Aminophenyl-X-azolopyridines as Precursors of Heterocyclic Azo Dyes

P. Savarino, G. Viscardi, R. Carpignano, A. Borda and E. Barni*

Istituto di Chimica Organica Industriale, Universita' di Torino, Corso Massimo D'Azeglio 48, 10125 Torino, Italy

Received July 28, 1988

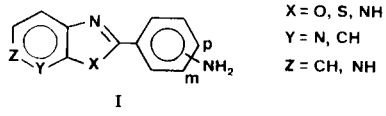
Aminophenyl-X-azolopyridines (X = O, S, NH) are interesting intermediates for the synthesis of disperse azo dyes and, provided the pyridine nitrogen is quaternized, of their cationic counterparts. A set of novel amines and nitro derivatives is described, and their physical properties and spectral parameters are discussed in comparison with those of analogous compounds. Some dyes in the oxazole series function as probes of the reactivity of the pentatomic ring.

J. Heterocyclic Chem., **26**, 289 (1989).

Anilines containing a hetaryl moiety are interesting intermediates for the synthesis of heterocyclic dyes.

Besides the obtainment of usual azo dyes, whose application mainly depends on the structure of the coupling component, the hetaryl moieties allow us to transform the dyes, by quaternization, into their cationic counterparts which are suitable for further applications, *i.e.* the dyeing of polyacrylonitrile substrates.

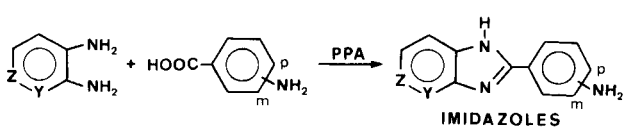
From an historical point of view, 'Primuline' dyes could be mentioned [1] and so far as the recent period is concerned, some papers from our laboratories are citable [2,3]. Going deeply into this topic, we have described new amines in this class, reporting their amazing behaviour in the course of the preparation of dyes [4]. This paper deals with the synthesis of other amines of the general formula **I**, including their physico-chemical and spectroscopic characterization [5].



I

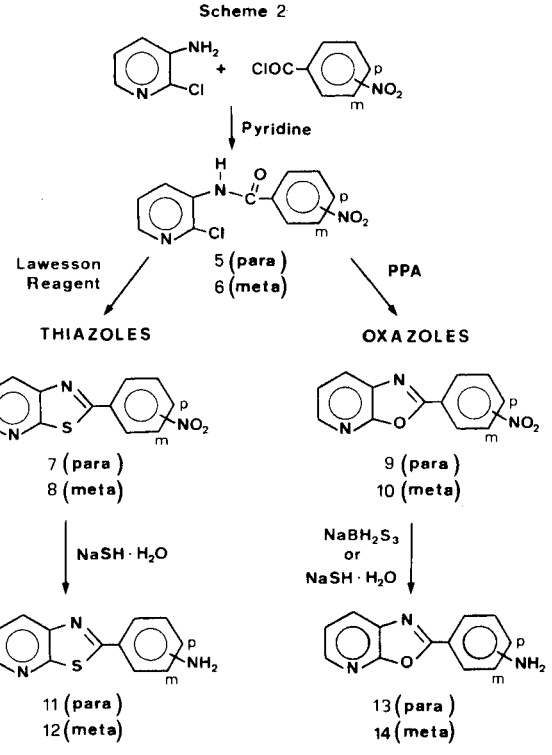
Distinct reaction pathways were followed in the synthesis of the amines. In Scheme 1, the classical reaction of diamines with carboxylic acids in polyphosphoric acid [6] to give imidazoles, is depicted. Scheme 2 shows the formation of the amines *via* reduction of nitro derivatives obtained, in turn, from chloroamides; 3-amino-2-chloropyridine, the commercially available precursor of chloroamides, was preferred to 3-amino-2-pyridone, a potentially alternative starting product for the synthesis of oxazoles (directly) and thiazoles (*via* thiolation).

Scheme 1



1 (Z = CH, Y = N, para) 2 (Z = CH, Y = N, meta)
3 (Z = N, Y = CH, para) 4 (Z = N, Y = CH, meta)

Scheme 2



Awaiting to have a complete chart available [5], we have chosen a set of ten amines whose structure allows a self-consistent discussion. Table 1 reports the selected amines, with their physical and spectroscopic features (for compounds whose preparation has been formerly described, R_f values and spectral parameters have been detected in view of a suitable discussion).

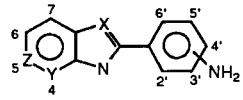
As observed for heterocycles belonging both to the present series [9] and to substantially different ones [10,11], benzimidazole derivatives, because of intermolecular hydrogen bonding, show melting points higher than those of their benzothiazoles and benzoxazole counterparts. Furthermore, in each pair of *para-meta* isomers, the former melt above the latter, in the range of 21-80°. The R_f values show an opposite trend. The more polar structures are more easily retained on the polar substrate. In fact, imida-

Table 1

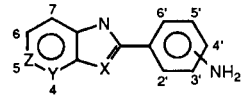
Characterization Data of Amines

General Structure

Compounds 1, 2, 15, 16



Compounds 3, 4, 11-14



Compound number [a]	Structure X	Y	Z	Isomer [b]	Mp °C	Electronic absorption spectra λ max nm log ε [c]	R_f	¹H NMR spectra (δ, ppm) [d] 4	5	6	7	2'	3'	4'	5'	6'	NH_2	Reference number
15	O	N	CH	*p*, [4,5-*b*]	262-263	347 (4.51)	0.83		8.43	7.33	8.08	7.93	6.74		6.74	7.93	6.18	2
16	O	N	CH	*m*, [4,5-*b*]	182-183	303 (4.38)	0.79		8.55	7.47	8.23	7.51		6.87	7.30	7.41	5.40	2
1	NH	N	CH	*p*, [4,5-*b*]	294-296	336 (4.38)	0.75		8.23	7.15	7.86	7.92	6.69		6.69	7.92	5.80	7
2	NH	N	CH	*m*, [4,5-*b*]	265-267	308 (4.40)	0.70		8.33	7.23	7.97	7.50		6.74	7.21	7.36	5.35	7
13	O	N	CH	*p*, [5,4-*b*]	246-247	345 (4.58)	0.91		8.24	7.41	8.09	7.90	6.73		6.73	7.90	6.13	4
14	O	N	CH	*m*, [5,4-*b*]	225-226	299 (4.46)	0.89		8.37	7.50	8.25	7.48		6.85	7.27	7.38	5.55	4
11	S	N	CH	*p*, [5,4-*b*]	220-221	356 (4.51)	0.94		8.48	7.51	8.24	7.80	6.69		6.69	7.80	6.04	
12	S	N	CH	*m*, [5,4-*b*]	170-171	308 (4.33)	0.90		8.61	7.61	8.41	7.38		6.80	7.24	7.24	5.52	
3	NH	CH	N	*p*, [5,4-*c*]	329-331	312 (4.30)	0.42	8.93		8.31	7.59	8.20	7.80		7.80	8.20	[e]	
4	NH	CH	N	*m*, [5,4-*c*]	289-291	288 (4.30)	0.40	8.92		8.31	7.56	7.48		6.75	7.22	7.33	5.39	

[a] Numbers in the range 1-14 correspond to those reported in Schemes 1 and 2. [b] Due to their tautomerism, imidazoles can be indifferently considered as [4,5] or [5,4] isomers. [c] The λ max and log ε values correspond to the most intense peak of the long-wave band. [d] All the signals correspond to first order spectra. [e] In the range 5.35-6.18 ppm no neat signal is appreciable.

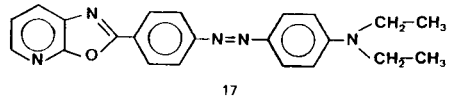
zoles exhibit the lowest R_f values with particular evidence for the [5,4-*c*] isomers.

The data on electronic spectra further confirm some fundamental effects previously observed for analogous amines, *i.e.*: (i) The absorption of *para* isomers compared to their *meta* counterparts shows a bathochromic shift (24-46 nm) [7]; (ii) the shift to longer wavelengths is more pronounced for the *para* isomers, in the 'pyrido' series with respect to the carbocyclic analogues (due to the participation of the pyridine nitrogen atom to the conjugation of the main chromogen) [7]; and (iii) the following sequence of absorptions, for corresponding compounds is: S > O > N (X in formula I) [9]. Besides the above reported regularities, it is worth mentioning the singular behaviour of [5,4-*c*] isomers whose absorptions are markedly hypsochromic. A similar effect is reflected on the related disperse and cationic dyes (under investigation); therefore, as shown by the overall data in Table 1, anellation on the '*c*' side deserves wider attention.

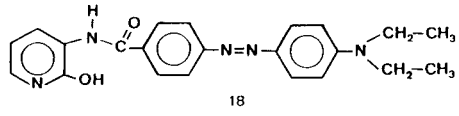
From the ¹H nmr data in Table 1, some general effects can be observed. Protons in the phenyl ring are subjected to the opposite effects from the hetaryl (deshielding) and the amino group (shielding). In particular, the *ortho* positions to the above groups are influenced, *i.e.* 2' and 6' by the hetaryl, 3' and 5' by the *p*-amino, 2' and 4' by the *m*-amino. The amino group also exherts a shielding effect on protons in the pyridine ring (**5**, **6**, and, more strongly, **7**) *para* isomers being more affected (0.08-0.17 ppm) than the corresponding *meta* ones. So far as the X heteroatom is concerned, a particular shift towards low fields is percieved in the thiazole derivatives. The data of compounds **3**, a [5,4-*c*] isomer, appear to be completely contradictory towards the diffuse regularities shown by other compounds. Indeed, the reported assignments are tentative,

the signals being quite complicated: repeated purifications of the product did not change the situation. Variations of the sample temperature caused changes of the positions and of the intensities of several signals. The presence of tautomers which at last are converted to the amino isomers in definite media (*e.g.* in the course of diazo-coupling), could be hypothized, but we prefer to delay this item when further '*c*' isomers will be available, also in view of the apparently regular behaviour of compounds **4**, a *meta* [5,4-*c*] isomer [12].

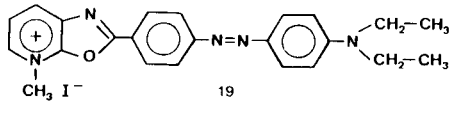
So far as amine **13** is concerned, it is worth mentioning our most recent findings in the area of its coloristic applications. We have reported [4] the possibility of obtaining both dyes **17** (closed) and **18** (opened), depending on experimental conditions, focussing the great sensitivity to the temperature during the formation of the amine hydrochloride. On the other hand, as mentioned above, we are preparing and testing the whole series of dyes, including cationic derivatives obtained by quaternization, such as



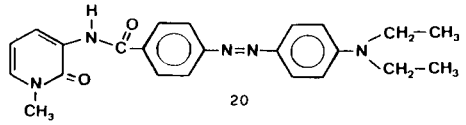
17



18



19



20

dye **19**. At this point, it appeared as a fixed step the hydrolysis of dye **19** which gave rise to the *N*-methylpyridone dye **20** (characterization data in the Experimental). As we have observed for dye **18**, the hydroxypyridine tautomer appeared to be more reliable for the presence, in its ir spectrum, of a band at 3360 cm^{-1}, consistent with the formation of an intramolecular hydrogen bond between the hydroxyl and the carbonyl of the amido group. In dye **20**, the presence of the N-CH_3 group prevents the hydroxypyridine-pyridone tautomerism and the above band is lost.

The sequence of R_f values in dyes **17-20** is in agreement with the assigned structures. Dye **19** (R_f 0.33), due to its ionic character, strongly interacts with the polar substrate, whereas the remainder, for their lower polarity, are less retained, in the order **20** (R_f 0.84), **18** (R_f 0.87), and **17** (R_f 0.91).

The mass spectrum of dye **20** closely supports the given structure. The main fragmentations are completely similar to those observed for dye **18** [4].

Finally, the positions of absorption maxima are strongly consistent with the assigned structures **17-20** as donor-acceptor substituted azobenzene chromogens [13]. Dye **19**, with an attracting hetarylium moiety, is the most bathochromic (λ max 481 nm), followed by dye **17**, containing a benzoxazole (λ max 479 nm) [14], and by 'opened' dyes **18** (λ max 460 nm) and **20** (λ max 459 nm) which show absorption maxima essentially not different, as predicted by their structural closeness.

EXPERIMENTAL

The R_f values were determined on silica gel 60 F_{254} tlc plates (Merck), using as eluent B.A.W. (butanol:acetic acid:water) 4:1:5. Electronic spectra were recorded on a Pye Unicam SP 8-100 spectrophotometer in ethanol. The ^1H nmr spectra were obtained with a Jeol GX 270 spectrometer in DMSO-d_6 solution (2.5%). Infrared spectra were detected in potassium bromide with a Perkin-Elmer 781 infrared spectrophotometer. Mass spectra were obtained with a Kratos MS 80 mass spectrometer.

The following compounds, among those listed in Schemes 1 and 2 and in Table 1, were previously described: **1**, **2**, reference [3]; **3**, reference [8]; **5**, **6**, **9**, **10**, **13**, **14**, reference [4]; **15**, **16**, reference [2].

Compound **4**, 2-(*m*-aminophenyl)imidazo[5,4-*c*]pyridine, was prepared condensing *m*-aminobenzoic acid, 1 mole, with 3,4-diaminopyridine, 1 mole, in polyphosphoric acid (85% phosphorus pentoxide), over a period of five hours at 210°, following the general procedure indicated in reference [6]. The reaction mixture was poured into water, the *p*H was adjusted to 5 with sodium hydroxide solution, the precipitate was collected and slurried in dilute sodium carbonate. The base was finally collected by filtration, dried and crystallized from dioxane/*n*-heptane, yield 93%.

Anal. Calcd. for $C_{12}H_{10}N_4$: C, 68.56; H, 4.79; N, 26.65. Found: C, 68.69; H, 4.81; N, 26.63. Other data in table 1.

Compounds **7** and **8**, 2-(*p*- or *m*-nitrophenyl)thiazolo[5,4-*b*]pyridines, were prepared treating in an oil bath at 140° for three hours 27.8 g of **5** or **6** (0.1 mole), 21 g (0.05 mole) of Lawesson's reagent (Merck) and 100 ml of hexamethylphosphoric-triamide. The mixture was poured into water and the nitro derivatives were collected and crystallized from ethanol. Data for the *para* isomer and, in parenthesis, for the *meta* isomer, yields, 71% (74%), mp 276-277° (199-200°).

Anal. Calcd. for $C_{12}H_7N_3O_2S$: C, 56.02; H, 2.74; N, 16.33. Found: C, 56.00 (55.89); H, 2.85 (2.84); N, 16.27 (16.25).

Compounds **11** and **12**, 2-(*p*- or *m*-aminophenyl)thiazolo[5,4-*b*]-pyridines, were prepared refluxing for six hours 1 g of **7** or **8** (4.4 × 10^{-3} mole) and sodium hydrogen sulfide 2 g (2.7 × 10^{-2} mole) dissolved in 80% aqueous methanol (25 ml). After cooling, the product was collected by filtration and washed with water. Data for the *para* isomer and, in parenthesis, for meta isomer are: crystallization solvent, ethanol/water (isobutyl alcohol), yields, 65% (50%).

Anal. Calcd. for $C_{12}H_9N_3S$: C, 63.41; H, 3.99; N, 18.49. Found: C, 63.35 (63.42); H, 4.10 (4.07); N, 18.39 (18.39). Other data are in Table 1.

Compound **19** was prepared by refluxing 1 g of **17** (2.69×10^{-3} mole) with a large excess of methyl iodide dissolved in *t*-butyl alcohol (30 ml) for twenty hours. After cooling, the product was collected by filtration, repeatedly washed with boiling *t*-butyl alcohol to give 0.9 g (65%), mp 198-200°; λ max 481 nm, log ε 4.38; R_f 0.33.

Anal. Calcd. for $C_{23}H_{24}IN_5O$: C, 53.81; H, 4.71; N, 13.64. Found: C, 53.68; H, 4.79; N, 13.70.

Compound **20** was prepared by refluxing 1 g of **19** (1.95×10^{-3} mole) with concentrated hydrochloric acid (10 ml) for two hours. After cooling, distilled water was added (50 ml) and the *p*H adjusted to 4.5 with a solution of sodium acetate. The crude dye was collected, washed with water and crystallized from ethanol/water to give 0.57 g of **20** (72%), mp 99-100°; λ max 459, log ε 4.39; R_f 0.84; ei/ms: (m/z) 403 (M^+), 388, 280, 252, 148, 120, 105.

Anal. Calcd. for $C_{23}H_{25}N_5O_2$: C, 68.47; H, 6.24; N, 17.36. Found: C, 68.39; H, 6.33; N, 17.35.

REFERENCES AND NOTES

[1] A. G. Green, *J. Soc. Dyers Col.*, **4**, 39 (1888).

[2] E. Barni, S. Pasquino, P. Savarino, G. Di Modica and G. Giraudo, *Dyes Pigments*, **6**, 1 (1985).

[3] P. Savarino, G. Viscardi, R. Carpignano, E. Barni and G. Ferrero, *ibid.*, in press.

[4] P. Savarino, G. Viscardi, R. Carpignano and E. Barni, *J. Heterocyclic Chem.*, in press.

[5] Indeed, the complete series of 2-phenylbenzo (or pyrido)-X-azoles (X = O, S, NH) having in the phenyl ring one substituent (amino, nitro) in the three possible positions (*o*-, *m*-, *p*-), amounts to 78 compounds; of these, a part has been described since a long time ago, a part has been described by us in previous papers and in the present paper, and the remainder has not yet been prepared.

[6] D. W. Hein, R. J. Alheim and J. J. Leavitt, U. S. Patent, 2,985,661 (1961); *Chem. Abstr.*, **57**, 11203 (1962).

[7] P. Savarino, G. Viscardi, E. Barni and R. Carpignano, *Dyes Pigments*, **9**, 295 (1988).

[8] A. V. Tretyakov, L. I. Rudaya, A. V. El'tzov, M. F. Larin and V. A. Lopirev, *Magn. Reson. Chem.*, **23**, 7 (1985).

[9] E. Barni, P. Savarino, M. Marzona and M. Piva, *J. Heterocyclic Chem.*, **20**, 1517 (1983).

[10] E. Barni and P. Savarino, *ibid.*, **14**, 937 (1977).

[11] E. Barni and P. Savarino, *ibid.*, **16**, 1579 (1979).

[12] The problem of tautomerism in imidazo[5,4-*c*]pyridines comes up again also in other assembled systems under investigation and will be the subject of a proper article.

[13] J. Griffiths, "Colour and Constitution of Organic Molecules", Academic Press, London, 1976, p 140.

[14] Changing from pyridooxazole to pyridinium-oxazole one could expect a more intense shift (Δλ observed, 2 nm). Data from our files indicate that such an effect is usually small (the maximum value so far obtained is 19 nmn).