

The Kinetics of Quaternisation of Some Naphthyridines and Methylnaphthyridines

BY RICHARD A. Y. JONES* and NIGEL WAGSTAFF

(School of Chemical Sciences, University of East Anglia, Norwich, NOR 88C)

WE have determined the second-order rate constants for the reaction of methyl iodide with some naphthyridines and methylnaphthyridines in acetonitrile solution by a conductimetric method.¹ The results are recorded in the Table together with values for quinoline and isoquinoline.

N-methyl group of 1-methyl-1,6-naphthyridinium iodide; relative areas suggest that this isomer is present to the extent of *ca.* 5–10%, in accord with the ratio of the rate constants.

1,8-Naphthyridine reacts nearly twenty times faster

TABLE

Second order rate constants (10^{-4} l. mole⁻¹ sec.⁻¹) for methiodide formation in acetonitrile at 24.8° ± 0.1°

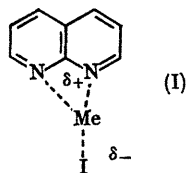
Quinoline	0.517	2-Methyl-1,8-naphthyridine	3.61
Isoquinoline	4.23	3-Methyl-1,8-naphthyridine	5.74
1,5-Naphthyridine	0.232	4-Methyl-1,8-naphthyridine	7.26
1,6-Naphthyridine	1.66	2,7-Dimethyl-1,8-naphthyridine	1.85
1,8-Naphthyridine	4.25		

The rate of quaternisation of a single nitrogen atom of 1,5-naphthyridine is less than that of the quaternisation of quinoline by a factor of 4.5, which accords with a greatly reduced charge density at the nitrogen atoms of 1,5-naphthyridine relative to quinoline.² The rate constant for 1,6-naphthyridine is the sum of the separate rate constants for reaction at the two nitrogen atoms; reaction at the 1-position will presumably be about as fast as in the 1,5-isomer so that the rate constant for reaction at the 6-position is *ca.* 1.5×10^{-4} l. mole⁻¹ sec.⁻¹, *ca.* 2.8 times less than for isoquinoline. The ¹H n.m.r. spectrum of the crude reaction product in deuteriodimethyl sulphoxide is essentially similar to that described by Paudler and Kress,³ except that in addition to the *N*-methyl singlet at τ 5.38 we observed a small singlet at 5.30 which we assign to the

than 1,5-naphthyridine and (allowing for the double degeneracy) four times faster than quinoline and nearly as fast as pyridine.¹ We suggest that this enhanced rate may arise partly because in the transition state the steric interactions of the methyl group with the *peri*-lone pair are less than with the *peri*-hydrogen atom,⁴ and partly because of neighbouring-group participation by one nitrogen atom in the transition state for quaternisation of the other, as in (I).

3-Methyl-1,8-naphthyridine quaternises to give almost exactly equal quantities of the 1- and 8-methyl salts, as indicated by the ¹H n.m.r. spectrum of the reaction product. For 4-methyl-1,8-naphthyridine the ratio of 1-methyl to 8-methyl salts is 3 : 2. Thus, for both compounds the rate constant for quaternisation at the 8-nitrogen atom is 2.9×10^{-4} l. mole⁻¹ sec.⁻¹. At the 1-nitrogen atom the

rates are 2.9 and 4.4×10^{-4} l. mole $^{-1}$ sec. $^{-1}$, respectively; the difference may indicate a hyperconjugative effect of the 4-methyl group⁵ or that steric hindrance by the 2-hydrogen atom is buttressed by the 3-methyl group. 2-Methyl-1,8-naphthyridine quaternises predominantly at the 8-nitrogen atom. The product ratio could not be accurately determined



by ^1H n.m.r. but less than 20% of the 1-methyl salt is formed. If the quaternisation in the 8-position is faster than in 1,8-naphthyridine itself by the same factor that quaternisation in the 1-position is slower than in 2,7-dimethyl-1,8-naphthyridine the rate constant for reaction at the 8-nitrogen atom is again 2.9×10^{-4} l. mole $^{-1}$ sec. $^{-1}$, so that the effect of the methyl group in the remote ring is the same regardless of its position. The rate constant for reaction at the sterically hindered 1-nitrogen atom is only 0.67×10^{-4} l. mole $^{-1}$ sec. $^{-1}$.

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³ W. W. Paudler and T. J. Kress, *J. Heterocyclic Chem.*, 1968, **5**, 561.

⁴ Cf. J. M. Bobbitt, A. R. Katritzky, P. D. Kennewell, and M. Snarey, *J. Chem. Soc. (B)*, 1968, 550.

⁵ H. C. Brown and A. Cahn, *J. Amer. Chem. Soc.*, 1955, **77**, 1715.