol), anhydrous potassium carbonate (1·38 g, 0·01 mol) and phenol (0·94 g, 0·01 mol) was refluxed in dry xylene (30 ml) for 7–8 h. The reaction mixture was filtered hot to remove impurities and the filtrate, on cooling to room temperature, yielded a white solid, which was filtered, washed with water and dried. The product was recrystallised from benzene to give **11a** as colourless needles (82%), m.p. 189°. Calculated for $C_{14}H_9N_3O_3$: C, 62·9; H, 3·4; N, 15·7. Found: C, 62·9; H, 3·1; N, 15·4%.

3.9. 6-Nitro-2-(4′-methylphenoxy)quinoxaline (11b)

The compound **11b** was synthesised similarly using the typical procedure described in Section 3.8. Crystallised from benzene as colourless needles (84%), m.p. 185°. Calculated for $C_{15}H_{11}N_3O_3$: C, 64·0; H, 3·9; N, 14·9. Found: C, 63·7; H, 3·7; N, 14·8%.

3.10. 6-Amino-2-(*n*-butylamino)quinoxaline (6a)

A stirred mixture of 6-nitro-2-(*n*-butylamino)quinoxaline (**5a**) (2·46 g, 0·01 mol) and water (200 ml) was heated to 65–70° and iron (1·68 g) soaked with concentrated hydrochloric acid (0·05 mol) was slowly added to it with stirring. After the addition was complete, the mixture was stirred under reflux for 8–9 h. The mixture was filtered hot and the filtrate concentrated to 50 ml and then repeatedly extracted with ethyl acetate–benzene (1:1) mixture. The amino compound, extracted in the organic layer, was recovered by distillation of the solvents. The compound thus obtained was filtered, dried and recrystallised from benzene to give colourless crystals (65%), m.p. 125°. Calculated for $C_{12}H_{16}N_4$: C, 66·7; H, 7·4; N, 25·9. Found: C, 66·6; H, 7·2; N, 25·8%.

The synthesis of other 6-amino-2-substituted aminoquinoxalines (**6b**–**6d**) was carried out in a similar way using the typical procedure described above. 6-Amino-2-alkoxyquinoxalines (**9a**–**9b**) and 6-amino-2-aryloxyquinoxalines (**12a**–**12b**) were synthesised similarly, except that these compounds were readily isolated on cooling the filtrate. 6-Amino-2-alkoxyquinoxalines (**9a**–**9b**) and 6-amino-2-aryloxyquinoxalines (**12a**–**12b**) separated and were recrystallised for purification as described below.

3.11. 6-Amino-2-piperidinoquinoxaline (6b)

Crystallised from benzene to give colourless crystals (62%), m.p. 160°. Calculated for $C_{13}H_{16}N_4$: C, 68·4; H, 7·0; N, 24·6. Found: C, 68·2; H, 6·8; N, 24·4%.

3.12. 6-Amino-2-morpholinoquinoxaline (6c)

Crystallised from benzene to give pale yellow needles (66%), m.p. 163°. Calculated for $C_{12}H_{14}N_4O$: C, 62·6; H, 6·0; N, 24·4. Found: C, 62·3; H, 5·9; N, 24·3%.

3.13. 6-Amino-2-*N*,*N*-dimethylaminoquinoxaline (6d)

Crystallised from benzene to give colourless needles (64%), m.p. 120°. Calculated for $C_{10}H_{12}N_4$: C, 63·8; H, 6·4; N, 29·8. Found: C, 63·5; H, 6·1; N, 29·7%.

3.14. 6-Amino-2-methoxyquinoxaline (9a)

Crystallised from ethanol to give colourless crystals (66%), m.p. 160°.

Calculated for $C_9H_9N_3O$: C, 61·7; H, 5·1; N, 24·0. Found: C, 61·4; H, 5·0; N, 23·8%.

3.15. 6-Amino-2-ethoxyquinoxaline (9b)

Crystallised from ethanol to give colourless crystals (65%), m.p. 110°. Calculated for $C_{10}H_{11}N_3O$: C, 63·5; H, 5·8; N, 22·2. Found: C, 63·1; H, 5·4; N, 22·1%.

3.16. 6-Amino-2-phenoxyquinoxaline (12a)

Crystallised from ethanol to give colourless crystals (69%), m.p. 180°. Calculated for $C_{14}H_{11}N_3O$: C, 70·9; H, 4·6; N, 17·7. Found: C, 70·6; H, 4·2; N, 17·6%.

3.17. 6-Amino-2-(4′-methylphenoxy)quinoxaline (12b)

Crystallised from ethanol to give colourless crystals (68%), m.p. 185°. Calculated for $C_{15}H_{13}N_3O$: C, 71·7; H, 5·2; N, 16·7. Found: C, 71·4; H, 5·0; N, 16·5%.

3.18. 6-Acetamido-2-(*n*-butylamino)quinoxaline (7a)

A mixture of 6-amino-2-(*n*-butylamino)quinoxaline (**6a**) (2·16 g, 0·01 mol) and acetic anhydride (35–40 ml) was refluxed for 3 h. The liquor was cooled and added to ice water, neutralised with sodium acetate and the solid which separated was filtered, washed with a little cold water and dried. It was recrystallised from ethanol to give colourless crystals (65%), m.p. 115°. Calculated for $C_{14}H_{18}N_4O$: C, 65·1; H, 6·9; N, 21·7. Found: C, 65·0; H, 6·6; N, 21·4%.

The synthesis of other 6-acetamido-2-substituted quinoxalines (**7b–7d**, **10a–10b** and **13a–13b**) was carried out in a similar way using the typical procedure described above for compound **7a**.

3.19. 6-Acetamido-2-piperidinoquinoxaline (7b)

Crystallised from ethanol as colourless needles (63%), m.p. 165°. Calculated for $C_{15}H_{18}N_4O$: C, 66·7; H, 6·7; N, 20·7. Found: C, 66·3; H, 6·4; N, 20·5%.

3.20. 6-Acetamido-2-morpholinoquinoxaline (7c)

Crystallised from ethanol as off-white needles (64%), m.p. 215°. Calculated for $C_{14}H_{16}N_4O_2$: C, 61·7; H, 5·9; N, 20·6. Found: C, 61·4; H, 5·8; N, 20·4%.

3.21. 6-Acetamido-2-*N*,*N*-dimethylaminoquinoxaline (7d)

Crystallised from ethanol as colourless crystals (61%), m.p. 205°. Calculated for $C_{12}H_{14}N_4O$: C, 62·6; H, 6·1; N, 24·3. Found: C, 62·4; H, 6·0; N, 24·2%.

3.22. 6-Acetamido-2-methoxyquinoxaline (10a)

Crystallised from ethanol as colourless needles (69%), m.p. 162°. Calculated for $C_{11}H_{11}N_3O_2$: C, 60·8; H, 5·1; N, 19·4. Found: C, 60·5; H, 5·0; N, 19·2%.

3.23. 6-Acetamido-2-ethoxyquinoxaline (10b)

Crystallised from ethanol as colourless needles (67%), m.p. 238°. Calculated for $C_{12}H_{13}N_3O_2$: C, 62·3; H, 5·6; N, 18·2. Found: C, 62·0; H, 5·4; N, 18·0%.

3.24. 6-Acetamido-2-phenoxyquinoxaline (13a)

Crystallised from ethanol as off-white crystals (70%), m.p. 230°. Calculated for $C_{16}H_{13}N_3O_2$: C, 68·8; H, 4·7; N, 15·1. Found: C, 68·7; H, 4·4; N, 14·8%.

3.25. 6-Acetamido-2-(4′-methylphenoxy)quinoxaline (13b)

Crystallised from ethanol as off-white crystals (71%), m.p. 222°. Calculated for $C_{17}H_{15}N_3O_2$: C, 69·6; H, 5·1; N, 14·3. Found: C, 69·4; H, 5·0; N, 14·1%.

3.26. 6-Benzamido-2-methoxyquinoxaline (14)

6-Amino-2-methoxyquinoxaline (0·875 g, 0·005 mol) was dissolved in pyridine (5–7 ml) and the mixture was cooled to 0°. To this mixture was added benzoyl chloride (0·59 ml, 0·005 mol) slowly with stirring. The reaction mixture was refluxed for 3 h, cooled to room temperature and added to ice water. The solid which separated was filtered, washed with water and dried. It was recrystallised from ethanol to yield colourless crystals (64·7%), m.p. 185°. Calculated for $C_{16}H_{13}N_3O_2$: C, 68·8; H, 4·7; N, 15·1. Found: C, 68·5; H, 4·4; N, 14·9%.

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