

Methylpyridylbenzimidazoles. Part II.
Bridged Mono and bis-Quaternary Salts
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The reaction of 2-(4-methyl-2-pyridyl)benzimidazole and of its *N* long alkyl chain derivatives with 1,3-dibromopropane led to cyclic bis-charged salts. Their spectroscopic (nmr and uv) and surface properties are briefly discussed. It turned out to be interesting to compare the similar behaviour of these salts and the corresponding well known derivatives of 2,2'-bipyridyl.

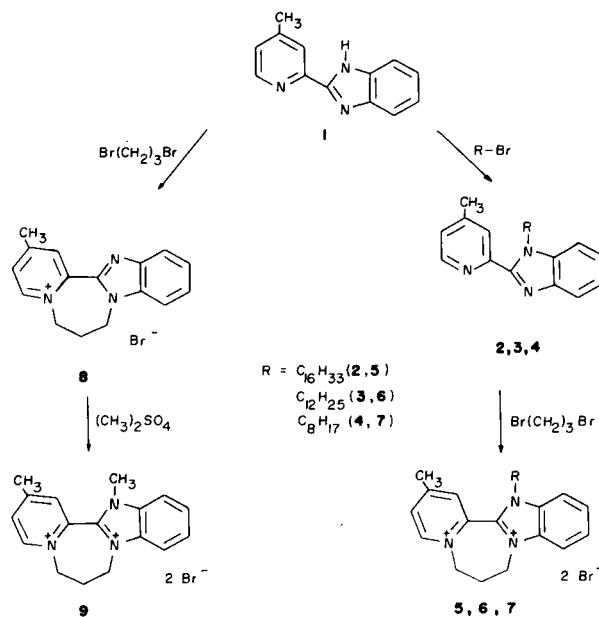
J. Heterocyclic Chem., **20**, 29 (1983).

In previous papers we described the synthesis of 2-(4-methyl-2-pyridyl)benzimidazole (1) and its behaviour to the quaternisation with short and long chain alkyl bromides and with dimethylsulphate (1-4). It proved to be interesting to extend the investigation and, in this paper, new types of salts obtained by reaction with bifunctional agents are described.

The following route was used to prepare the salts as indicated in the scheme.

The interest in cyclic salts is highly opportune, particularly in view of their redox properties, as shown, for example, by the closely related cyclic viologens (5). One important application of viologens (cyclic or not) is for the photodecomposition of water, in which connection a recent investigation in micellar solutions has been made (6,7). The idea of developing similar amphiphilic active structures is also supported by the reported use of a self-micellizing 1-ethyl-1'-cetyl-4,4'-bipyridinium dibromide (8).

The starting base 1 is readily alkylated with long chain alkyl bromides and the products obtained 2-4 (3) are active towards bifunctional reagents giving, in theory, different results. Using 1,3-dibromopropane, the salts 5-7 were obtained. Their analytical and spectroscopic data, reported in Tables I and II, agree with the assigned cyclic



structures. The melting points and R_f values are higher and lower respectively than in the starting products, according to similar previously observed effects (3). The nmr signals from the methyl and aromatic protons also support

Table I
 Characterisation Data on Bridged Mono and bis-Quaternary Salts

Compound number	Yield %	Mp °C	R_f	Empirical formula	C%		Elemental analyses H%		N%		log CMC	Amin(a) (Å ²)
					Calcd.	Found	Calcd.	Found	Calcd.	Found		
5	17	238-240	0.23	C ₃₂ H ₄₆ Br ₂ N ₃	60.47	60.60	7.77	7.83	6.61	6.53	-2.54	122
6	7	229-231	0.20	C ₂₈ H ₄₁ Br ₂ N ₃	58.04	57.91	7.13	7.14	7.25	7.37	-1.70	115
7	8	232-234	0.17	C ₂₄ H ₃₃ Br ₂ N ₃	55.08	55.11	6.36	6.49	8.03	7.98	-1.18	114
8	50	295-296	0.15	C ₁₆ H ₁₆ BrN ₃	58.19	58.10	4.88	5.01	12.72	12.73	—	—
9	8	272-274	0.11	C ₁₇ H ₁₉ Br ₂ N ₃	48.02	48.17	4.50	4.54	9.88	9.96	—	—

(a) Minimum areas per molecule.

Table II
Spectroscopic Data on Bridged Mono and bis-Quaternary Salts

Compound number	Electronic absorption spectra (a)		$\geq\text{C-CH}_3$ (b)	Methylene protons	NMR Spectra			Benzimidazole protons (g)
	λ max (nm)	log ϵ			τ (ppm)	H_β	H_α	
5	319	4.20	7.18	6-4.5 (c)	1.47	1.73 (f)	0.43	2.33-1.50
6	319	4.20	7.18	6-4.5 (c)	1.47	1.73 (f)	0.43	2.33-1.50
7	319	4.20	7.18	6-4.5 (c)	1.47	1.73 (f)	0.43	2.33-1.50
8	344	4.23	7.28	5.66-5.08 (d)	1.45	1.88	0.80	2.70-2.07
9 (h)	319	4.20	7.18	6-4.83 (e)	1.41	1.82	0.75	2.27-1.58

(a) The main absorptions above 250 nm are indicated. (b) Partially superimposed to the signals of the central methylene group of the bridge. (c) Multiplet corresponding to three methylene groups (the first of the long chain linked to the azole nitrogen and the two extreme of the bridge). The resonance range is indicated. (d) Multiplet corresponding to the two extreme methylene groups of the bridge. The resonance range is indicated. (e) See (c) instead of the long chain methylene group the signal of the *N*-methyl is present. (f) Partially superimposed to the signals of benzimidazole protons. (g) The resonance range for the multiplet is indicated. (h) The nmr spectrum was recorded in DMSO- d_6 /deuterium oxide (8:2).

doubly-charged structures. Marked downfield shifts (referred to 2-4) are observed not only for methyl and pyridine, but also for benzimidazole protons. Especially noteworthy is the downfield resonance of the methyl groups which is the highest observed for the pyridinium salts of the series. Signals from the bridged methylene protons are quite complex and in Table II their resonance range is reported. The electronic absorption spectra, whose maxima are independent of the alkyl chain length, show strong bathochromic and weak hypochromic effects compared to **1** and **2-4**.

Owing to the low reaction yields, an alternative route to compounds **5-7** was tried. Reacting **1** with 1,3-dibromopropane, compound **8** was isolated in good yield, but it failed to react with long chain alkyl halides. This cyclic monoquaternary salt shows a higher melting point and a lower R_f value than long chain bis salts. A strong bathochromic effect is observed, not only with respect to the alkylated bases, but also to the bis salts, whereas the intensity of the absorption bands were only very slightly affected. These effects suggest that the presence of the trimethylene chain allow the pyridine and benzimidazole rings to resume a less twisted position. The cyclic mono-charged structure is confirmed by nmr data. The chemical shifts of methyl and pyridine protons are downfield with respect to the starting compound but smaller than in the bis salts. Their absolute values are in agreement with the presence of a charge on the pyridine ring, while the position of the benzimidazole signals confirms the absence of a charge on that ring.

It was however possible to alkylate compound **8** with dimethylsulphate, obtaining **9**, whose structure differs from **5-7** only in the alkyl chain length. The methyl derivative has a higher melting point than its long chain counterparts but the same electronic spectrum (Figure 1); the nmr signals lie in the same regions. The position of maxima in the cyclic bis-charged salts show the effect of long chains which twist the system independently of the chain length.

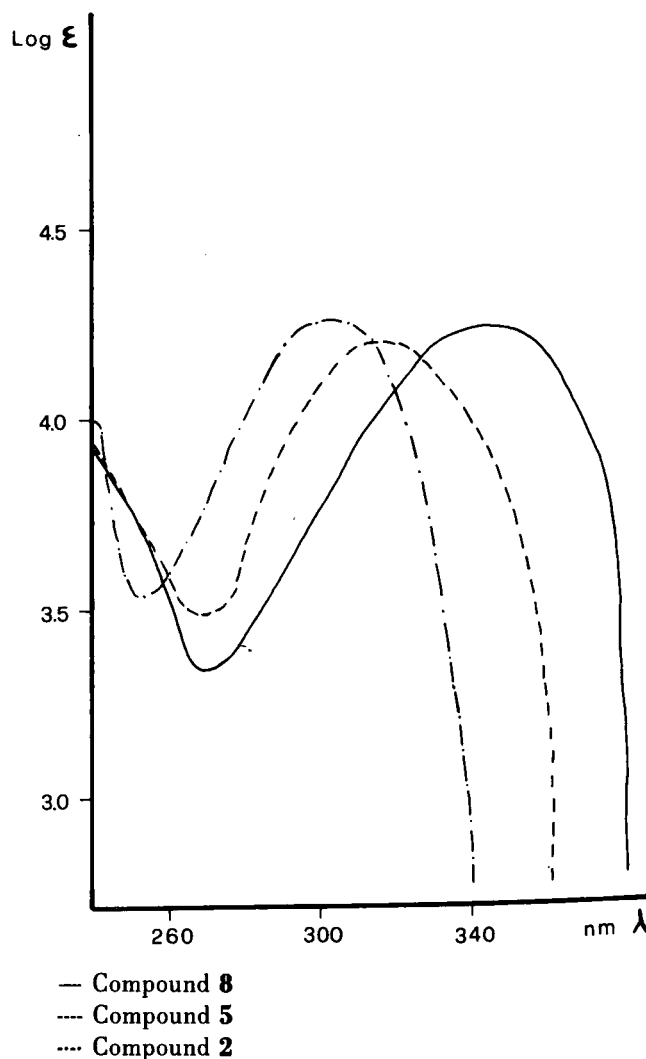
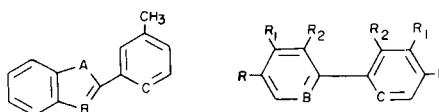


Figure 1. Electronic absorption spectra.

It is interesting, at this point, to make a comparison between the spectral behaviour of compounds related to **1**

Table III

Comparison of Electronic Absorption Spectra of 2,2'-Bipyridyls and Pyridylbenzimidazoles



Structure			R	R ₁	R ₂	λ	log ε	Δλ (a)	Δlog ε (a)	Ref	λ	log ε	Δλ (b)	Δlog ε (b)	Ref
A	B	C	H	H	H	308	4.40	—	—	1	283	4.11	—	—	12
NH	N	N	H	H	H	302	4.28	-6	-0.12	3					
N-C ₈ H ₁₇															
N-C ₁₂ H ₂₅	N	N													
N-C ₁₆ H ₃₃															
	N	N	H	H	CH ₃						271	3.50	-12	-0.61	12
	N	N	H	CH ₃	H						284	4.10	+1	-0.01	12
	N	N	CH ₃	H	H						289	4.30	+6	+0.19	12
N-C ₈ H ₁₇															
N-C ₁₂ H ₂₅	*N-CH ₃	N	H	H	H	282	4.19	-26	-0.21	3	277	3.97	-6	-0.14	9
N-C ₁₆ H ₃₃															
N-C ₈ H ₁₇															
N-C ₁₂ H ₂₅	*N-CH ₃	*N-CH ₃	H	H	H	284	4.04	-24	-0.36	3	270	4.13	-13	+0.02	9
N-C ₁₆ H ₃₃															
N-C ₈ H ₁₇															
N-C ₁₂ H ₂₅	*N	*N	H	H	H	319	4.20	+11	-0.20		287	4.19	+4	+0.08	10
N-C ₁₆ H ₃₃	CH ₂ -CH ₂ -CH ₂	CH ₂ -CH ₂ -CH ₂													
N-CH ₃	*N	*N	H	H	CH ₃	319	4.20	+11	-0.20		298	4.17	+15	+0.06	11
	CH ₂ -CH ₂ -CH ₂	CH ₂ -CH ₂ -CH ₂													
	*N	*N	H	CH ₃	H						284	4.17	+1	+0.06	11
	CH ₂ -CH ₂ -CH ₂	CH ₂ -CH ₂ -CH ₂													
	*N	*N	CH ₃	H	H						297	4.01	+14	-0.10	11
	CH ₂ -CH ₂ -CH ₂	CH ₂ -CH ₂ -CH ₂													
N	*N	*N				344	4.23	+36	-0.17						
	CH ₂ -CH ₂ -CH ₂	CH ₂ -CH ₂ -CH ₂													

(a) Differences related to 2-(4-methyl-2-pyridyl)benzimidazole (compound 1). (b) Differences related to 2,2'-bipyridyl.

and the analogous 2,2'-bipyridyls. For this purpose, comparative data from the electronic spectra of pyridyl benzimidazole, 2,2'-bipyridyl and their derivatives, are summarized in Table III. Accurate nmr and uv studies on the conformation of bipyridyls have been extant for a long time (9-12).

The data in Table III indicate a hypsochromic effect in both series when an alkyl system is inserted next to the joining portion of the two rings. Similarly, a bathochromic shift is observed if the nitrogen atoms are bridged with a methylene chain. This similar behaviour of bipyridyls and pyridylbenzimidazoles led us to infer that analogous effects are operating in the two systems.

As mentioned above, a peculiar property of these cyclic

salts is their reduction potential. Compounds 5-7 display their r.p. in the range -490/-630 mV (measured by cyclic voltametry) which, again, is closely related to the r.p. range of the analogous bipyridyls (9).

Owing to the presence of long chains and of two positive charges, compounds 5-7 exhibit surface active properties (data in Table I). The minimum areas per molecule (A_{\min} in \AA^2) at the liquid-air interface are calculated from the equations (13):

$$\Gamma = \frac{i}{2.303 m RT} \left(\frac{\delta \gamma}{\delta \log c} \right)_T \quad \begin{matrix} m = 3 \text{ (bis charged ions)} \\ N_A = \text{Avogadro's number} \end{matrix}$$

$$A_{\min} = \frac{10^{16}}{N_A \Gamma} \left(\frac{\delta \gamma}{\delta \log c} \right)_T = \text{slope of the } \gamma/\log c \text{ plot (Figure 2)}$$

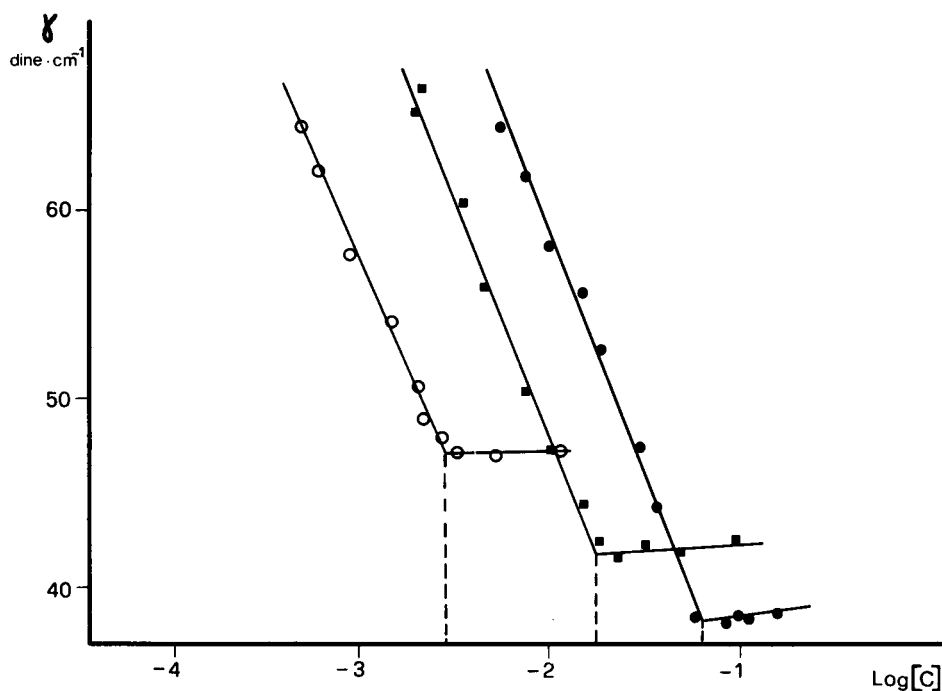


Figure 2. O Compound 5 ($R = C_{16}H_{33}$)
 ■ Compound 6 ($R = C_{12}H_{25}$)
 ● Compound 7 ($R = C_8H_{17}$)

Figure 2. Surface tension (γ) as a function of the logarithm of the molar concentration of bridged long chain salts.

The critical micellar concentrations (CMC) and the values of γ at the CMC are dependent on the chain length.

EXPERIMENTAL

The nmr spectra were obtained with a Varian T 60 spectrometer in DMSO- d_6 solution (6%) using TMS as an internal standard. Electronic spectra were recorded in ethanol, on a Pye Unicam SP 8-100 spectrophotometer. Surface tension measurements were obtained with a Dognon-Abribat tensiometer. The R_f values were determined by tlc on silica gel 60 F 254 (Merck) plates using, as eluent, BAW (4:5:1).

Compounds 1-4 were prepared as previously reported (1-3).

Compounds 5-7 were prepared mixing equimolecular amounts (2.3×10^{-2} mole) of 1,3-dibromopropane and of the suitable alkylated base (2-4) in toluene (10 ml) and refluxing for 90 minutes. After cooling, ethyl ether was added and the solid collected. The crude products were well washed with ethyl ether and crystallized from acetonitrile.

Compound 8 was prepared by refluxing equimolecular amounts (5×10^{-2} mole) of 1 and 1,3-dibromopropane in 40 ml of DMF for 4 hours. After cooling, the crude product was collected, washed with ethyl ether and crystallized from ethanol.

Compound 9 was prepared by refluxing 8 (1×10^{-2} mole) with dimethylsulphate (5×10^{-2} mole) in 40 ml of toluene for 4 hours. The solvent was removed and the residue slurred with ethyl ether and treated with a saturated aqueous solution of potassium bromide. The crude dibromide was extracted with ethanol, the solution evaporated to dryness and the residue crystallized from aqueous ethanol.

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REFERENCES AND NOTES

- (1) E. Barni and P. Savarino, *J. Heterocyclic Chem.*, **14**, 937 (1977).
- (2) E. Barni and P. Savarino, *ibid.*, **16**, 1583 (1979).
- (3) E. Barni, P. Savarino, G. Viscardi and E. Pelizzetti, *ibid.*, **20**, 23 (1983).
- (4) E. Barni, P. Savarino, E. Pelizzetti and G. Rothenberger, *Helv. Chim. Acta*, **64**, 1943 (1981).
- (5) B. Kok, H. Ruraimski and O. V. H. Owens, *Biochim. Biophys. Acta*, **109**, 347 (1965).
- (6) P. A. Brugger and M. Grätzel, *J. Am. Chem. Soc.*, **102**, 2461 (1980).
- (7) M. P. Pieloni, A. M. Braun and M. Grätzel, *Photochem. Photobiol.*, **31**, 423 (1980).
- (8) K. Takuma, T. Sakamoto, T. Nagamura and T. Matsuo, *J. Phys. Chem.*, **85**, 619 (1981).
- (9) R. F. Homer and T. E. Tomlinson, *J. Chem. Soc.*, 2498 (1960).
- (10) I. C. Calder, T. McL. Spotswood and C. I. Tanzer, *Aust. J. Chem.*, **20**, 1195 (1967).
- (11) T. McL. Spotswood and C. I. Tanzer, *ibid.*, **20**, 1213 (1967).
- (12) T. McL. Spotswood and C. I. Tanzer, *ibid.*, **20**, 1227 (1967).
- (13) M. J. Rosen, "Surfactants and Interfacial Phenomena", Wiley Interscience, New York, 1978.