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^{1}H NMR Spectra and Structure of Safranines. Hindered Rotation of the 3-Dialkylamino Group in 7-Azo Derivatives

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ABSTRACT

The ^{1}H NMR spectra of safranine derivatives are reported. Semiempirical calculations indicate that the high shielding of the 4- and 6-proton adjacent to an amino or hydroxyl group (resonating between 5.5 and 6.0 ppm) is due to accumulation of negative charge on the 4—and 6-C atoms, augmented by the magnetic anisotropy effect of the orthogonal 5-phenyl ring. The ortho protons of the latter resonate up field to the meta and para protons. Hindered rotation of dialkylamino groups, altogether unexpected in view of the rather low barriers in similar anilines, is observed only in the azo derivatives. AM1 suggest that this is due to destabilization of the transition state when an amino group is substituted for an azo group.
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INTRODUCTION

The discovery of safranines began with Perkin's mauveine and most safranine based dyes were commercially available in the previous century and their chemical constitution was established in the ensuing decades [1]. No NMR spectra of this type of phenazinium salts were reported until very recently, when, in 1994, Meth-Cohn and Smith [2] challenged the textbook structure of mauveine from retrosynthetic considerations. They showed convincingly that an original sample from Perkin's factory consisted mainly

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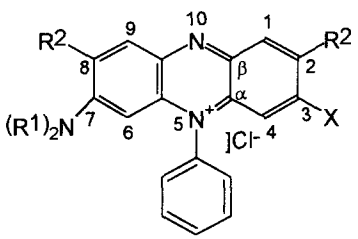
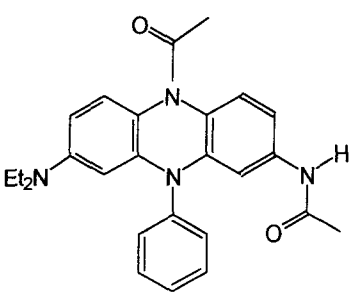
of two purple safranine dyes, neither of which had a methyl group in position 2, as shown by the generally accepted formula.

Meth-Cohn and Smith drew attention to the unusually high field chemical shifts of the protons in positions 4 and 6; they assigned the highest field signal of the protons of the 5-phenyl group in safranine to the *ortho* protons, although this is not the expected chemical shift in the case of a phenyl group attached to a positive nitrogen atom. Our experience with dialkylamino safranines showed another interesting feature; while simple safranines showed sharp signals for the dialkylamino groups, azo compounds exhibited broad lines, indicating slow rotation. The reason for this considerable difference in the barriers to rotation is not obvious. This prompted a molecular orbital study on the phenazinium cations in an attempt to relate their NMR characteristics to structure.

We now report on the ^1H NMR spectra of safranines **1–7** and the acetylated 5,10-dihydro derivative **8**:



	R^1	R^2	X
1	H	H	NH_2
2	H	Me	NH_2
3	Me	H	NH_2
4	Et	H	NH_2
5	Et	H	OH
6	Me	H	4-$(Me_2N)C_6H_4$-N=N
7	Et	H	4-$(Me_2N)C_6H_4$-N=N



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Although safranines and their azo derivatives are no longer used for dying textiles, they still find many applications. Some recent ones include brighteners in galvanics [3], the preparation of leucko dyes for thermographic imaging [4], and photography [5].

EXPERIMENTAL

^{1}H NMR spectra were taken on a Bruker WM 250 or DRX 250. AM1[6] calculations were carried by means of the MOPAC 6.00 package [7].

Dyes

3,7-Diamino-5-phenylphenazinium chloride **1** (Phenosafranine, Safranine B Extra) was obtained by the usual procedure of oxidizing p-phenylenediamine and two moles of aniline with dichromate and hydrochloric acid [8]. A dry sample of the salted out product was extracted with dry ethanol and precipitated with ethyl acetate to give a thin layer chromatography (TLC) and ^{1}H NMR pure product.

3,7-Diamino-2,8-dimethyl-5-phenylphenazinium chloride **2** (safranine T, C. I. Basic Red 2) was a commercial product (Chemapol, former Czechoslovakia). This showed after developing twice on DC-Alufolien Kieselgel 60 F_{254} (Merck) with heptane:dry ethanol 1:1 or with BuOH:EtOH:AcOH:H_2O 9:1:1:1 [9] two red admixtures moving faster than the main dye. The product was purified by preparative TLC on Kieselgel 60 PF_{254} (Merck) developing with heptane: dry ethanol, extracting with dry ethanol and precipitating with ethyl acetate.

3-Amino-7-(dimethylamino)-5-phenylphenazinium chloride **3** *and 3-amino-7-diethylamino-5-phenylphenazinium chloride* **4** *were obtained by the modified* [3] *procedure of Cobenzl* [10] from *p*-nitroso-*N,N*-dialkylanilines and aniline. Repeated recrystallization from water gave pure products.

8-Diethylamino-10-phenyl-2-phenazinone **5** was isolated as a side product upon preparation of Janus Green B and prepared also according to the procedure of Fischer and Hepp [11] by heating in a sealed tube at 150°C 100 mg of *N,N*-diethylsafranine **4** with 200 mg of sodium acetate hydrate in 10 ml of water for 30 h. TLC with dry ethanol: heptane 1:1 indicated incomplete conversion. The reaction mixture was made alkaline with 25% aqueous ammonia, allowed to crystallize, filtered and washed several times with water. Yield 23 mg (25%). The dry precipitate extracted with hot benzene was pure according to NMR. m.p. 270–2°C (lit. [12] m.p. 261–264°C).

3-Dimethylamino-7-(4-dimethylaminophenylazo)-5-phenylphenazinium chloride **6** *and 3-diethylamino-7-(4-dimethylaminophenylazo)-5-phenylphenazinium chloride* **7** (Janus Green B) were obtained by diazotization of safranines **3** and **4** and coupling with *N,N*-dimethylaniline [13]. The salted out product was dried and extracted with dry ethanol and the extract chromatographed under pressure on Kieselgel 60 PF_{254} (Merck). Substance:packing ratio was 1:30 and elution was carried out with heptane:dry ethanol starting with a 4:1 ratio and gradually increasing the ethanol content. After two

insignificant yellow fractions at a heptane:dry ethanol ratio of 1:2, a third fraction was isolated containing the safranone **5** in the case of **7**. The azo dye was eluted as a fourth fraction at a 1:3 ratio of the solvents.

10-Acetyl-3-acetylamino-7-diethylamino-5,10-dihydro-5-phenylphenazine **8** was obtained by the reductive acylation procedure of Barry *et al.* [14] used with anilinosafranines. The base of **4**, 175 mg, (obtained from making alkaline an aqueous or ethanolic solution of **4** and drying the precipitate) was suspended in 25 ml acetic anhydride, 25 mg of Adam's catalyst was added and the mixture stirred under hydrogen until the reaction mixture lost its colour. The product was poured onto ice and the precipitate filtered rapidly, washed with water and dried *in vacuo*. In air, the compound readily oxidized to coloured products, and because of this, it was identified only by ^{1}H NMR.

RESULTS AND DISCUSSION

Assignment of spectra

With the exception of tolusafranine **2**, all compounds studied are 3,7-substituted 5-phenylphenazine derivatives, which gives rise to characteristic splitting patterns, i.e. doublets of large and small couplings for protons 1,9 and 4,6, respectively, and doublets of doublets for protons 2,8. For the symmetrical phenosafranine **1** this suffices for the assignment [2] of the protons bound to the phenazine moiety, as has been reported for simple phenazines [15]. When the 3,7-substituents are different, the two sets of protons could in some cases be distinguished by slight differences in the coupling constants as in the 7-dialkylamino derivatives **3** and **4**. Which set of protons belongs to which ring is a question not readily solvable from chemical shift considerations: the dialkylamino group shifted one of the neighbouring protons (6) up field while the other one (8) down field. The assignment shown in Table 1 is based on an NOE difference experiment with compound **3**. Irradiation of the methyl signal at 3.036 ppm increased the intensity of the doublet at 5.578 by 2.7% and of the doublet of doublets at 7.146 ppm by 3.1%. HH-COSY experiments with compound **3** and **5** confirmed the connections from the coupling constants.

The 'safranol' **5** (see formula in introduction) was isolated as the neutral safranon. The similarity of its spectrum obtained in $CDCl_3$ to those of safranines **3** and **4** suggested that it could be present in the cationic form. The conversion of the latter into the neutral form is expected [16] to take place at pH 5–6 in water. Shaking the $CDCl_3$ with 10% KOH in D_2O to remove any traces of acid, however left the spectrum unchanged. The assignment of the two sets of protons is tentative, the slightly broader set of lines being attributed to the nucleus bearing the oxygen atom.

TABLE 1

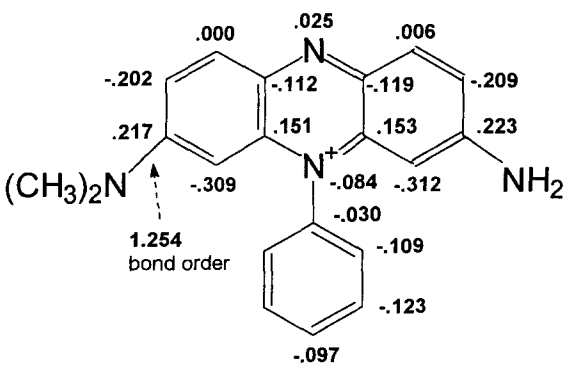
^{1}H NMR Chemical Shifts (ppm) and Splittings in Brackets (Hz) of 5-Phenylphenazinium Derivatives (Numbering of Protons is as indicated in the Formula, and Differs in Some Cases from That of Standard Names of the Compounds)

Compound	*Solvent*	$H_{(1)}$	$H_{(2)}$	$H_{(4)}$	$H_{(6)}$	$H_{(8)}$	$H_{(9)}$	$H^a_{(o)}$	$H^a_{(m)}$	$H^a_{(p)}$
1[b]	D_2O	7.529d	6.996dd	5.858d	5.858d	6.996dd	7.529d	7.364q	7.863t[c,d]	7.863t[b,c,d]
		(9.3)	(9.2,2.2)	(2.2)	(2.2)	(9.2,2.2)	(9.3)			
2[b,e]	D_2O	6.853s		5.722s	5.722s		6.853s	7.490dd	7.974m[c]	7.938m[c]
3[f]	D_2O	7.507d	6.975dd	5.841d	5.578d	7.146dd	7.495d	7.406m	7.883–7.927m[c]	7.883–7.927m[c]
		(9.2)	(9.2,2.2)	(2.2)	(2.4)	(9.7,2.4)	(9.7)			
4[g]	D_2O	7.376d	6.868dd	5.795d	5.484d	7.149dd	7.403d	7.279t	7.869m[c]	7.869m[c]
		(9.2)	(9.2,2.1)	(2.1)	(2.2)	(9.5,2.2)	(9.4)			
	CF_3CO_2D	8.270d	7.668d[h]	6.505d	6.555s[h]	7.848d[h]	8.408d	7.549m	7.949m[c]	7.949m[c]
		(9.4)	(9.4)	(1.7)		(9.8)	(9.6)			
5[i]	$CDCl_3$	7.793d	6.841dd[h,j]	5.610d[hk]	5.562d	6.929dd	7.587d	7.308d[l]	7.690t[l]	7.606t[i]
		(9.3)	(9.3,2.7)	(2.7)	(2.2)	(9.7,2.2)	(9.7)			
6[m]	$CDCl_3$	8.309d	8.223dd	7.369d[h]	5.845d[h]	7.973dd	8.125d	7.518d[h]	7.886m[c]	7.886m[c]
		(9.2)	(9.1,2.0)	(ca 2)	(ca 2)		(9.2)			
7[n]	$CDCl_3$	8.310d	8.220dd	7.384d	5.808[h,k]	7.92[h,j]	8.159d	7.53d[h]	7.90m[c]	7.90m[c]
		(9.0)	(9.0,1.6)	(1.6)			(9.3)			
8[o]	$CDCl_3$	7.160d[h]	7.045dd[h]	6.613d[h]	5.556d	6.287dd	7.366d[p]	7.364d[p]	7.613t	7.502t
		(8.5)	(8.5,1.8)	(1.7)	(2.8)	(8.9,2.8)		(7.2)	(7.4)	(7.4)
9[q]	CF_3CO_2D	7.95		7.14	7.06d	7.80dd	8.14d			
					(2.0)	(9.5,2.0)	(9.5)			

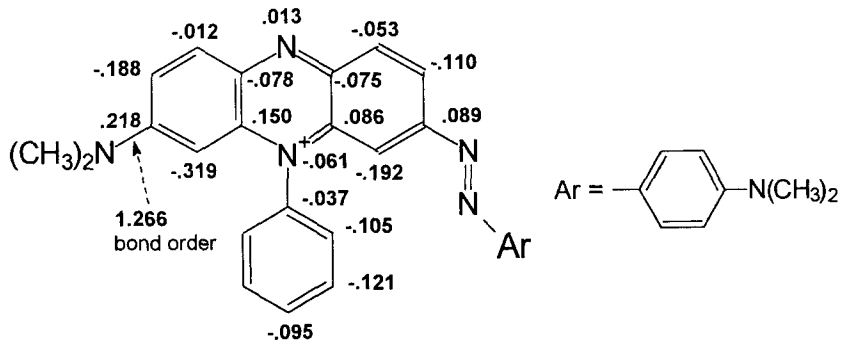
[a]Protons of the 5-phenyl ring. [b]ref.2 reports data in CD_3OD. [c]m—and p-signals overlap. [d]Three lines of equal intensity. [e]δ-CH_3 1.995s. [f]δ-CH_3 3.036s. [g]δ-CH_3 1.082t (6.5); δ-CH_2 3.396q (6.5)(in CF_3CO_2Hδ-CH_3 1.316t(7.0); δ-CH_2 3.733q[h](7.0)). [h]Broad lines. [i]δ-CH_3 1.094t(7.1), δ-CH_2 3.317q(7.1). [j]Unresolved dd. [k]Unresolved d. [l]Fine structure evident. [m]2′,6′-H 7.850d(9.2), 3′,5′-H 6.732d(9.2), 4′-$(CH_3)_2N$ 3.162s, 7-$(CH_3)_2N$ see text. [n]2′,6′-H 7.856d(9.2), 3′,5′-H 6.736d(9.2), 4′-$(CH_3)_2N$ 3.166s, 7-$(C_2H_5)_2$ see text. [o]CH_3CO 2.040s, 2.244, 7-$(CH_2H_5)_2N$ CH_3 0.974t(7.0), CH_2 3.113q(7.0), NH7.127s. $PH_{(1)}$ and o-H overlap. [q]ref.13

The assignment with the two azo dyes, **6** and **7**, relies on chemical shift considerations. Only one of the doublets with a small splitting is observed below 6 ppm. The other one is shifted to lower fields, presumably due both to a diamagnetic effect of the neighbouring azo double bond and a change in the electron density at $C_{(4)}$, (see below). Line intensities show the connection between protons 1 and 2 and between 8 and 9. Similar considerations were used to identify these protons in the case of the dihydro derivative **8**. The signals of the protons bound to the ring carrying the acetylamino group are broad, indicating a slow rotation.

The protons attached to the 5-phenyl ring in the case of **8** conform to the expected pattern of a phenyl linked to a nitrogen atom with a free lone pair. Those of compounds **1–7**, surprisingly, did the same with the *ortho* protons appearing at higher field, a multiplet of two protons around 7.3–7.5. The *meta* and *para* protons more or less overlapped showing a multiplet of three protons around 7.6–7.9 ppm. It is well known that when a phenyl ring is bound to a positively charged nitrogen as in $PhNH_3^+$, it is the *meta* and not the *ortho* protons that are more shielded. The AM1 calculations also yield larger negative charges to the meta protons (Schemes 1 and 2). The splitting pattern of the higher field signal defied this; a very clear-cut case was presented by tolusafranine **2** where a typical doublet of doublets for *ortho* protons was observed which apparently led Meth-Cohn and Smith [2] to the correct assignment. LAOCOON simulations of the AA'BXX' system in several compounds reproduced the observed patterns only when XX' were assumed to be ortho protons. In the case of phenosafranine **1** a 1D NOE difference experiment confirmed the assignment. Irradiation of protons 4 and 6 (the doublet at 5.858 ppm) increased by 8.2% the intensity of the signal at 7.364 ppm and left the multiplet at 7.863 ppm unchanged. According to the AM1 calculations, the distance from proton 4 to the *ortho* proton is 3.3 Å,



Scheme 1



Scheme 2

and 4.4 Å to the *meta* one (the 5-phenyl group perpendicular to the phenazine moiety).

While with the simple safranines **3,4** and **5**, the usual sharp signals for the 7-dialkylamino groups were observed, with the azo compounds **6** and **7**, broad pairs of signals of equal intensity were observed:

		CH_3, δ ppm	CH_2 δ ppm
6	298 K	3.69, 3.25	
	338 K	3.479	
7	298K	1.12, 1.415	3.52, 4.00
	333K	1.265	3.78

That this is due to slow rotation was demonstrated by the coalescence of the signals at higher temperatures although with the temperatures accessible in $CDCl_3$, sharpening of the coalesced signals could not be achieved.

The ^{13}C chemical shifts of phenosafranine **1** (Table 2) were assigned from an HC-COSY experiment correlating the ^{13}C shifts with the shifts of the protons bonded to them. A quaternary C atom of smaller intensity was identified as the ipso atom of the 5-phenyl ring, the lowest field signal was attributed to the carbons carrying the amino groups, while the quarternary carbons designated α and β were ordered according to their AM1 charges.

TABLE 2
^{13}C Chemical Shifts of Phenosafranine **1** in D_2O[a]

Carbons	*1,9*	*2,8*	*3,7*	*4,6*	*i*	*o*	*m*	*p*	*α*	*β*
δ ppm	132.3	121.0	156.5	94.2	135.5	127.0	131.2	131.0	136.6	135.0

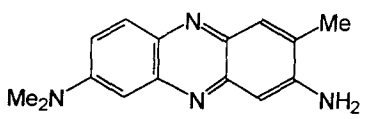
[a]Ref. 2 gives data in CD_3OD.

Structural interpretation of spectra.

The unusual chemical shifts of protons 4 and 6 when neighbouring to an amino or hydroxy group, of the *o*-protons in the phenyl rings and, most importantly the observed hindered rotation of the dialkyl groups in the azo safranines, prompted an MO study of their structure.

The structures of the cations of compounds **1–7** were calculated by the AM1 procedure of the MOPAC program [6, 7]. According to the calculations, the phenazine moiety is planar, agreeing with X-ray data for the parent phenazine [17]. The 5-phenyl group is perpendicular to this plane. Zero torsion angles were obtained for the dimethylamino groups. The best conformation for the diethylamino group is with the methyls 'sticking' perpendicularly against the benzene ring while the torsion CH_2–N–$C_{(7)}$–$C_{(8)}$ is 10°. The charges on the carbon atoms of a diamino derivative **(3)** are illustrated on Scheme 1 while those of an azo compound **(6)** on Scheme 2.

Meth-Cohn and Smith [2] attributed the shielding of protons in positions 4 and 6 to the magnetic ring current effect of the orthogonal 5-phenyl group and the electronic effect of the neighbouring amino groups. With respect to the shift quoted [18] for benzene, the shifts observed by these authors are 1.3 ppm up field; 1.7 ppm for some cases listed in Table 1. A shielding of 0.45 ppm is predicted from the Tables of Haigh and Mallion [19] due to the magnetic anisotropy of the phenyl ring. A practical estimate of the ring current effect can be made by comparison with a suitable phenazine without the phenyl group. A rough reference is provided by Neutral Red **9** (2-amino-3-methyl-8-dimethylaminophenazine) for which the ^1H NMR has been



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reported [20] in F_3CCO_2H. Protonation evens somewhat the electronic effects. Comparison with the spectrum of the *N,N*-diethyl seafaring **4** in F_3CCO_2D suggests the effect of the phenyl ring to be 0.5–0.6 ppm. The *ortho* protons in aniline and dimethylaniline resonate [18] 0.8 and 0.7 ppm, respectively, up field from benzene. Direct comparison is not, however, appropriate because of the formal positive charge on the neighbouring N atom, and further demonstrated by the shifts of protons in positions 2 and 8, which were 0.1–0.3 ppm up field from benzene. The observed shifts $H_{(4)}$ and $H_{(6)}$ are in complete agreement with the large negative charge around −0.3 obtained for carbons 4 and/or 6 with AM1 when the substituents at positions 3 and/or 7 are an amino or a hydroxy group. Magnetic anisotropy effects are

insignificant with ^{13}C shifts. Carbons 4 and 6 in phenosafranine **1** (Table 2) appear rather high up field for aromatic carbons at 94.2 ppm, confirming negative charge accumulation.

The appearance of the *o*-protons of the 5-phenyl group up field from the *m* and *p* ones could not be explained along these lines. As regards charges on the *ortho* carbons, AM1 calculates intermediate ones between those for the *meta* (most negative) and the *para*-carbons (least negative). The tables of Haigh and Mallion [19] predict the *o*-protons to be on the border between the shielding and deshielding zones exerted by the phenazine rings modeled as benzene rings. We believe that this small effect of *ca* 0.4 ppm, persistent in all phenazinium compounds **1–7**, is probably an anisotropy ring current effect caused by the phenazine moiety and not properly accounted for by the benzene model.

Hindered rotation of the dialkylamino group in the azosafranines

The indication of hindered rotation of the dialkylamino groups in the ^1H NMR spectra of the azo derivatives at ambient temperature was unexpected because the rotational barriers in sterically unhindered *N,N*-dimethylanilines with moderately electron withdrawing substituents are small [21]. The barrier in *p*-nitroso-*N,N*-dimethylaniline is quoted as $\Delta G^{\ddagger}_{-76°C} = 10.6$ kcal mol^{-1}. Accordingly, no hindered rotation was observed with the simple dialkyl safranines **3** and **4**. The barriers to the observed slow rotation in **6** and **7** can be estimated very crudely from the experimental data by means of the formula [22]

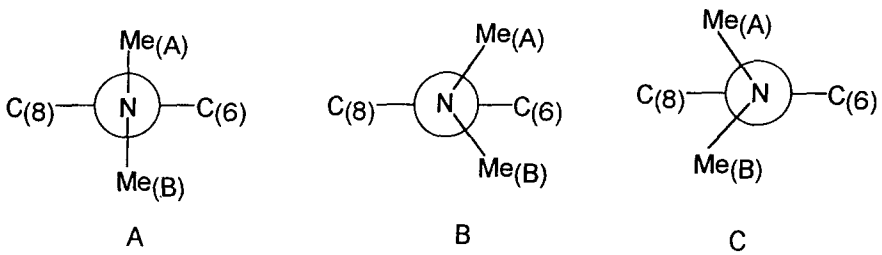
$$k = \frac{\pi \delta \nu}{\sqrt{2}}$$

where k is the rate of exchange at the coalescence temperature and $\delta\nu$ the difference in frequency between the two signals of the exchanging groups. Assuming that the frequencies of the already broadened signals are those at slow rotation, and the temperature where a single signal was observed is the one at coalescence, this gives for the dimethyl azo dye **6** $\Delta G^{\ddagger} = 16$ kcal mol^{-1} at 338K. If the coalescence temperature is assumed to be 318K, 15.2 kcal mol^{-1} obtains. Around 16 kcal mol^{-1} are estimated in the same way from data found for the diethyl derivative **7**.

The azo group in the Janus Green dyes is in an 'extended' *m* position with respect to the dialkylamino group and thus there be should no significant resonance interaction between the two groups, which could increase the barrier to rotation. As can be seen in Schemes 1 and 2, the $N–C_{(7)}$ bond order in the azo compound **6** is slightly greater that of the simple safranine **3**

but the difference is too small to explain a substantial increase in the rotational barrier. That the azo group does not perturb strongly the ring bearing the dialkyamino group in the ground state is evidenced by the very similar charges on the carbon atoms in this ring of the two safranines.

In an attempt to elucidate the difference in behaviour, the barriers of rotation of the dialkylamino groups in compounds **3, 4, 6** and **7** were estimated by varying stepwise the $C_{(8)}$–$C_{(7)}$–N–$C_{(alkyl)}$ torsion angle. The AM1 procedure used by us has been recommended [23] to give the best results among the semi-empirical methods for calculating barriers to rotation in amides and ureas. The torsion angle $C_{(2)}$–$C_{(3)}$–N=N was kept fixed at 180° because of the very small variation of the energy upon rotation, around 0.5 kcal/mole, (Figs 1 and 2), which was considered as a possible source of the small differences in the minimized energies. The results obtained are presented in Figs 1 and 2. As can be seen, maximum energies are calculated for torsions 110–125° because the nitrogen atom becomes tetrahedral in the transition state:



Contrary to a planar nitrogen atom giving rise to a single transition state A, with a tetrahedral nitrogen two transition states B and C are possible. In the 'calculation experiment', transition state B was approached by varying the torsion angle $Me_{(A)}$-N-$C_{(7)}$-$C_{(8)}$ (zero when $Me_{(A)}$ and $C_{(8)}$ are eclipsed) and the step between 90 and 130 degrees was reduced to 5°. The calculated torsion angle of the other methyl group, $Me_{(B)}$-N-$C_{(7)}$-$C_{(6)}$, lags behind. The dependence of the two torsions is illustrated in Fig. 3. The points denoted with x are the heats calculated for fixed values of torsion of $Me_{(B)}$ leading to C; the circles denote the same heats plotted against the torsions for $Me_{(A)}$ obtained in the calculation. At some time, inversion at the nitrogen atom takes place and $Me_{(A)}$ flips over to return to the planar geometry.

The estimates of the barriers of rotation (Table 3) were obtained as the difference between the highest heat of formation calculated upon rotation and that of the ground state (an attempt to find the 'true' transition state was deemed unnecessary). The results indicate no significant difference between transition states B and C.

Qualitatively, the AM1 predictions agree with the experiment results, giving 1.0–1.4 kcal higher barriers for rotation of the azo compounds. These results suggest that the explanation for the higher barriers is greater destabilization

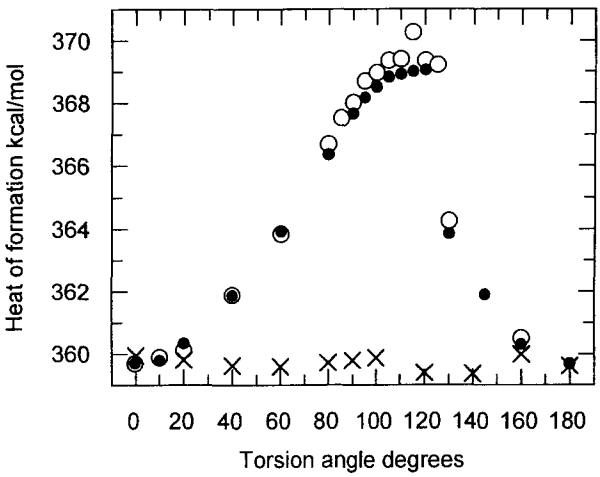


Fig. 1. Plots of AM1 heat of formation against torsion angle: (○)s—rotation of the dimethylamino group ($Me_{(A)}$–N–$C_{(7)}$–$C_{(8)}$) in 'dimethyl Janus Green' **6**, (●)s—$\triangle H_f + 91.9$ kcal mol^{-1} for the same rotation in 'dimethyl safranine' **3**, ×—rotation of the azo group around the $C_{(3)}$ N bond in **6**.

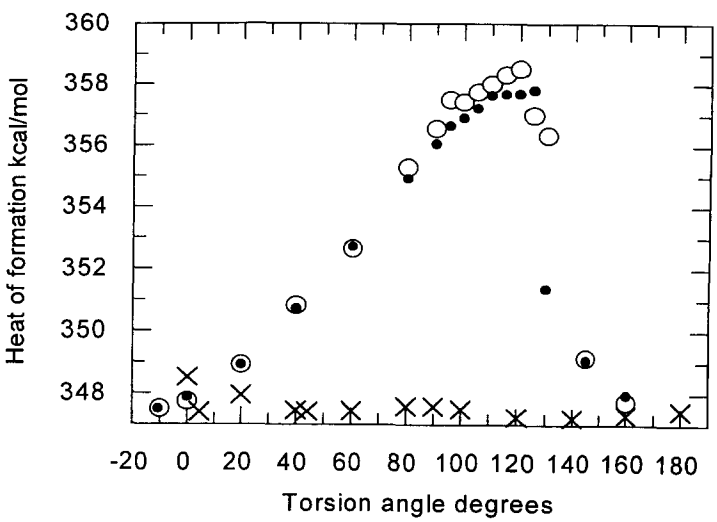


Fig. 2. Plots of AM1 heat of formation against torsion angle: (○)s—rotation of the dimethylamino group ($Et_{(A)}$–N–$C_{(7)}$–$C_{(8)}$) in 'dimethyl Janus Green' **7** (●)s—$\triangle H_f + 91.8$ kcal mol^{-1} for the same rotation in 'dimethyl safranine'**4**, ×—rotation of the azo group around the $C_{(3)}$ N bond in **7**.

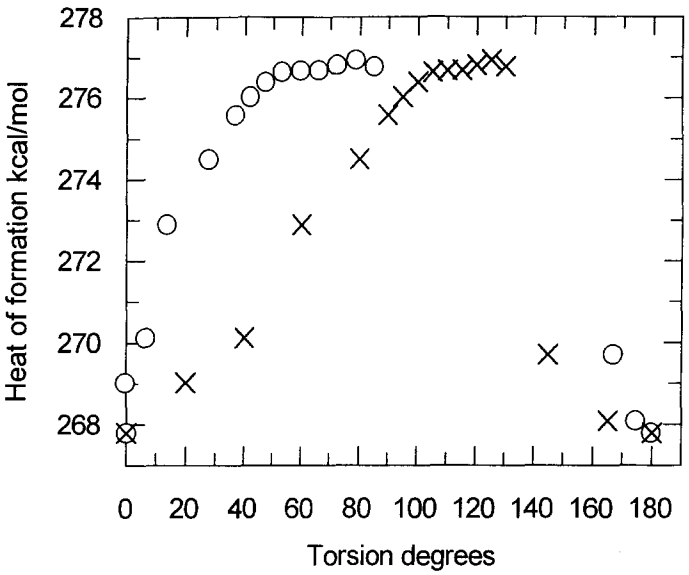


Fig. 3. Dimethyl safranine **3**: comparison of the dependence of the energy on the 'free' torsion $Me_{(A)}$–N–$C_{(7)}$–$C_{(8)}$—(○)s and on the fixed $Me_{(B)}$–N–$C_{(7)}$–$C_{(6)}$—(×). At zero degrees $Me_{(A)}$ and $Me_{(B)}$ are eclipsed with $C_{(8)}$ and $C_{(6)}$, respectively.

when the lone pair becomes orthogonal to the π-system of the phenazininium cation: in the transition state the π-system is conjugated with the lone pair of the remaining amino group with the simple safranines **3** and **4** and apparently less effectively with the lone pair on the azo group in the azo derivatives **6** and **7**.

Quantitatively, the calculated barriers are low. Feigel and Strassner [23] recommended a linear correlation as the best approach to bring calculated and experimental barriers together:

$$\Delta G^{\ddagger}_{liquid} = 1.6\Delta H^{\ddagger}_{(AM1)} + 4.5$$

TABLE 3

AM1 Estimates of the Energy Barriers to Rotation of the Dialkylamino Gropus kcal/mol. Data with Azo Compounds Obtained with Torsion $C_{(2)}$–$C_{(3)}$–N = N Fixed at 180°

Compound	*State B*	*State C*	$\Delta\Delta H^{\ddagger}$
3	9.31	9.13	
4	10.18	10.02	
6	10.57	11.05	1.4
7	11.05	11.12	1.0

The crude estimates of the barriers, made above, can be brought into line with the values in Table 3, either if they are multiplied by 1.6 or if 4.5 were added; however, good quantitative values for transition state are not readily obtained by semi-empirical methods.

An interesting problem is how great is the difference in barriers between the azo and parent safranines. Attempts to detect slow rotation with the N,N-dimethyl safranine **3** through increasing the chemical shift difference in Hz by taking the spectrum at 600 MHz in $CDCl_3$ and lowering the temperature to 273K remained unsuccessful.

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