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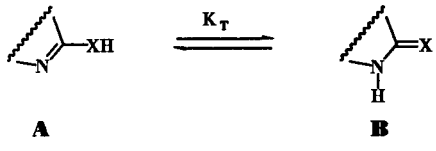
Received February 25, 1992

With the aim of checking potential amino/imino tautomerism in heterocyclic series, some uv/visible spectroscopic properties of 2-*N*-(2,4,6-trinitrophenyl)pyridine, 2-*N*-(2,4,6-trinitrophenyl)pyrimidine and of 2-*N*-(2,4,6-trinitrophenyl)thiazoleamine are reported and discussed. In dimethyl sulphoxide the imino tautomer of the thiazole derivatives is the more populated form, while in toluene the amino aromatic form predominates. The more populated tautomer of the pyridine and pyrimidine derivatives is the amino aromatic form in both polar and apolar solvents. For the thiazole derivatives the tautomeric equilibrium in toluene is shifted toward the imino form by adding small amounts of tetrabutylammonium bromide or of dimethyl sulphoxide. The position of the tautomeric equilibrium is quantitatively evaluated and discussed.

*J. Heterocyclic Chem.*, **29**, 1461 (1992).

"Aza" containing heterocycles with potential amino, hydroxy or mercapto groups exist in at least two tautomeric forms [1], as shown in Scheme 1.

**Scheme 1**




X = O, S, N-Y

Generally, Y is an electronwithdrawing group. Our interest lies with the amino group in the α-position with respect to the aza nitrogen, in order to check the amino-imino tautomerism (X = NY in Scheme 1).

Several years ago we calculated some $K_T$ values of some 2-thiazoleamino derivatives from p*K*a values [2]. In these studies, a strong effect of the presence of a phenyl group bonded to the exocyclic nitrogen was observed. The 2-*N*-phenylthiazolamine shows $K_T$ values favourable to the contemporaneous presence of both species in solutions. Usually the electron-withdrawing groups (bonded to the exocyclic nitrogen), can shift the tautomeric equilibrium towards the imino form **B** [3]. However the amino aromatic form **A** clearly predominates in some nitro derivatives of 2-*N*-phenylthiazolamine [4,5].

Recently [6], on the basis of $^1$H nmr spectral data we suggested that 2-*N*-(2,4,6-trinitrophenyl)thiazolamine is mainly in the imino form **B** in dimethylsulphoxide, while the amino aromatic form **A** predominates in chloroform.

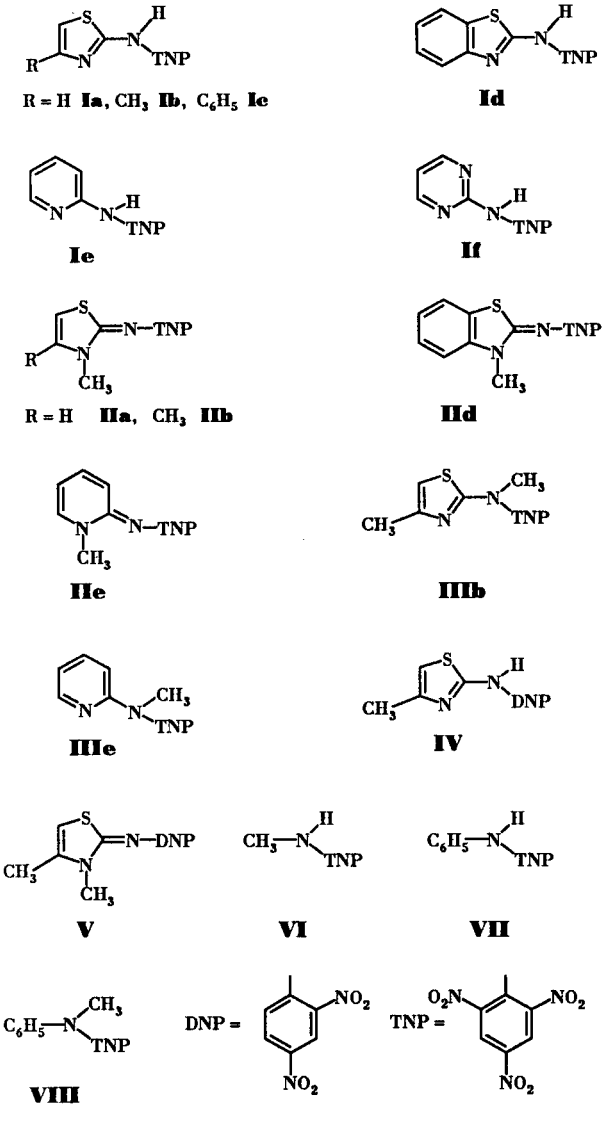
This conclusion agrees with the general statement that solvent "polarity" may be a very important factor in shifting the position of tautomeric equilibrium [1].

We now present some data regarding the uv/visible spectroscopic properties and the tautomerism [in toluene (TOL) and in dimethyl sulphoxide (DMSO)] of some derivatives of 2-*N*-(2,4,6-trinitrophenyl) heteroarylamine.

## Results and Discussion.

Table 1 presents some uv/visible spectroscopic data on the derivatives of thiazoleamine, pyridineamine, pirimi-

**Scheme 2**



dineamine and benzothiazoleamine examined as shown in Scheme 2.

Table 1

UV/Visible Spectroscopic Properties of the Compounds Considered

| Compound | **Ia** | **Ib** [a] | **Ic** | **Id** | **Ie** [a] | **If** [a] |
|---|---|---|---|---|---|---|
| TOL λ max (nm) | 381 | 389 | 407 | 388 | 376 | 359 |
| (ε x $10^2$) | (105) | (94) | (95) | (90) | (138) | (139) |
| DMSO λ max (nm) | 428 | 447 | 471 | 425 | 396 | 372 |
| (ε x $10^2$) | (90) | (118) | (130) | (80) | (122) | (115) |

| Compound | **IIa** | **IIb** [a] | **IId** | **IIe** | **IIIa** | **IIIe** [b] |
|---|---|---|---|---|---|---|
| TOL λ max (nm) | 410 | 419 | 404 | 422 | 438 | 421 |
| (ε x $10^2$) | (70) | (83) | (60) | (160) | (44) | (47) |
| DMSO λ max (nm) | 419 | 427 | 403 | 429 | 435 | 421 |
| (ε x $10^2$) | (89) | (93) | (65) | (214) | (37) | (39) |

| Compound | **IV** [c] | **V** [c] | **VI** | **VII** [b] | **VIII** [b] |
|---|---|---|---|---|---|
| TOL λ max (nm) | 358 | 422 | 415 | 364 | 430 |
| (ε x $10^2$) | (110) | (180) | (59) | (117) | (59) |
| DMSO λ max (nm) | 382 | 438 | 417 | 389 | 437 |
| (ε x $10^2$) | (100) | (200) | (60) | (133) | (62) |

[a] Data from ref [7]. [b] Data from ref [8]. [c] Data from ref [9].

In the same table, some data on fixed parents of the potential tautomers are also presented.

The use of the fixed amino and imino parents of possible tautomeric species is a useful approach in evaluating the presence and the position of tautomeric equilibria. Some criticisms of the use of this method which certainly includes some approximations were reported by Katritzky [1]. The possibility of using the absorptivity of fixed amino parents **III** to evaluate the concentration of amino **A** and imino **B** tautomers of compounds **I** can be completely disregarded because in the trinitroaniline system, the substitution of the hydrogen of the amino group with a methyl group strongly affects the spectrum; in previous papers [7,8], a strong red shift was reported for the substitution of a hydrogen with a methyl group on the exocyclic nitrogen.

However, it is interesting to observe that the differences in λ max by passing from TOL to DMSO in compounds **III** were close to zero Δ = λ max DMSO - λ max TOL for **IIIa** = -3 and for **IIIe** = 0 nm. The Δ values for compounds **I** are high, at least for the thiazole derivatives: 47, 58, 64, 37, 20, 19 nm for compounds **Ia**, **Ib**, **Ic**, **Id**, **Ie**, and **If**, respectively.

The spectral data of the fixed imino forms [compounds **II**] are of some utility. The λ max in TOL and in DMSO of compounds **II** shows only slight differences: Δ = λ max DMSO - λ max TOL = 9, 8, -1, 7 nm, for **IIa**, **IIb**, **IId** and **IIe**, respectively. These differences may be ascribed to mere medium effect. It is interesting to note that the solvent change from TOL to DMSO shows small effects in the absence of protons on the amino nitrogen, but it is more marked when the proton is present [6] [for *N*-2,4,6-trinitrophenylaniline **VII** and *N*-methyl-*N*-2,4,6-trinitrophenylaniline **VIII** Δ values are 25 and 7 nm respectively]. Probably DMSO acts as a proton acceptor. In agreement with previous findings [6] and conclusions on the basis of $^1$H nmr spectral data, the above reported differences support the hypothesis that at least for thiazole derivatives in toluene the amino aromatic form **A** predominates, while in DMSO the imino form **B** is more populated.

In order to change medium polarity, we recorded spectra in toluene and in the presence of varying amounts of salts. The choice of the salts was conditioned by the solubility of salts in the poorly polar solvent.

Addition of tetrabutylammonium bromide (TBAB) to the solutions in toluene produced a red shift of the maximum of visible spectrum in type **I** compounds, while the maximum of the spectrum in compounds **II** (fixed imino forms), of compounds **III** (fixed amino forms) or of compounds **IV**, **V**, **VI**, **VII** and **VIII**, was unaffected by the addition of TBAB. Compounds **I** presented a narrow range of [TBAB] values in which the wavelength maximum was unchanged. Beyond this range, the increase of concentration value of TBAB produces a red shift up to a constant value of λ max which is near to the value in toluene of the parent fixed imino forms, when they are available.

The λ max in the presence of excess of TBAB are: 412, 419, 425, 411 nm for compounds **Ia**, **Ib**, **Ic** and **Id**, respectively and 408, 419, 404, 423 nm for compounds **IIa**, **IIb**, **IId** and **IIe**, respectively. The maximum value of λ max was checked also in the presence of TBAB as a solid (satu-

Table 2

Effect of the Addition of Tetrabutylammonium Bromide (TBAB) to a Solution of 4-Methyl-2-(2,4,6-trinitrophenyl)thiazolamine (**Ib**) in Toluene at 25°

| $10^3$ [TBAB] (mole $dm^{-3}$) | 0 [a] | 0.20 | 0.25 | 2.02 | 3.37 | 4.06 | |
|---|---|---|---|---|---|---|---|
| λ max (nm) | 389 | 389 | 390 | 397 | 400 | 402 | |
| $10^3$ [TBAB] (mole $dm^{-3}$) | 4.42 | 4.72 | 6.74 | 8.85 | 13.5 | 16.0 | [b] |
| λ max (nm) | 403 | 405 | 409 | 414 | 418 | 419 | 419 |

[a] The Lambert-Beer law was checked for the range of [**Ib**] x $10^4$ values from 0.5 to 1.5 mole $dm^{-3}$. [b] Saturated solution.

rated solutions). Table 2 reports an instance of this behaviour. Unfortunately the solubility of TBAB in toluene is too low to have allowed us to use a large range of salt concentrations. In particular the derivative of 2-pyridinamine **Ie** and that of 2-pyrimidinamine **If** are scarcely sensitive to salt addition and very slight λ max shifts were observed. In the same way, the spectrum of compound **IV**, which in a previous study was reported to be in amino aromatic form also in polar solvent, was unaffected by addition of TBAB.

Addition of tetrabutylammonium trifluoromethanesulphonate (TBAM) to solutions in toluene of **Ic** and **Id** produced very slight shifts of λ max values, even when high concentration values of TBAM (0.05 mole $dm^{-1}$) were used.

The same behaviour of TBAB was observed by adding to the solutions in toluene of type **I** compounds small amounts of DMSO, at least in the concentration range used here. The λ max values in toluene were shifted by addition of DMSO, reaching a maximum value lower than the value of λ max recorded in DMSO. There were small but significant differences between the λ max values in toluene and in the presence of TBAB and DMSO in excess of compounds **I** and the spectrum of the related imino parent recorded in the same experimental conditions. This fact is an indication that the use of the physical parameters of fixed parents may be a source of error in calculating $K_T$ values. It appears reasonable to assume that in toluene without addition of TBAB or of DMSO the more populated tautomer was the amino aromatic form **A**, while in the presence of the excess of salt or of DMSO the imino aromatic form predominated. For the intermediate situations, *i.e.* moderate addition of TBAB or of DMSO it was possible to evaluate the position of the tautomeric equilibrium expressed by the ratio $c_B/c_A$ [$c_B$ is the concentration of the imino form, **B**, $c_A$ is the concentration of the amino form **A**]. From the plots of the $c_B/c_A$ values against the concentration values [TBAB] or [DMSO] it was possible to evaluate the sensitivity of the amino/imino equilibrium to medium polarity changes.

Table 3 collects the slopes of these plots. In every cases the intercept values are very close to zero, as required by the assumption that in the absence of salts or of DMSO the $c_A$ value is greater than the $c_B$ value.

In this way it is possible to obtain $K_T$ values at a definite concentration of salt or of DMSO, for instance, when [TBAB] = 0.01 mol $dm^{-3}$, $K_T = c_B/c_A$ = 4.0, 2.0, 1.8, 45.5, for **Ia**, **Ib**, **Ic** and **Id** respectivley. $K_T$ values for the six-membered rings heterocycles **Ie** and **If** can be evaluated 1 power of ten lower than the values of the thiazole derivatives.

The observed spectral differences in toluene caused by addition of TBAB or DMSO may be related to the equilibrium of Scheme 1.

In principle, other equilibria may be considered to be operating, such as an equilibrium between differently populated rotameric species. The presence of rotational isomers has been suggested on systems similar to those reported here [10]. Rotamers are expected also for the considered compounds in particular **Ie**, **IIIb** and **IIIa** which present spectra unaffected by addition of salt or of DMSO.

Although the method reported here includes some assumptions and simplifications, it is an evaluation of the position of tautomeric equilibrium without the use of physical parameters measured on fixed parent compounds.

An interesting observation concerns the different behaviour of five-membered rings compared with six-membered rings. Under the experimental conditions used here, pyridine, and pyrimidine derivatives, tend not to show evidence of the presence of their imino tautomers **B**, while under the same experimental conditions thiazole derivatives present evidence of the presence of both tautomers. 2-Aminothiazole was indicated [11] to be more prone to exist in the imino form than 2-aminopyridine also by *p*Ka measurements. Present data agree with this conclusion.

The amino aromatic form may be considered to be more stable than the imino form because the resonance energy is partially lost in the imino form. In the thiazole system resonance is a less important stabilising factor than in the pyridine system. In this way the loss of the stabilisation from amino form to imino form is less relevant in five-membered heterocycles than in six-membered heterocycles. The effect of benzo condensation ($K_T$ **Id**/$K_T$ **Ia** = 11) agrees with this explanation.

In any case, for the thiazole derivatives, the addition of small amount of salt (TBAB) or of DMSO greatly affects

Table 3

Slopes of Plots of $C_B/C_A$ Values Against [TBAB] or [DMSO] Values, in Toluene at 25°

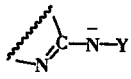
| Compound | λ [a] (nm) | slope [b] | n [c] | R [d] |
|---|---|---|---|---|
| [TBAB] | | | | |
| **Ia** | 460 | 398±13 | 6 | 0.998 |
| **Ib** | 460 | 316±5 | 7 | 0.999 |
| **Ic** | 460 | 183±8 | 7 | 0.996 |
| **Id** | 480 | 4,554±7 | 5 | 0.999 |
| [DMSO] | | | | |
| **Ia** | 440 | 28±2 | 7 | 0.998 |
| **Ib** | 460 | 43±1 | 7 | 0.999 |
| **Ib** | 360 | 39±2 | 7 | 0.993 |
| **Ic** | 420 | 15±1 | 8 | 0.989 |
| **Id** | 460 | 58±1 | 9 | 0.999 |

[a] Used in the determinations. [b] Errors are standard deviations. [c] Number of points. [d] Correlation coefficient.

the position of the tautomeric equilibrium. All the compounds considered are more sensitive to addition of TBAB than to addition of DMSO. This fact may be explained by a simple enhancement of the polarity of the medium, different for the added substances, or by some specific solute-solute interaction.

Up to now, it has been difficult to discriminate between the two explanations because experimental conditions do not allow us more extended investigation; for instance the solubility in toluene of salts other than TBAB is too low to have appreciable concentration values. The absence of effects caused by addition of an anion trifluoromethanesulphonate with dispersed negative charge may be considered only a feeble indication of the presence of specific interaction. Probably the present data are the result of an overlap between the two interactions.

The importance of the presence of the electron withdrawing group bonded to the exocyclic nitrogen (Y in Scheme 1) is worthy of comment. Previously [4,5] we found that when Y = 4-nitrophenyl and 2,4-dinitrophenyl, compound **IV** the amino form also predominates in polar solvents. Present data confirm this conclusion and emphasize that the acidity of the exocyclic N-H group is an essential condition for having a significant population of the imino form **B**. It may be assumed that the stabilization of the negative charge, after the dissociation of the exocyclic



N-H bond which is clearly favoured by the increased polarity of the medium, or by the presence of hydrogen ion acceptors is an important factor in shifting the tautomeric equilibrium towards the imino form.

For instance the $\Delta pKa$ between 2,4,6-trinitroaniline and 2,4-dinitroaniline is about 5 $pKa$ units.

On the other hand the electron withdrawing power of the heterocyclic moiety is probably of little importance. In fact the 2-thiazolyl group can be considered to have a similar electron withdrawing effect to that of the 2-pyridinyl group as tested by the $\sigma$ het values [12].

## EXPERIMENTAL

### Materials.

Melting points are uncorrected. Compounds considered were prepared by described procedures [6]. Compounds **Ic** [mp 201-202° (methanol); $M^+$ (m/z) found 387.0273; calculated: 387.02734], **Id** [mp 196-197° (methanol); $M^+$ (m/z) found 361.0110; calculated: 361.01170] and **(IId)** [mp 225-226° (acetone); $M^+$ (m/z) found 375.0278; calculated 375.02734] were prepared according to a previous report [6].

Toluene was purified by distillation from sodium [13]. Dimethyl sulphoxide was distilled over calcium hydride [13]. Tetrabutylammonium bromide (TBAB) and tetrabutylammonium trifluoromethanesulphonate were commercial specimens (Fluka) recrystallised from anhydrous tetrahydrofuran and dried by gently warming in a vacuum for 5 hours. The uv/visible spectra were recorded using a Perkin Elmer spectrophotometer (Model Lamda 5). The Labert-Beer law was checked in the range 0.3-1.5 x $10^{-4}$ mole $dm^{-3}$ of the concentration values; in accordance with the fact that the trinitro derivtive considered may be expected to be poorly self associated.

### Determination of $c_B/c_A$ Ratios.

The $c_B/c_A$ ratios were calculated by following equations:

$A = \epsilon_B c_B + \epsilon_A c_A$ and $c_{st} = c_B + c_A$

where $c_A$ and $c_B$ are the concentration values of amino and imino forms respectively, of the considered compound dissolved in toluene ($c_{st}$ is the total concentration value); A is the experimental absorbance value measured at appropriate $\lambda$ value, see Table 3, $\epsilon_A$ is the absorptivity in the absence of TBAB (or DMSO) and $\epsilon_B$ is the absorptivity measured in the presence of excess of TBAB or DMSO.

### Acknowledgements.

This work was carried out with the financial assistance of the CNR (Roma).

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