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Short Communication

Synthesis of 1,2-Fused Benzimidazo Heterocycles from Benzimidazole-2-acetonitrile and Heterocyclic *ortho*-Chloroaldehydes

SUMMARY

The condensation of 5-chloro-4-formyl-3-methyl-1-phenylpyrazole with benzimidazole-2-acetonitrile led to the formation of the fused heterocycle 3-methyl-1-phenyl-1H-pyrazolo[4,3:5,6]pyrido[1,2-a]benzimidazole-5-carbonitrile. Similar condensation of 2-chloro-3-formylquinoline derivatives gave the corresponding 1,2-fused benzimidazo heterocycles. These heterocycles underwent oxidative cyanation.

We have previously reported[1] the chloroformylation of 3-methyl-1-phenyl-5-pyrazolone and during the course of our investigations into the synthesis of new fluorescent whitening agents, the reaction of the chloroformyl pyrazole (**1**) with a bifunctional reagent such as benzimidazole-2-acetonitrile (**2**) was investigated. The product of this reaction was strongly fluorescent and the benzimidazole structure **3** is assigned to it on the basis of elemental analysis, mass spectrum (M^+ at *m/e* 323) and PMR spectrum (see Table 1).

In view of the strong fluorescence of compound **3**, the reaction of benzimidazole-2-acetonitrile (**2**) with other chloroaldehydes was investigated. Thus benzimidazole-2-acetonitrile (**2**) was reacted with 2-chloro-3-formyl-7-methyl-quinoline (**8**) and with 2-chloro-3-formyl-7*H*-benzoquinoline (**13**). The products obtained were bright yellow and were evaluated as dyes for polyester.

Moeckli[2] has recently reported cyanation at the 4-position of coumarins

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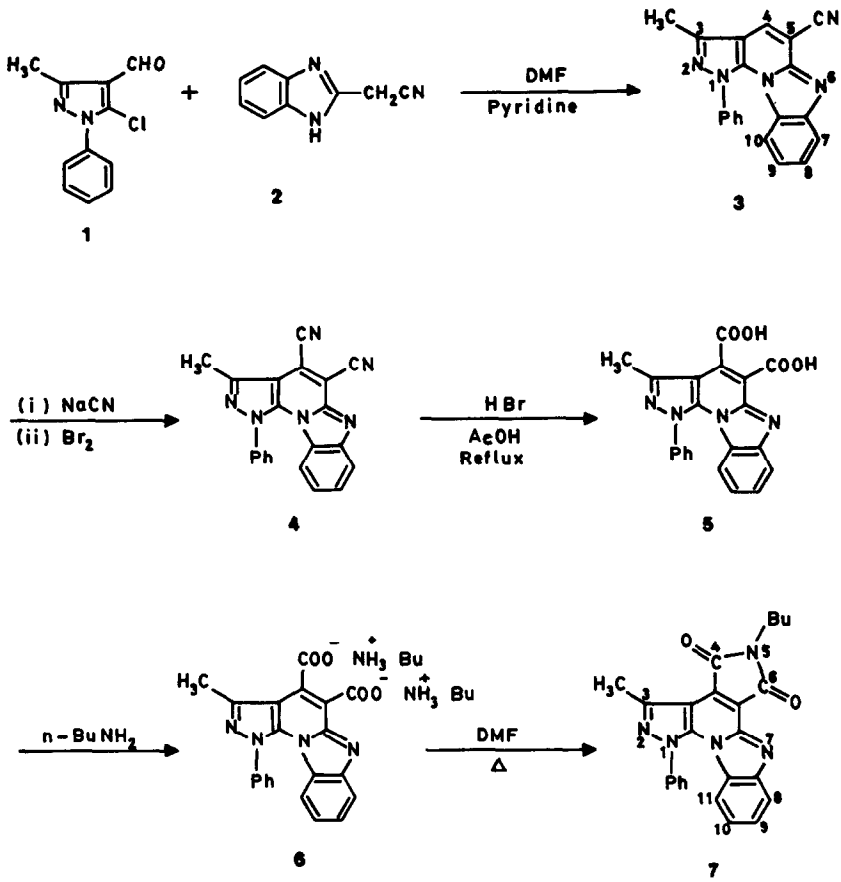
TABLE 1
Physical and Spectral Data

Compd.	*Molecular formula*[a]	*M.p.*[b] (°C)	*Yield* (%)	*Absorption max. (nm)*	*Emission max. (nm)*	*log ε*	*Solvent*	*PMR data*
3	$C_{20}H_{13}N_5$	300	83	355	455	3·95	TFA	2·9, 3H CH_3; 9·0, S, 1H Ar at C-4; 6·1, $J_{10-9}=8$Hz, 1H Ar at C-10 (upfield due to ring current of phenyl at C-1); 7–8, *m*, 8H Ar.
9	$C_{20}H_{12}N_4$	323	85	402	495	4·20	TFA	2·9, s, 3H CH_3; 9·1–9·15, s, 2H Ar at C-8, C-7; 9·8,[c] d, 1H Ar at C-1; 7·8–8·3, *m*, 6H Ar.
14	$C_{23}H_{12}N_4$	354	87	416	497	4·23	—	Not sufficiently soluble.
4	$C_{21}H_{12}N_6$	348	80	421	512	3·87	TFA	2·9, s, 3H CH_3; 6·1, d, 1H AR at C-10, $J_{10-9}=8$Hz; 7–8, m, 8H Ar.
5	$C_{21}H_{24}N_4O_4$	258–60 (d)	93	—	—	—	—	—
6	$C_{29}H_{36}N_6O_4$	224	55	—	—	—	—	—
7	$C_{25}H_{21}N_5O_2$	226	80	452	—	3·58	$CDCl_3$	1·0, t, 3H CH_3 (of —C_4H_9); 1·2, m, 4H CH_2 (of —C_4H_9); 2·9, s, 3H CH_3 at C-3; 3·7, t, 2H CH_2 (α to $-NC_4H_9$); 6·0, d, $J_{11-10}=8$Hz, 1H Ar at C-11; 8·0, d, 1H Ar at C-8, $J^{8-9}=6·8$, t(dd), 1H Ar at C-10; 7·2–7·7, *m*, 6H Ar.
15	$C_{25}H_{10}N_6$	360	65	—	—	—	—	Not soluble.
10	$C_{22}H_{10}N_6$	360	70	464	524	3·90	TFA	2·9, *s*, 3H CH_3; 9·9, s, 1H Ar at C-1; 8–8·7, m, 6H Ar (3H of ring A and 3H of ring E).
12	$C_{22}H_{12}N_6$	360	60	421	520	3·83	—	Not soluble.

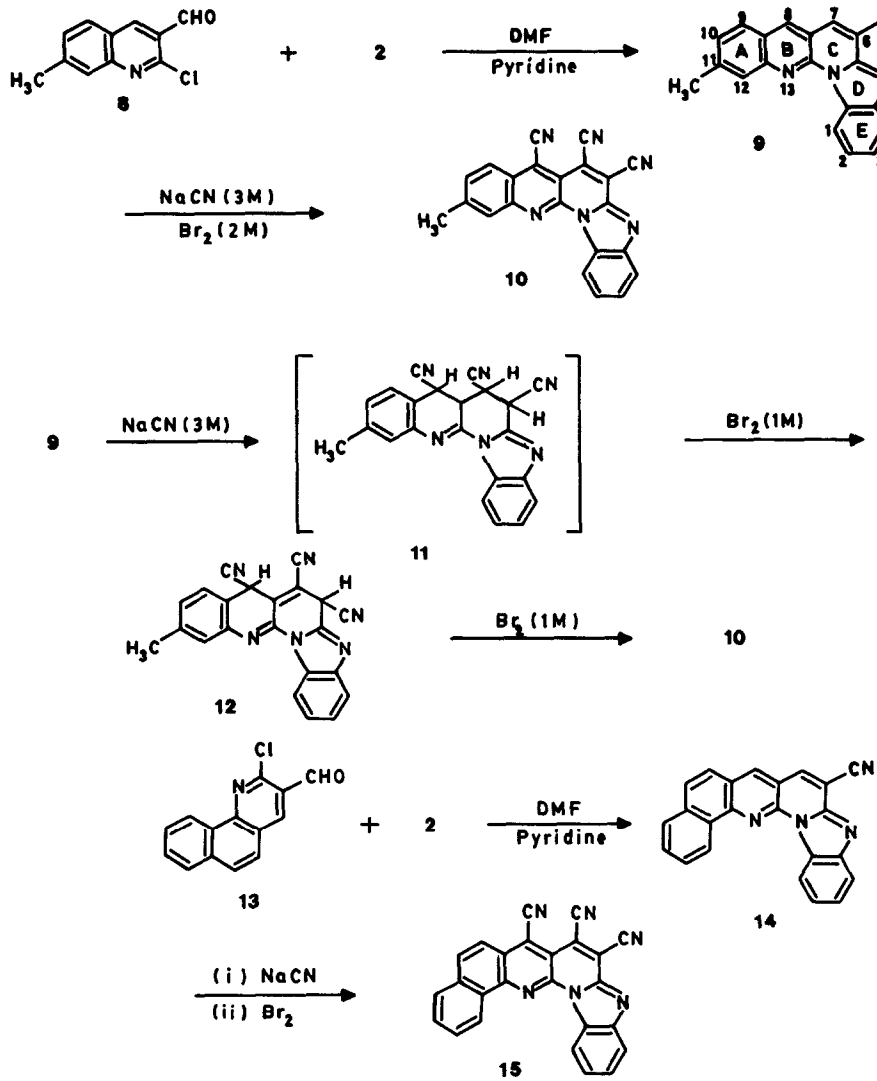
[a] All compounds gave satisfactory elemental analysis.
[b] All compounds were crystallised from DMF.
[c] Downfield due to protonation (TFA) of the quinoline nitrogen.



Scheme 1

containing a negative group at the 3-position. The condensed benzimidazoles (**3**, **9** and **14**) containing the cyano group are closely related to 3-cyanocoumarins and hence should also undergo nucleophilic attack by the cyanide ion. The product derived from the pyrazole (**3**) was therefore submitted to the cyanation reaction and the dicyano compound (**4**) was obtained, as indicated by elemental analysis, mass spectrum and the PMR spectrum, which showed absence of a signal at 9·0 indicating that the proton at the 4-position has been substituted. This dinitrile was then hydrolysed to the dicarboxylic acid **5** and the acid then converted to the *n*-butylimide (**7**).

In the cyanation reaction of the fused benzimidazoles **9** and **14** there are two possible sites of attack by the nucleophile. In both these cases cyanation occurred at both the sites leading to the formation of the tricyano derivatives **10** and **15**. These compounds were deeply coloured in



Scheme 2

comparison to the monocyanate starting materials. To ascertain whether the cyanation could be effected selectively at either of the reactive sites, addition of 1 mole equivalent of cyanide, followed by oxidation with bromine, gave only a mixture of the tricyano compound (**10**) and of unreacted monocyano compound (**9**), i.e. no selective cyanation occurred. The controlled aromatisation of the intermediate **11** to the tricyano compound (**10**) was investigated and it was observed that the use of 1 mole equivalent of bromine gave a dihydro derivative to which we assigned the

structure **12** on the basis of its colour. PMR spectroscopy was not useful in structural characterisation because of very small differences between the alternative structures. The structures of the tricyano compounds (**10** and **15**) show some analogy to the tricyanoethylene class of dyes, but when they were applied to polyester the dyes showed only poor tinctorial values and the resultant dyeings had lightfastness. Absorption data and other moderate characteristics are given in Table 1.

EXPERIMENTAL PROCEDURE

All melting points are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 397 spectrophotometer from nujol mull. Absorption spectra were recorded on a Bausch and Lomb-2000 spectrophotometer and the fluorescence spectra on an Aminco–Bowman spectrophotofluorimeter. The PMR spectra were recorded on a Varian EM-360L spectrophotometer using TMS as internal standard and the mass spectrum on a Varian Mat CH-7 spectrometer.

Benzimidazole-2-acetonitrile (**2**),[3] 5-chloro-4-formyl-3-methyl-1-phenyl-pyrazole (**1**),[4] 2-chloro-3-formyl-7-methylquinoline (**8**)[5] and 2-chloro-3-formylbenzo[*h*]quinoline (**13**)[6] were prepared by known methods.

General method for the preparation of condensed pyridobenzimidazoles (3, 9, 14).

A mixture of the appropriate chloroaldehyde (**1**, **8** or **13**) (0·01 mol) and benzimidazole-2-acetontrile (**2**) (0·01 mol) was refluxed in DMF (20 ml) containing pyridine (0·011 mol) for 4–5 h and the liquor cooled to room temperature. Crystalline products were filtered, washed with MeOH and dried. Data on yields, m.p., crystallisation solvents, molecular formula, etc., of the pyridobenzimidazoles **3**, **9** and **14** are given in Table 1.

General method of cyanation of compounds 3, 9 and 14

*Synthesis of 3-methyl-1-phenyl-1*H*-pyrazolo[4',3':5,6]pyrido[1,2-*a*]benzimidazole-4,5-dicarbonitrile* (*4*), *11-methylbenzimidazolo[1,2-*a*]benzo*[g]-[*1,8*]*naphthyridine-6,7,8-tricarbonitrile* (**10**), *and benzimidazo* [*1,2-*a*]*naphtho*[*2,1-*g][*1,8*]*naphthyridine-7,8,9-tricarbonitrile* (**15**)

A mixture of the appropriate pyridobenzimidazole derivative (**3**, **9** or **14**) (0·005 mol) and finely powdered sodium cyanide (0·015 mol) was stirred at room temperature in DMF (20 ml in the case of **9** or **14** and 60 ml in the case of **3**) for 4 h (30 h in the case of **3**). The reaction mixture was then

cooled to 0–5°C and Br_2 (0·005 mol in the case of **3**, and 0·015 mol in the case of **9** and **14**) was added dropwise during 15 min. The reaction mixture was stirred at room temperature and then poured into ice-water (150 ml) and the residue filtered and washed with water. The yields, m.p., crystallisation solvent and spectral data of the cyanated products are given in Table 1.

Synthesis of 3-methyl-1-phenyl-1*H*-pyrazolo[4′,3′:5,6]-pyrido[1,2-*a*]benzimidazole-4,5-dicarboxylic acid (5)

The dinitrile **4** (0·006 mol) was refluxed in a solution of HBr in acetic acid (40%, 50 ml) for 17 h under anhydrous conditions. The reaction mixture was then cooled in an ice-bath and the product (**5**) was filtered, washed initially with water and then with ethyl acetate (15 ml) and dried. The yield, m.p., crystallisation solvent and other physical data are given in Table 1.

Synthesis of 3-methyl-1-phenyl-1*H*-pyrazolo[4′,3′:5,6]pyrido[1,2-*a*]benzimidazole[4,5-*c*]-*N*-butylimide (7)

The dicarboxylic acid (**5**) (3·0 g) was heated with *n*-butylamine (15 ml) for 2 h and the dibutylammonium salt (**6**) which separated on cooling was filtered (yield 50%). This dibutylammonium salt (1·3 g) was heated in DMF (15 ml) for 15–16 h, the reaction mixture cooled and the orange coloured product filtered, washed with *n*-hexane and dried. Yield, m.p., crystallisation solvent and spectral data of **7** are given in Table 1.

Synthesis of 11-methylbenzimidazole[1,2-*a*]benzo[*g*][1,8]naphthyridine-6*H*,8*H*-dihydro-6,7,8-tricarbonitrile (12)

A mixture of the monocarbonitrile (**9**) (0·005 mol) and sodium cyanide (0·015 mol) was stirred in DMF (25 ml) at room temperature for 4 h. The reaction mixture was cooled to 0–5°C, bromine (0·005 mol) added and the reaction liquor stirred for a further 2 h at room temperature and then poured into ice water and filtered to give **12**. Yield, m.p., crystallisation solvent, etc., are given in Table 1.

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