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KINETIC STUDY OF THE FORMATION OF MEISENHEIMER COMPLEXES : INTERACTION OF OH^- AND CH_3O^- IONS WITH 3,5-DINITROPYRIDINE IN WATER, METHANOL AND THEIR MIXTURES WITH DIMETHYLSULFOXIDE.

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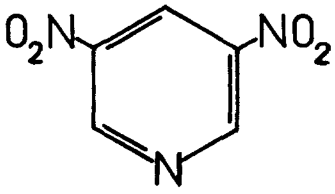
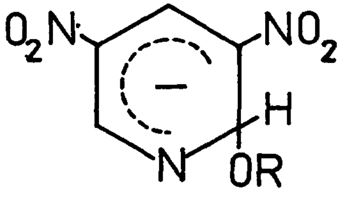
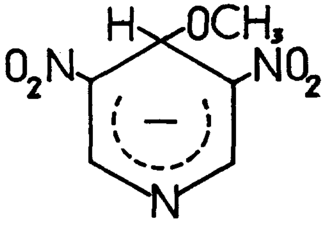
The development of apparatus suitable to the study of fast reactions now allows the accumulation of kinetic date concerning the formation of Meisenheimer complexes. Important results have already been obtained for the interaction of OH^- and CH_3O^- ions with various dinitro and trinitro derivatives of benzene in water, methanol and methanol-DMSO mixtures (1,2,3,4,5,6). However, except for a recent study relative to the behavior of 3,5-dinitro-4-methoxypyridine in methanol (7), practically no kinetic measures have been done on heterocyclic compounds ; this situation led us to undertake a detailed study of the interaction, in varying conditions, of OH^- and CH_3O^- ions with 3,5-dinitropyridine I. We present here the first results of this work.



I



II



III

OH^- and CH_3O^- ions react rapidly with 3,5-dinitropyridine in water or methanol to form, according to the equation below, the yellow addition complex ($\lambda_{max}^{CH_3OH}$ = 455 mμ , ε = 19.900), whose structure is well established (8) and whose appearance has been followed spectrophotometrically by stopped flow.

$$I + RO^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} II \qquad RO^- = OH^- , CH_3O^-$$

As the concentration of the substrate is always very small (around 10^{-5}M), the amount of base consumed in establishing equilibrium can be neglected, and the rate equation gives pseudo-first order kinetics. The variations in the apparent rate constant $\lambda = k_{-1} + k_1 b$ as a function of the base concentration b are represented on a logarithmic diagram (Fig. 1). Since the graphs of $\log \lambda = f(\log b)$ give on the one hand a straight line of slope 1 at high base concentrations ($\log \lambda = \log k_1 + \log b$) and on the other hand a flat line of slope 0 at low base concentrations ($\log \lambda = \log k_{-1}$), we have been able to obtain the rate constants of formation k_1 and of decomposition k_{-1} for II, and thus the equilibrium constant K.

The nucleophilic attack of OH^- in water occurs at a rate close to that observed for trinitrobenzene (Table I) ; however, 3,5-dinitropyridine seems more strongly acidic than TNB because the complex II is more stable. In methanol, although complex II is less stable than in water $\left[\frac{\overset{CH_3OH}{k_{-1}}}{\overset{H_2O}{k_{-1}}} \simeq 12\right]$, the acidity is significantly increased ($\Delta pK = 0,63$) because CH_3O^- ions are more reactive than OH^- ions $\left[\frac{\overset{CH_3OH}{k_1}}{\overset{H_2O}{k_1}} \simeq 50\right]$

TABLE I

Kinetic and Thermodynamic Parameters at 20°C.

PARAMETERS	3,5-DINITROPYRIDINE					TRINITROBENZENE
	(a) H_2O	H_2O-DMSO (b) 89.2-10.8 in weight	(c) CH_3OH	CH_3OH-DMSO (d) 86.65-13.35 in weight	CH_3OH-DMSO (e) 74.67-25.33 in weight	H_2O
k_1 $l.mole^{-1}sec^{-1}$	33.2	50.2	1 740	3 020	4 560	27
k_{-1} sec^{-1}	2	1.1	24	13.2	7.6	10.5
K $l.mole^{-1}$	16.6	45.5	72.5	229	600	2.57

There is a strong increase in the equilibrium constant with addition of DMSO to the aqueous and methanolic solutions : this is the result not only of the expected increase in k_1 but also of a decrease in k_{-1} , each factor contributing about 50 % of the variation in K. The decrease in k_{-1}, which corresponds to a considerable increase in the stability of the complex, is probably due to a better solvation of II in the mixtures of CH_3OH-DMSO. Parker (9,10) has in fact shown that large polarizable anions such as the transition states in nucleophilic aromatic substitutions, whose structure is close to II, are more strongly solvated by DMSO than by methanol, as opposed to small anions with localized charge (CH_3O^-, OH^-).

FIG 1

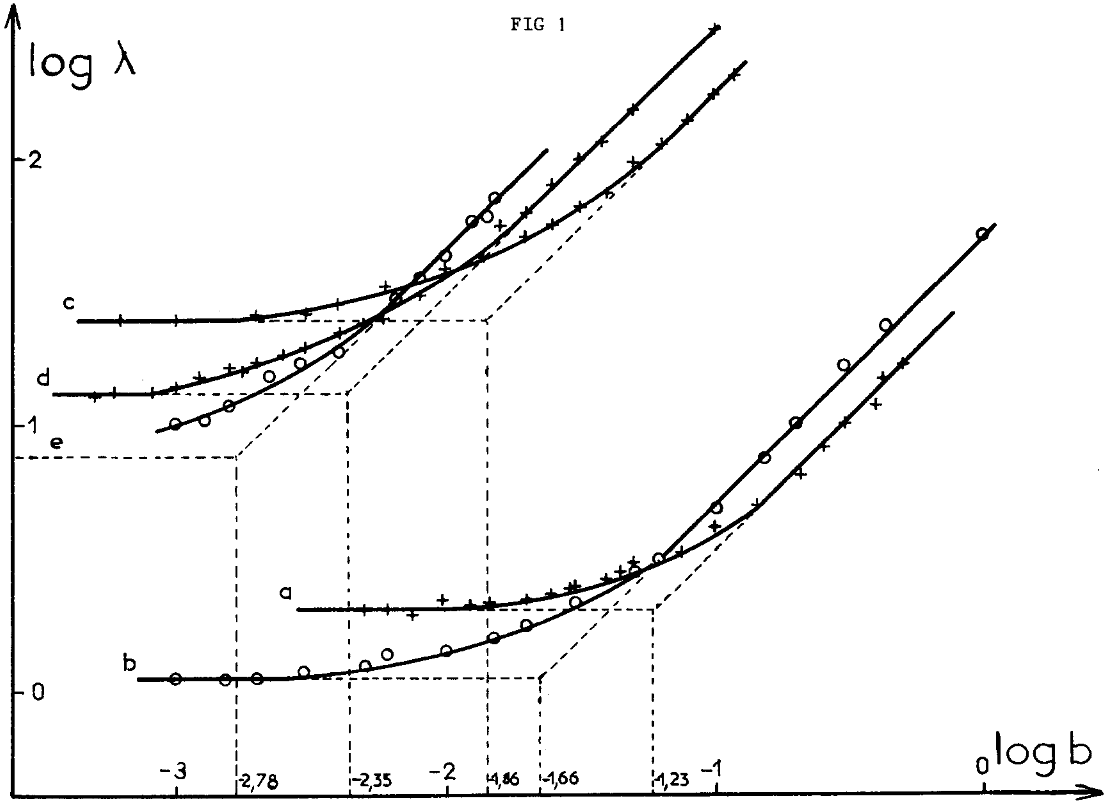
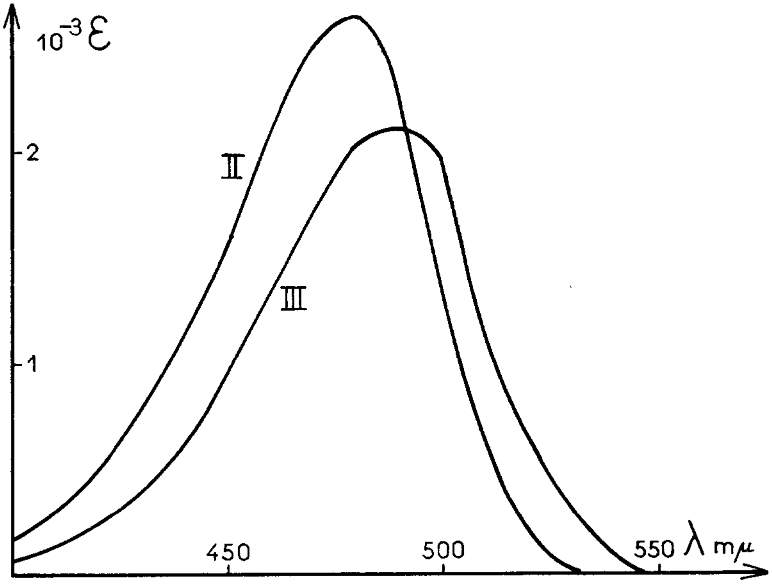

log λ
2
1
0
c
d
e
a
b
-3
-2,78
-2,35
-2
-1,86
-1,66
-1,23
-1
0
log b

FIG 2


$10^{-3}\varepsilon$
2
1
II
III
450
500
550
λ mμ

In solutions rich in DMSO and specifically in mixtures of CH_3OH and DMSO, the behavior of 3,5-dinitropyridine becomes very different. The kinetic curves obtained by stopped flow show that the appearance of the complex II is preceeded by the rapid formation of another less stable thermodynamically complex III, which is probably due to an attack by CH_3O^- ions on the carbon 4 of I. We were able to determine the absorption spectrum of III, that disappears progressively to give II, in a mixture of CH_3OH and DMSO (92.6 % DMSO in weight - Fig. 2) and to follow kinetically its conversion to II. This conversion is faster at high methanol concentrations and, in agreement with the kinetic scheme previously postulated during the study of various 4-substituted 2,6-dinitroanisoles (4), the rate reaches, in a given medium, a maximum at the highest concentrations of methoxide ion ; thus, in a mixture containing 92.6 % DMSO, the half time of reaction is around 5 seconds, and in pure DMSO the lifetime of III is sufficiently long so that rapid NMR measures permitted us to confirm the structure of the complex which was not identified by FYFE (8). The addition of one drop of potassium methoxide 5.85 M, practically exempt of methanol (11) to a solution of 3,5-dinitropyridine in DMSO-d_6 causes in fact the immediate appearance of a doublet at 8.33 ppm, which can be assigned to the equivalent protons of III and which disappears rapidly to give the signals of II (doublet at 8.61, quadruplet at 8.37 and doublet at 6.10 ppm).

REFERENCES

1 - F. TERRIER and F. MILLOT - C.R. Acad. Sci. 268 C, 808 (1969)

2 - F. MILLOT and F. TERRIER - Bull. Soc. Chim. Fr., 2692 (1969)

3 - R. GABORIAUD and R. SCHAAL - Bull. Soc. Chim. Fr., 2683 (1969)

4 - F. TERRIER and F. MILLOT - Bull. Soc. Chim. Fr., 1970, submitted for publication

5 - J.H. FENDLER, E.J. FENDLER and C.E. GRIFFIN - J. Org. Chem., 34, 689 (1969)

6 - E.J. FENDLER, J.H. FENDLER, C.E. GRIFFIN and J.W. LARSEN - J. Org. Chem. 35 (1970) submitted for publication

7 - P. BEMPORAD, G. ILLUMINATI and F. STEGEL - J. Am. Chem. Soc. 91, 6742 (1969)

8 - C.A. FYFE - Tetrahedron Lett. 659 (1968)

9 - A.J. PARKER - Chem. Rev. 69, 1, (1969)

10 - R. ALEXANDER, E.C.F. KO, A.J. PARKER and T.J. BROXTON - J. Am. Chem. Soc., 90 5049 (1968)

11 - F. TERRIER - C.R. Acad. Sci. 265 C, 1433, (1967)