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^1H NMR Study of the Hydrolysis of some Model Pyrimidyl Reactive Dyes

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ABSTRACT

The kinetics and mechanisms of the hydrolysis of some model pyrimidyl reactive dyes have been studied using ^1H *NMR. Evidence indicating that Meisenheimer complexes (or* σ*-adducts) should occur in the hydrolysis process was obtained from the experiments and it is also shown that a quantitative measurement of the kinetic data is possible. The molecular mechanics method was used to interpret the experimental results.*

1 INTRODUCTION

The various techniques used for kinetic studies of chemical reactions all have advantages and disadvantages. Thus, UV–visible spectroscopy, titration, and high-pressure liquid chromatography (HPLC) are widely used in dye chemistry, but have a disadvantage in that they are relatively non-diagnostic. In addition, with HPLC, considerable time is needed for the measurement of the kinetic data, although the method can separate effectively each component in the reaction system.

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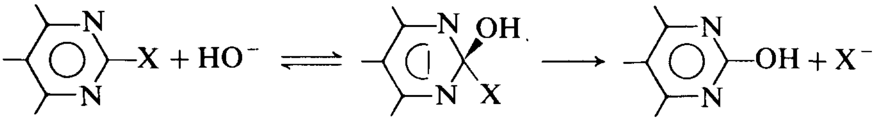
High-resolution nuclear magnetic resonance spectroscopy is much less sensitive than UV–visible spectroscopy (often by several orders of magnitude) but has a great advantage as a diagnostic tool and can provide much more information about the detailed molecular structure of the species observed. Because of this, it has become one of the most widely used spectroscopy techniques for the identification of compounds in equilibrium systems and in chemical reaction systems.

The object of this paper is to use NMR to study the reactions of reactive dyes. The system chosen for the study was the hydrolysis of pyrimidyl reactive dyes, an area in which there has been considerable interest.

In general considerations,[1] the hydrolysis of 2-methylsulfonoyl-4-chloro-(or methyl-)-pyrimidyl and 2-chloro-4-methyl-pyrimidyl reactive dyes has been suggested as a typical nucleophilic hetero-aromatic substitution.



(A) (B) (A---B) (C) (D)

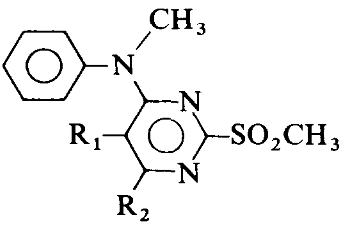
According to the reaction mechanism hypothesized above, a Meisenheimer complex (or σ-adduct) should occur in the hydrolysis process, and the rate expression of the second-order reaction can be deduced by using the steady-state approximation, as follows:

$$\frac{1}{C_{BO} - 2C_{AO}}\left(\ln \frac{C_{AO}(C_{BO} - 2y)}{C_{BO}(C_{AO} - y)}\right) = kt \tag{1}$$

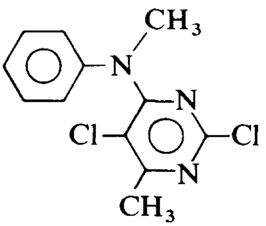
where C_{AO} and C_{BO} are the initial concentrations of components A and B, and y is the concentration of the product C.

To simplify the problem, a series of model reactive dyes was used. The hydrolysis of these compounds was studied by NMR and some evidence that Meisenheimer complexes occurred in the hydrolysis was obtained, and a second-order hydrolytic reaction constant was evaluated based on eqn (1).

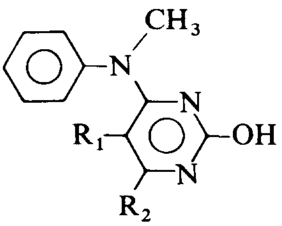
For the actual measurements, the substrates used were of the general formulae **I** and **II**, attack of hydroxyl ion on which may yield products **III**.



I



II



III

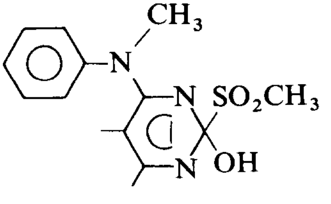
PY-2: $R_1 = CH_3$, $R_2 = Cl$, PY-4: **II**,
PY-8: $R_1 = Br$, $R_2 = CH_3$, PY-9: $R_1 = H$, $R_2 = Cl$,
PY-11: $R_1 = Br$, $R_2 = Cl$.

PY-10, PY-20, etc., correspond to the σ-adducts which occur in the hydrolysis.

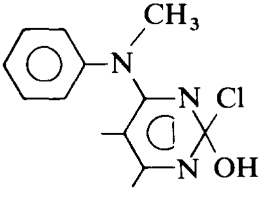
2 RESULTS AND DISCUSSION

Figure 1 shows the ^1H NMR spectra of PY-2 in the CD_3COCD_3–NaOH–H_2O system. In the range 5–6·5 ppm, two peaks were observed at the beginning of the hydrolysis and these decreased with the reaction time. Similar peaks were observed in the ^1H NMR spectra of PY-4, PY-9 and others, which were hydrolyzed in the CD_3COCD_3–NaOH–H_2O system (see Figs 2–5). However, these peaks were not observed in the ^1H NMR spectra of the CD_3COCD_3–NaOH–H_2O system (see Fig. 6), in the spectra of the model reactive dyes on hydrolysis in CD_3COCD_3–NaOD–D_2O (see Fig. 7), or in the CD_3COCD_3–NaOH–D_2O system (see Fig. 8). It is therefore apparent that these peaks correspond to 'active hydrogen' and relate to the hydrolysis reaction.

One reasonable suggestion is that the peaks in the range 5–6·5 ppm are probably due to the formation of hydrolysis intermediates having structures such as **IV** or **V**. The hydrogen in —OH is 'active hydrogen', and no signals can be found in the spectra of systems which contain deuterium oxide.



IV



V

When the reaction temperature was raised to 60°C, the peaks, chemical shift and shape are the same as those at 30°C (see Fig. 9). But, with decrease in the amount of sodium hydroxide the peaks become sharper, and the distance between the two peaks increases (see Figs 1 and 10). The explanation of this phenomenon is that the decrease in hydroxyl ions will slow down the exchange rate of the 'active hydrogen' which is displayed by the two peaks.

Attempts were made to define the steric effects in the intermediate (structure **IV** or **V**) by application of the molecular mechanics method.[2] One of the parameters given by the molecular mechanics calculation is the steric co-ordinates for the arrangement of the molecule for minimum energy.

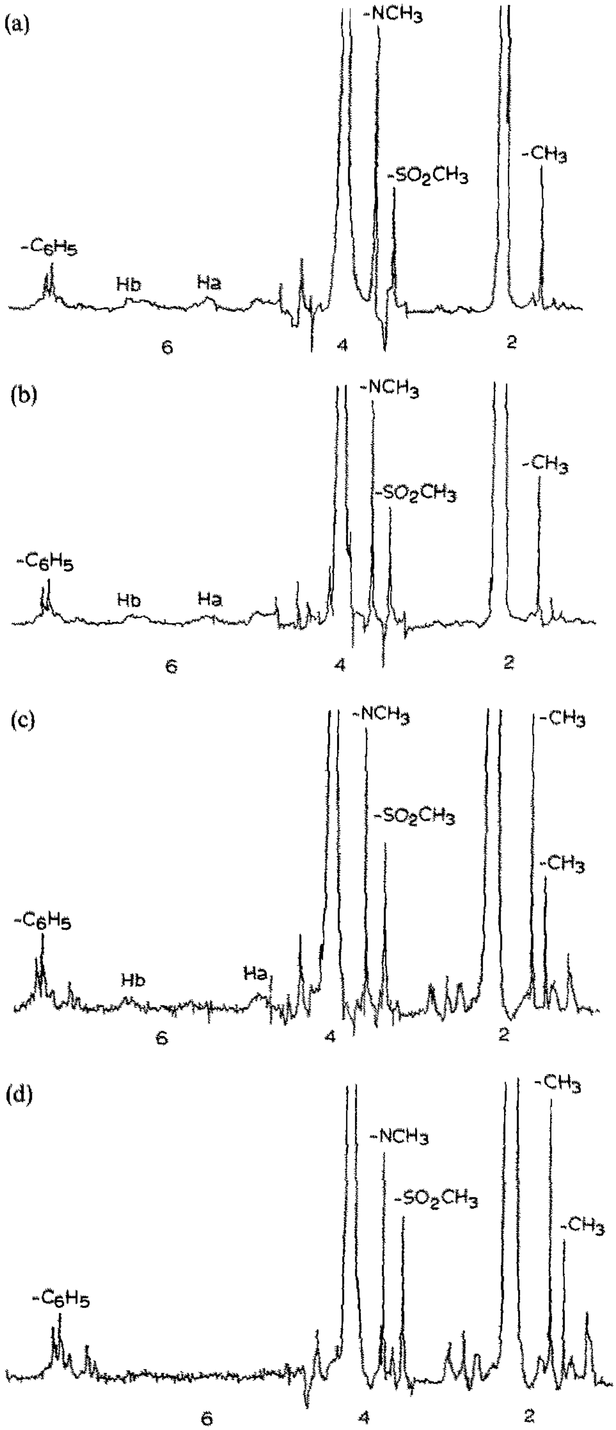


Fig. 1. ^{1}H NMR spectra following the hydrolysis of PY-2 in alkaline solution, at 30°C. (a) $t = 1{\cdot}5$ min; (b) $t = 3$ min; (c) $t = 16$ min; (d) $t = 31$ min.

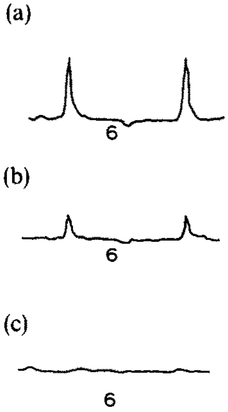


Fig. 2. ^{1}H NMR spectra following the hydrolysis process of PY-4, at 30°C. (a) $t = 4$ min; (b) $t = 11{\cdot}5$ min; (c) $t = 20$ min.

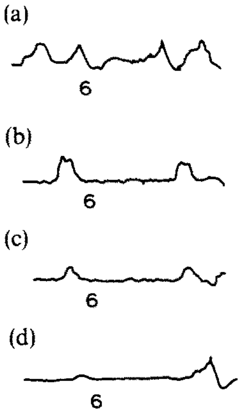


Fig. 3. ^{1}H NMR spectra following the hydrolysis process of PY-8, at 30°C. (a) $t = 1$ min; (b) $t = 17$ min; (c) $t = 27$ min; (d) $t = 42$ min.

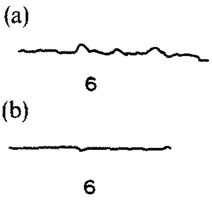


Fig. 4. ^{1}H NMR spectra following the hydrolysis process of PY-11 in alkaline solution, at 30°C. (a) $t = 1$ min; (b) $t = 7$ min.

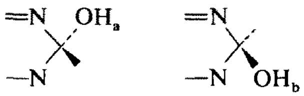


Fig. 5. Modes of attacking of OH$^-$.

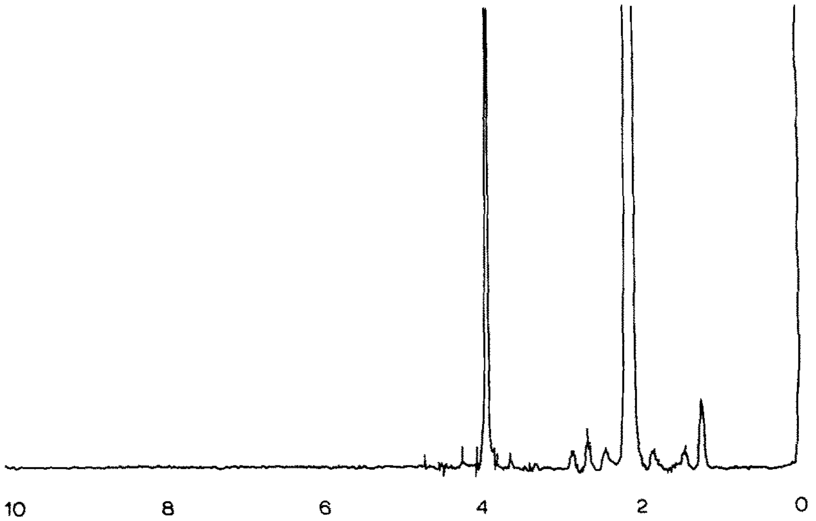


Fig. 6. ^{1}H NMR spectrum of alkaline solution (containing 0·1 ml NaOH solution, 0·5 ml acetone).

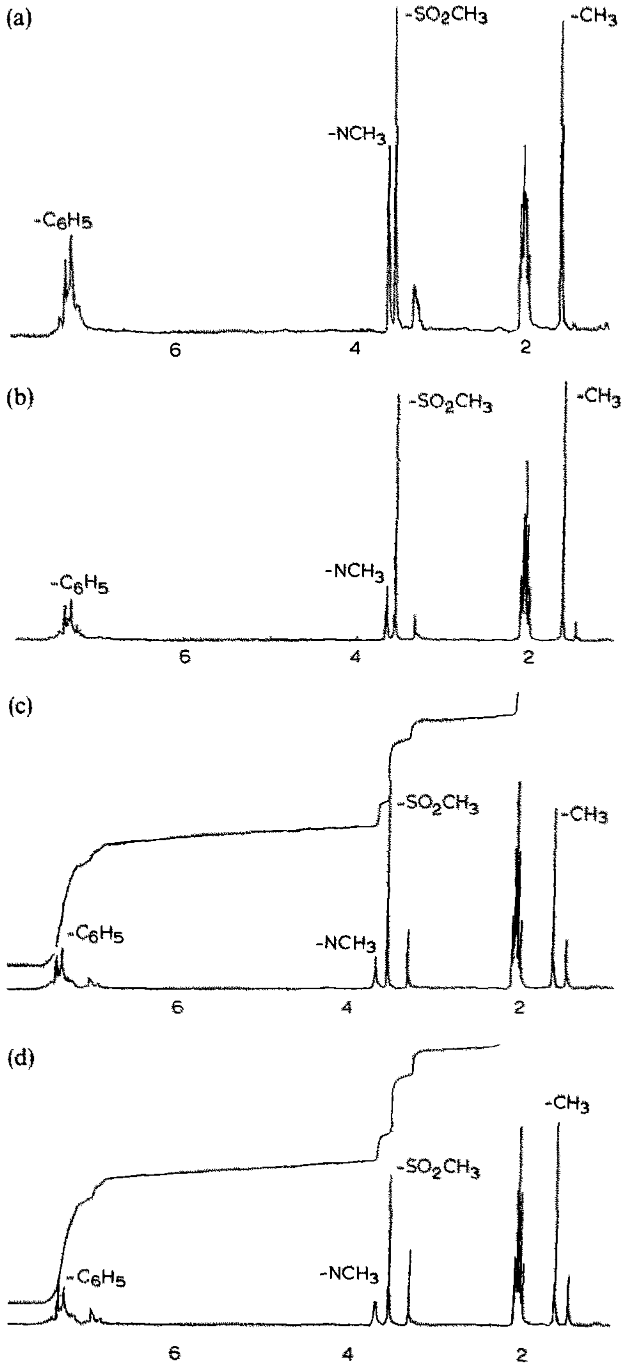


Fig. 7. ^{1}H NMR spectra following the hydrolysis of PY-2 in alkaline solution (NaOD, D_2O, CD_3COCD_3), at 30°C. (a) $t = 3$ min; (b) $t = 20$ min; (c) $t = 45$ min; (d) $t = 60$ min.

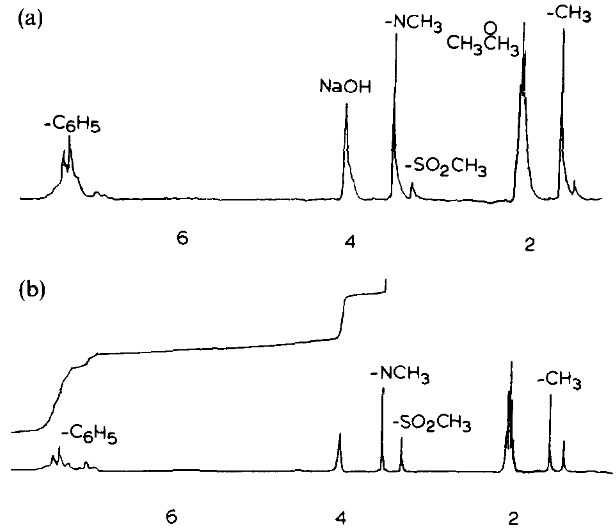


Fig. 8. ^1H NMR spectra following the hydrolysis of PY-2 in alkaline solution (NaOH, D_2O, CD_3COCD_3), at 30°C. (a) $t = 3$ min; (b) $t = 20$ min.

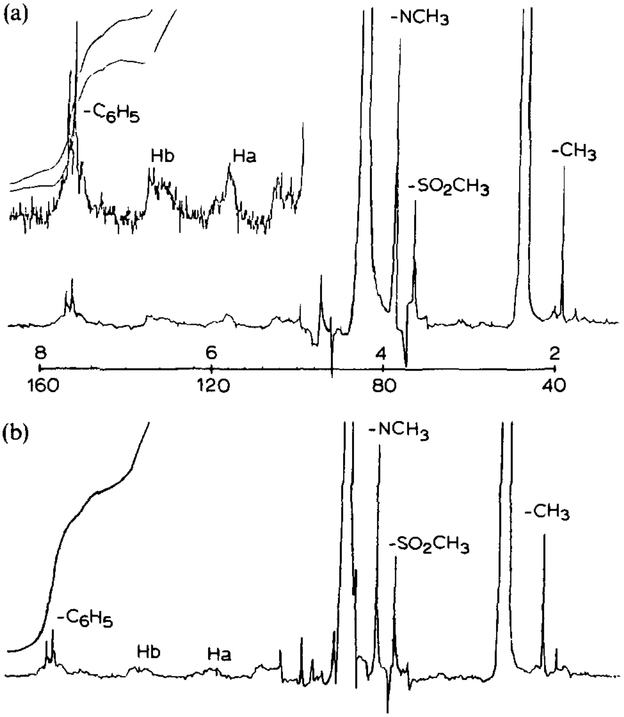


Fig. 9. ^1H NMR spectra following the hydrolysis of PY-2 in alkaline solution, at 60°C. (a) $t = 1{\cdot}5$ min; (b) $t = 3$ min.

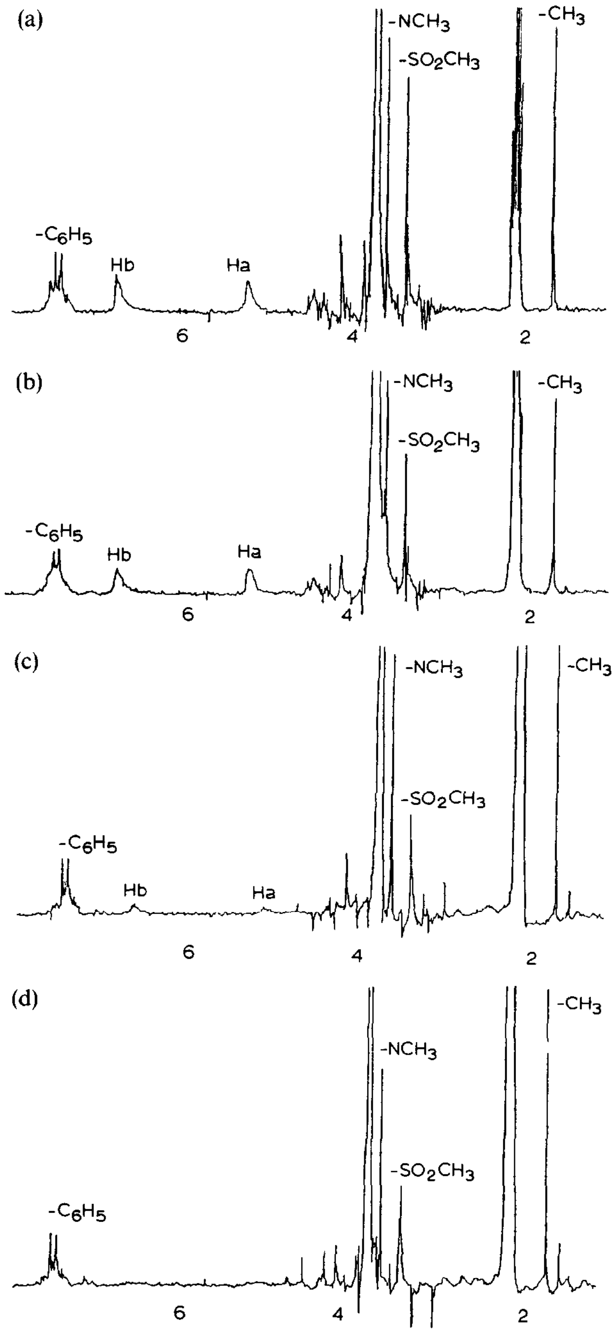


Fig. 10. ^{1}H NMR spectra following the hydrolysis of PY-2 in alkaline solution (0·05 ml NaOH solution added to 0·5 ml acetone), at 30°C. (a) $t = 1$ min; (b) $t = 4$ min; (c) $t = 22$ min; (d) $t = 30$ min.

TABLE 1

The Co-ordinates of PY-2, Calculated by the Molecular Mechanics Method

x	*y*	*z*	*Atom*	*No.*
−0·253 12	0·055 95	−0·382 18	C	1
−1·339 71	0·261 93	−1·234 14	C	2
−1·586 61	1·532 07	−1·755 11	C	3
−0·742 12	2·587 08	−1·410 10	C	4
0·341 91	2·370 27	−0·556 11	C	5
0·617 23	1·099 41	−0·031 05	C	6
2·535 44	−0·182 87	0·397 61	C	7
3·259 42	−2·374 20	0·781 55	C	8
4·153 85	−1·242 58	−1·035 54	C	9
3·377 85	−0·113 87	−0·725 87	C	10
2·369 14	1·942 28	1·501 62	C	11
1·943 80	−3·606 02	3·081 39	C	12
4·439 43	−4·068 78	2·430 44	O	13
2·673 22	−4·945 80	0·952 18	O	14
1·682 70	0·837 32	0·836 65	N	15
2·502 13	−1·323 14	1·117 91	N	16
4·081 29	−2·347 81	−0·277 34	N	17
5·257 28	−1·275 06	−2·422 67	Cl	18
3·154 23	−3·860 82	1·788 23	S	19
3·474 75	1·103 44	−1·614 99	C	20
3·042 19	1·548 43	2·298 79	H	21
1·869 83	−4·523 79	3·707 25	H	22
2·992 48	2·540 30	0·799 55	H	23
1·634 19	2·613 84	2·003 46	H	24
2·253 33	−2·748 71	3·720 80	H	25
0·950 77	−3·389 26	2·626 80	H	26
−0·090 58	−0·958 35	0·019 80	H	27
−2·005 18	−0·578 54	−1·494 41	H	28
−2·443 68	1·701 28	−2·428 59	H	29
−0·933 43	3·596 07	−1·813 14	H	30
0·977 14	3·236 30	−0·310 62	H	31
2·774 55	1·920 63	−1·351 56	H	32
3·240 92	0·836 78	−2·670 60	H	33
4·500 15	1·535 44	−1·568 08	H	34

By using the steric co-ordinates obtained from the molecular mechanics calculation (see Tables 1 and 2) the least-squares equation of the plane of the phenyl ring and pyrimidyl ring in PY-2 or PY-20 are

(a) phenyl ring in PY-2:

$$x - 0{\cdot}3601y - 1{\cdot}366z - 0{\cdot}2543 = 0 \qquad (2)$$

$$(\mathrm{R} = 0{\cdot}9999)$$

TABLE 2

The Co-ordinates of PY-20, Calculated by the Molecular Mechanics Method

x	*y*	*z*	*Atom*	*No.*
0·063 15	0·068 99	−0·957 77	C	1
−0·808 58	0·489 83	−1·962 52	C	2
−0·905 17	1·845 46	−2·279 39	C	3
−0·128 11	2·766 36	−1·577 44	C	4
0·741 59	2·333 37	−0·573 26	C	5
0·867 22	0·974 92	−0·246 88	C	6
2·595 31	−0·517 34	0·346 29	C	7
3·177 07	−2·827 58	0·387 37	C	8
4·678 09	−1·369 99	−0·708 94	C	9
3·735 54	−0·298 15	−0·512 01	C	10
2·305 73	1·434 68	1·712 65	C	11
0·640 11	−4·121 84	0·084 43	C	12
2·850 05	−5·047 86	−1·037 25	O	13
1·897 43	−2·947 77	−1·937 17	O	14
3·406 24	−3·71064	1·476 42	O	15
1·719 55	0·498 90	0·755 77	N	16
2·356 95	−1·685 61	0·836 28	N	17
4·476 50	−2·550 45	−0·249 10	N	18
6·203 26	−1·108 85	−1·575 62	S	19
2·155 05	−3·799 00	−0·792 32	Cl	20
4·031 48	1·042 30	−1·141 89	C	21
2·805 29	0·876 14	2·538 53	H	22
−0·040 43	−4·709 19	−0·571 96	H	23
4·049 58	−4·363 56	1·264 95	H	24
3·067 54	2·096 41	1·242 04	H	25
1·512 76	2·061 03	2·183 77	H	26
0·845 86	−4·709 40	1·006 88	H	27
0·137 28	−3·168 41	0·359 37	H	28
0·106 88	−1·007 55	−0·726 92	H	29
−1·423 71	−0·247 79	−2·505 23	H	30
−1·592 60	2·185 06	−3·072 40	H	31
−0·201 97	3·84063	−1·817 47	H	32
1·332 28	3·101 30	−0·048 85	H	33
3·180 38	1·751 31	−1·112 20	H	34
4·272 46	0·925 46	−2·222 52	H	35
4·891 77	1·529 66	−0·629 43	H	36

(b) pyrimidyl ring in PY-2:

$$x + 0{\cdot}4701y + 0{\cdot}7841z - 2{\cdot}758 = 0 \qquad (3)$$
$$(\mathrm{R} = 0{\cdot}9999)$$

and (c) phenyl ring in PY-20:

$$x - 0{\cdot}1415y - 0{\cdot}9308z - 0{\cdot}9503 = 0 \qquad (4)$$
$$\mathrm{R} = 0{\cdot}9999)$$

Excluding the C_6 atom, the least squares equation of the plane of the pyrimidyl in PY-20 is

$$x + 0{\cdot}4954y + 1{\cdot}563z - 2{\cdot}842 = 0 \qquad (5)$$
$$(\mathrm{R} = 0{\cdot}9992)$$

Substituting the co-ordinates of N_7 (1·682 70, 0·837 32, 0·836 65), (1·719 55, 0·498 90, 0·755 77) into eqn (3) or eqn (5) gives

$$\text{PY-2:} \quad \text{left} = -0{\cdot}0257$$
$$\text{PY-20:} \quad \text{left} = 0{\cdot}3060$$

The amino nitrogen N_4 atom is displaced significantly above or below the plane of the pyrimidyl ring in PY-20 and the equation of the least squares plane of the pyrimidyl ring, including all 6-atoms, in PY-20 is

$$x + 0{\cdot}3913y + 1{\cdot}613z - 2{\cdot}927 = 0 \qquad (6)$$
$$(\mathrm{R} = 0{\cdot}9876)$$

Substituting the co-ordinates of C_6 (3·177 07, 2·827 58, 0·387 37) into eqn (5) gives

$$\text{PY-20:} \quad \text{left} = 0{\cdot}4603$$

Both the results deduced above mean that the C_6 atom is out of the plane which consists of N_1, N_2, C_3, C_4, C_5 (see Figs 5 and 11), so, around the hydrogen atoms Ha and Hb, the chemical environments are not the same. Two peaks would be observed due to the absorption of Ha and Hb. This explains why there are two peaks in the range 5–6·5 ppm in the ^{1}H NMR spectra following the hydrolysis process of the model reactive dyes.

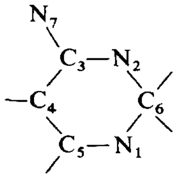


Fig. 11. Labelling of the constituent atoms in the pyrimidine ring.

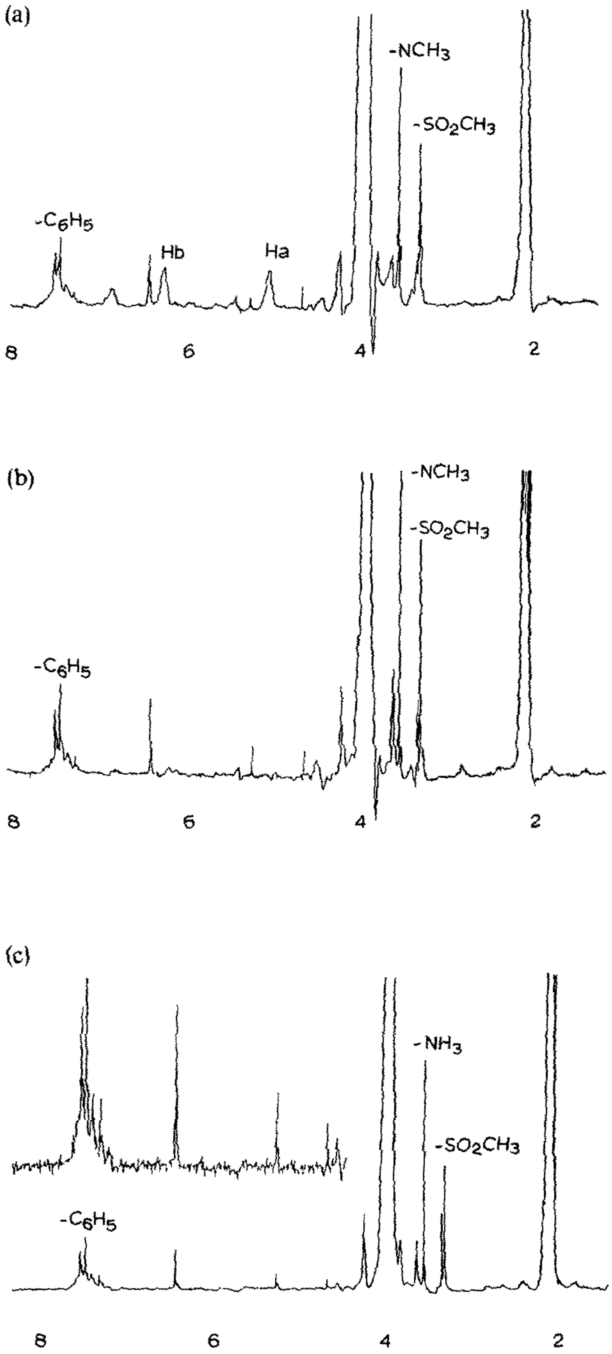


Fig. 12. ^{1}H NMR spectra following the hydrolysis of PY-9 in alkaline solution (0·05 ml alkaline solution and 0·5 ml acetone), at 30°C. (a) $t = 1$ min; (b) $t = 6$ min; (c) $t = 75$ min.

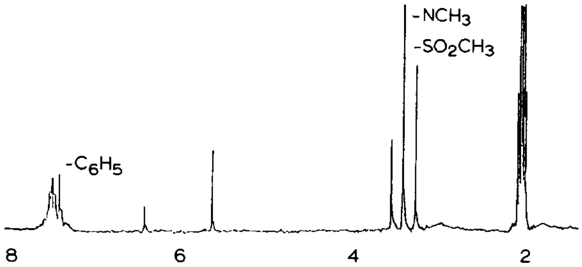
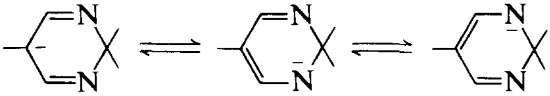


Fig. 13. ^{1}H NMR spectra of the mixture of PY-9 and its hydrolysis product.

More exact evidence is given by the spectra of PY-9 during hydrolysis in the CD_3COCD_3–NaOH–H_2O system (Fig. 12). Besides the two broad peaks noted above, three narrow peaks are observed at 6·44, 5·28 and 4·69 ppm, respectively. The lower field signals (6·44 and 5·28 ppm) correspond to the hydrogens in the pyrimidyl ring of PY-9 (the substrate) and PY-90 (the hydrolysis product) (see Fig. 13). The signal which is observed at 4·69 ppm is due to the formation of the hydrolysis intermediate. The broken hetero-aromatic system and large electron density in the pyrimidyl ring force the absorption of the hydrogen in the pyrimidyl ring to shift to the higher field. Such phenomena have been noted by other workers.[3]



Hydrolysis of the model reactive dye in acidic medium was also attempted. Even after 5 h (Fig. 14) no signals of the hydrolysis product were apparent in the ^{1}H NMR spectra. The hydrolysis of the pyrimidyl model dyes is thus negligible in acidic medium. A peak at 5·1 ppm may be due to the formation of hydrogen-bonding between a hydrogen and a nitrogen atom.

Since the area of a signal due to a given nucleus is proportional to the concentration of this nucleus in solution, NMR can be used to make kinetic measurements, provided there are no saturation effects. The measurement of kinetic data of hydrolysis was carried out in the CD_3COCD_3–NaOD–D_2O system. The rate of hydrolysis of PY-2 was determined from the areas of the respective signals of the methyl substituent in the pyrimidyl ring signal at 1·48 ppm. Under the conditions stated in the experimental section, the hydrolysis follows second-order kinetics. A linear relation between the concentration of species and reaction time t was found (Fig. 15) and the constant of hydrolysis calculated by eqn (1) was 0·071 94 mol^{-1} min^{-1}.

Even though the ^{1}H NMR spectra of the hydrolysis in CD_3COCD_3–NaOH–H_2O also changes regularly, from the viewpoint of evaluating the

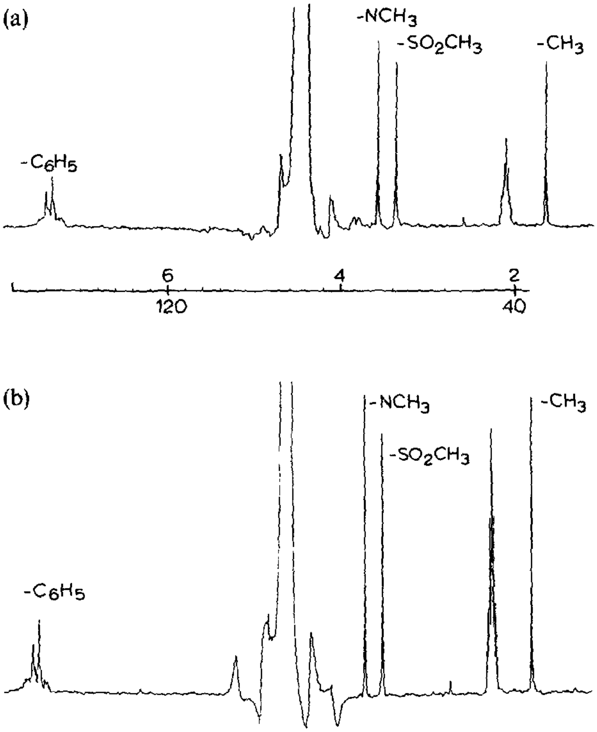


Fig. 14. ^{1}H NMR spectra following the hydrolysis of PY-2 in acidic solution, at 30°C. (a) $t = 1{\cdot}5$ min; (b) $t \approx 5$ h.

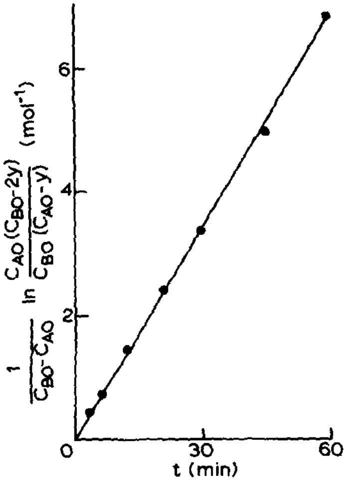


Fig. 15. Kinetic plot for the hydrolysis of PY-2.

TABLE 3

[a]The Kinetic Data of PY-2, Measured by NMR

t (min)	*y*	*k* (mol^{-1} min^{-1})
3	0·001 29	0·083 64
6	0·002 17	0·072 00
12	0·004 17	0·073 08
20	0·006 44	0·072 30
30	0·008 50	0·067 80
45	0·011 33	0·066 00
60	0·014 12	0·068 64

[a] $C_{A0} = 0·000\,042\,5$ mol, $C_{B0} = 0·000\,075\,0$ mol.

kinetic parameters it is not favourable for calculating the area of the peaks accurately (see Table 3).

CD_3COCD_3 is used as a field lock and to dissolve the model compounds to make a homogeneous reaction system. During the hydrolysis process, CD_3COCD_3 plays a role in the proton exchange reaction (see Fig. 16)

$$CD_3COCD_3 \overset{HO^-}{\rightleftharpoons} CD_2HCOCD_3 + DO^- \overset{HO^-}{\rightleftharpoons}$$

and this is shown in the ^2H NMR spectra following the D–H exchange (see Fig. 17). Because of this, the concentration of deuterium in the hydrolysis system continuously increases and this leads to the fast disappearance of the peaks which are due to the absorption of the 'active hydrogen' in the intermediate. As mentioned above, the hydrogen in the pyrimidyl ring of the hydrolysis intermediate (PY-8) is not an 'active hydrogen', and does not take part in the exchange reaction with deuterium. After 75 min reaction time, the signal of this hydrogen was still observed in the ^1H NMR spectrum.

Fig. 16. ^2H NMR spectrum of acetone (CD_3COCD_3).

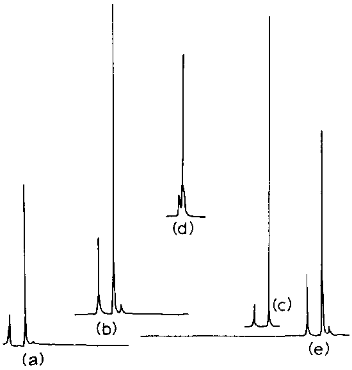


Fig. 17. ^2H NMR spectra following D–H exchange reaction. (a) CD_3COCD_3–NaOH–H_2O system, at 15 min. (b) CD_3COCD_3–NaOH–H_2O system, at 60 min. (c) The peaks of the alkaline system which contain PY-2, at 30 min. (d) The peaks of acetone in alkaline system, as (c). (e) The peaks of the alkaline system, as (a), at 120 min.

3 EXPERIMENTAL

MS and NMR data for the model reactive dyes are shown in Table 4.

^1H NMR spectra were measured on an FX-900 instrument at the specified temperatures. Neutral molecules were examined in solution in CD_3COCD_3 tetramethylsilane as internal standard.

The alkaline hydrolysis of the model dyes were carried out in the CD_3COCD_3–NaOH–H_2O system which comprised 0·5 ml CD_3COCD_3 and 0·1 ml or 0·05 ml of 3% aq. NaOH. For the other systems, the volumes of the components were as above.

The acidic medium used was of 0·1 ml HCl solution (3·4 ml of 36% HCl diluted to 50 ml) and 0·5 ml of CD_3COCD_3.

TABLE 4

The Data of Mass Spectra and NMR Spectra

Name	*N Element analysis*		*M*	*H NMR spectra (ppm)*		
	Calc.	*Obs.*		SO_2CH_3	NCH_3	$py\text{-}CH_3$
PY-2	13·48	13·19	311	3·33	3·58	2·48
PY-4	15·67	15·69	267	—	3·48	2·36
PY-8	11·79	11·54	357	3·32	3·56	2·52
PY-9	14·11	13·80	297	3·30	3·57	—
PY-11	11·16	11·13	377	3·32	3·60	—

The concentration of the product was calculated by the following equation:

$$y = \frac{\text{area of the methyl signal}}{3} \times \frac{5}{\text{total area of the phenyl signal}} \times (\text{initial concentration of the substrate})$$

REFERENCES

1. Tong-Gen, Yu, Zheng-Hua, Zhu & Zhu-Sheng, Chen, *J. East China Inst. Chem. Technol.*, **1** (1985) 10.
2. Burkert, U. & Allinger, N. L., Molecular Mechanics. ACS Monograph 177. Am. Chem. Soc., Washington DC, 1982.
3. Clark, J., *Spectrochim. Acta*, **40A** (1984) 75.