Ermanno Barni and Piero Savarino

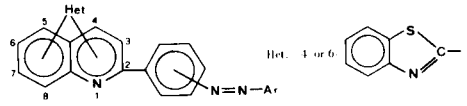
Istituto di Chimica Organica Industriale, Università di Torino, 10125 C. so M. D'Azeglio 48, Italy

Received March 23, 1977

In view of the preparation of heterocyclic polymethine dyes, 2-(methylpyridyl or quinolyl)-benz-X-azoles were synthesized with the general reaction between carboxylic acids (or derivatives) and *o*-bifunctional compounds. The electronic spectra and the methyl proton chemical shifts are briefly discussed.

J. Heterocyclic Chem., 14, 937 (1977)

Our studies of the reaction of heterocyclic amines with α,β-unsaturated carbonyl compounds (2) led us recently to consider the effect of heterocyclic substituents on the properties of disperse azo dyes of general structure I (3):



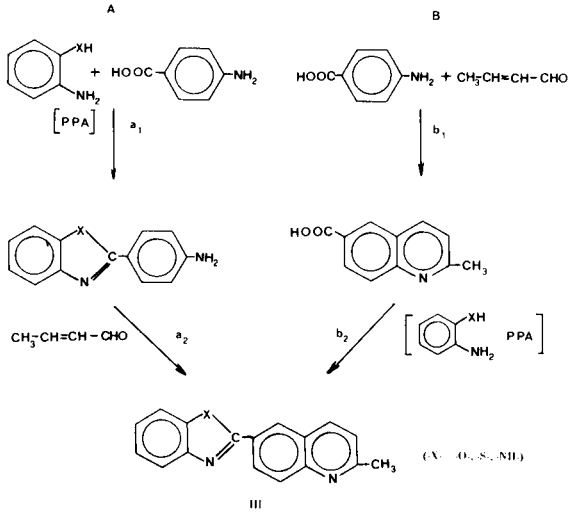
I

When the reagents are 2-(*p*-aminophenyl)benzothiazole and crotonic aldehyde or methylvinylketone, methylquinolines of structure II (2- or 4-CH_3, 6-Het, -X- = -S-) could be obtained and the effect of 6-(2-benzothiazolyl) on the properties of the related polymethine dyes (obtained by

II

reaction of activated methyl groups) could be investigated.

The route A of the scheme indicates the sequence of steps in the synthesis of III (-X- = -S-): the same compound may be prepared with reversed procedure according to the route B.



III

These results using the latter procedure are more satisfactory and suggests the possibility of an extensive investigation. Following the b_2 step (4), we can easily change the nature of the X heteroatom and, starting from suitable carboxylic acids, we can also change the position of a given hetaryl in the quinoline nucleus. Furthermore, in a similar manner, the analogous pyridine derivatives become available. In the a_2 step, it is difficult to change the X atom when 2-(*p*-aminophenyl)benzoxazole (-X- = -O-) or benzimidazole (-X- = -NH-) are employed.

In Table I the data for 2-(*m*-methyl-*n*-pyridyl)benz-X-azoles and in Table II the data for 2-(*m*-methyl-*n*-quinolyl)benz-X-azoles are reported respectively.

The melting points of the benzimidazole derivatives are distinctly higher in comparison with compounds in the benzoxazole and benzothiazole series. This is not unexpected if we consider the presence of hydrogen bonding in benzimidazoles. When the benz-X-azolyl group occupies the 6 position of the quinoline ring the melting points are, for a given X atom, generally higher if compared with other structural isomers. Furthermore the melting points are in the order pyridine < quinoline, provided that the X atom and the position of the benz-X-azolyl on the azine ring are identical.

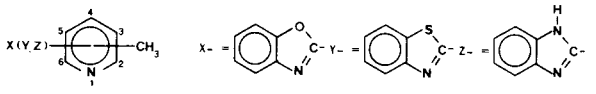
The chemical shifts of methyl protons on the quinoline ring are practically the same, whereas those on the pyridine ring are somewhat different. The values are: 2- and 4-methylquinoline (τ 2-CH_3 = 7.31; τ 4-CH_3 = 7.32 (8)) and 2- and 4-methylpyridine (τ 2-CH_3 = 7.49; τ 4-CH_3 = 7.70 (9)). The benz-X-azolyl group, however, exerts a weak deshielding effect on methyl protons (in the range 1.5-10 Hz) nearly irrespective of the nature of the X heteroatom.

Electronic absorption spectra of pyridine derivatives (No. **1-9**) show an intense broad band in the region 290-350 nm with the maxima in the range 299-312 nm. A broad absorption mainly due to the benzylidene-imine chromophore (-N=C-C_6H_5) is analogously observed in the spectra of 2-phenylbenz-X-azoles (10-12). A similar behaviour is also typical for the compounds of the quinoline series in which the benz-X-azolyl is linked to the 4 position (No. **10-12**). Figure 1 reports the spectra of compounds **2**, **8**, **11**. The spectra of compounds **14**, **17**, **20** are reported in Figure 2 as an example of 2- and 6-hetarylquinolines; the general pattern of these molecules is characterized by the presence of another absorption in the region 250-290 nm.

From a general point of view the situation in our structures appears to be different from that of isolated systems;

Table I

Pyridine Derivatives



Compound number	Structure	Yield %	M.p. °C	Crystallization solvent	Empirical formula	Elemental Analyses C% Calcd.	C% Found	H% Calcd.	H% Found	N% Calcd.	N% Found	Electronic absorption spectra λ max (log ε) nm (a)	Nmr spectra τ-CH_3 (ppm)
1	4-X 2-CH_3	67	103-104	DMSO/water	$C_{13}H_{10}N_2O$	74.27	74.18	4.79	4.83	13.33	13.30	302 (4.33)	7.41
2	4-Y 2-CH_3	70	90-91	DMSO/water	$C_{13}H_{10}N_2S$	69.00	69.14	4.45	4.58	12.38	12.40	299 (4.26)	7.40
3	4-Z 2-CH_3	70	208-209	Water	$C_{13}H_{11}N_3$	74.62	74.43	5.30	5.20	20.08	19.89	312 (4.35)	7.41
4	2-X 6-CH_3	70	124-125	DMSO/water	$C_{13}H_{10}N_2O$	74.27	74.40	4.79	4.69	13.33	13.46	305 (4.40)	7.39
5(b)	2-Y 6-CH_3	70	147-148	Ethanol/water	$C_{13}H_{10}N_2S$	69.00	69.08	4.45	4.56	12.38	12.26	313 (4.34)	7.41
6(c)	2-Z 6-CH_3	87	224-225	DMSO/water	$C_{13}H_{11}N_3$	74.62	74.62	5.30	5.36	20.08	20.01	312 (4.42)	7.39
7	2-X 4-CH_3	71	124-125	Ethanol/water	$C_{13}H_{10}N_2O$	74.27	74.30	4.79	4.85	13.33	13.26	303 (4.36)	7.56
8	2-Y 4-CH_3	93	134-135	DMSO	$C_{13}H_{10}N_2S$	69.00	68.87	4.45	4.49	12.38	12.39	308 (4.30)	7.55
9(d)	2-Z 4-CH_3	91	225-226	Benzene	$C_{13}H_{11}N_3$	74.62	74.60	5.30	5.40	20.08	20.13	308 (4.40)	7.60

(a) The main absorption above 250 nm is indicated. (b), (c), (d) In references 5, 6, 7, respectively, the synthesis of these compounds with alternative procedures are reported.

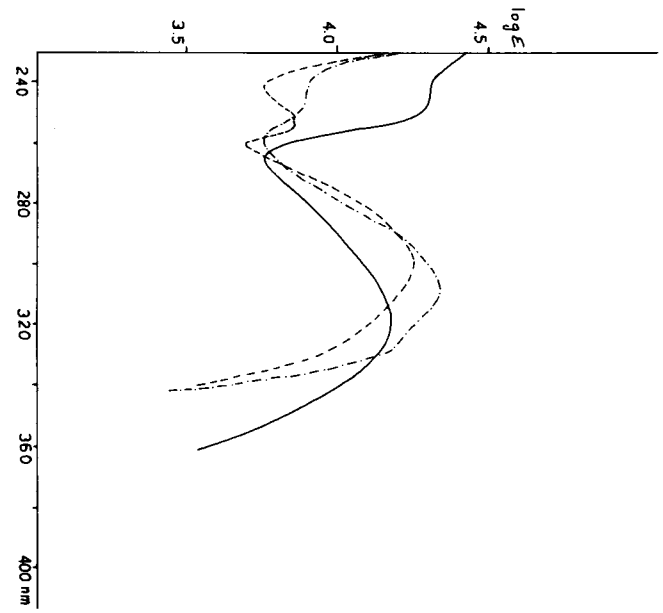


Figure 1. Electronic absorption spectra in ethanol of compounds:
No. **11** ——— 2-(2-methyl-4-quinolyl)benzothiazole
No. **8** —·—·— 2-(4-methyl-2-pyridyl)benzothiazole
No. **2** ---------- 2-(2-methyl-4-pyridyl)benzothiazole

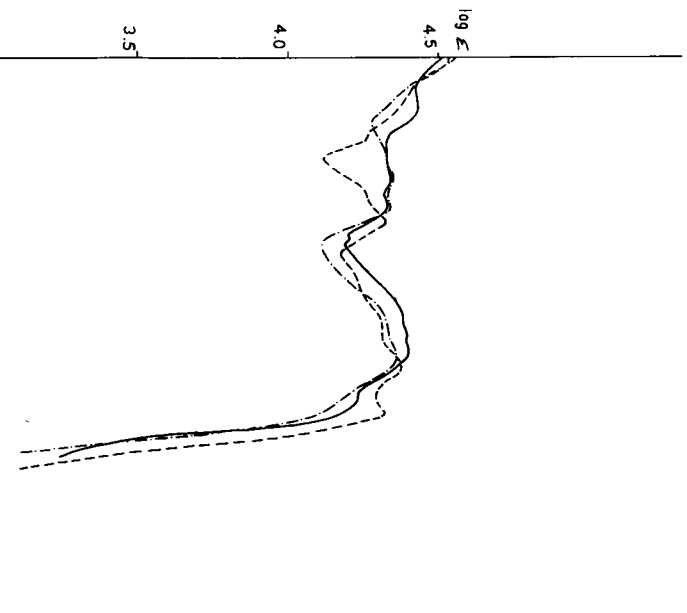
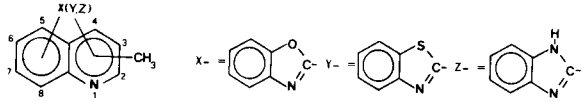


Figure 2. Electronic absorption spectra in ethanol of compounds:
No. **14** ——— 2-(2-methyl-6-quinolyl)benzothiazole
No. **20** —·—·— 2-(4-methyl-6-quinolyl)benzothiazole
No. **17** ---------- 2-(4-methyl-2-quinolyl)benzothiazole

Table II

Quinoline Derivatives



Compound number	Structure	Yield %	M.p. °C	Crystallization solvent	Empirical formula	Elemental Analyses C% Calcd.	C% Found	H% Calcd.	H% Found	N% Calcd.	N% Found	Electronic absorption spectra λ max (log ε) nm (a)	Nmr spectra τ-CH_3 (ppm)
10	4-X 2-CH_3	71	144-145	Ligroin	$C_{17}H_{12}N_2O$	78.44	78.59	4.65	4.63	10.76	10.81	321 (4.26)	7.23 (b)
11	4-Y 2-CH_3	87	90-91	Ligroin	$C_{17}H_{12}N_2S$	73.88	74.00	4.38	4.38	10.14	10.00	320 (4.17)	7.23
12	4-Z 2-CH_3	81	239-240	Dioxane/water	$C_{17}H_{13}N_3$	78.74	78.65	5.05	5.16	16.21	16.10	321 (4.19)	7.20
13	6-X 2-CH_3	73	172-173	Ligroin	$C_{17}H_{12}N_2O$	78.44	78.35	4.65	4.70	10.76	10.69	340 (4.20); 317 (4.47) 304 (4.42); 263 (4.39)	7.23 (b)
14	6-Y 2-CH_3	82	165-166	Ligroin	$C_{17}H_{12}N_2S$	73.88	73.70	4.38	4.41	10.14	10.03	343 (4.23); 326 (4.40) 313 (4.37); 279 (4.33) 269 (4.34)	7.25 (b)
15	6-Z 2-CH_3	75	254-255	Dioxane	$C_{17}H_{13}N_3$	78.74	78.70	5.05	5.09	16.21	16.12	339 (4.34); 319 (4.43) 308 (4.37); 281 (4.33)	7.30
16	2-X 4-CH_3	91	137-138	Ligroin	$C_{17}H_{12}N_2O$	78.44	78.42	4.65	4.71	10.76	10.70	345 (4.23); 330 (4.39) 318 (4.40); 280 (4.37)	7.20
17	2-Y 4-CH_3	91	173-174	Ligroin	$C_{17}H_{12}N_2S$	73.88	73.97	4.38	4.44	10.14	10.22	348 (4.33); 333 (4.37) 316 (4.30); 284 (4.32)	7.17
18	2-Z 4-CH_3	93	227-228	Dioxane/water	$C_{17}H_{13}N_3$	78.74	78.84	5.05	4.98	16.21	16.17	350 (4.44); 330 (4.38) 322 (4.30); 285 (4.32)	7.18
19	6-X 4-CH_3	71	176-177	Ligroin	$C_{17}H_{12}N_2O$	78.44	78.38	4.65	4.60	10.76	10.79	340 (4.16); 320 (4.42) 313 (4.40); 266 (4.39)	7.23 (b)
20	6-Y 4-CH_3	70	173-174	Ligroin	$C_{17}H_{12}N_2S$	73.88	73.79	4.38	4.43	10.14	10.09	329 (4.35); 280 (4.34) 270 (4.35)	7.20 (b)
21	6-Z 4-CH_3	79	270-272	Dioxane/water	$C_{17}H_{13}N_3$	78.74	78.59	5.05	5.15	16.21	16.09	323 (4.36); 282 (4.34)	7.18

(a) The main absorptions above 250 nm are indicated. (b) Taken in saturated solution.

i.e. benz-X-azoles, picolines and methylquinolines which show absorptions at shorter wavelengths and with lower intensities. The compounds **13-21**, which show an extention of the molecule along the long axis of the quinoline ring, have a spectral behaviour similar (apart from obvious bathochromic and hyperchromic effects) to that of 2- and 6-halo and alkylquinolines probably for the enhancement of polarized bands according to this axis (13). On the other hand the 4-hetaryl quinolines pattern (*i.e.* No. **11**, Figure 1) (these structures are extended along the short axis of the quinoline ring) is quite dissimilar compared with the above compounds and closely resembles the pattern of pyridine derivatives.

Quaternisation studies of these heterocyclic bases and the preparation and technologic testing of the related polymethine dyes are in progress.

EXPERIMENTAL

Nmr spectra were obtained with a Jeol C-60 HL spectrometer, in DMSO-d_6 solution (6%) using TMS as internal standard. Electronic spectra were recorded, in ethanol, on a Unicam SP 1700 spectrophotometer.

Commercial 6-methylpicolinic acid, *o*-aminophenol, *o*-aminothiophenol and *o*-phenylenediamine were employed. The following carboxylic acids and carboxamides were prepared according to literature methods: 2-methylisonicotinic acid (14), 2-methyl-4-quinolinecarboxylic acid (15), 4-methyl-6-quinolinecarboxylic acid (16), 2-methyl-6-quinolinecarboxylic acid (17), 4-methyl-2-quinolinecarboxamide (18). 4-Methylpicolinamide was prepared by homolytic amidation of 4-methylpyridine by the general procedure (18) and resulted in a product identical with that described (19).

Compounds **1-21** were prepared condensing a suitable carboxylic acid or amide (b_2 step) with *o*-aminophenol (or *o*-aminothiophenol or *o*-phenylenediamine) in polyphosphoric acid (85% phosphorus pentoxide) over a period of three hours at 200° following the general procedure indicated in reference (4). The reaction mixture was poured into water, excess acid was neutralized (*p*H 4), the precipitate was collected and slurried in dilute sodium carbonate. The base was finally collected by filtration, dried and crystallised.

Compound No. **14** was prepared by an alternate method following step a_2. This consists of reaction of 2-(*p*-aminophenyl)-benzothiazole with crotonaldehyde in ethanolic solution of 36% hydrochloric acid in the presence of sodium *m*-nitrobenzenesulphonate and zinc chloride, following the detailed procedure reported in reference (20).

REFERENCES AND NOTES

(1) This work was supported by the National Research Council (CNR).

(2) G. Di Modica, E. Barni and F. Delle Monache, *J. Heterocyclic Chem.*, **2**, 242 (1965).

(3) E. Barni and G. Di Modica, *Ann. Chim. (Rome)*, **66**, 385 (1976).

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

(5) P. J. Palmer, R. B. Trigg and J. Warrington, *J. Med. Chem.*, **14**, 248 (1971).

(6) W. Krüger and G. Krüger, East German Patent, 99787 (1973); *Chem. Abstr.*, **80**, 95953$_b$ (1974).

(7) F. H. Case, *J. Heterocyclic Chem.*, **4**, 157 (1967).

(8) R. Mondelli and R. Merlini, *Tetrahedron*, **22**, 3253 (1966).

(9) J. C. N. Ma and E. W. Warnhoff, *Can. J. Chem.*, **43**, 1849 (1965).

(10) R. Passerini, *J. Chem. Soc.*, 2256 (1954).

(11) R. Passerini and A. Cerniani, *ibid.*, 2261 (1954).

(12) M. Gelus and J. M. Bonnier, *J. Chim. Phys.*, 1602 (1967).

(13) H. H. Jaffè, M. Orchin, "The Theory and Applications of Ultraviolet Spectroscopy", John Wiley and Sons, New York-London, 1962, Ch. 14.

(14) A. D. Campbell, E. Chan, S. Y. Chooi, L. W. Deady and R. A. Shanks, *Aust. J. Chem.*, **24**, 377 (1971).

(15) W. Pfitzinger, *J. Prakt. Chem.*, **56**, 283 (1897).

(16) A. P. Shroff, H. Jaleel and F. M. Miller, *J. Pharm. Sci.*, **55**, 844 (1966).

(17) M. A. Kunz, G. Kochendoerfer and K. Köberle, German Patent, 567,273 (1931); *Chem. Abstr.*, **27**, 1362 (1933).

(18) A. Arnone, M. Cecere, R. Galli, F. Minisci, M. Perchinunno, O. Porta and G. Gardini, *Cazz. Chim. Ital.*, **103**, 13 (1973).

(19) K. Watanabe and K. Murayama, *Bull. Chim. Soc. Japan*, **47**, 1948 (1974).

(20) E. Barni and G. Di Modica, *J. Heterocyclic Chem.*, **8**, 693 (1971).