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Synthesis of 5-Hetarylpyrazolo[3,4-*b*]pyrazines and their Use as Disperse Dyes for Polyester Fibres

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ABSTRACT

*4-Nitroso-1-phenyl-3-methyl-5-aminopyrazole was condensed with ethylacetoacetate, ethyl benzoylacetate and diethyl malonate to give ethyl pyrazolo[3,4-*b*]pyrazine-5-carboxylates or the corresponding carboxylic acids in the first two cases. Similar condensations with malononitrile or cyanoacetamide gave 6-aminopyrazolo[3,4-*b*]pyrazine derivatives. Further condensation of these products with* o*-phenylenediamine or with* o*-aminophenol yielded 5-benzimidazolo- or 5-benzoxazolo-6-substituted pyrazolo[3,4-*b*]pyrazines, and with benzoyl hydrazide 5-(2-phenyloxadiazol-5-yl)-6-substituted pyrazolo[3,4-*b*]pyrazines were obtained. The resultant 5-hetaryl pyrazolo[3,4-*b*]pyrazines were applied to polyester and their fastness properties studied.*

1 INTRODUCTION

We have previously reported the synthesis of a number of fused heterocyclic systems such as pyrido[1,2-*a*]benzimidazoles,[1–4] fused quinoxalines[5–8] and pyrazolo-1,2,3-triazoles.[9]

We report here the synthesis of novel 5-hetarylpyrazolo[2,3-*b*]pyrazine derivatives (Scheme 1) and their use as disperse dyes for polyester fibres.

2 RESULTS AND DISCUSSION

Various 5-hetarylpyrazolo[2,3-*b*]pyrazines (**9a**–**9c**, **10a**–**10c**, **11a**–**11c**, **12a** and **12b**) were synthesised from 4-nitroso-1-phenyl-3-methyl-5-aminopyrazole (**1**) as starting material. Compound **1** was reacted with

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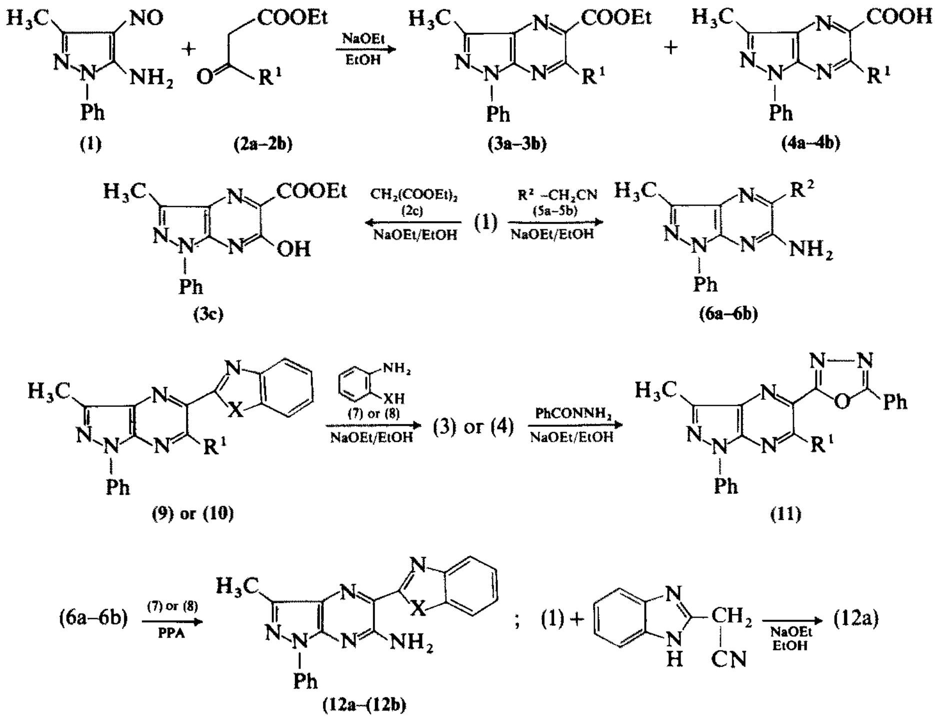

Compound						R^1
2a	3a	4a	9a	10a	11a	CH_3
2b	3b	4b	9b	10b	11b	Ph
—	3c	—	9c	10c	11c	OH

Compound					X
7	9a	9b	9c	12a	—NH—
8	10a	10b	10c	12b	—O—

5a, 6a $R^2 = CN$; 5b, 6b $R^2 = CONH_2$

Scheme 1

active-methylene keto compounds such as ethyl acetoacetate (**2a**) and ethyl benzoylacetate (**2b**) in refluxing ethanol containing sodium ethoxide. In each case, two compounds resulted. Reaction of **2a** gave the 6-methyl-5-carbethoxypyrazolopyrazine derivative (**3a**) together with the 6-methyl-5-carboxylic acid derivative (**4a**), whereas reaction of **2b** yielded the 6-phenyl-5-carbethoxy derivative (**3b**) and the 6-phenyl-5-carboxylic acid derivative (**4b**). The structures of compounds **3a**, **4a** and **3b**, **4b** were confirmed by elemental analyses and infrared spectra. The mass spectra of compounds **3a** and **4a** showed molecular ion peaks at 296 and 268 respectively. Compounds **3b** and **4a** were also confirmed by their ^1H-NMR spectra in deuterated chloroform. Thus, ^1H-NMR of compound **3b** showed a triplet centred at 1·1 ppm corresponding to $3\underline{H}$ of the —CH_3 in the carbethoxy group at C-5, a sharp singlet at 2·8 corresponding to $3\underline{H}$ of the —CH_3 group at C-3, a quartet centred at 4·3 corresponding to $2\underline{H}$ of the —CH_2— in the carbethoxy group at C-5, a broad multiplet between 7·1 and 7·9 corresponding to aromatic 8$\underline{H}$ (aromatic 5$\underline{H}$ due to protons of the phenyl group at C-6 and aromatic 3$\underline{H}$ due to protons 3′, 4′ and 5′ of the phenyl group at C-1), and a split doublet between 8·2 and 8·5 corresponding to aromatic 2$\underline{H}$ due to protons 2′ and 6′ of the phenyl group at O-1. The ^{1}H-NMR spectrum of compound **4a** showed a sharp singlet at 2·6 corresponding to 3$\underline{H}$ of the —CH_3 group at C-6, a sharp singlet at 2·8 corresponding to 3$\underline{H}$ of the —CH_3 group at C-3, a broad aromatic multiplet due to protons 3′, 4′ and 5′ of the phenyl group at C-1, a finely split doublet between 7·9 and 8·1 corresponding to aromatic 2$\underline{H}$ due to protons 2′ and 6′ of the phenyl group at C-1 and a singlet at 10·0 corresponding to 1$\underline{H}$ of the carboxylic acid group at C-5.

Compound **1**, when reacted with diethyl malonate (**2c**) in refluxing ethanol containing sodium ethoxide, yielded the 6-hydroxy-5-carbethoxypyrazolo[3,4-*b*]pyrazine derivative (**3c**) in excellent yield, no formation of the corresponding carboxylic acid being observed. The structure of compound **3c** was confirmed by its elemental analysis, infrared and ^{1}H-NMR spectra. Thus, its ^{1}H-NMR spectrum in deuterated chloroform showed a triplet centred at 1·4 corresponding to 3$\underline{H}$ of the —CH_3 in the carbethoxy group at C-5, a sharp singlet at 2·5 corresponding to 3$\underline{H}$ of the —CH_3 group at C-3, a quartet centred at 4·4 corresponding to 2$\underline{H}$ of the —CH_2— in the carbethoxy group at C-5, a multiplet between 7·0 and 7·4 corresponding to aromatic 3$\underline{H}$ due to protons 3′, 4′ and 5′ of the phenyl group at C-1, a doublet between 8·0 and 8·2 corresponding to aromatic 2$\underline{H}$ due to protons 2′ and 6′ of the phenyl group at C-1 and a broad singlet at 12 corresponding to 1$\underline{H}$ of the —OH group at C-6.

Compound **1** when reacted with malononitrile (**5a**) and cyanoacetamide (**5b**) in similar manner gave the 6-amino-5-cyano- and 6-amino-5-carboxamido-pyrazolo[3,4-*b*]pyrazines, **6a** and **6b**. The structures of these compounds were confirmed by elemental analyses and by infrared and mass spectra.

The compounds **3a**–**3c**, **4a**, **4b**, **6a** and **6b** were yellow to yellowish-brown solids and exhibited a moderate fluorescence in common organic solvents in daylight. 5-Hetarylpyrazolo[3,4-*b*]pyrazole derivatives were synthesised by converting the carbethoxy groups in **3a**–**3c** or the carboxylic acid groups in **4a** and **4b** to 5-benzimidazole, 5-benzoxazole and 5-(2-phenyl-oxadiazol-5-yl derivatives of 6-methyl-, 6-phenyl- and 6-hydroxy-pyrazolo[3,4-*b*] pyrazine (**9a**–**9c**, **10a**–**10c** and **11a**–**11c**). The 5-cyano and 5-acetamido groups in **6a** and **6b**, respectively, were similarly converted to 5-benzimidazolo- and 5-benzoxazolo-6-aminopyrazolo[3,4-*b*]pyrazines, **12a** and **12b**.

The structures of compounds **9a**–**9c**, **10a**–**10c**, **11a**–**11c**, **12a** and **12b** were confirmed by elemental analysis and by infrared and mass spectra, e.g. the mass spectra of compounds **9a**, **9c** and **12b** showed molecular ion peaks at 341, 343 and 341 respectively. The structures of compounds **11c**, **12a** and **12b** were further confirmed by their ^{1}H-NMR spectra. Thus, the ^{1}H-NMR spectrum of **11c** in DMSO-d_6 showed a sharp peak at 2·8 corresponding to 3H of the —CH_3 group at C-3, a broad multiplet between 7·2 and 7·8 corresponding to aromatic 6H (aromatic 3H due to protons 3′, 4′ and 5′ of the phenyl group in the 2-phenyloxadiazol-5-yl moiety at C-5, and aromatic 3H due to protons 3′, 4′ and 5′ of the phenyl group at C-1), a multiplet between 8·0 and 8·4 corresponding to aromatic 4H (aromatic 2H due to protons 2′ and 6′ of the phenyl group in the 2-phenyloxadiazol-5-yl moiety at C-5 and aromatic 2H due to protons 2′ and 6′ of the phenyl group at C-1) and a broad singlet at 11·5 corresponding to 1H of the —OH group at C-5. The ^{1}H-NMR spectrum of compound **12a** in trifluoroacetic acid showed a sharp singlet at 3·0 corresponding to 3H of the —CH_3 group at C-3 and a multiplet between 7·7 and 8·3 corresponding to aromatic 9H (aromatic 5H due to protons of the phenyl group at C-1 and aromatic 4H due to protons of the benzimidazolyl phenyl group at C-5). The ^{1}H-NMR spectrum of compound **12b** in deuterated chloroform showed a sharp singlet at 2·6 corresponding to 3H of the —CH_3 group at C-3, a multiplet between 7·2 and 7·8 corresponding to 2H of the NH_2 group at C-6 and aromatic 5H (aromatic 3H due to protons 3′, 4′ and 5′ of the phenyl group at C-1 and aromatic 2H due to protons 2′ and 3′ of the benzoxazolyl phenyl group at C-5) and a multiplet between 8·1 and 8·4 corresponding to aromatic 4H (aromatic 2H

TABLE 1
Absorption and Emission Spectra of 5-Hetarylpyrazolo[3,4-*b*]pyrazines

Compound	*Absorption* λ_{max} *(nm)*	*Absorbance* *A*	*Emission* λ_{max} *(nm)*	*Molar extinction coefficient* $\varepsilon \times 10^4$
9a	352	0·45	480	1·67
9b	360	0·63	498	2·03
9c	389	0·55	525	1·93
10a	317	0·39	490	1·59
10b	330	0·60	501	1·70
10c	358	0·51	529	1·56
11a	335	0·38	502	1·82
11b	348	0·58	508	2·54
11c	373	0·48	534	2·09
12a	379	0·54	497	1·74
12b	355	0·50	500	1·86

due to protons 2′ and 6′ of the phenyl group at C-1 and aromatic 2$\underline{H}$ due to protons 1′ and 4′ of the benzoxazolyl phenyl group at C-5).

Compound **12a** was also obtained directly, and in quantitative yield, by reaction of **1** with 2-cyanomethylbenzimidazole.

The 5-hetarylpyrazolo[3,4-*b*]pyrazines were bright yellow to yellow-brown crystalline solids. They exhibited a fair to intense green fluorescence, except for **12a** which showed blue fluorescence in daylight in DMF. The absorption maxima and emission maxima of the 5-hetarylpyrazolo[3,4-*b*] pyrazines were recorded in DMF and are given in Table 1. The absorption maxima and emission maxima of these compounds were in the ranges 317–389 nm and 480–534 nm, respectively. In general, comparing the 5-hetaryl derivatives in which the substituent of the 6-position is the same, it was observed that the presence of the 5-(2-phenyl-oxadiazol-5-yl) moiety showed a bathochromic shift in emission maxima compared with the 5-benzoxazolyl analogue, which in turn showed a bathochromic shift compared with the 5-benzimidazolyl analogue.

TABLE 2
Hues, Pick-Up and Fastness Properties of 5-Hetarylpyrazol[3,4-*b*]pyrazines on Polyester Fibres

Compound	*Hue*	*Pick-up*	*Light-fastness*	*Sublimation fastness*
9a	Orange	2	3	3
9b	Orange	3	4	3
9c	Greenish yellow	3	5	4
10a	Yellow	3	4	5
10b	Yellow	2	4	4
10c	Orange	2	5	4
11a	Greenish yellow	2	4	3
11b	Greenish yellow	2	4	3
11c	Orange	2	3	3
12a	Greenish yellow	2	2	2
12b	Greenish yellow	2	2	2

The 5-hetarylpyrazolo[3,4-*b*]pyrazines were applied to polyester as disperse dyes and gave fluorescent yellow, yellowish-brown and orange dyeings. The results of the dyeings are given in Table 2. The dyeings on polyester showed good pick-up (2 to 3), moderately good lightfastness (in most cases 4 to 5) and good sublimation fastness (mostly between 3 and 5). Dyeings of compounds **12a** and **12b** showed inferior fastness.

3 EXPERIMENTAL

All melting points are uncorrected and are in °C. Absorption and fluorescence emission spectra in DMF 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 ^{1}H-NMR spectra were recorded on a Varian 60-MHz instrument EM-360-L using TMS as internal standard and the chemical shifts, δ, are given in ppm.

3.1 Preparation of starting materials

4-Nitroso-1-phenyl-3-methyl-5-aminopyrazole (**1**),[10] benzoylhydrazide[11] and 2-cyanomethylbenzimidazole[12] were prepared by known methods.

3.2 Ethyl 3,6-dimethyl-1-phenylpyrazolo[3,4-*b*]pyrazine-5-carboxylate (3a) and 3,6-dimethyl-1-phenyl[3,4-*b*]pyrazine-5-carboxylic acid (4a)

Ethyl acetoacetate (**2a**) (3·9 g, 0·03 mol) was added to a previously prepared solution of sodium (0·46 g, 0·02 mol) in absolute ethanol (80 ml) and the mixture stirred at room temperature for 30 min. 4-Nitroso-1-phenyl-3-methyl-5-aminopyrazole (**1**) (4·04 g, 0·02 mol) was added, the temperature was raised to reflux and refluxing continued until the reaction was complete (6 h, monitored by TLC). The mixture was cooled to room temperature, poured onto an ice–water mixture (about 100 g) and the solid was filtered. The filtrate was used for the isolation of **4a**. The solid was thoroughly washed with water and dried. It crystallised from ethanol to give **3a** as pale yellow needles (55%), m.p. 311°. Calculated for $C_{16}H_{16}N_4O_2$: C, 64·9; H, 5·4; N, 18·9. Found: C, 65·1; H, 5·2; N, 18·3%.

The aqueous filtrate obtained in the above was treated with conc. hydrochloric acid (30%) until the pH was brought to 2, when a solid separated. The solid was filtered and washed with ice-cold water and dried. It was recrystallised from ethanol to give **4a** as yellow fine crystals (35%), m.p. 262°. Calculated for $C_{14}H_{12}N_4O_2$: C, 62·7; H, 4·5; N, 20·9. Found: C, 62·4; H, 4·5; N, 21·3%.

Compounds **3b**, **4b**, **3c**, **6a** and **6b** were synthesised in the same manner as above except that no carboxylic acids corresponding to **3c**, **6a** and **6b** were obtained.

3.3 Ethyl 1,6-diphenyl-3-methylpyrazolo[3,4-*b*]pyrazine-5-carboxylate (3b) and 1,6-diphenyl-3-methylpyrazolo[3,4-*b*]pyrazole-5-carboxylic acid (4b)

3b: Crystallised from ethanol as yellow needles (60%), m.p. 144–145°.

Calculated for $C_{21}H_{18}N_4O_2$: C, 70·4; H, 5·0; N, 15·6. Found: C, 71·0; H, 5·1; N, 15·5%.

4b: Crystallised from ethanol as pale yellow crystals (32%), m.p. 194–195°. Calculated for $C_{19}H_{14}N_4O_2$: C, 69·1; H, 4·2; N, 17·0. Found: C, 69·0; H, 4·2; N, 16·7%.

3.4 Ethyl 6-hydroxy-1-phenyl-3-methylpyrazolo[3,4-*b*]pyrazine-5-carboxylate (3c)

Crystallised from ethanol as yellow needles (77%), m.p. 156°. Calculated for $C_{15}H_{14}N_4O_3$: C, 60·4; H, 6·7; N, 18·8. Found: C, 60·4; H, 6·5; N, 18·7%.

3.5 6-Amino-5-cyano-1-phenyl-3-methylpyrazolo[3,4-*b*]pyrazine (6a)

Crystallised from acetic acid as yellow crystals (87%), m.p. 310° (decomp.). Calculated for $C_{13}H_{10}N_6$: C, 59·1; H, 3·8; N, 31·8. Found: C, 58·9; H, 3·6; N, 31·1%.

3.6 6-Amino-5-carboxamido-1-phenyl-3-methylpyrazolo[3,4-*b*]pyrazine (6b)

Crystallised from ethanol as yellow crystals (79%), m.p. 245–246°. Calculated for $C_{13}H_{12}N_6O$: C, 58·2; H, 4·5; N, 31·3. Found: C, 58·1; H, 4·3; N, 31·0%.

3.7 5-(Benzimidazol-2-yl)-3,6-dimethyl-1-phenylpyrazolo[3,4-*b*]pyrazine (9a)

A mixture compound **3a** (2·96 g, 0·01 mol) or **4a** (2·68 g, 0·01 mol) and *o*-phenylenediamine (**7**) (1·08 g, 0·01 mol) in ethane-1,2-diol (5 ml) was refluxed until the reaction was complete (5 h, monitored by TLC). The mixture was allowed to cool overnight to room temperature when a dark brown solid separated. This was crystallised from ethanol to give **9a** as dark brown microcrystals (68%), m.p. >350°. Calculated for $C_{20}H_{16}N_6$: C, 76·9; H, 5·1; N, 17·9. Found: C, 76·8; H, 5·0; N, 17·9%.

Compounds **9b**, **9c**, 10a–**10c** and **11a**–**11c** were synthesised in the same manner as described above for **9a** except that for **10a**–**10c**, *o*-aminophenol (**8**) and for **11a**–**11c** benzoyl hydrazide was used for the condensation instead of **7**.

3.8 5-(Benzimidazol-2-yl)-1,6-diphenyl-3-methylpyrazolo[3,4-*b*]pyrazine (9b)

Crystallised from DMF/ethanol (1:1) as yellow crystals (77%), m.p. 120°. Calculated for $C_{25}H_{18}N_6$: C, 72·6; H, 4·2; N, 19·6. Found: C, 72·5; H, 4·1; N, 19·5%.

3.9 5-(Benzimidazol-2-yl)-6-hydroxy-1-phenyl-3-methylpyrazolo[3,4-*b*] pyrazine (9c)

Obtained as fine yellow crystals (82%), m.p. 247–249°. Calculated for $C_{19}H_{14}N_6O$: C, 66·7; H, 4·1; N, 24·6. Found: C, 66·8; H, 3·9; N, 24·1%.

3.10 5-(Benzoxazol-2-yl)-3,6-dimethyl-1-phenylpyrazolo[3,4-*b*]pyrazine (10a)

Crystallised from ethanol as brown microcrystals (66%), m.p. 305–310° (decomp.). Calculated for $C_{20}H_{15}N_5O$: C, 70·4; H, 4·4; N, 20·5. Found: C, 70·4; H, 4·3; N, 20·1%.

3.11 5-(Benzoxazol-2-yl)-1,6-diphenyl-3-methylpyrazolo[3,4-*b*]pyrazine (10b)

Crystallised from DMF as yellowish brown crystals (69%), m.p. 121–122°. Calculated for $C_{25}H_{17}N_5O$: C, 74·4; H, 4·2; N, 17·4. Found: C, 74·4; H, 4·2; N, 17·2%.

3.12 5-(Benzoxazol-2-yl)-6-hydroxy-3-methyl-1-phenylpyrazolo[3,4-*b*] pyrazine (10c)

Crystallised from DMF as light brown crystals (80%), m.p. 286°. Calculated for $C_{19}H_{13}N_5O_2$: C, 66·5; H, 3·8; N, 20·4. Found: C, 66·1; H, 3·6; N, 20·1%.

3.13 5-(5-Phenyl-1,3,4-oxadiazol-2-yl)-3,6-dimethyl-1-phenylpyrazolo [3,4-*b*]pyrazine (11a)

Crystallised from ethanol as yellow crystals (75%), m.p. 340° (decomp.). Calculated for $C_{21}H_{16}N_6O$: C, 68·5; H, 4·3; N, 22·8. Found: C, 68·4; H, 4·3; N, 22·8%.

3.14 5-(5-Phenyl-1,3,4-oxadiazol-2-yl)-1,6-diphenyl-3-methylpyrazolo [3,4-*b*] pyrazine (11b)

Crystallised from DMF as yellow crystals (74%), m.p. 164–165°. Calculated for $C_{26}H_{18}N_6O$: C, 72·6; H, 4·2; N, 19·6. Found: C, 72·5; H, 4·1; N, 19·5%.

3.15 5-(5-Phenyl-1,3,4-oxadiazol-2-yl)-6-hydroxy-1-phenyl-3-methyl pyrazolo[3,4-*b*]pyrazine (11c)

Crystallised from benzene/ethyl acetate (4:1) as yellow crystals (79%), m.p. 128–130°. Calculated for $C_{20}H_{14}N_6O$: C, 67·8; H, 4·0; N, 23·7. Found: C, 67·9; H, 3·7; N, 23·9%.

3.16 5-(Benzimidazol-2-yl)-6-amino-1-phenyl-3-methylpyrazolo[3,4-*b*] pyrazine (12a)

Method A

A mixture of orthophosphoric acid (6 ml) and phosphorus pentoxide (10 g) was heated to 180°C with vigorous stirring and the temperature was maintained for 1 h, after which it was cooled to 100°C. Compound **6a** (1 g, 4 mmol) or **6b** (1 g, 3·75 mmol) and *o*-phenylenediamine (**7**) (0·54 g. 5 mmol) were then added with vigorous stirring and the temperature was raised to 140°C and maintained for the next 3 h. The mixture was cooled to room temperature and poured onto crushed ice (about 100 g) with stirring. The yellow solid obtained was filtered, washed with water until free of acid and dried. Recrystallisation from acetic acid gave **12a** as fine yellow crystals (49%), m.p. 220–221°. Calculated for $C_{19}H_{15}N_7$: C, 66·9; H, 4·4; N, 28·7. Found: C, 65·5; H, 4·3; N, 28·5%.

Method B

2-Cyanomethylbenzimidazole (1·88 g, 0·012 mol) and compound **1** (2·02 g, 0·01 mol) were condensed using sodium (0·23 g, 0·01 mol) in absolute ethanol (50 ml), following the procedure described above for **3a**. The crude product was obtained almost in quantitative yield and was recrystallised from acetic acid to give **12a** as fine yellow crystals (91%), m.p. 220–221°, identical to the product obtained by Method A.

3.17 5-(Benzoxazol-2-yl)-6-amino-1-phenyl-3-methylpyrazolo[3,4-*b*] pyrazine (12b)

This was prepared in the same manner as Method A above for **12a**. It was crystallised from acetic acid as yellow crystals (54%), m.p. 224°. Calculated for $C_{19}H_{14}N_6O$: C, 66·7; H, 4·1; N, 24·6. Found: C, 66·6; H, 3·9; N, 24·1%.

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