Assembled Systems [X-Azolopyridine][quinoline]. Bases and Salts [1].

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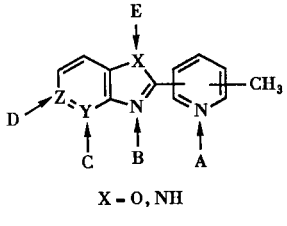
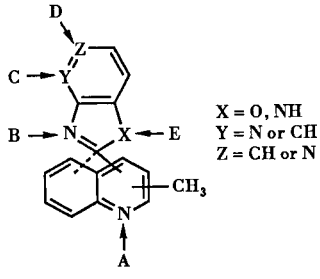
A series of bases containing X-azolopyridines (X = O, NH) and methylquinolines, assembled in different ways, was prepared by reaction of methylquinolinecarboxylic acids (or carboxamides) with diamino (or hydroxyamino) pyridines. The bases were quaternized with methyl iodide. The physical and spectroscopic data of both the bases and the salts were correlated and compared with those of [X-azolopyridine][pyridine] systems previously studied. The structure of the salts was markedly influenced by a balance of basicity-hindrance factors in the heteroaromatic substrates.

J. Heterocyclic Chem., **29**, 185 (1992).

Assembled heterocyclic systems have many uses in the chemical and pharmaceutical industries [2,3]. Basic members of this category, such as X-azolopyridine systems **I**, have been studied by us in recent years [4,5] due to their relevance in the field of dye chemistry.

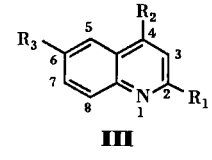


I

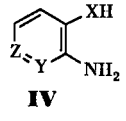


II

The new derivatives **II** which are now reported were desirable to study the effect of the bulkier quinoline ring on the basicity of the system. Twelve X-azolopyridines **II**, assembled with methylquinolines in various positions, have been obtained from acids or amides **III** and disubstituted pyridines **IV** in polyphosphoric acid, according to a versatile procedure previously tested on other azole compounds [6]. The system reactivity has then been tested through the synthesis of the corresponding salts from **II** and methyl iodide. Physical and spectroscopic data for bases and salts are reported in Tables 1 and 2 respectively. Properties as a function of the structure are



III



IV

IIIa $R_1 = CH_3$, $R_2 = COOH$, $R_3 = H$
IIIb $R_1 = CONH_2$, $R_2 = CH_3$, $R_3 = H$
IIIc $R_1 = CH_3$, $R_2 = H$, $R_3 = COOH$
IIId $R_1 = H$, $R_2 = CH_3$, $R_3 = COOH$
IVa X = NH, Y = N, Z = CH
IVb X = NH, Y = CH, Z = N
IVc X = O, Y = N, Z = CH

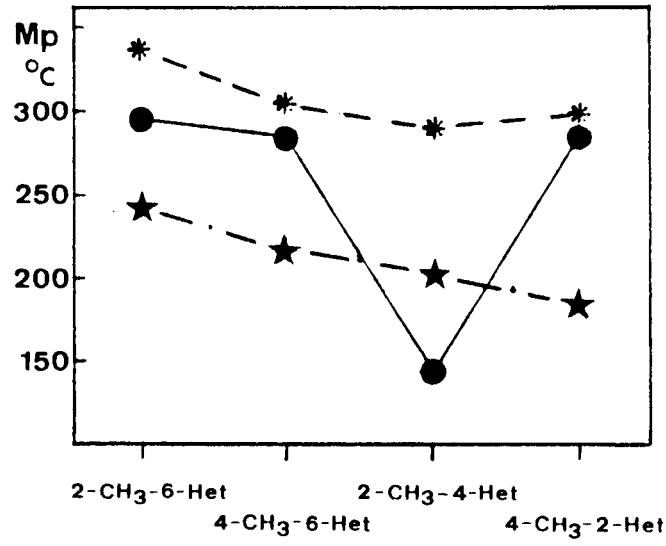


Figure 1. Comparison of melting points of compounds **1-12**. Hetaryl: ● 2-imidazo[4,5-*c*]pyridyl, * 2-imidazo[4,5-*b*]pyridyl, ★ 2-oxazo-[4,5-*b*]pyridyl.

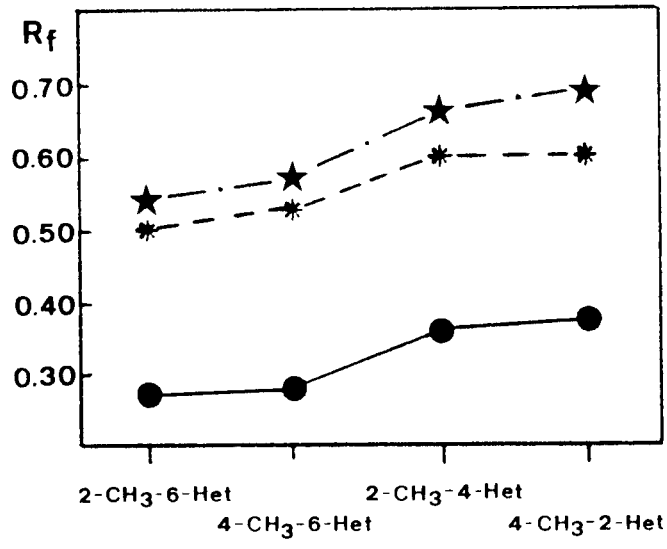
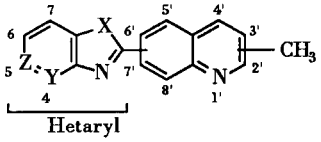


Figure 2. Comparison of Rf values of compounds **1-12**. For key see Figure 1.

Table 1

Characterization Data of Bases



Compound number	Hetaryl position	Structure CH_3 position	X	Y	Z	Electronic absorption spectra λ max (log ε) nm		Mp °C	Rf	Empirical formula	Elemental Analyses Calcd./Found C	H	N
1	2'	4'	NH	N	CH	242 (4.51)	290 (4.27)	288-289	0.60	$C_{16}H_{12}N_4$	73.83	4.65	21.52
						331 (4.49)	347 (4.50)				73.99	4.70	21.63
2	2'	4'	NH	CH	N	246 (4.65)	278 (4.36)	274-276	0.37	$C_{16}H_{12}N_4$	73.83	4.65	21.52
						314 (4.33)	326 (4.33)				73.77	4.73	21.48
						342 (4.22)							
3	2'	4'	O	N	CH	247 (4.43)	289 (4.31)	180-181	0.69	$C_{16}H_{11}N_3O$	73.55	4.24	16.08
						324 (4.46)					73.51	4.31	16.08
4	4'	2'	NH	N	CH	242 (4.31)	320 (4.27)	280-281	0.61	$C_{16}H_{12}N_4$	73.83	4.65	21.52
											73.68	4.71	21.55
5	4'	2'	NH	CH	N	243 [a]	311 (4.08)	141-143	0.36	$C_{16}H_{12}N_4$	73.83	4.65	21.52
											73.80	4.62	21.64
6	4'	2'	O	N	CH	247 (4.23)	325 (4.26)	197-198	0.66	$C_{16}H_{11}N_3O$	73.55	4.24	16.08
											73.49	4.23	16.12
7	6'	2'	NH	N	CH	244 (4.55)	286 (4.17)	324-326	0.50	$C_{16}H_{12}N_4$	73.83	4.65	21.52
						322 (4.51)	342 (4.30)				73.84	4.59	21.58
8	6'	2'	NH	CH	N	244 (4.66)	277 (4.33)	285-286	0.27	$C_{16}H_{12}N_4$	73.83	4.65	21.52
						312 (4.36)	337 (4.03)				73.78	4.66	21.53
9	6'	2'	O	N	CH	248 (4.52)	284 (4.20)	235-236	0.54	$C_{16}H_{11}N_3O$	73.55	4.24	16.08
						323 (4.41)	341 (4.39)				73.56	4.19	16.02
10	6'	4'	NH	N	CH	242 (4.48)	288 (4.20)	294-295	0.53	$C_{16}H_{12}N_4$	73.83	4.65	21.52
						327 (4.44)	342 (4.25)				73.75	4.65	21.49
11	6'	4'	NH	CH	N	243 (4.65)	277 (4.33)	275-276	0.28	$C_{16}H_{12}N_4$	73.83	4.65	21.52
						315 (4.32)					73.86	4.65	21.49
12	6'	4'	O	N	CH	246 (4.48)	284 (4.26)	212-213	0.57	$C_{16}H_{11}N_3O$	73.55	4.24	16.08
						325 (4.53)	341 (4.35)				73.58	4.29	16.10

[a] Shoulder.

discussed hereinafter by comparison with the data reported for compounds of the *benzo* series **II** (Y = Z = CH) [7].

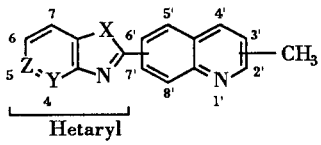
Figure 1 and 2 have been drawn for a more immediate comparison of the melting points and chromatographic data. Imidazo[4,5-*b*] isomers show melting points higher than imidazo[4,5-*c*] ones and than oxazole derivatives. Compound **5** is an exception, its melting point is surprisingly low. A minor effect is represented by the decreasing of melting points, according to the relative positions of the rings, which follows the order: 2-CH_3-6-Het > 4-CH_3-6-Het > 2-CH_3-4-Het > 4-CH_3-2-Het. The *benzo* derivatives [7] show values lower than their *pyrido* counterparts.

The above trends are consistent with the ability to establish intermolecular hydrogen bonds, a phenomenon which has been frequently noticed by us with heterocyclic systems. If melting points and chromatographic R_f's were approximately controlled by the same polar and intermolecular factors, one should expect R_f values (on silica gel, eluent BAW) in Figure 2, to change in the opposite order to melting points. This happens in most cases (the sequence of R_f is 2-CH_3-6-Het < 4-CH_3-6-Het < 2-CH_3-4-Het < 4-CH_3-2-Het, oxazoles show highest values) but, as the annellation is concerned (*i.e.* [4,5-*b*] or [4,5-*c*]), the upsetting is not observed. Chromatographic elution, may indeed be ruled by other factors, in addition to H-bonding.

The electronic spectra may be divided in two types (Figure 3, compounds **1** and **4** as examples). The first type, exhibited by compounds **1**, **2**, **3**, **7-12**, shows a well structured absorption in the long-wavelength region and one

Table 2

Characterization Data of Salts

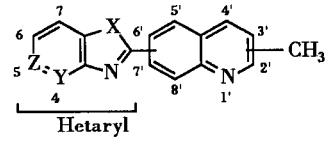


Compound number	Hetaryl position	Structure CH_3 position	X	Y	Z	Electronic absorption spectra λ max (log ε) nm		Δλ max [a]	Δlog ε [a]	Mp °C	Rf	Empirical formula	Elemental Analyses Calcd./Found C	H	N
13	2'	4'	NH	$\overset{+}{N}$-CH_3	CH	247 (4.52)	292 (4.06)	+10	+0.1	275-277	0.29	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
						341 (4.57)	357 (4.60)						50.69	3.80	13.88
14	2'	4'	NH	CH	$\overset{+}{N}$-CH_3	252 (4.70)	280 (4.24)	+3	+0.02	283-285	0.24	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
						317 (4.35)							50.67	3.82	13.92
15	2'	4'	O	$\overset{+}{N}$-CH_3	CH	249 (4.47)	295 (4.20)	+16	+0.10	207-211	0.32	$C_{17}H_{14}IN_3O$	50.64	3.50	10.42
						340 (4.56)	355 [b]						50.48	3.63	10.34
16	4'	2'	NH	$\overset{+}{N}$-CH_3	CH	336 (4.30)		+16	+0.03	245-247	0.24	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
													50.79	3.77	13.98
17	4'	2'	NH	CH	$\overset{+}{N}$-CH_3	316 (4.20)		+5	+0.12	254-256	0.21	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
													50.82	3.71	13.90
18	4'	2'	O	$\overset{+}{N}$-CH_3	CH	336 (4.31)		+11	+0.50	247-248	0.22	$C_{17}H_{14}IN_3O$	50.64	3.50	10.42
													50.59	3.52	10.45
19	6'	2'	NH	$\overset{+}{N}$-CH_3	CH	245 (4.56)	343 (4.58)	+21	+0.70	265-266	0.18	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
						358 (4.55)							50.76	3.83	13.96
20	6'	2'	NH	CH	$\overset{+}{N}$-CH_3	250 (4.82)	317 (4.55)	+5	+0.19	288-289	0.16	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
													50.66	3.86	13.89
21	6'	2'	O	$\overset{+}{N}$-CH_3	CH	244 (4.42)	342 (4.49)	+19	+0.08	207-208	0.21	$C_{17}H_{14}IN_3O$	50.64	3.50	10.42
						358 (4.42)							50.67	3.62	10.47
22	6'	4'	NH	$\overset{+}{N}$-CH_3	CH	244 (4.56)	296 (4.04)	+16	+0.12	263-264	0.20	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
						343 (4.56)	359 (4.53)						50.78	3.67	14.01
23	6'	4'	NH	CH	$\overset{+}{N}$-CH_3	250 (4.71)	318 (4.42)	+3	+0.1	295-297	0.16	$C_{17}H_{15}IN_4$	50.76	3.76	13.93
													50.71	3.76	13.97
24 [c]	6'	4'	O	N	CH	247 (4.39)	300 (4.37)	+15	-0.31	226-227	0.12	$C_{17}H_{14}IN_3O$	50.64	3.50	10.42
						324 (4.21)	340 (4.22)						50.68	3.57	10.49

[a] Δ is the difference salt-base of main absorption in the long wavelength region. [b] Shoulder. [c] *N*-Methylquinolinium salt.

Table 3

^1H NMR Data of Bases



Compound number	Hetaryl position	Structure CH_3 position	X	Y	Z	Chemical Shifts (ppm) Pyridine-ring protons 4	5	6	7	2'	Quinoline-ring protons 3'	4'	5'	6'	7'	8'	2' CH_3	4' CH_3
1	2'	4'	NH	N	CH	–	8.46	7.33	8.00	–	8.40	–	8.20	7.88	7.73	8.20	–	2.83
2	2'	4'	NH	CH	N	9.07	–	8.39	7.62	–	8.40	–	8.19	7.89	7.73	8.19	–	2.82
3	2'	4'	O	N	CH	–	8.64	7.57	8.37	–	8.34	–	8.20	7.89	7.77	8.20	–	2.83
4	4'	2'	NH	N	CH	–	8.49	7.37	8.19	–	8.00	–	9.20	7.69	7.83	8.06	2.78	–
5	4'	2'	NH	CH	N	9.12	–	8.40	7.73	–	8.02	–	9.19	7.69	7.83	8.06	2.78	–
6	4'	2'	O	N	CH	–	8.67	7.60	8.35	–	8.20	–	9.29	7.76	7.86	8.07	2.79	–
7	6'	2'	NH	N	CH	–	8.38	7.29	8.09	–	7.52	8.38	8.82	–	8.55	8.09	2.71	–
8	6'	2'	NH	N	CH	9.00	–	8.35	7.65	–	7.52	8.39	8.80	–	8.53	8.09	2.71	–
9	6'	2'	O	N	CH	–	8.58	7.50	8.26	–	7.56	8.47	8.88	–	8.51	8.12	2.72	–
10	6'	4'	NH	N	CH	–	8.40	7.30	8.10	8.83	7.47	–	9.00	–	8.61	8.17	–	2.82
11	6'	4'	NH	CH	N	9.03	–	8.36	7.67	8.83	7.48	–	8.97	–	8.59	8.18	–	2.82
12	6'	4'	O	N	CH	–	8.59	7.50	8.30	8.88	7.50	–	8.88	–	8.50	8.21	–	2.82

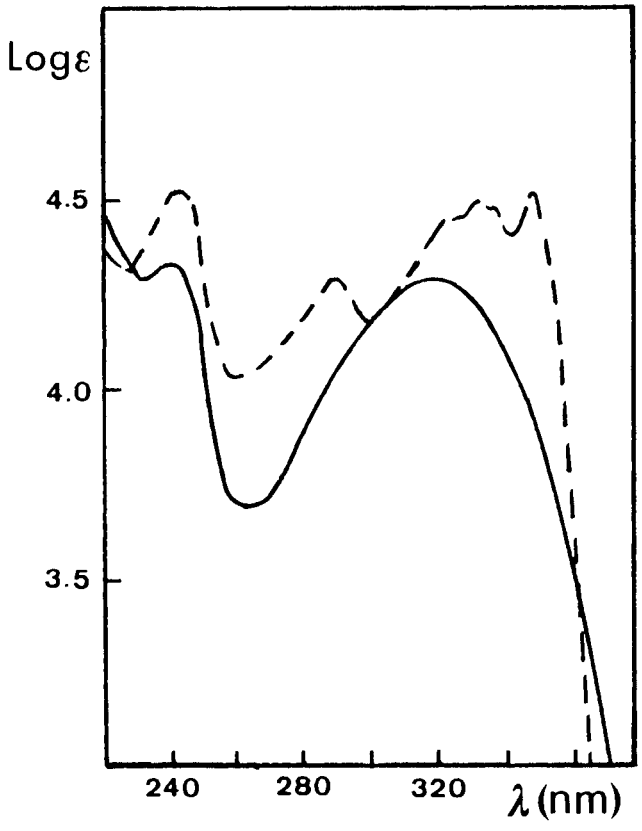


Figure 3. Electronic absorption spectra of compounds:——**1** and —**4**.

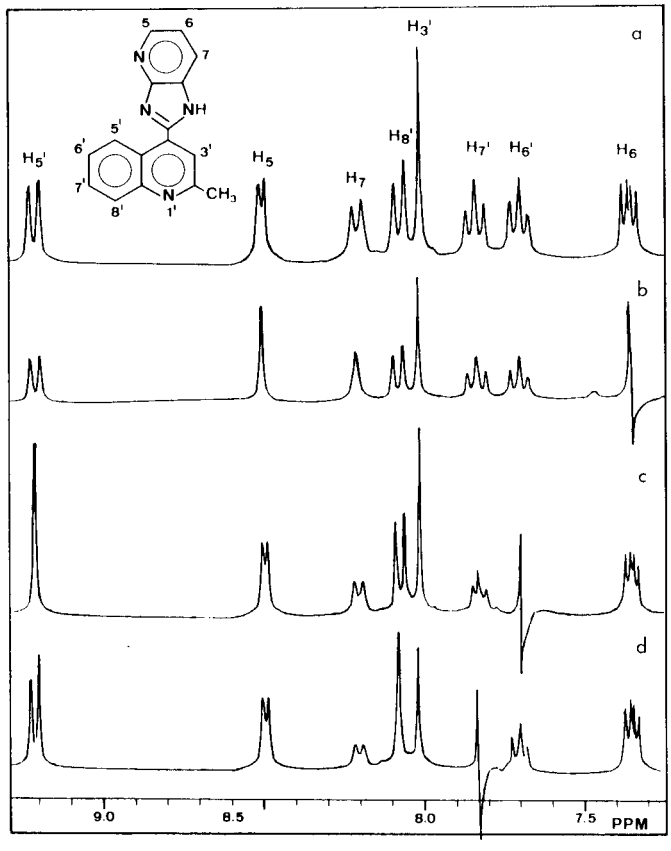


Figure 4. Selective decoupling of compound **4**: a) without decoupling, b) irradiated at 7.37 ppm, c) irradiated at 7.69 ppm, d) irradiated at 7.83 ppm.

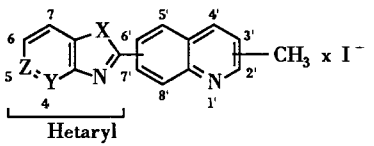
band at 277-290 nm. The second type, shown by compounds **4**, **5**, **6**, features one broad band in the long-wavelength range and no band at 277-290 nm. This behaviour closely follows the trend observed in the *benzo* series **II**, (Y = Z = CH) [7], thus confirming that in type **1** compounds the hetaryl moiety, linked to the 2 or 6 positions of the quinoline ring, causes an extention of the molecule along the long axis of quinoline, accompanied by the enhancement of polarized bands along to this axis [8]. In type **4** compounds, the hetaryl moiety is linked to the 4 position, thus giving rise to a structure extended along the short axis of the quinoline ring. In both of the families the main effect is the shift of the bands to short wavelengths observed for the [4,5-*c*] condensed systems, in agreement with the observed behaviour of pyridines (Formula **I**) [5]. The above effect is greater by far than that due to the nature of the X heteroatom. In fact, the spectra of oxazoles (X = O) and of the [4,5-*b*] condensed imidazoles (X = NH) are practically superimposable.

The ^{1}H nmr spectra recorded at 270 MHz (Table 3) are interpreted by means of spin-spin decoupling experiments and in relation to data obtained on other similar compounds. For compound **4** (the example in Figure 4), the undecoupled spectrum in deuterated dimethyl sulphoxide (4a) shows a doublet of doublets at 7.37 ppm assigned to proton 6, this being adjacent to two protons. The position of the above multiplet is expected for a pyridoimidazole system. Irradiation at 7.37 ppm (4b) allows us to assign the doublets at 8.19 and 8.49 ppm to protons 7 and 5 respectively. Similarly, irradiation at 7.69 ppm (4c) and at 7.83 ppm (4d) allows us to assess coupling of the signal at 7.69 ppm with that at 9.20 ppm and of the signal at 7.83 ppm with that at 8.06 ppm. These signals are then respectively assigned to the 5′-6′ pair and to the 7′-8′ pair, based on the deshielding effect exerted by the 4′-hetaryl moiety.

Methyl proton signals of the quinoline ring are shifted downfield by hetaryl moieties dependending on their mutual positions. When the hetaryl moieties are at the 2′ position (compounds **1**, **2**, **3**) or at 6′ (compounds **10**, **11**, **12**) the strongest effect is effect is exerted at the 4′ methyl groups. The following effect is in regard to the 2′ methyl protons if the hetaryl moieties are at the 4′ position (compounds **4**, **5**, **6**) whereas, as expected for their mutual distance, methyl groups at the 2′ position are weakly deshielded by the 6′ hetaryl moieties (compounds **7**, **8**, **9**).

The protons of the quinoline ring adjacent to the

Table 4
NMR Data of Salts



Compound number	Hetaryl position	CH_3 position	X	Y	Z	Pyridine-ring protons 4	5	6	7	Chemical Shifts (ppm) quinoline-ring protons 2'	3'	4'	5'	6'	7'	8'	2' CH_3	4' CH_3	4 $\overset{+}{N}$-CH_3	5 $\overset{+}{N}$-CH_3
13	2'	4'	NH	$\overset{+}{N}$-CH_3	CH	–	8.92	7.87	8.67	–	8.39	–	8.22	7.94	7.79	8.22	–	2.87	4.55	–
14	2'	4'	NH	CH	$\overset{+}{N}$-CH_3	9.59	–	8.66	8.14	–	8.38	–	8.21	7.92	7.78	8.21	–	2.84	–	4.44
15	2'	4'	O	$\overset{+}{N}$-CH_3	CH	–	9.17	8.23	9.22	–	8.45	–	8.29	7.97	7.87	8.27	–	2.91	4.61	–
16	4'	2'	NH	$\overset{+}{N}$-CH_3	CH	–	8.89	7.80	8.81	–	8.22	–	9.22	7.84	7.95	8.14	2.87	–	4.57	–
17	4'	2'	NH	CH	$\overset{+}{N}$-CH_3	9.71	–	8.74	8.32	–	8.09	–	9.02	7.74	7.89	8.11	2.82	–	–	4.48
18	4'	2'	O	$\overset{+}{N}$-CH_3	CH	–	8.91	7.82	8.83	–	8.23	–	9.20	7.86	7.96	8.15	2.88	–	4.57	–
19	6'	2'	NH	$\overset{+}{N}$-CH_3	CH	–	8.84	7.81	8.70	–	7.60	8.52	8.93	–	8.55	8.17	2.74	–	4.52	–
20	6'	2'	NH	CH	$\overset{+}{N}$-CH_3	9.29	–	8.61	8.09	–	7.53	8.43	8.91	–	8.41	8.03	2.72	–	–	4.36
21	6'	2'	O	$\overset{+}{N}$-CH_3	CH	–	9.06	8.25	8.65	–	7.63	8.58	9.13	–	8.56	8.22	2.76	–	4.56	–
22	6'	4'	NH	$\overset{+}{N}$-CH_3	CH	–	8.85	7.83	8.75	8.91	7.56	–	9.10	–	8.64	8.27	–	2.86	4.54	–
23	6'	4'	NH	CH	$\overset{+}{N}$-CH_3	9.56	–	8.66	8.25	8.89	7.54	–	9.05	–	8.61	8.23	–	2.84	–	4.45
24 [a]	6'	4'	O	$\overset{+}{N}$-CH_3	CH	–	8.67	7.61	8.41	9.48	8.20	–	9.23	–	8.98	8.75	–	3.17	4.66	–

[a] N-Methylquinolinium salt.

hetaryl moieties are markedly deshielded, as expected. In fact, the 3′ proton resonances are downfield (chemical shift range 8.00-8.40 ppm) if the hetaryl moieties are at both the 2′ (compounds **1**, **2**, **3**) and the 4′ position (compounds **4**, **5**, **6**) compared to the 6′ position (compounds **7-12**, chemical shift range 7.47-7.56 ppm). Similar behaviour is shown by 5′ and 7′ protons if the hetaryl moieties are in at the 6′ position (compounds **7-12**) compared to the more distant 2′ position (compounds **1**, **2**, **3**). Protons 5′ position in compounds **4**, **5**, **6**, having a 4′ hetaryl moiety show the highest δ values. It seems reasonable to refer to a possible magnetic anisotropy arising by a *peri* effect.

As to hetaryl moieties (X-azolylpyridine, [4,5-*b*] anellation), protons **5**, **6**, **7** in oxazoles (X = O) are deshielded relatively to the same protons in imidazoles (X = NH) (pairs **1-3**, **4-6**, **7-9**, **10-12**), due to the stronger electron attracting power of oxazole. If the mutual assemblage of heterocycles is considered, protons at positions 4-7 are more deshielded as the hetaryl moieties are more affected by the quinoline nitrogen. This again happens if the hetaryls moieties are at the 2′ position (compounds **1**, **2**, **3**) or at the 4′ position (compounds **4**, **5**, **6**), compared to the 6′ position (compounds **7-12**).

Reactivity to methyl iodide is deduced from the structure of salts **13-24**. In these compounds the presence of a positive charge seems to be the most important structural factor, causing the range of melting points to be narrower than for the bases and absolute Rf values to be lower (Figures 5 and 6). Melting points follow the sequence imidazo[4,5-*c*] > imidazo[4,5-*b*] > oxazolo [4,5-*b*], whereas R_f values show the opposite trend, as expected. Electronic spectra exhibited similar patterns as those of bases.

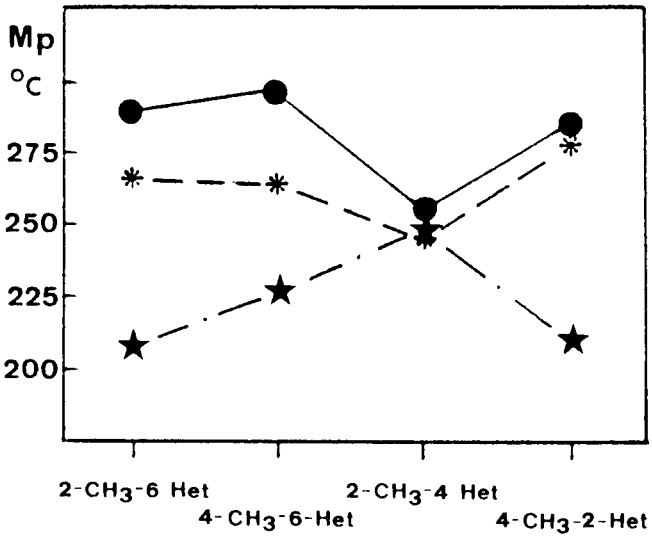


Figure 5. Comparison of melting points of compounds **13-24**. Hetaryl: ● imidazo-2-yl-[4,5-*c*]-5-methylpyridinium * imidazo-2-yl-[4,5-*b*]-4-methylpyridinium ★ oxazo-2-yl-[4,5-*b*]-4-methylpyridinium.

Values of λ max and log ϵ in Table 2 show that quaternization causes a systematic batho-hyperchromic shift of bands. Furthermore, the amount of the bathochromic effect is markedly lower in the series imidazo[4,5-*c*] (compounds **14**, **17**, **20**, **23**). Compound **24** appears to be an exception to the general trend, because quaternization shifts the bands to longer wavelengths but their intensity is appreciably depressed. The exception is only apparent, being **24** the lone example of a quinolinium salt. In fact, in formula **II**, five sites (A, B, C, D, E) are potentially reactive to methyl iodide: compounds **13-23** are monoquaternary pyridinium salts (quaternization at C or D), whereas compound **24** is a monoquaternary quinolinium salt (quaternization at A).

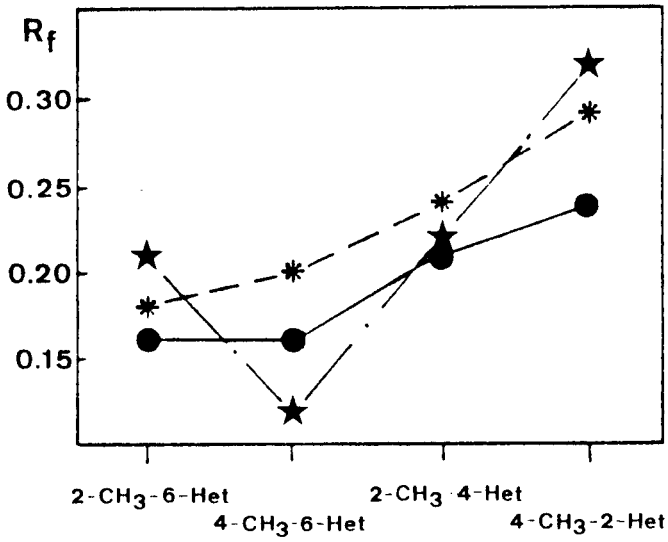
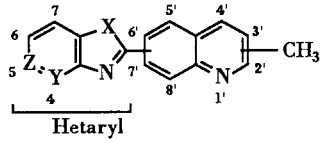


Figure 6. Comparison of Rf values of compounds **13-24**. For Key see Figure 5.

The ^{1}H nmr spectra (Tables 4 and 5) for compounds **13-24** give one singlet at 4.30-4.66 ppm, equivalent to three protons and assigned to one *N*-methyl group. The monomethiodide structure was also confirmed by elemental analysis. Except salt **24**, the C-CH_3 signals of the quinoline ring are shifted downfield very weakly compared to the starting bases (0.01-0.09 ppm), thus indicating that the positive charge is *far* from the site A. In contrast, the 0.35 ppm value of salt **24** confirms its *lepidinium* structure. The quaternization at B,E (X-azolium salts) can be excluded by the following considerations: (i) quaternization of imidazoles, usually accompanied by *N*-alkylation [9], is excluded in the present series (one methyl group is inserted), (ii) the nitrogen atom in oxazoles has low basicity [10], (iii) hypsochromic shifts in the electronic spectra should be observed if X-azolium salts were formed [11,12]. Values for proton and methyl protons chemical shift (Table 4) and for chemical shift difference ($\Delta\delta$, Table 5) are strictly consistent with the quaternization at pyridine

Table 5

Δδ values ($\delta_{salt} - \delta_{base}$), ppm [a]



Compound number	Pyridine-ring protons				Quinoline-ring protons								
	4	5	6	7	2'	3'	4'	5'	6'	7'	8'	2'CH_3	4'CH_3
13-1	–	0.46	0.54	0.67	–	0.01	–	0.02	0.06	0.06	0.02	–	0.04
14-2	0.52	–	0.27	0.52	–	0.02	–	0.01	0.03	0.05	0.01	–	0.02
15-3	–	0.53	0.66	0.85	–	0.11	–	0.09	0.08	0.10	0.07	–	0.08
16-4	–	0.40	0.43	0.62	–	0.22	–	0.02	0.15	0.12	0.08	0.09	–
17-5	–	0.34	0.59	–	0.07	–	0.18	0.05	0.06	0.05	0.04	–	–
18-6	–	0.24	0.22	0.48	–	0.03	–	0.10	0.10	0.10	0.08	0.09	–
19-7	–	0.45	0.51	0.61	–	0.08	0.14	0.11	–	0.00	0.08	0.03	–
20-8	0.29	–	0.26	0.44	–	0.01	0.04	0.11	–	0.12	0.06	0.01	–
21-9	–	0.48	0.65	0.39	–	0.07	0.11	0.25	–	0.05	0.10	0.04	–
22-10	–	0.45	0.53	0.65	0.08	0.09	–	0.10	–	0.03	0.10	–	0.04
23-11	0.53	–	0.30	0.62	0.22	0.06	–	0.08	–	0.02	0.05	–	0.02
24-12	–	0.08	0.11	0.11	0.60	0.70	–	0.35	–	0.48	0.54	–	0.35

[a] The structures are depicted in Tables 1 and 2.

nitrogens C or D. In particular, except for the pair **12-24**, one can point out the very low values of the quinoline ring protons (range 0.01-0.25 ppm) compared to those of the pyridine ring (range 0.22-0.85 ppm), which are affected by the proximity of the positive charge. In the pair **12-24** the situation is obviously reversed.

The data prove that the availability of the new compounds **II** provides additional evidence of the combined roles of both electronic and steric effects on the reactivity of basic assembled heterocyclic systems. In compounds **I**, the A site is the most basic [13]. In fact, by reaction with methyl iodide, monoquaternary salts at site A or bisquaternary salts at sites A and C or A and D are obtained. The only exceptions are the 2-2'-assembled isomers, where site A is markedly hindered and only site C or D is quaternized. In contrast to the above case, if the A site is the quinoline nitrogen [10,13] (compounds **II**), only monoquaternary salts are obtained. Reaction with methyl iodide occurs either at site C or D, unless favourable structural features are present. This is the case of compound **12**, in which steric hindrance at site A is partly removed due to the absence of the methyl group at the 2' position and the availability of the lone pair electrons at C to the electrophilic reagent is reduced by the strong electron withdrawing effect of the oxygen atom in oxazole (X = O).

EXPERIMENTAL

Electronic spectra were recorded on a Pye Unicam SP8-100 spectrophotometer in ethanol. R_f values were determined on silica gel 60 F_{254} tlc plates (Merck), using as eluent butanol:acetic acid:water, 4:1:5. The ^1H nmr spectra were obtained with Jeol GX270 spectrometer in DMSO-d_6 solution (6%).

The following carboxylic acids and carboxamide were prepared according to literature methods: 4-methyl-6-quinolinecarboxylic acid [14], 2-methyl-6-quinolinecarboxylic acid [15], 2-methyl-4-quinolinecarboxylic acid [16], and 4-methyl-2-quinolinecarboxamide [17].

Compounds **1-12** were prepared by reacting the suitable methylquinolinecarboxylic acid (or amide) (0.15 mole) with equimolecular amounts of 3,4-diaminopyridine (**2**, **5**, **8**, **11**) or 2,3-diaminopyridine (**1**, **4**, **7**, **10**), or 2-amino-3-hydroxypyridine (**3**, **6**, **9**, **12**) in the presence of polyphosphoric acid (85% phosphorus pentoxide, 200 g) for 2 hours at 210°. The cooled reaction mixture was poured into water, neutralized and the precipitate filtered and slurried in dilute sodium carbonate. The crude products were washed with water and crystallized from ethanol (except compound **3** that was crystallized from ligroin). The yields were good, in the range 85-95%.

Compounds **13-24** were prepared by refluxing the corresponding bases (0.03 mole) with a large excess of methyl iodide (10 ml) in presence of acetone (20 ml) for 24 hours. The cooled mixture was filtered, the precipitate washed with ether and crystallized from ethanol [18].

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[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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[18] Salt **15** was kept as the crude product. The crystallization from ethanol caused cleavage of the oxazole ring.