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THE POSITION OF QUATERNISATION IN METHYL AND DIMETHYL THIAZOLOQUINOLINES

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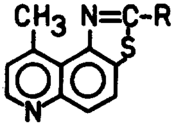
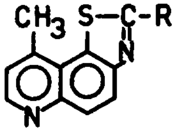
In a previous work (1) we have described the synthesis and properties of heterocyclic compounds in the series of thiazoloquinolines. These compounds reacts readily with methyl iodide to give salts used as intermediates for the preparation of polymethine dyes.

This paper deals with the determination of the position of quaternisation in 9-methylthiazolo-(4,5-f)-quinolines (I) and 9-methylthiazolo-(5,4-f)-quinolines (II) which react with methyl iodide giving a monomethiodide.



Ia R = -H

Ib R = $-CH_3$



IIa R = -H

IIb R = $-CH_3$

The reaction is carried out by refluxing the base with an excess of methyl iodide for one hundred hours; the solid salt is washed with anhydrous ethyl ether and crystallised from absolute ethanol (Methiodides: Ia m.p. 246-248°. Calcd. for

TABLE I (*)

Compd.	H_2	H_7(d)	H_8(d)	H_4-H_5(q)	C_2-Me	C_9-Me (d)	$J_{H_7-H_8}$	$J_{H_4-H_5}$
Ib	- - -	525,5 556,5 31	448,5 489,5 (b) 41 (b)	484,5 521,0 36,5	175,0 186,0 11	181,0 209,0 28	4,5 6,5 2	9,0 9,5 0,5
Ia	566,5 587,5 21	528,5 559,5 31	451,5 492,5 (b) 41 (b)	491,5 528,5 37	- - -	183,0 211,5 28,5	4,5 6,5 2	9,0 9,5 0,5
IIb	- - -	524,0 561,0 37	449,5 496,0 (b) 46,5 (b)	480,5 524,0 43,5	175,0 187,0 12	158,0 196,5 38,5	4,5 6,5 2	9,0 9,5 0,5
IIa	568,0 593,0 25	524,0 563,0 39	448,5 498,0 (b) 49,5 (b)	485,0 532,0 47	- - -	160,0 201,0 41	4,5 6,5 2	9,0 9,5 0,5

(*) Spectra recorded on a Varian A-60 spectrometer in 2% solution in CD_3COCD_3/D_2O (1/1 by volume) with tetramethylsilane (1%) as internal standard. Values given in cps. The left hand of each column gives values for the free base, the right hand gives values for the methiodide, and the intermediate position gives $\Delta\delta$ values, being $\Delta\delta = \delta_{\text{methiodide}} - \delta_{\text{free base}}$ (cps). Singlets are unmarked, multiplets are described as follows: (d) doublet, (q) quartet, (b) each of the doublet components is split again into a quartet. All signals in first three columns correspond to one proton, all signals in fourth column to two, all signals in fifth and sixth columns to three protons.

$C_{12}H_{11}IN_2S$: C 42.11; H 3.24; N 8.18. Found: C 42.13; H 3.31; N 8.14. Ib m.p. 245-248°. Calcd. for $C_{13}H_{13}IN_2S$: C 43.83; H 3.67; N 7.86. Found: C 44.03; H 3.78; N 7.82. IIa m.p. 268-270°. Calcd. for $C_{12}H_{11}IN_2S$: C 42.11; H 3.24; N 8.18. Found: C 42.36; H 3.26; N 8.11. IIb m.p. 261-264°. Calcd. for $C_{13}H_{13}IN_2S$: C 43.83; H 3.67; N 7.86. Found: C 43.77; H 3.79; N 7.83).

The assignement of the site of quaternisation was made using NMR by comparison of chemical shift and J values both in the bases and their methiodides. Spectra were recorded on a Varian A-60 spectrometer in 2% solution in CD_3COCD_3/D_2O (1/1 by volume) with tetramethylsilane (1%) as internal standard.

Fig. 1 shows, for example, the type of spectra of compounds IIa and its methiodide. In Table I are summarized spectral data.

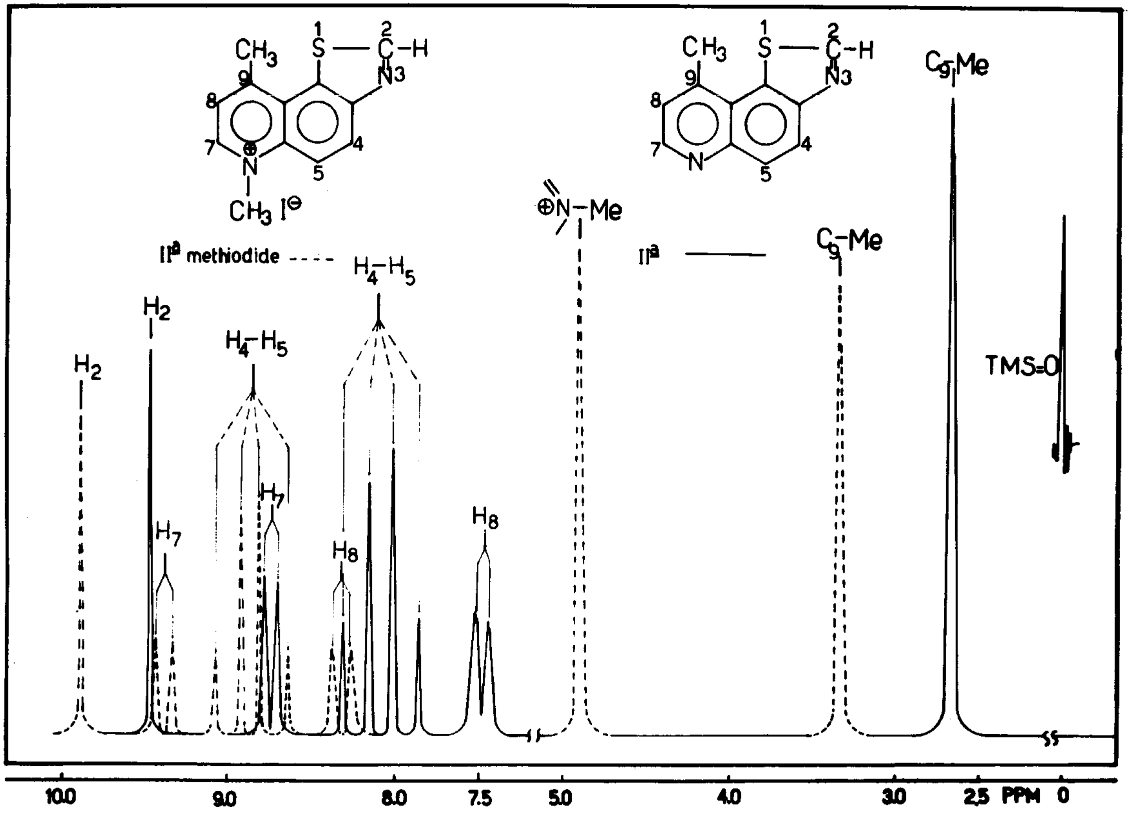
A comparison of $\Delta\delta$ values between H_2 (Ia and IIa) and H_7 (Ia and IIa) protons, wich roughly results in the ratio 1:1,5-2 suggests that -7 position is more markedly affected than -2 position on methylation.

Also a comparison of $\Delta\delta$ values between C_2-Me (Ib and IIb) and C_9-Me (Ib and IIb) protons wich roughly results in the ratio 1:3 suggests that -9 position is even more markedly affected than -2 position on methylation.

Furthermore we observe that $\Delta\delta$ values for H_8 protons are in all cases higher than corresponding values for H_7 protons.

Moreover, the values of $J_{H_7-H_8}$ increase from 4.5 cps in the base to 6.5 cps in the methiodide. We have observed a similar effect in 4-methylquinoline and its methiodide under the same conditions. J constants obtained from spectra of the bases in trifluoroacetic acid show the same value of 6.5 cps.

FIG. 1


II^a methiodide ----
II^a ——
H_2
H_2
H_7
H_4-H_5
H_7
H_8
H_4-H_5
H_8
⊕N-Me
C_9-Me
C_9-Me
TMS=0
10.0
9.0
8.0
7.5
5.0
4.0
3.0
2.5 PPM
0

A similar increase of $J_{H_2-H_3}$ from 4.0-4.5 cps (in DMSO, $CDCl_3$, CCl_4) to 6-7 cps (in TFA) for 4-methylquinoline was observed (2).

The reported data suggest that the quaternisation in the above compounds takes place on the quinoline nitrogen atom.

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

(2) R. Mondelli and L. Merlini, Tetrahedron, in the press.