Heterocyclic Intermediates for the Synthesis of Disperse and Cationic Dyes [1]

Guido Viscardi*, Piero Savarino, Ermanno Barni,
Rosarina Carpignano, Enzo Montoneri and Pierluigi Quagliotto

Università degli Studi di Torino,
Dipartimento di Chimica Generale ed Organica Applicata,
Corso Massimo D'Azeglio, 48,
10125 Torino, Italia

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Nitro derivatives and amines containing X-azolo[4,5-*c*]pyridine moieties were prepared choosing more favourable synthetic pathways. Their physical and spectroscopic data were discussed in correlation with those of previously studied systems. The heteroaromatic amines were shown to be suitable precursors for the synthesis of disperse dyes and of their cationic counterparts.

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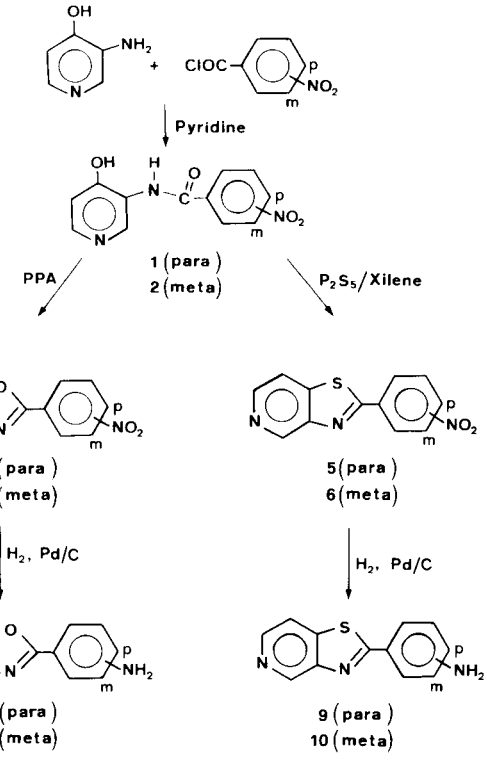
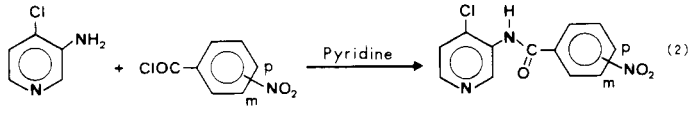
Based on a long lasting tradition, the dye industry has largely benefited from the advancement of heterocyclic chemistry: indeed, many commercial dyes are heterocyclic compounds. A recent review [2] of our work covers, for instance, heterocyclic bases and quaternary salts with reactive methyl groups as a source of polymethine dyes and heterocyclic amines and phenols as precursors of azo dyes. We report now the synthesis of new intermediates belonging to a recently described class of amines [3], which shows high potential for being expanded.

Most of the new compouds **1-10** (Table 1) have been obtained according to Scheme 1, where 3-amino-4-hydroxypyridine is converted to the hydroxyamide isomers, followed by cyclization to oxazoles or thiazoles and by reduction of the nitro groups to amines. Other alternative one step syntheses, although more attractive, were discarded. Step (2) was disadvantageous because of the high reactivity of chlorine towards nucleophiles (*e.g.* water or alcohols) [4]. In step (3) complex product mixtures were obtained probably due to the hydroxypyridine-pyridone tautomerism of the starting amine. The method outlined in step (3) proved successful for the synthesis of compouds **11** and **12**. The reaction pathway is shown in Scheme 2. The new products have properties which are common to other simi-

Scheme 1





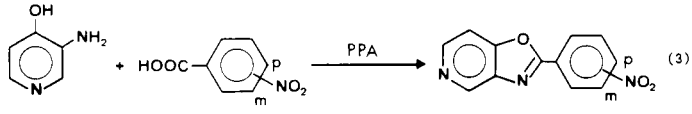
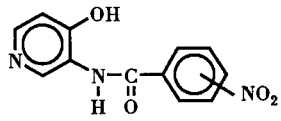
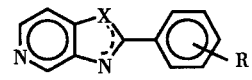


Table 1

Analytical and Spectroscopic data compounds **1-14**



1-2



3-14

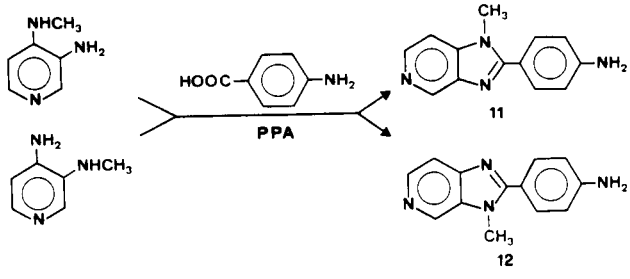
Compound Number	Structure Isomer	X	R	Mp °C	Rf [a]	Rf [b]	Empirical fromula	Elemental Analyses Calcd./Found C	H	N	Yield %	Electronic Absorption Spectra λ max in nm (log ε) [c] [d]	Ref
1	*p*			326-328	0.74	0.68	$C_{12}H_9N_3O_4$	55.60	3.50	16.21	82	310 (3.89) 2.65 (4.31)	
								55.48	3.61	16.34			
2	*m*			315-316	0.72	0.72	$C_{12}H_9N_3O_4$	55.60	3.50	16.21	77	s 300 (4.00) 270 (4.21)	
								55.69	3.55	16.08			
3	*p*	O	NO_2	224-226	0.78	0.47	$C_{12}H_7N_3O_3$	59.75	2.93	17.42	63	300 (4.36)	
								59.87	2.86	17.51			
4	*m*	O	NO_2	175-176	0.77	0.50	$C_{12}H_7N_3O_3$	59.75	2.93	17.42	57	281 (4.32) s 262 (4.28)	
								59.62	3.00	17.48			
5	*p*	S	NO_2	242-244	0.78	0.43	$C_{12}H_7N_3O_2S$	56.02	2.74	16.33	53	314 (4.35) 266 (4.13)	
								55.90	2.79	16.40			
6	*m*	S	NO_2	170-172	0.77	0.46	$C_{12}H_7N_3O_2S$	56.02	2.74	16.33	50	s 290 (4.33) 254 (4.46)	
								56.18	2.64	16.34			
7	*p*	O	NH_2	326-328	0.75	0.63	$C_{12}H_9N_3O$	68.24	4.29	19.89	85	337 (4.65)	
								68.10	4.35	20.00			
8	*m*	O	NH_2	226-227	0.73	0.63	$C_{12}H_9N_3O$	68.24	4.29	19.89	86	s 335 (3.65) 287 (4.35)	
								68.13	4.40	19.80		s 252 (4.03)	
9	*p*	S	NH_2	343-345	0.77	0.57	$C_{12}H_9N_3S$	63.41	3.99	18.49	89	345 (4.42)	
								63.30	4.06	18.57		s 260 (4.00)	
10	*m*	S	NH_2	188-191	0.74	0.57	$C_{12}H_9N_3S$	63.41	3.99	18.49	80	s 346 (3.56) 294 (4.24)	
								63.25	4.10	18.48			
11	*p*	NCH_3	NH_2	307-309	0.29	0.17	$C_{13}H_{12}N_4$	69.62	5.39	24.98	65	312 (4.36) 2.61 (4.03)	
								69.50	5.48	24.96			
12	*p*	N [e]	NH_2	254-255	0.31	0.15	$C_{13}H_{12}N_4$	69.62	5.39	24.98	60	314 (4.32) s 290 (4.13)	
								69.66	5.30	25.00			
13	*p*	NH	NH_2	329-331	0.43	0.13						s 326 (4.12) 312 (4.30) 258 (3.88)	[3]
14	*m*	NH	NH_2	289-291	0.40	0.15						s 330 (3.58) 288 (4.30)	[3]

[a] BAW/Silica Gel. [b] Methanol/hptlc RP-18. [c] The main absorptions above 240 nm are reported. [d] s = shoulder. [e] Instead of the azole nitrogen (position 3) N-CH_3 is present.

lar heterocycles, but show some surprising peculiarities.

Regardless of the functional group (*i.e.* amide, nitro or amino derivatives), the *para* isomers have distinctly higher melting points than the *meta* isomers (Table 1, pairs **1-2**, **3-4**, **5-6**, **7-8**, **9-10**, **13-14**, compounds **11-12** are both *para*); the same order has been observed by us with other heterocycles [3]. As to the functional group effect, amines are higher melting than their nitro precursors (pairs **7-3**, **8-4**, **9-5**, **10-6**). These trends may be respectively due to the higher degree of crystallinity of the *para* isomers and to intermolecular hydrogen bonds in amines. R_f data (Table 1) may be ordered as follows: (i) values in BAW/silica gel are higher than those in methanol/RP-18, (ii) imidazoles (compounds **11-14**) show, in both systems, the lowest values in the series (compounds **1-12**), (iii) nitro derivatives are less retained than amines on silica gel (eluent BAW), whereas on RP-18 plates (eluent methanol) the opposite is true.

Scheme II



The electronic spectra of amides **1** and **2**, exemplified by that shown in Figure 1 for compound **1**, exhibit the following features. The absorption pattern (a main band

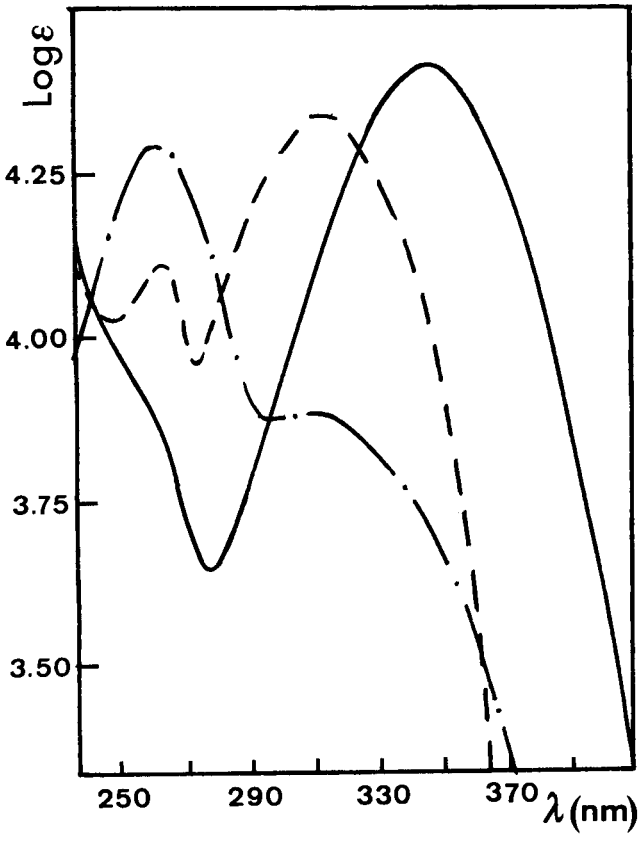
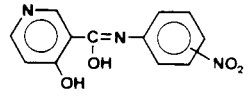


Figure 1. Electronic Absorption spectra of compounds: **1** —·—, **5** – – –, **9** ——.

with peak absorbance at 265-270 nm and a shoulder at 300-310 nm) closely resembles that of *N*-(4-hydroxyphenyl)-4-nitrobenzanilide [5,6] and allows to attribute the absorptions to the "imidol" chromogen **I**. After cyclization to X-



I

azoles, significant spectral changes occur due to the presence of the "benzylidene-imino" chromogen **II** [7]. Selected examples of thiazoles are reported in Figures 1

II

and 2. The overall data in Table 1 related to X-azoles **3-14**, may be rationalized as follows. The position of the long

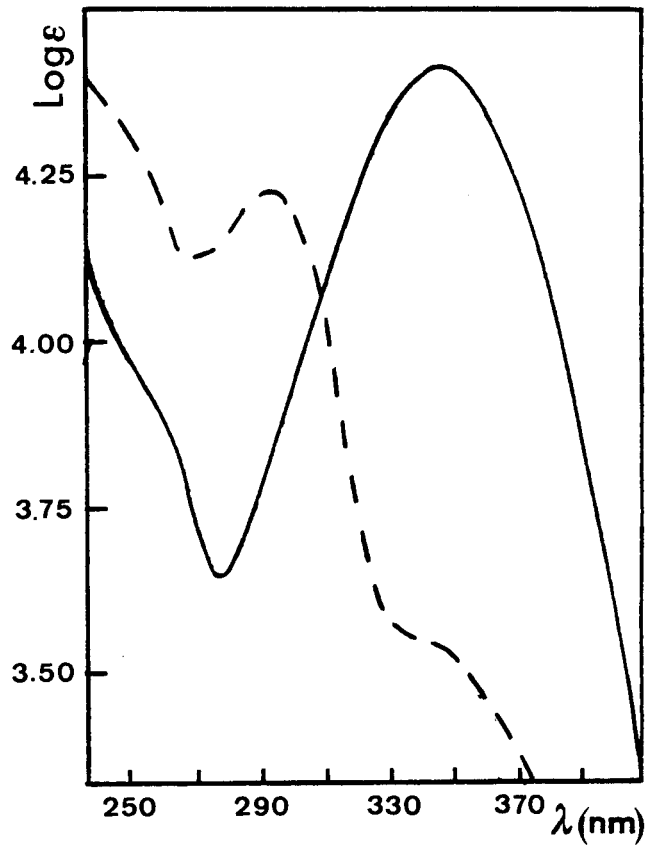


Figure 2. Electronic Absorption spectra of compounds: **9**——, **10** – – –.

wavelength absorption is strongly influenced by the electronic effects of the R substituent, the peak absorbance of amines is bathochromically shifted by comparison with the nitro derivatives. *Meta* isomers, relatively to *para* compounds, exhibit the long wavelength band as a shoulder, due to overlapping by the band of the more intense benzenoid transition. As observed with other heterocycles [3,8], the wavelength peak absorbance is a function of the nature of the X heteroatom and changes as follows: thiazoles > oxazoles > imidazoles.

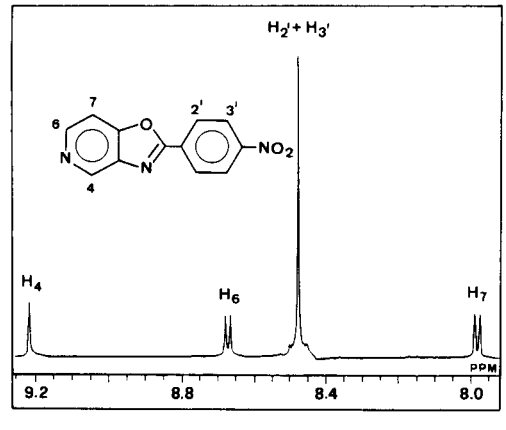
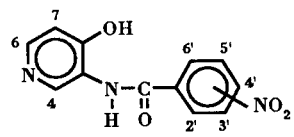


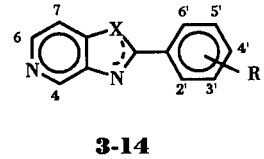
Figure 3. The ^{1}H nmr spectrum of compound **3**.

Table 2

^{1}H NMR Data



1-2



3-14

Compound Number	Isomer	Structure X	R	^{1}H NMR spectra (δ, ppm) [a] 4	6	7	2'	3'	4'	5'	6'	NH_2	NCH_3
1	*p*			8.77	7.73	6.34	8.17	8.38	-----	8.38	8.17		
2	*m*			8.75	7.75	6.34	8.67	-----	8.46	7.85	8.36		
3	*p*	O	NO_2	9.22	8.67	7.98	8.47	8.47	----	8.47	8.47		
4	*m*	O	NO_2	9.20	8.68	7.97	8.89	-----	8.64	7.97	8.52		
5	*p*	S	NO_2	9.41	8.61	8.27	8.42	8.42	-----	8.42	8.42		
6	*m*	S	NO_2	9.42	8.62	8.31	8.86	-----	8.56	7.92	8.46		
7	*p*	O	NH_2	8.97	8.50	7.77	7.92	6.76	-----	6.77	7.92	5.00	
8	*m*	O	NH_2	9.10	8.59	7.87	7.48	-----	6.85	7.27	7.38	5.55	
9	*p*	S	NH_2	9.14	8.47	8.12	7.82	6.70	-----	6.70	7.82	6.02	
10	*m*	S	NH_2	9.29	8.53	8.21	7.40	-----	6.80	7.24	7.24	5.51	
11	*p*	NCH_3	NH_2	8.88	8.33	7.61	7.61	6.73	-----	6.73	7.61	5.70	3.89
12	*p*	N [b]	NH_2	8.91	8.32	7.58	7.63	6.73	-----	6.73	7.63	5.74	3.96
13	*p*	NH	NH_2	8.82	8.24	7.48	7.92	6.71	-----	6.71	7.92	5.73	
14	*m*	NH	NH_2	8.92	8.31	7.56	7.48	-----	6.75	7.22	7.33	5.39	

[a] The numbering of pyridine positions in the amido derivatives **1-2** is arbitrary but useful for comparing them with cyclized compounds. [b] Instead of the azole nitrogen (position 3) N-CH_3 is present.

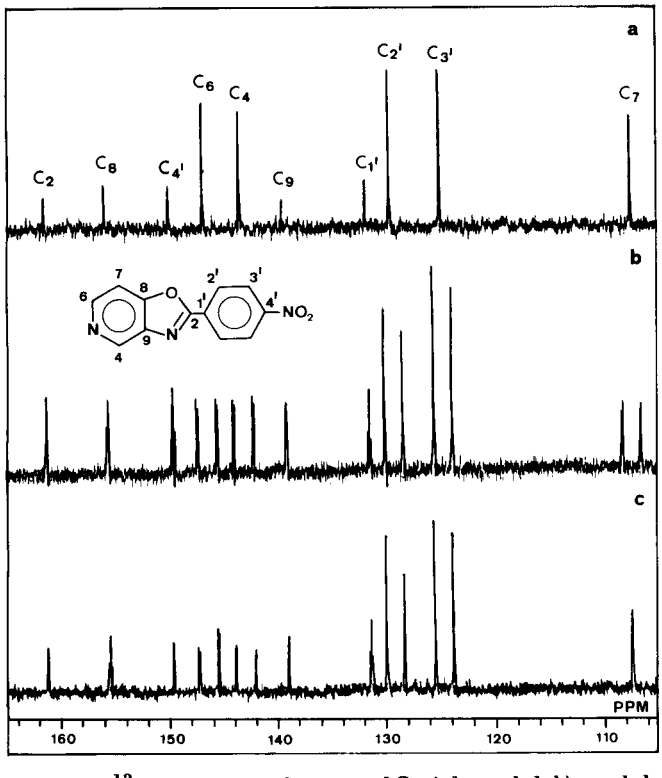


Figure 4. ^{13}C nmr spectra of compound **3**: a) decoupled, b) coupled, c) selectively decoupled by irradiation at 7.98 ppm.

The ^{1}H nmr spectra (Table 2) recorded at 400 MHz are interpreted in relation to data obtained for other similar compounds. The case of X-azoles requires some more detailed discussion. In the spectra of these compounds, the signals arising from protons 6 and 7 cannot be unequivocally identified. For compound 3, as an example (Figure 3), the doublets at 7.98 and 8.67 ppm do not show any evident *meta* coupling, as expected for proton 6. Electron density distribution considerations for pyridines suggest that the proton 6 (α) resonance should lie downfield from that of proton 7 (β). Final assignments were possible from ^{13}C spectra (Figure 4), which were interpreted in agreement with data available for related compounds [9]. Irradiation at 7.98 ppm simplifies the signal at 107.5 ppm in the spectrum, thus confirming that the proton at 7.98 ppm is H_7. Other features worth mentioning are as follows. The reduction of nitro groups to amines is generally accompanied by a shielding effect. This is more effective on protons of the benzene rings carrying *nitro* or amino substituents. The substituent position (*para vs. meta*) strongly influences the 2' and 6' protons: the 2' protons are more deshielded by nitro and shielded by amino group in the *para* substituted compound compared to the *meta* isomer. The X heteroatom of the pentatomic ring has different effects on benzene *versus* pyridine protons, shielding the former

in the order O > NH > S > NCH_3 and the latter in the order S > O > NCH_3 > NH.

These data show, once again, that the effect of heteroatoms can be surprising and that, even in a series derived from one parent structure, nothing can be taken for granted. With the present compounds, peculiarities due to the heteroatoms have been observed not only in relation to the physical and spectroscopic properties as reported above, but also in the chemical properties. The new products indeed offer broad synthetic possibilities for dye chemistry. Specifically, for the synthesis of dyes, the amines **7-14** may in principle yield disperse dyes by diazotization and coupling to *N,N*-diethylaniline and the reaction products may then by quaternized. Preliminary runs by this route, have shown peculiar behaviour of these compounds depending on the sequence of the reaction steps: *i.e.* preparation of dyes followed by quaternization or quaternization of amines followed by diazo-coupling. Investigation into this intriguing subject is in progress.

EXPERIMENTAL

Electronic spectra were recorded on a Pye Unicam SP 8-100 spectrophotometer in ethanol. The R_f values were determined (i) on silica gel 60 F_{254} tlc plates (Merck), using as eluent BAW (butanol:acetic acid:water) 4:1:5 and (ii) on hptlc RP-18 F_{254s} plates (Merck), using methanol as eluent. The ^1H nmr spectra were obtained with a Jeol EX 400 spectrometer in DMSO-d_6 solution (3%).

The synthesis of compounds **13** and **14** was previously described in references [10] and [3] respectively.

The following intermediates were prepared according to literature methods: 3-amino-4-hydroxypyridine [11,12], 3-amino-4-methylaminopyridine [11,4], and 4-amino-3-methylaminopyridine [4].

Amides **1** and **2** were prepared adding a solution of *para* or *meta* nitrobenzoyl chloride (0.50 mole) in pyridine (1.5 ℓ) to 0.60 mole of 3-amino-4-hydroxypyridine dihydrochloride dissolved in pyridine (1 ℓ) at 10° and stirring overnight. Water and glacial acetic acid were added to obtain neutralization of the solution. The precipitate was filtered and, after washing with 10% acetic acid, crystallized from ethanol. The amide **1** is also cited in reference [13].

Compounds **3** and **4** were prepared treating amides **1** and **2** (0.25 mole) respectively at 180° for six hours in 300 ml of polyphosphoric acid (85% phosphorus pentoxide). The reaction mixture was poured into distilled water and sodium hydroxide was added until *p*H 5 was obtained. The precipitate was collected, washed with water until neutral and crystallized from ethanol. Compound **4** is also cited in reference [13].

Compounds **5** and **6** were prepared refluxing amides **1** and **2** (0.25 mole) respectively with 120 g of phosphorus pentasulfide in 1.5 ℓ of xylene:pyridine (4:1) for 18 hours. The solid material was filtered out and the solvent evaporated in vacuum. The crude product was crystallized from ethanol.

Compounds **7**, **8**, **9** and **10** were prepared by catalytic hydrogenation of the corresponding nitro derivative (0.10 mole) in 1 ℓ of methanol at 25° using Pd/C as catalyst, until chromatographic analyses confirmed complete conversion. The catalyst was filtered off and the solvent evaporated. The crude product was crystallized from ethanol/water.

Compounds **11** and **12** were prepared by reaction of 3-amino-4-methylaminopyridine (0.25 mole) and 4-amino-3-methylaminopyridine (0.25 mole) respectivley with *p*-aminobenzoic acid (0.25 mole) in 300 ml of polyphosphoric acid (85% phosphorus pentoxide) following the procedure indicated for compounds **3** and **4**. The crude product was crystallized from ethanol.

REFERENCES AND NOTES

[1] This work was supported by a contribution of Progetto Finalizzato Chimica Fine of Consiglio Nazionale delle Ricerche (CNR) and of Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST) of Italy.

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