Protonation acidity constants for benzotoluidides in sulfuric acid solutions

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Abstract: The protonation of ω-, m- and p-benzotoluidide in sulfuric acid solutions is studied by UV spectroscopy in the 190–350 nm region. Principal component analysis is applied to estimate the contributions of the effect of protonation and the medium effect. For the substances studied in this work, the first principal component (PC) captures about 98 % of the variance and the second PC ∼100 % of the cumulative percentage variance in the 210–350 nm region. The same spectral region is used for calculation of the ionization ratio from the coefficients of the first PC and mole fractions of the base and its conjugate acid. Using these data and Hammett’s equation (pK_BH+ = H_X + log I), the pK_BH+ values for the protonation reaction are obtained. The dissociation constants as well as the solvent parameters m* (∼0.43) and φ (∼0.60) are calculated using the Excess Acidity Method (-pK_BH+= 2.28–2.30) and the Bunnett-Olsen Method (-pK_BH+= 2.24–2.28). The probable sites of protonation are discussed.

Keywords: Benzotoluidides, protonation, dissociation constants, spectrophotometry

1 Introduction

Protonation equilibria of weakly basic substrates are of central importance to the study of reaction mechanisms that take place in acidic media. Acidity constants are obtained by analysing the changes of some physical properties of the observed substrates at varying acid concentrations. The three most commonly studied properties are the observed
changes in the characteristics of UV-VIS, $^1$H, and $^{13}$C NMR spectra [1–4] that occur in going from the free base to the protonated base as the acidity of the solutions increases.

However, for carbonyl compounds such as amides, the situation is more complex, as the spectra of one or both forms are usually subject to substantial medium effects. Various methods have been widely employed to compensate for medium effects, e.g. principal component analysis (PCA) [5], target testing method of factor analysis [6, 7], and characteristic vector analysis (CVA) [1, 8–10].

In this work, the protonation of three benzotoluidides (Scheme 1) in sulphuric acid media is studied. These compounds were chosen partly because their structures resemble previously studied compounds of benzamide and benzanilide [4]. Further, to the best of our knowledge, no protonation data for these compounds have been published so far using UV spectroscopy. Thus, one can compare the values in this study with known values and discuss the influence of the different substituent positions in the structure on the protonation process.

The structures of the benzotoluidide compounds used in this study are presented in the following scheme.

\[
\begin{align*}
\text{O} & \quad \text{H}^+ & \quad \text{C} & \quad \text{N} & \quad \text{CH}_3 \\
\text{H} & & \text{O} & \quad \text{C} & \quad \text{N} & \quad \text{CH}_3 \\
\text{H} & & & & \text{C} & \quad \text{N} & \quad \text{CH}_3
\end{align*}
\]

\[
\begin{align*}
\text{o-benzotoluidide} & = N\text{-o-toly}l\text{benzamide} = N\text{-}(2\text{-methylphenyl})\text{benzamide} \\
\text{m-benzotoluidide} & = N\text{-m-toly}l\text{benzamide} = N\text{-}(3\text{-methylphenyl})\text{benzamide} \\
\text{p-benzotoluidide} & = N\text{-p-toly}l\text{benzamide} = N\text{-}(4\text{-methylphenyl})\text{benzamide}
\end{align*}
\]

Scheme 1 Protonation equilibria of the benzotoluidides.

Another reason to study $N$-substituted benzamides in acid solutions is their wide range of practical uses [11–15]. Derivatives of $N$-tolyl-benzamide are precursors for the synthesis of disubstituted amidrazones [11] and quinazolinones [12, 13]. They also serve as model compounds for the investigation of intramolecular charge transfer dual fluorescence of $p$-dimethylaminobenzanilides [14] and $N$-benzoylaminonaphthalenes [15]. Acid dissociation constants of acetooacet-$o$-toluidide and similar compounds have been determined potentiometrically [16].

2 Experimental

Benzotoluidides ($o$-, $m$- and $p$-) were synthesized and purified according to previously published procedures [11]. The purity of the toluindides was verified by FT-IR spectrometry (Perkin Elmer System 2000 FT-IR) and by gas chromatography (Hewlett Packard 5980 Series II plus, equipped with mass selective detector model MSD 5972). Stock solutions of the compounds were prepared in ethanol (Riedel-de Haën). Reagent grade
sulfuric acid (97 % by weight, Alkaloid – Skopje) was used. The exact concentration of sulfuric acid was determined by titration against 0.1000 ± 0.005 mol dm$^{-3}$ sodium hydroxide (Titrival, Alkaloid – Skopje).

The concentrations of the o-, m- and p-benzotoluidides for pK$_{BH^+}$ value determination were $3.31 \times 10^{-5}$, $4.62 \times 10^{-5}$, and $2.96 \times 10^{-5}$ mol dm$^{-3}$, respectively. The UV spectra of the substrates and appropriate blanks, were recorded in a range of sulfuric acid solutions (0.5 to 15.0 mol dm$^{-3}$).

The UV spectra were recorded from 190 to 350 nm immediately after preparing the solutions on a Varian Cary 50 Spectrophotometer in 1 cm quartz cells, with 1 nm resolution at room temperature ($25 \pm 1 ^\circ C$).

In order to compensate for the effect of the medium on the appearance of the spectra, PCA was employed using a procedure developed using Mathcad [17] on preprocessed experimental data (all data were normalized to unit area under the curves).

3 Results and discussion

The UV spectra of o-benzotoluidide in sulfuric acid solutions (Figure 1 shows 14 selected spectra from 25 that were recorded) exhibit four bands which result from $\pi \rightarrow \pi^*$ transitions. The bands $1B_a$, $1B_b$, $1L_a$ and $1L_b$, have been assigned and interpreted using the free-electron model [18] (Table 1).

![Fig. 1 Changes in the ultraviolet absorption spectra of o-benzotoluidide as a function of sulfuric acid concentration from 0.5 (curve 1) to 15.0 mol dm$^{-3}$ (curve 14).](image)

Because of the existing heavy overlap of $1B_a$ and $1B_b$ bands, it is very difficult to estimate their exact behavior during the medium acidity alteration. It is very probable that as the concentration of the mineral acid increases, the $1B_a$ band exhibits hypsochromic and hypochromic effects, i.e. it shifts towards shorter wavelengths and decreases in intensity, while the $1B_b$ band exhibits only a hypochromic effect.
Table 1 Experimental transitions in the UV spectra of benzotoluidides.

At the same time, the $^{1}L_{a}$ band shifts toward longer wavelengths (bathochromic effect). The $^{1}L_{b}$ absorption band appears as a shoulder at approximately 270 nm which can not be seen clearly, because it is submerged (hidden) under the high-intensity $^{1}L_{a}$ band.

These changes in the UV spectra of o-benzotoluidide result from the protonation of the benzotoluidide. The effect of the medium causes minor shifts of the absorption band $^{1}L_{a}$, so a precisely defined isosbestic point is not observed, as one might expect.

For this reason, we have tried to remove the undesired medium effect by the application of PCA. For a large number of carbonyl compounds [1] the absorbance at any acid concentration can be described as a mean absorbance of at least two principal components (PC). It is reasonable to associate the first PC with the effect of protonation and the second PC with the medium effect. The spectra were reconstructed according to eq. (1)

\[
A_{\lambda} = A_{\lambda}(mean) + q_{1}\nu_{1\lambda} + q_{2}\nu_{2\lambda} + \ldots
\]

where $A_{\lambda}$ is absorbance at wavelength $\lambda$, $A_{\lambda}(mean)$ is the average $A$ at that wavelength over the entire acidity range that was dealt with, $\nu_{1}, \nu_{2}, \ldots$, are principal components (PC) independent of acidity and weighting coefficients $q_{1}, q_{2}, \ldots$, independent of wavelength. When this method is used, which separates the protonation effects from medium effects, the protonation information is contained in $q_{1}$ [1, 9, 10].

The reconstructed spectra using the first principal components (Figure 2-4) intersect at isosbestic points. This gives additional support that, indeed, the first PC describes the behavior of the system due to the protonation that occurs in acidic media.

In Figure 2, the reconstructed spectra for o-benzotoluidide clearly show neat isosbestic points at 195 and 245 nm.

The experimental UV spectra of m-benzotoluidide and p-benzotoluidide are very similar to the spectra of the o-isomer in the region 190 – 210 nm.

The reconstructed spectra of m- (Figure 3) and p-toluidide (Figure 4) show isosbestic points at 267 nm and 275 nm, respectively, as a result of the bathochromic effect of the $^{1}L_{b}$ band originating from the unprotonated base. These changes in the UV spectra are

\[
\log \varepsilon \text{ for free (B) and protonated base (BH}^{+}\text{) determined in sulfuric acid solutions with concentration 0.5 and 15 mol dm}^{-3} \text{ respectively.}
\]
Fig. 2 Changes in the reconstructed absorption spectra of \( o \)-benzotoluidide as a function of sulfuric acid concentration from 0.5 (curve 1) to 15.0 mol dm\(^{-3} \) (curve 14).

Fig. 3 Reconstructed absorption spectra of \( m \)-benzotoluidide as a function of sulfuric acid concentration from 0.5 (curve 1) to 15.0 mol dm\(^{-3} \) (curve 14).

similar to those reported previously for benzanilide [4].

Major differences are observed in the position of the \( ^1L_a \) and \( ^1L_b \) band in the spectra of \( o \)-toluidide as compared to the spectra of the \( m \)- and \( p \)-isomers. The different behaviour is probably due to the steric effect of methyl group in ortho position [15, 19].

3.1 Determination of \( pK_{BH^+} \) values

In order to determine the strength of these weak bases, the thermodynamic \( pK_{BH^+} \) values are calculated using four different methods [20]: the equation proposed by Yates
Fig. 4 Reconstructed absorption spectra of \( p \)-benzotoluidide as a function of sulfuric acid concentration from 0.5 (curve 1) to 15.0 mol dm\(^{-3} \) (curve 14).

and McClelland (eq. 2), its modification (eq. 3), the excess acidity method (EAM) (eq. 4), and the Bunnett and Olsen method (eq. 5):

\[
\log I = m(-H_0) + pK_{BH+} \tag{2}
\]

\[
\log I = m'(-H_A) + pK_{BH+} \tag{3}
\]

\[
\log I - \log \{c_{H+}\}^\delta = mX + pK_{BH+} \tag{4}
\]

\[
\log I + H_0 = \Phi(H_0 + \log \{c_{H+}\}) + pK_{BH+} \tag{5}
\]

where \( H_0 \) is Hamett’s acidity function; \( H_A \) is its corrected value for amides, and \( X \) is the excess acidity function. Values of \( \log \{c_{H+}\} \) and \( X \) are available for aqueous H\(_2\)SO\(_4\) [21]. The data for \( H_0 \) and \( H_A \) are calculated using equations: \( -H_0 = X + \log \{c_{H+}\} \) [22] and \( H_A = 0.53H_0 + 0.68 \) [23], respectively.

Ionization ratios are calculated using the following equation:

\[
I = c_{BH+}/c_B = (A_B - A)/(A - A_{BH+}) \tag{6}
\]

where \( A_B \) and \( A_{BH+} \) are absorbances at selected wavelengths of the free and the protonated base, respectively. The same ionization ratios are obtained directly from the coefficients of the first PC [1, 4, 9] i.e. the weighting coefficients:

\[
I = c_{BH+}/c_B = (q_{1B} - q_1)/(q_1 - q_{1BH+}) \tag{7}
\]

The coefficients of the first PC are plotted (Figure 5) as a function of \( c(H_2SO_4) \), for illustrative purposes.

\( \delta \) \( \{c_{H+}\} = c_{H+}/\text{mol dm}^{-3} \)
Simple protonation should give a sigmoidal curve, changing from a constant $c_B$ to a constant $c_{BH^+}$. It is evident that $q_1$ behaves like this initially, but does not reach a stable final value. The equilibrium described in Scheme 1 likely produces two superimposed sigmoid curves, reaching a constant value at high acidity. However, the existence of only one step on the sigmoidal curve suggests that only one process in Scheme 1 occurs.

For the compounds studied here (Table 2), the first principal component in the 210–350 nm region always captures about 98 % of the variance, and the sum of the variances of the first and second principal components is $\sim 100 \%$. It is reasonable to associate the first PC with the effect of the protonation and the second PC with the medium effect, as was mentioned earlier [9].

| spectral region /nm | $190 - 350$ | $200 - 350$ | $210 - 350$ |
|---------------------|-------------|-------------|-------------|
|                      | $v_1$ /%    | $(v_1 + v_2)$ /% | $v_1$ /%    | $(v_1 + v_2)$ /% | $v_1$ /%    | $(v_1 + v_2)$ /% |
| Compound             |             |             |             |               |             |               |
| $\alpha$-benzotoluidide | 74.54       | 97.00       | 98.08       | 99.74         | 98.07       | 99.92         |
| $m$-benzotoluidide   | 79.75       | 96.06       | 98.27       | 99.58         | 98.11       | 99.86         |
| $p$-benzotoluidide   | 79.46       | 96.90       | 98.62       | 99.67         | 98.84       | 99.85         |

**Table 2** First PC and the sum of the first and second PC for the studied substances.

The values of the thermodynamic dissociation constants for the protonated benzotoluidides, calculated from the reconstructed spectra at 95 % confidence level using coefficients of the first principal components, are given in Table 3.

Because the slope of $\log I = -H_0 + pK$ is not equal to 1, the base does not seem to “follow” the Hammett acidity function, $H_0$. The investigated bases do not behave in the same way as the indicator bases used to define the acidity function. The best slope value
The values of the thermodynamic dissociation constant of the protonated benzotoluidides, calculated from the reconstructed spectra in the 210-350 nm region, using the first weighting coefficients.

The values of $pK_{BH+}$ that are calculated using equations proposed by the Excess Acidity Method and the Bunnett and Olsen method are presented in Table 3 and do not differ significantly.

The determination of the dissociation constants depends upon the method used and the wavelength selected [6]. Therefore, equilibrium concentrations of the base and its conjugate acid (their mole fractions at each sulfuric acid concentration) are obtained (Table 4) by the method of least squares, solving the system of 141 linear equations:

$$
\begin{align*}
A_1 &= A_B \cdot x_B + A_{BH+}^1 \cdot x_{BH+} \\
A_2 &= A_B^2 \cdot x_B + A_{BH+}^2 \cdot x_{BH+} \\
&\vdots  \\
A_{\lambda} &= A_B^\lambda \cdot x_B + A_{BH+}^\lambda \cdot x_{BH+}
\end{align*}
$$

where, $A_B^\lambda$ and $A_{BH+}^\lambda$ are the reconstructed absorbances at the wavelength ($\lambda$) of the free and protonated base, respectively. A similar method was applied in our previous investigations [24].

Ionization ratios were calculated according to the following equation:

$$
I = c_{BH+/c_B} = x_{BH+}/x_B
$$

The calculated results from the reconstructed spectra at the 95% confidence level are given in Table 5. The $pK_{BH+}$ values are in very good agreement with those of Table 3.

The values for the solvation parameter, $m^*$, are close to those characteristic for other amides [3, 4], indicating that the protonation site in the molecule is most probably the
Furthermore, the obtained \( \phi (\approx 1 - m^*) \) values presented in Table 3 and 5 are positive, as expected for oxygen Brønsted bases.

Also, methyl substitution in benzanilide \((-pK_{BH^+} = 2.42, m^* = 0.44) \) [4] increases the basicity relative to the unsubstituted compound. This fact is explainable in terms of the positive inductive effect of the methyl group, which stabilizes the conjugate acid of the benzotoluidides to a greater extent \((-pK_{BH^+} \approx -2.28, m^* = 0.43) \).

### 4 Conclusions

Principal Component Analysis is used for the purpose of separating the protonation effects of benzotoluidides from the medium effects in the spectral region 210–350 nm. The same spectral region was used for calculation of the ionization ratio from coefficients of the first component.
The values of the thermodynamic dissociation constant of the protonated benzotoluidides, calculated from the reconstructed spectra in the region 210-350 nm, using mole fractions of B and BH$^+$.principal component and molar fractions of the base and its conjugated acid.

The p$K_{BH^+}$ values for the benzotoluidides (-p$K_{BH^+}$ $\approx$ 2.24 – 2.30) do not differ significantly, when calculated using equations from either the Excess Acidity Method or Bunnett and Olsen method.

The different positions of the methyl group in the structures of the studied compounds do not influence protonation process, i.e. there are no significant differences in their p$K_{BH^+}$ values. Further, the calculated values for $m'$ and $m^*$ are close to those characteristic for amides, indicating that the protonation site on the molecule is the O-atom.

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