Quaternary Salts from 2-(Methylpyridyl or Quinolyl)benzimidazoles and Related Polymethine Dyes (1)

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The quaternisation of 2-(methylpyridyl or quinolyl)benzimidazoles with methyl iodide leads to a variety of salts depending on the relative position of the nuclei and on the experimental conditions: N-methylpyridinium, N-methylquinolinium, methyl and 1,3-dimethylbenzimidazolium iodides, and hydroiodides were isolated. Cyanine dyes were prepared from N-methylpyridinium and N-methylquinolinium methiodides. The main spectrospecopic features of these compounds are briefly discussed.

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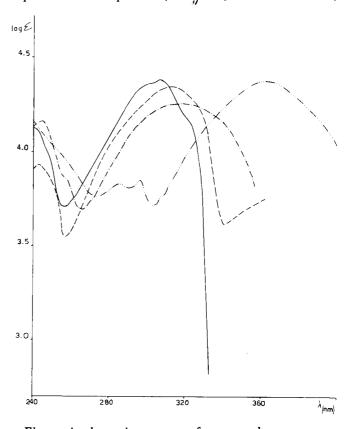
In previous papers (2-4) we described a series of 2-(methylpyridyl or quinolyl)benz-X-azoles (X = 0, S, NH), their quaternary salts and the related polymethine dyes when X = 0, S. This paper deals with salts and dyes of benzimidazoles (X = NH).

Together with the quaternisation at the azine (A) and azole (B) nitrogen atoms, typical of the oxazole and thiazole derivatives, the benzimidazoles show the possibility of N-alkylation (C) (I). Furthermore, the basicity of the A and B sites in the isolated systems is similar (p K_a values (5): benzimidazole 5.48, 2-picoline 5.97, 4-picoline 6.02, quinaldine 5.83, lepidine 5.67) and this results in a more marked competition in the quaternisation if compared with the previously described benzoxazole and benzothiazole derivatives (3,4,6,7).

Physical constants, analysis and spectroscopic data of the salts obtained reacting the bases with methyl iodide are reported in Table I.

The reaction with methyl iodide leads to the N-methyl-pyridinium or quinolinium iodides (compounds 1,2,4,6,7,9) and the benzimidazolium iodides (compounds 11-13), in which the 2-benzimidazolyl is α bonded to the azine nitrogen. In particular, compounds 12 and 13 (pyridine series) are 1,3-dimethylbenzimidazolium salts, in which both quaternisation and N-alkylation are observed, while in 11 (quinoline series), the N-alkylation is not active. Compounds 14 and 15 exhibit the hydroiodide structure instead of the expected methiodide structure, as in the corresponding compounds of the benzoxazole series (4).

The methiodide structure was established by nmr spectroscopy (Table I), following the procedure previously described (3). The $\Delta\delta$ values of the pyridinium and quinolinium salts are in the range of 13.8-22.2 Hz, while those of the benzimidazolium salts are in the range 4.2-8.4 Hz. The 5.48-5.95 τ absorptions assigned to +N-CH₃ protons and its integration value corresponds to three protons. The spectra of compounds 12 and 13 indicate the presence of six protons (τ +N-CH₃ = 5.91 and 5.95,



Electronic absorption spectra of compounds:
_____ methiodide 1 (------ free base)
____ methiodide 2 (_____ free base)

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Table I Salts

~		Δδ(b) Hz	15.6	20.4	17.4	15.6	18.0	22.2	19.8	25.2	13.8	21.0	4.8		4.2	8.4	1.8	3.6
	Compounds 14-15 Nmr Spectra	7+N·CH ₃	5.72	5.58	5.68	5.58	5.63	5.50	5.53	5.50	5.48	5.36	5.50		5.91 (f)	5.95 (f)		
	_	Ppm ppm	7.15	7.11	7.20	7.07	7.40	6.83	6.97	6.89	6.95	6.97	7.10		7.32	7.46	7.05	7.20
2-2-4-2-4	Compounds 12-13 Electronic Absorption	Spectra λ max (log ε), nm (a)	362 (4.38)	318 (4.26)	265 (3.78)	305 (4.06)	255 (3.81)	392 (4.25); 332 (4.12)	370 (3.91); 303 (4.42)	318 (4.00)	371 (3.89), 303 (4.44)	(3.90)	347 (4.31); 332 (4.37)	284 (4.36)	288 (4.17)	285 (4.18)	345 (4.24); 325 (4.18)	345 (4.00); 320 (4.06)
		6 Found	11.85	11.85		11.80		10.49	10.61		10.36		10.48		11.50	11.40	10.89	10.71
		N% Calcd.	11.97	11.97		11.97		10.47	10.47		10.47		10.47		11.51	11.51	10.85	10.85
	Compound 11 Elemental Analyses	Found	4.09	4.11		4.12		4.16	4.00		4.14		4.14		4.56	4.53	3.77	3.78
		H% Calcd.	4.02	4.02		4.02		4.02	4.02		4.02		4.02		4.42	4.42	3.64	3.64
		% Found	48.01	47.61		47.63		53.73	53.80		53.73		54.01		49.20	49.26	52.61	52.85
£	•	C% Calcd.	47.88	47.88		47.88		53.88	53.88		53.88		53.88		49.33	49.33	52.73	52.73
" " " " " " " " " " " " " " " " " " "	Compounds 6-10 Empirical	Formula	H. IN.	C H IN	C14**14***3	C H IN	-14-143	NI H		C18111611 3	N	0181416113	C.H.IN.	0 01 01				$C_{17}H_{14}IN_3$
IZ Z	Jo a		983.984	207-507	207-007	990-931	107-777	958.950	971.979	717.117	274.975	017	221-222		263-264	305.306	325-327 dec	303-305 dec
, , , , , , , , , , , , , , , , , , ,	S		HJ'6	L-CII3	ocu,	117-7 TUT		E E	2-CII3				+0113		6-CH.	4-CH	2.CH.	4-CH ₃
· (i)z-ō	Compounds 1-5	Number	1 4.7	3.4		3 (c) 4 3 7		(n) c			(a) 0		10 (c) 11	:	13	1 2	14	12

(a) The main absorptions above 250 nm are indicated. (b) Δδ values (Hz) are defined as follows: Δδ = δC-CH₃(methiodide) - δC-CH₃(base). (c) References 8,9. (d) References 9,10.
 (e) Reference 11. (f) The integration of this signal corresponds to six protons.

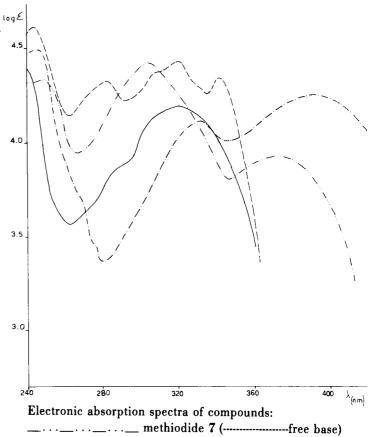
Table II
Polymethine Dyes

General Formulas	Compound Number			M.p. °C	Electronic Absorption Spectra λ max, nm (log ε)			
z (+ +) (**)								
6 N1 2	16	4-Z	2-K	275-276	507 (4.56)			
CH31	17	4-Z	2-W	271-273	558 (4.85)			
Compounds 16:25	18	5-Z	2-K	274-276	515 (4.74)			
5 Z 4	19	5-Z	2-W	250-252	559 (5.03)			
"(T) + 1 'k(w)	20 (a)		2-K		460 (4.57)			
, , , , , , , , , , , , , , , , , , , ,	21 (b)		2-W		536 (4.93)			
e ch ₃ i	22	3-Z	4-K	204-206	515 (4.57)			
Compounds 26-35	23	3-Z	4-W	197-199	564 (4.84)			
A LA	24 (a)		4-K		480 (4.62)			
z-= C-	25 (b)		4-W		557 (4.98)			
₩ N	26	4-Z	2-K	290-291	565 (4.73)			
	27	4-Z	2-W	250-251	605 (4.81)			
	28	6-Z	2-K	284-285	557 (4.85)			
K = CH-CH ₃	29	6-Z	2-W	288-289	599 (5.12)			
K- = -CH=CH-(CH ₃	30 (c)	3 2	2-K	200 209	525 (4.78)			
styryl dyes	31 (b)		2-W		582 (5.12)			
	32	6-Z	4-K	261-262	581 (4.61)			
su	33	6-Z	4-W	310-311	654 (5.14)			
W- = - CH= CH-CH=C	34 (c)	0 L	4-K	5.5 51.	544 (4.65)			
Сн _з	35 (d)		4-W		630 (5.14)			
unsymmetrical dyes	00 (u)		. "		333 (0.14)			

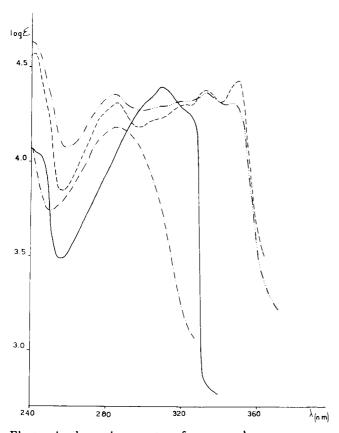
(a) Reference 15. (b) Reference 16. (c) Reference 17. (d) Reference 18. $\log \mathcal{L}$ respectively), in agreement with the usual behaviour of 1,3-dialkylbenzimidazolium salts. Besides, compound 11, obtained under more drastic conditions (see Experimental), is a monomethyl benzimidazolium salt (τ + N-CH₃ = 5.50; three protons). The salts 14 and 15 show low $\Delta \delta$ values (1.8 and 3.6 Hz), without + N-CH₃ signals and with a broad + N-H peak which rapidly exchanges with deuterated water. This suggests an hydroiodide structure similar to that of the analogous 8-(2-benzoxazolyl)methylquinoline hydroiodides (4). Owing to the low $\Delta \delta$ value, however, the site of protonation is the azole nitrogen atom (13).

A comparison of nmr data of the quaternary salts containing 2-benzoxazolyl and 2-benzothiazolyl (3,4) with our data suggest some generalizations. Both pyridinium and quinolinium salts show a deshielding effect of the hetaryl moiety on the chemical shifts (τ values) of C-CH₃ and +N-CH₃ protons and a magnitude of $\Delta\delta$ values in a given series (that is a fixed position of methyl and rings) in the order: 2-benzoxazolyl > 2-benzothiazolyl > 2-benzimidazolyl. Furthermore, if a comparison is made with unsubstituted compounds (2 or 4 picolinium, quinaldinium and lepidinium methiodides) the same effects are observed (14) (the 2-benzimidazolyl even plays, in few cases a shielding role).

The main absorptions above 240 nm of the electronic spectra of salts 1-15 are reported in Table I. The spectral



__.__. methiodide **6** (__



Electronic absorption spectra of compounds:
_____ methiodide 11 (------ free base)
____ methiodide 13 (_____ free base)

patterns of the bases and the salts of the benzimidazole series are similar to the corresponding ones of the benz-oxazole and benzothiazole series (2,3,4). Depending on the relative position of the nuclei, characteristic patterns are found, as reported in Figures 1-3.

The spectra of pyridinium salts (Figure I) reveal a bathochromic shift due to the quaternisation, which is more intense when the benzimidazolyl may be conjugated with the quaternised nitrogen. The spectra of the quinolinium salts (Figure 2) show a behaviour similar to that of the corresponding pyridinium ones, when the benzimidazolyl is γ -linked. However, in the case of substitution on the benzo ring of quinoline (6 position), the typical pattern of the methiodide, which changes with respect to the corresponding base, is evident. When quaternisation occurs at the benzimidazole nucleus, the spectral patterns are generally maintained (Figure 3). However, the pyridine derivatives show an appreciable hypo- and hypsochromic effect. The spectra of the hydroiodides 14 and 15 are quite similar to these of the related bases with very feeble shifts of the maxima.

The pyridinium and quinolinium methiodides (com-

pounds 1-10) react with aldehydes to give the corresponding polymethine dyes, reported in Table II, while compounds 11-15 do not react as expected. Apart from obvious considerations of a bathochromic effect of the unsymmetrical versus styryl dyes and of the γ -linked versus α -linked polymethine chains, the benz-X-azolyl ring gives rise, in a series, to a bathochromic shift which is less evident in the benzimidazole derivatives.

EXPERIMENTAL

Nmr spectra were obtained with a Jeol C-60 HL spectrometer, in DMSO-d₆ solution (6%) using TMS as internal standard. Electronic spectra were recorded, in ethanol, on a Unicam SP 1700 spectrophotometer. Salts.

The salts of the pyridine series were prepared by refluxing the suitable free bases with a strong excess of methyl iodide over a period of 5-6 hours. The salts of the quinoline series were obtained by adding acetone to the reaction mixture and refluxing over a period of 12 hours. The crude products were collected, washed with ethyl ether and crystallized from ethanol. The crude methiodide 6 was thrice slurried with boiling dioxane before the crystallization from ethanol.

The methiodide 11, which can not be prepared as above, was obtained by reaction in sealed tube at 105° for 12 hours. The hydroiodides 14 and 15 can be prepared either by refluxing or in a sealed tube. The three crude salts were washed once with ethyl ether and thrice with boiling acetone before recrystallization from ethanol. The yields of pyridinium and quinolinium methiodides, of benzimidazolium methiodides and of the hydroiodides were ca. 60-70%, ca. 30-40% and ca. 16-18%, respectively.

Dyes.

The dyes were prepared by refluxing a suitable methiodide (3×10^{-3} mole) for 45 minutes in acetic anhydride (20 ml. for pyridinium salts and 40 ml. for quinolinium salts) with p-dimethylaminobenzaldehyde (3.4×10^{-3} mole) (styryl dyes) or (3-methyl-2-benzothiazolynilydene)-ethanal (19) (3.5×10^{-3} mole) (unsymmetrical dyes). Styryl dye 18 was obtained by reaction of methiodide 2 in absolute ethanol (piperidine as catalyst) under milder conditions (45° , 30 minutes). The crude products were collected, washed with ethyl ether and crystallized from ethanol (dyes 16, 17, 18 from methanol).

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experimental conditions of the reaction with methyl iodide are important factors in determining the structure of the salts in these series. As a further proof of this situation it is interesting to note that compound 6 is recovered refluxing the proper base with methyl iodide. If the reaction is carried out in a sealed tube at 95° for several hours, besides this product, the formation of a 1,3-dimethylbenzimidazolium derivative and a bis iodide (each of the three nitrogens is methylated) is observed.

(14) In the case of 1,4-dimethyl-3-(2-benzothiazolyl)pyridinium iodide (compound 16 in reference 4), τ and $\Delta\delta$ values are lowered presumably due to a steric effect caused by the substituent methyl group. This results

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