NMR Study of the Configuration and Protonation Equilibria of a Pyrazolotriazole Azomethine Dye

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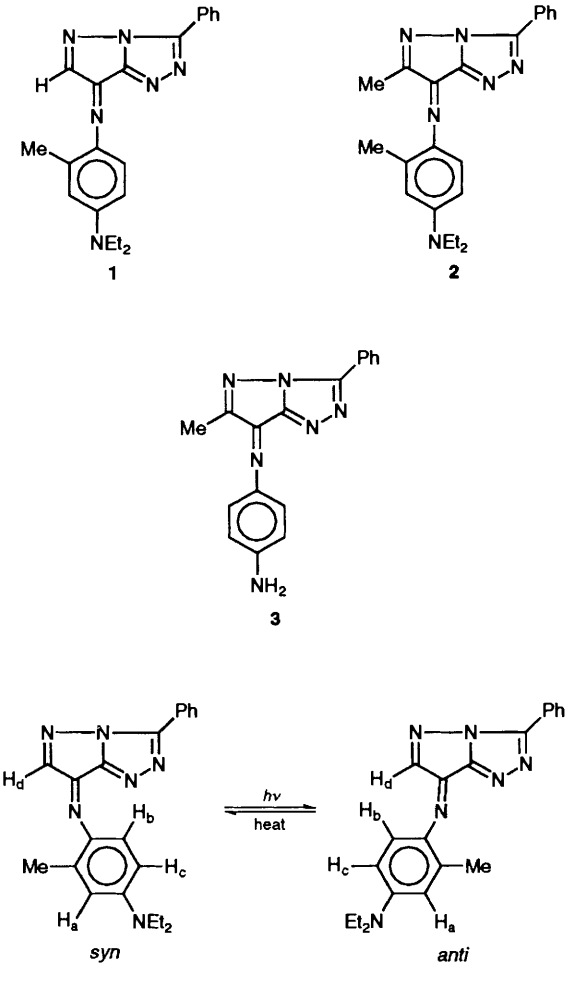
^{1}H NMR and NOE spectroscopy have been used to investigate the ground state configuration and proton equilibria of a 7*H*-pyrazolo[5,1-*c*][1,2,4]triazole phenylamino azomethine dye. NOE experiments show that the dye exists in the *syn* configuration at room temperature. Two protonation equilibria can be identified in $CDCl_3$–CF_3CO_2H at 1.6 ± 0.2 and 0.0 ± 0.2 −log[acid] units. The first equilibrium involves protonation of the azomethine nitrogen and leads to changes in the NMR spectrum which are interpreted as arising from increasing deviation from planarity about the azomethine bond because of steric interactions. The second equilibrium involves protonation of the phenylamino nitrogen.

Bailey introduced the 7*H*-pyrazolo[5,1-*c*][1,2,4]triazole azomethine dyes as potential magenta image dyes for conventional colour photography.[1] *syn* or *anti* configurations are possible. Microsecond flash photolysis studies show that interconversion between these isomers can be induced photochemically,[2–6] and UV–VIS and NMR data show that, for dyes studied to date, only one isomer predominates at room temperature.[6] However, there has been little conclusive evidence to indicate whether this is the *syn* or *anti* isomer. PPP MO calculations indicate that the *anti* configuration is the lowest energy π arrangement, but show the *anti* isomer to have the longer wavelength, lower oscillator strength, transition.[7] Unfortunately, this is in direct conflict with results from flash photolysis which show that, for all dyes studied to date, the unstable photoisomer absorbs to the red of the stable isomer with a reduced extinction coefficient.[2–6] This common spectral feature suggests that all of the dyes exist in the same configuration at room temperature.

These dyes also undergo at least two protonation equilibria which can be identified by changes in the UV–VIS absorption spectra.[8] Although UV–VIS spectroscopy has been used to provide accurate equilibrium data[8] it does not give direct information about the sites of protonation.

In this work we present results from NMR studies in which we used ^{1}H NMR, and NOE spectroscopy (Fig. 1) to investigate the ground state configuration of the dye and the sites and structural effects of protonation. We chose to work predominantly with dye **1** for the following reasons: the presence of proton H_d gives useful NOE experiments; the slow interconversion rate constant for *syn–anti* isomerisation of this dye means that NMR spectra cannot be due to the time averaged signal from interconverting isomers;[6] we have also characterised the protonation equilibria of dye **1** using UV–VIS spectroscopy.[8]

Rotation about the –C–N= bond is rapid on the NMR timescale, and the signals observed reflect the time averaged environment of the protons under study. The *predominant* conformations for the dyes are in the *syn* and *anti* forms bearing in mind the relative steric effects of the *ortho*-methyl and H-b substituents.



Experimental

Materials.—The dyes were prepared as described earlier.[6] Deuteriochloroform was obtained from Aldrich and trifluoroacetic acid obtained from Fluka.

Methods.—^{1}H NMR studies of protonation equilibria were carried out using a Perkin-Elmer R-24B 60 MHz spectrometer with $CDCl_3$–CF_3CO_2H as solvent and dye concentration of *ca.* 0.12 mol dm^{-3}. Hydroxylic solvents could not be used because of hydrolysis of the dye at high acid concentrations.[8] We have used equilibrium data for the dye at low concentration in $CHCl_3$–CF_3CO_2H obtained from UV–VIS studies to calculate free acid

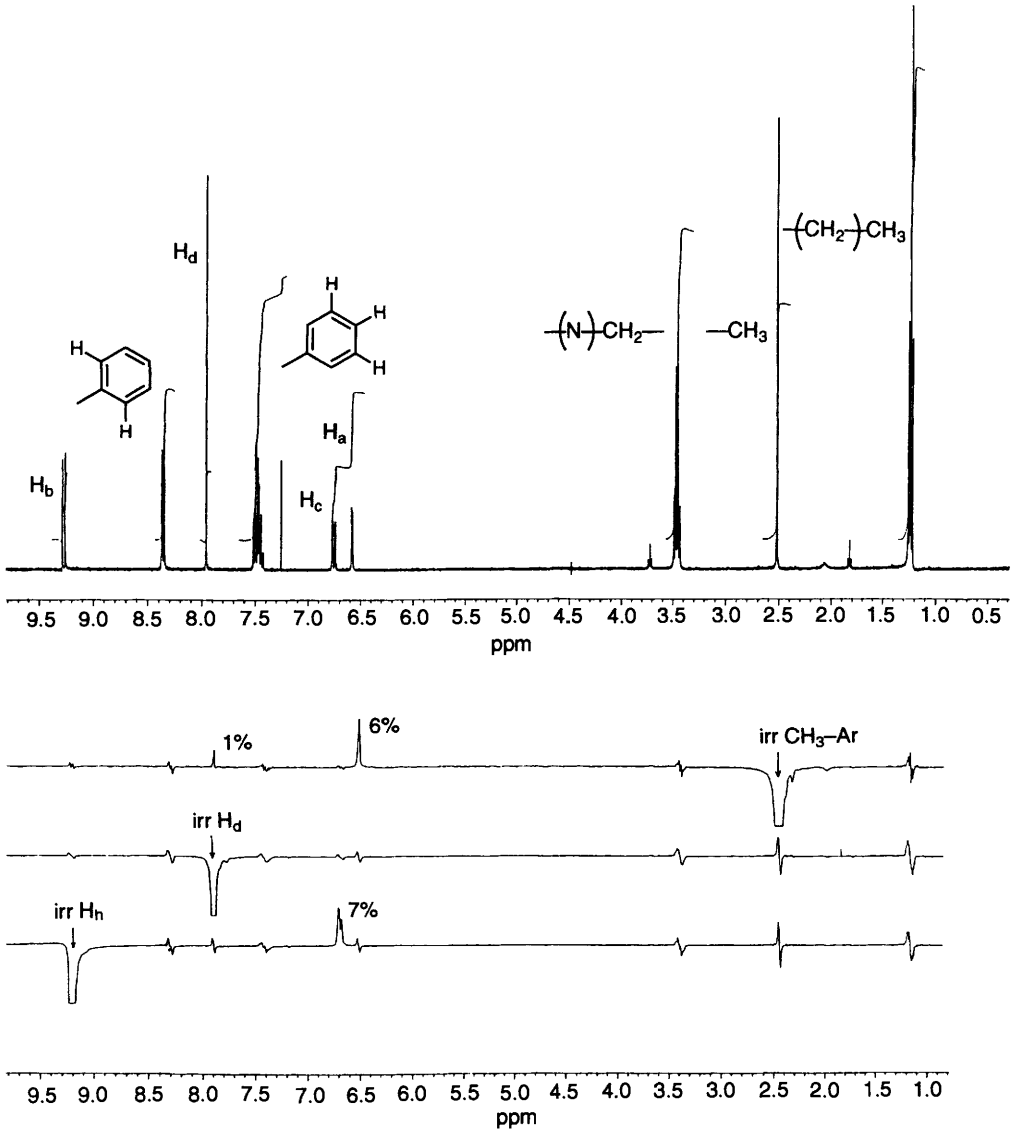


Fig. 1 NOE spectra for dye **1**, in $CDCl_3$ at 20 °C

Table 1 Data for proton equilibria in $CDCl_3$–CF_3CO_2H at 25 °C derived from Figs. 2 and 3

	pK_a	*n*	C.coeff(no.)
First protonation			
H-b	1.6 (±0.2)	0.87 (±0.3)	0.98 (5)
UV–VIS[a]	2.0 (±0.1)	1.1 (0.12)	0.998 (11)
Second protonation			
H-a	0.0 (±0.2)		
H-b	0.1 (±0.2)		
H-c	0.0 (±0.2)		
UV–VIS[a]	0.3 (0.1)		

[a] At low concentration in $CHCl_3$–CF_3CO_2H at 25 °C, from ref. 8.

concentrations (*i.e.* [acid added] − [protons transferred to dye]) at any $CDCl_3$–CF_3CO_2H ratio for Figs. 2 and 3 (see also Table 1 which compares results from UV–VIS and NMR studies).[8a] Data given in Table 2 were obtained using a Bruker 250 MHz instrument. NOE studies were carried out at the Edinburgh University Ultra High Field NMR Centre using a Bruker 360 MHz instrument.

Results and Discussion

Spectra.—Table 2 gives NMR assignments for dyes **1**–**3**. The H-b and H-b′ signals are at very low field, presumably because of the deshielding effect of the pyrazolotriazole rings. Rapid rotation about the –C–N= bond results in only one signal for the H-b,b′ protons of dye **3**. Replacement of the *ortho*-methyl group by H-b′ results in *ca.* 1 ppm upfield shift of the H-b,b′ signal for dye **3** compared to the H-b signal of dyes **1** and **2**. Substitution by the *ortho*-methyl group presumably increases the dihedral angle between the planes of the heterocycle and the aminophenyl ring resulting in H-b being displaced towards the shielding region above, or below, the heterocyclic plane.

NOE Experiments.[9]—Table 3 gives results from NOE experiments for irradiation at different proton resonances of dye **1**, and Fig. 1 gives the most relevant spectra. As expected, irradiation of the *ortho*-H resonance enhances that of the *meta*-H, irradiation of H-c enhances H-b and also the ethyl proton resonances, and irradiation of the aliphatic methyl resonance enhances those at $-CH_2-$, H-a and H-c. All of these are consistent for either the *syn* or *anti* isomer. However, irradiation of the H-b resonance enhances that of H-c but not of H-d, and irradiation of the aromatic methyl resonance enhances both that of H-a and H-d. These results show that H-d is far from H-b

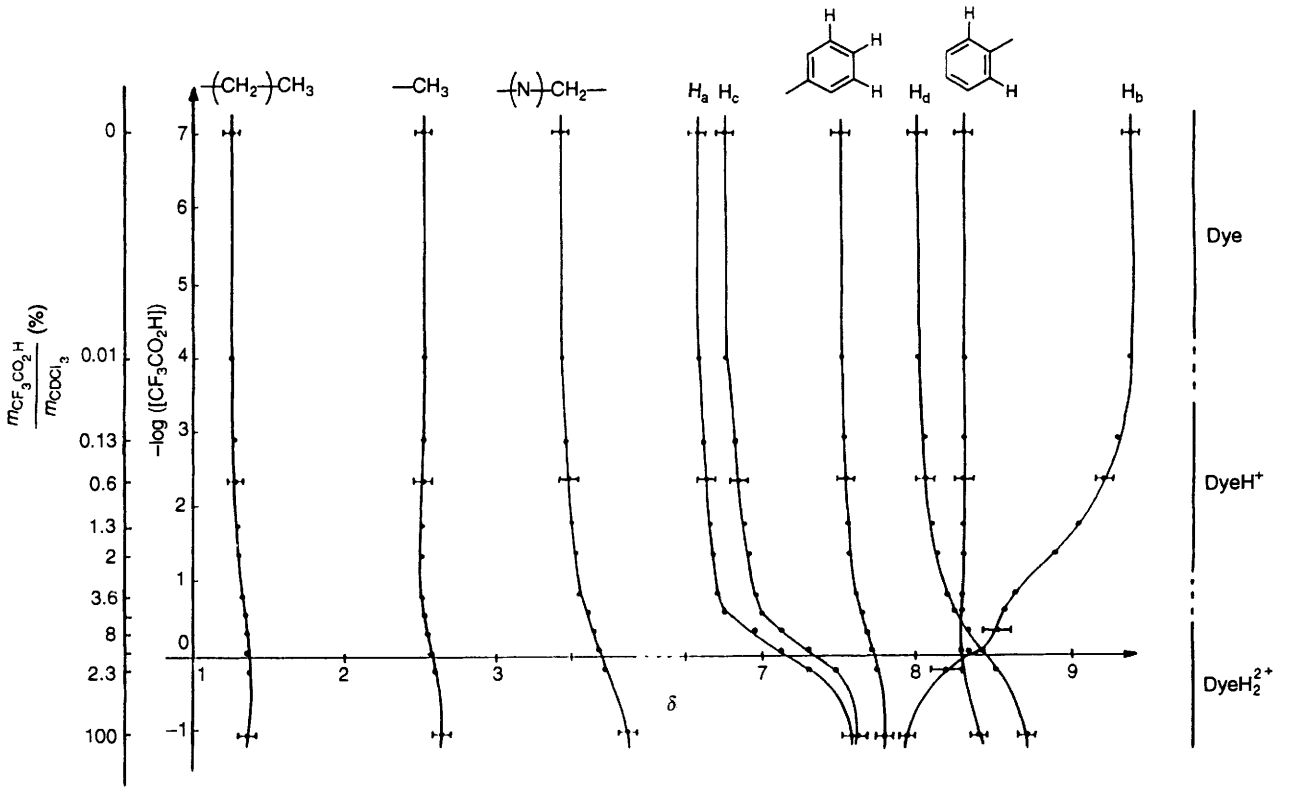


Fig. 2 Acid dependent NMR chemical shifts for dye **1** in $CDCl_3$–CF_3CO_2H at 25 °C

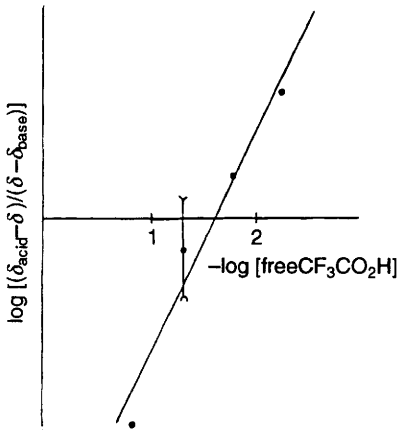


Fig. 3 Determination of first acid dissociation constant for dye **1** in $CDCl_3$–CF_3CO_2H at 25 °C from chemical shift data of proton H-b using eqn. (1)

Table 2 Peak positions and assignments for NMR spectra of dyes **1–3**

	δ (intensity; nature[a])		
	1	**2**	**3**
H-a	6.62 (1, d)	6.60 (1, d)	—
H-b	9.27 (1, d)	9.25 (1, d)	8.33 (2, d)
H-c	6.79 (1, d, d)	6.80 (1, d, d)	6.81 (2, d)
H-d	8.12 (1, s)	—	—
Ar-CH_3	2.54 (3, s)	2.53 (3, s)	—
$-CH_2-$	3.50 (4, q)	3.50 (4, q)	—
$-CH_2CH_3$	1.27 (6, t)	1.27 (6, t)	—
o-Ph	8.40 (2, c)	8.39 (2, c)	8.25 (2, c)
m,p-Ph	7.53 (3, c)	7.52 (3, c)	7.58 (3, c)
Pyr-CH_3		2.57 (3, s)	2.46 (3, s)

[a] Main structural features: s = singlet; d = doublet; d,d = double doublets; t = triplet; q = quarter; c = complex.

and close to the aromatic methyl group. These findings are consistent only with the *syn* configuration. In the *anti* configuration H-b is very close to H-d even if the molecule is not truly planar, and the aromatic methyl is too far away to enhance H-d. Also, in the *anti* configuration an enhancement of H-b on irradiation of H-d might be expected but none is observed.

Effects of Protonation.—Fig. 2 gives the proton chemical shifts as a function of free acid concentration. Two distinct transitions occur at *ca.* 1.6 and 0.0 $-\log$ [acid] units. We have used UV–VIS spectroscopy using a thin pathlength optical cell to confirm that these transitions, observed in the highly concentrated solutions necessary for NMR studies, give rise to qualitatively the same UV–VIS spectral shifts identified previously and attributed to the first and second protonation steps.[8] In solvents of known acidity function, H_0, acid dissociation constants can be obtained from acid dependent changes in chemical shifts using eqn. (1),[10] where δ_{acid} and δ_{base}

$$pK_a = nH_0 + \log[(\delta_{acid} - \delta)/(\delta - \delta_{base})] \quad (1)$$

are limiting chemical shifts at high and low acid concentrations, δ is the chemical shift at any intermediate acid concentration, n is the number of protons involved in the pK_a transition, and H_0 is the acidity function for the solvent mixture. If we assume that H_0 varies linearly with log [free CF_3CO_2H] in the CF_3CO_2H–$CHCl_3$ mixture below a concentration of *ca.* 0.1 mol dm^{-3} then chemical shift data for proton H-b can be rationalised *via* eqn. (1) as shown in Fig. 3. We have not analysed the second equilibrium in terms of eqn. (1) because H_0 is unlikely to vary linearly with log [free CF_3CO_2H] at the very high acid concentrations used[11] and we have few data points for this transition. However, the sharpness of the transition is also evident in UV–VIS studies, where analysis using the UV–VIS equivalent of eqn. (1) gives a slope of 2.3 ($\pm$ 0.3) and a pK_a value of 0.3 ($\pm$ 0.1).[8] Table 1 gives pK_a values for this second transition estimated from the mid-point of the second titration

Table 3 Results from NOE experiments

Irradiated resonance	Increase in signal (%)							
	H-a	H-b	H-c	H-d	Ar-CH_3	$-CH_2-$	CH_2-CH_3	*m,p*-Ph
H-b			7					
H-c		17				2	< 1	
H-d								
Ar-CH_3	6			1				
CH_2-CH_3	3		3			2		
o-Ph								9

curve seen in Fig. 2. As shown in Table 1 there is good agreement between data obtained from NMR and UV–VIS studies,[8] although the relatively large errors in the measurement of chemical shifts results in less precise values for the pK_as determined by NMR as compared to those obtained from UV–VIS.

The effects of the first protonation are most obvious on the protons in the vicinity of the azomethine nitrogen, in particular there is a *ca.* 0.8 ppm upfield shift for the proton H-b signal. This is consistent with protonation at the azomethine nitrogen causing either an increased deviation from planarity about the azomethine bond because of steric interaction with the *ortho*-methyl group, or a change in configuration. We prefer the former explanation because flash photolysis of the protonated dye generates a transient, the protonated *anti* isomer, which also absorbs to the red of the protonated ground state *syn* isomer.[8]

The effects of the second protonation are most obvious on the protons in the vicinity of the amino nitrogen, where the H-a and H-c signals undergo *ca.* 0.7 ppm downfield shifts, H-b shifts *ca.* 0.5 ppm upfield and the ethyl proton signals shift a few tenths of a ppm downfield. Clearly this second protonation involves the amino nitrogen, and in addition to causing changes in chemical shift, protonation at high ($\geqslant$0.8 mol dm^{-3}) acid concentration causes the well resolved quartet of the $-CH_2-$ group to collapse to a broad, poorly resolved, band. We interpret this as arising from the coupling of the ethyl proton resonances to the rapidly exchanging proton on the adjacent N atom in strongly acidified solution.[12] It is interesting to note that the second protonation also influences the chemical shift of H-d and those of the phenyl substituent on the pyrazolotriazole group and it is possible that protonation of the nitrogen atoms of the ring system also occurs at these high acid concentrations. An alternative explanation may lie in the effect that protonation of the aromatic amino nitrogen has on the electron distribution throughout the molecule. UV–VIS studies show very large spectral shifts associated with the second pK_a transition, and MO calculations show that the phenylamino lone-pair are delocalised across the whole molecule.[7] Protonation at this nitrogen will result in significant changes in electron density throughout the molecule, and this may lead to the changes in chemical shifts for protons well removed from the protonation site as seen in Fig. 2.

Conclusions

NOE experiments show that dye **1** exists in the *syn* configuration at room temp. The fact that all dyes show similar transient spectra following flash photolysis[2–6] suggests that all of the pyrazolotriazole azomethine dyes studied to date also exist in the *syn* configuration at room temp.

The two protonation equilibria, previously identified by UV–VIS spectroscopy, can also be identified by NMR spectroscopy, and occur at 1.6 ± 0.2 and 0.0 ± 0.2 $-\log$ [acid] units in $CDCl_3$–CF_3CO_2H. The first equilibrium involves protonation of the azomethine nitrogen. The *ca.* −0.8 ppm shift in the position of the H-b proton resonance associated with this transition is interpreted as arising from increased deviation from planarity about the azomethine bond because of steric interaction with the *ortho*-methyl group. The second equilibrium involves protonation of the phenylamino nitrogen atom.

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