

Studies on the Acid–Base Equilibrium of Some Benzotriazolium Ylides

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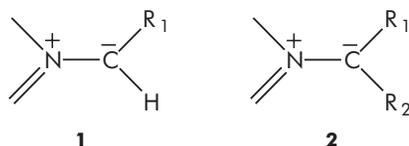
RECEIVED APRIL 4, 2005; REVISED MARCH 14, 2006; ACCEPTED MARCH 16, 2006

Keywords
benzotriazolium salts
ylides
acidity constants
theoretical parameters

Acidity constants of benzotriazolium salts and the corresponding ylides represent quantitative parameters for the estimation of their stability. Experimental pK_a values were determined using UV-spectrometry. For each species involved in acid-base equilibria, the theoretical total energies E_t , solvation energies E_s and UV-VIS electronic transitions were calculated by AM1, PM3, RHF/6-31G*, AM1/H₂O and ZINDO methods, respectively. Theoretical parameters confirm the experimental pK_a values. Acidity constants together with theoretical energies constitute critical parameters for achieving good yields for the synthesis of ylides from their corresponding benzotriazolium salts.

INTRODUCTION

All cycloimmonium ylides contain a carbanion bonded to a positively charged nitrogen atom, which belongs to an azaheterocycle^{1,2} (Scheme 1). These compounds reveal interesting properties and have been used as analytical reagents^{3,4} and semi-conducting materials.⁵ Few pa-



Scheme 1. Monosubstituted **1** and disubstituted **2** cycloimmonium ylides.

pers report biological activity for such compounds.^{6,7} Their best-known application is in organic chemistry as intermediates in various heterocyclic synthesis of new azaheterocyclic compounds.^{8–10} Up to this moment, thirteen disubstituted cycloimmonium ylides **2** have been measured as crystals, by X-ray diffraction.¹¹ This is not possible for the less stable monosubstituted ylides **1**. According to the different theoretical data, these monosubstituted systems are thermodynamically stable, but their high reactivity renders them experimentally unstable.¹² The ratio of tautomeric carbanion monosubstituted ylides in solution as well as their stability and chemical behaviour represent complementary data relating to the choice of the appropriate experimental conditions for some new heterocyclic syntheses. In this work, a spectro-

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metric study on the acid-base equilibrium, in aqueous solution, between benzotriazolium cations, the corresponding ylides, and the corresponding anions has been carried out in order to determine the equilibrium constants for acid dissociation (acidity constants). The experimental data are correlated to some theoretical parameters obtained by semi-empirical AM1, PM3, *ab initio* RHF/6-31G* and ZINDO methods.

EXPERIMENTAL

Apparatus

The pH values of solutions were measured on a CONSORT P 901 pH-meter using a glass saturated calomel-combined electrode. All measurements were performed on a Jasco V 530 UV-VIS spectrometer coupled with a personal computer, running the Jasco spectrophotometric software supplied by Jasco. The spectrometer was validated. The measurements were made in quartz cells of 1 cm pathlength and the optimal conditions for recording the spectra were: wavelength range 200–800 nm; scan speed 100 nm/min; slit width 2 nm; wavelength interval 1nm; smooth, 5.

Reagents

All chemicals and solvents used were commercially available and were of analytical grade (obtained from Merck or Aldrich). Double-distilled water was used. Stock solutions of benzotriazolium salts, 0.001 mol L⁻¹, were prepared by dissolving an appropriate quantity of each substance in EtOH 95 %. Solutions of 1.000 mol L⁻¹ of NaOH and HCl were prepared from standard Merck products.

Determination of Acidity Constants

The procedure for determination of acidity constants was adapted from Lachmann and Polster.¹³ A volume of 1 mL stock solution of benzotriazolium salt was diluted to 250 mL with water in a volumetric flask. 200 mL of this solution was used for determination. The pH of the solution was adjusted, by means of a micropipette, using small volumes of two concentrated solutions of NaOH and HCl, respectively. In this way, the dilution during the experiments is of only ≈ 0.5 mL (1–2 mL if a burette is used for titration) and the error of dilution is < 0.06 %. Therefore, this error can be ignored in titration spectra that are recorded in an analogue mode and the sharp isosbestic points are preserved throughout the experiment. Evaluation of the apparent pK_a values was carried out using the Henderson-Hasselbach¹⁴ equation adapted for spectrometric titration:

$$\text{p}K_{\text{a}} = \text{pH} + \lg [(A_{\text{max}} - A)/(A - A_{\text{min}})] \quad (1)$$

where A_{max} and A_{min} are the absorbance of the solution which contains only acid and base forms of the reagent, respectively, and A is the absorbance, at a given pH, of a solution containing both acid and base forms. All these absorbances were measured at the same wavelength.

RESULTS AND DISCUSSION

Compound **3**, which is colourless, is in equilibrium with the chemical species **4**, which is yellow and is in turn in equilibrium with the chemical species **5**, of an intense yellow colour. Similar families of spectra were recorded for salts **3b** and **3c**. The existence of such equilibria has already been proved by means of NMR spectroscopy and synthesis.¹⁶ The pK_a values were calculated using relation (1). The results obtained for the pK_a values are summarized in Table I.

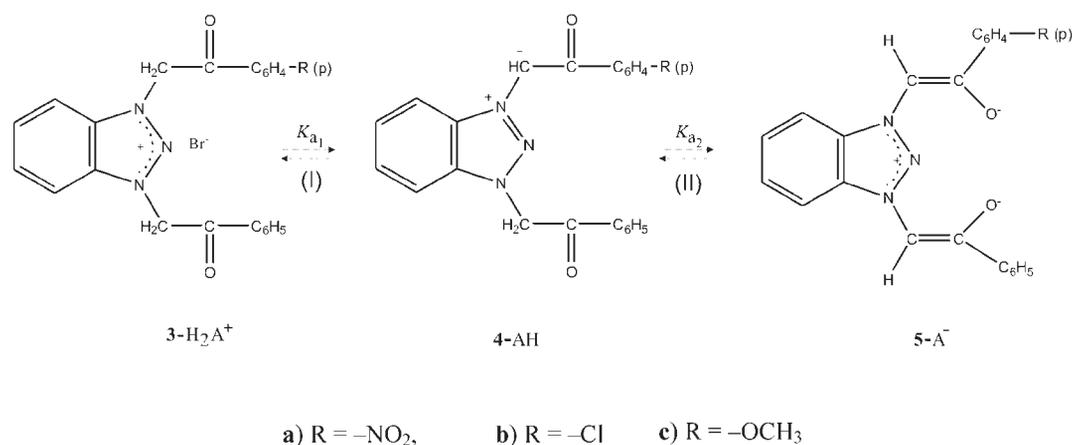
TABLE I. Values of pK_a at 25° C

salt	pK _{a1}	pK _{a2}	pH range	isosbestic points λ / nm	
3a	7.21 ± 0.12	9.62 ± 0.11	5.21 – 12.40	260	345
3b	9.71 ± 0.10	10.53 ± 0.10	5.39 – 12.49	275	310
3c	10.38 ± 0.17	11.82 ± 0.12	5.39 – 12.64	275	318

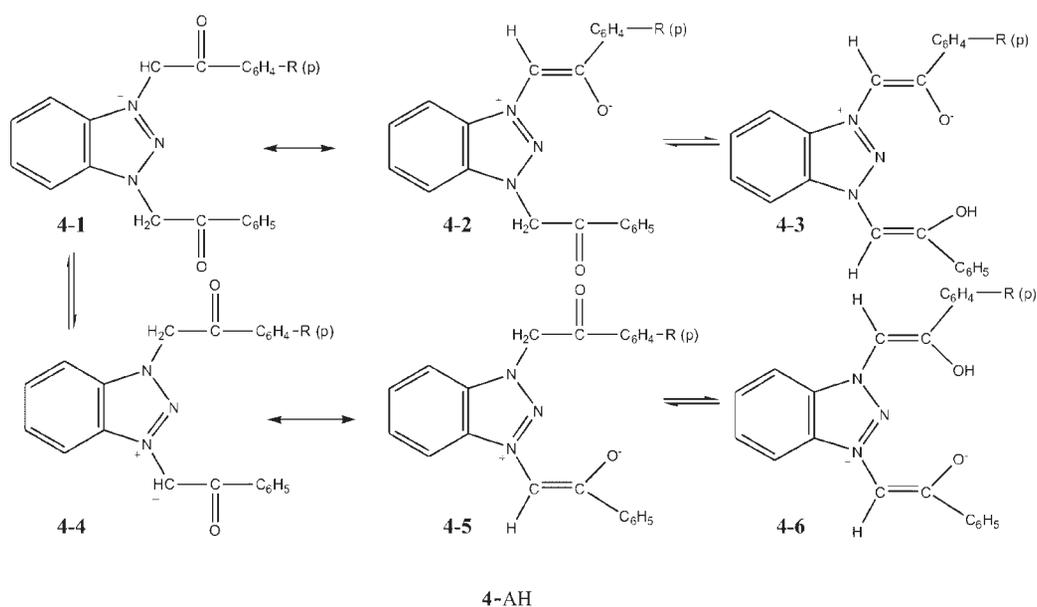
Each pK_a value represents an average of five determinations ± standard deviation.

As shown in Scheme 3, compound **4** can exist in many tautomeric and stereoisomeric forms. In order to assign a certain absorbance value to each of these forms, the theoretical spectrum of each compound was computed and its spectral parameters were compared with the experimental ones. Thus, the geometry of each compound was optimized using the semi-empirical AM1 and PM3 procedures in Spartan Pro Package¹⁷ and the *ab initio* RHF/6-31G* method in Spartan 02 Package.¹⁸ Both the AM1 and PM3 procedures reach the most stable conformation after a multi-conformational search, developed at the level of all single bonds of the involved systems.¹⁹ Then the most stable conformer is subjected to a new geometrical optimization without constraints. The choice of this conformer is based on ΔH (heat of formation) and E_t (total energy) values. This conformer, found by a semi-empirical study, was submitted to geometry optimization, using the *ab initio* RHF/6-31G* procedure and finally the theoretical spectrum was computed by means of a ZINDO procedure. Table II shows the spectral parameters of the theoretic spectrum computed for each form of ylide **4**. As shown (Figure 1), the computed spectrum for all three forms having the positive charge on atom N, which is near to the para-substituent of the benzene cycle of benzoyl fragment, has its maximum located at 275 nm. The theoretical spectrum of compound **4-1** fits best the experimental one and its structure was chosen to represent ylide **4** in Scheme 2.

Similarly, molar absorptivities for the UV–VIS electronic transitions, calculated for compounds **3a** and **5a**, were determined. It can be seen from Table IV that there are no significant differences between the theoretical



Scheme 2. Acid-base equilibria between benzotriazolium salts and the corresponding ylides.

Scheme 3. Tautomeric forms of ylides **4**.TABLE II. The UV-VIS electronic transitions calculated for all species of ylide **4a**

Wavelength λ_{\max} / nm	Molar absorptivities ϵ / mol ⁻¹ cm ⁻¹						Observations
	4-1	4-2	4-3	4-4	4-5	4-6	
216		38067.0					
242			23390.1				
258	24516.1						
264				50115.6	46431.6	22632.8	
275	34838.7	31056.1	35985.1				Real spectrum has absorbance max. at 271 nm
282						26943.8	
404		50819.8		59434.2		56043.2	
326			19339.6				
394					54301.1		
478			58475.8				

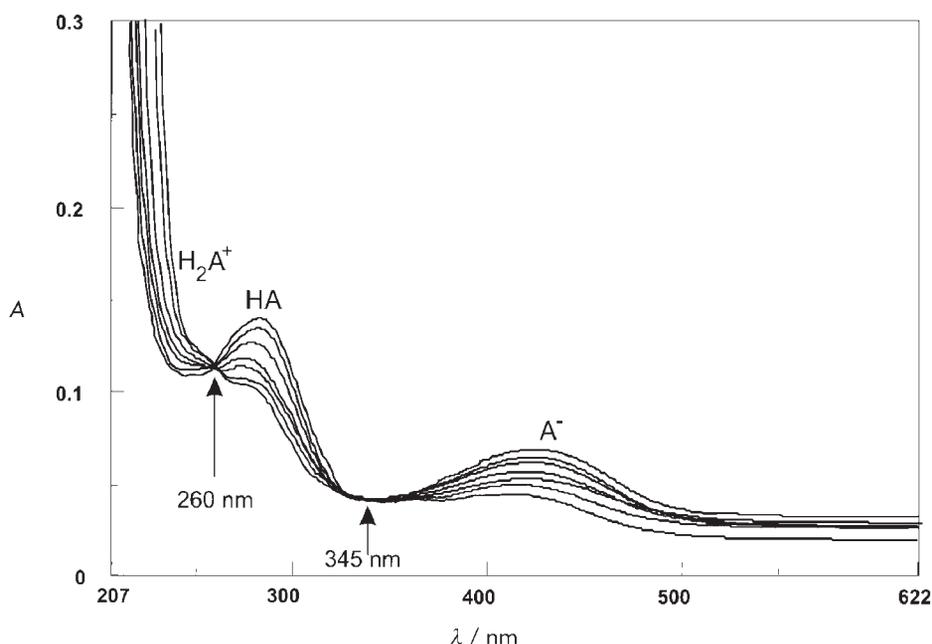


Figure 1. Variation $A = f(\lambda)$ for **3a**: 1) pH = 5.21; 6) pH = 12.40.

and experimental spectra. Therefore, one may deduce that the first value belongs to the formation of the first pK_{a_1} ylidic form **4-1**, according to equilibrium (I), in Scheme 2. Normally, the second pK_{a_2} value corresponds to the formation of the ylidic form **5**, according to equilibrium (II). The difference between pK_{a_1} and pK_{a_2} in every acid-base equilibrium could be taken as a measure of the stability of ylides. Thus, Table IV presents the differences between pK_{a_1} and pK_{a_2} together with σ substituent constants of $-\text{Cl}$, $-\text{OCH}_3$ and $-\text{NO}_2$ groups.²⁰ According to the ΔpK_a values and the para-substituent nature of the benzene cycle of benzoyl fragment, it is only the equilibria presented in Scheme 2 that could validate such pK_a differences. Indeed, a stronger electron-with-

drawing group $-\text{NO}_2$ favours the positive charge, increasing on the nitrogen atom bonded to the unsubstituted phenacyl fragment (see below the corresponding ΔpK_a for the **4a-5a** transfer). Direct dehydrohalogenation of the benzotriazolium salt **3** to both corresponding benzotriazolium ylides **4** and **5** should entail opposite pK_a values. The succession of equilibria, as described in Scheme 2, is supported by the fact that dehydrohalogenation of compound **3** with simultaneous configuration of chemical species **4** and **5** takes the existence of opposite pK_a values as a fact.

Experimentally, this theoretical conclusion was validated through a synthesis involvings tautomeric benzotriazolium ylides at some time after generation of the

TABLE III. The UV-VIS electronic transitions calculated for compounds **3a**, **4-1a** and **5a**

Wavelength $\lambda_{\text{max}} / \text{nm}$	Molar absorptivities $\epsilon / \text{mol}^{-1} \text{cm}^{-1}$			Observations
	3a	4-1a	5a	
208	54912.6	13924.7	45161.2	Real spectra show maximum absorbance at 206 nm
258	24517.3	24516.1	24516.1	Experimental isobestic point at 260 nm
275	19430.4	34838.7	27634.4	Real spectra show maximum absorbance at 271 nm
349	0.00	7741.91	7741.94	Experimental isobestic point at 345 nm
425	0.00	2150.52	40860.2	Real spectra show maximum absorbance at 423 nm

TABLE IV. Values of substituent constants, σ , and internal difference of acidity constants, ΔpK_a , for ylides **4** and **5**

	Substituent		
	a) $-\text{NO}_2$	b) $-\text{Cl}$	c) $-\text{OCH}_3$
σ	0.77	0.22	0.27
ΔpK_a	2.41	0.82	1.44

tautomeric mixture.¹⁶ The fact that the ratio and the chemical behaviour of the two species **4** and **5** are known permits the control of the compound concentration in the final reaction mixture. We should emphasise the fact that each tautomeric form leads to its specific reaction product. Finally, the stability of salts **3** and ylides **4** and **5** out of the pH range given in Table I was studied. In acidic solutions up to pH = 2.18, 3.24 and 3.57, salts **3a**, **3b** and **3c**, respectively, are stable for 20 minutes. On the other hand, ylides **4abc** and **5abc** decompose at pH = 12.45, 12.49 and 12.64, respectively, in an interval of 15–20 minutes. Practically, all experimental data presented in this paper recommend the use of such forms in aqueous solutions as reagents with respect to the pH ranges. Figure 2 presents a diagram of the distribution of the acid-base species of compound **3** as a function of pH. This diagram can be used to achieve good yields for the synthesis of ylides from their corresponding benzotriazolium salts.

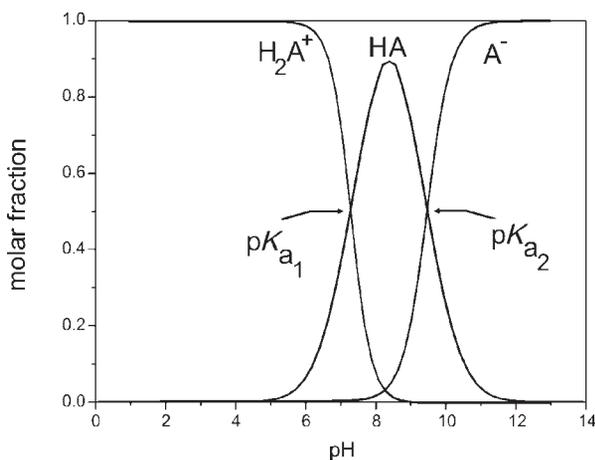


Figure 2. Distribution diagram of acid-base species of benzotriazolium salts as a function of pH.

CONCLUSIONS

The pK_a values for transformation of the benzotriazolium salts **3** to the corresponding benzotriazolium ylides **4** and **5** have been determined using a spectrometric procedure. The theoretical data obtained by AM1, PM3, RHF/6-31G*, AM1/H₂O and ZINDO point out the fact

that the formation of ylide **4** is in the first stage of the salt-ylide transformation. The benzotriazolium ylides **5** could be formed only after an acid-base equilibrium, $4 \rightleftharpoons 5$ according to the correlation between substituent constants σ and ΔpK_a internal differences of the two pK_{a1} and pK_{a2} values. The pH range in which the benzotriazolium salts **3** and the corresponding benzotriazolium ylides **4** and **5** are stable has been established.

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SAŽETAK

Istraživanja kiselo-bazne ravnoteže u nekim benzotriazolijevim ilidima

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Konstante kiselosti benzotriazolijeve soli i odgovarajućih ilida predstavljaju kvantitativne parametre za određivanje njihove stabilnosti. Eksperimentalne pK_a vrijednosti određene su korištenjem UV-spektrometrije. Za svaku vrstu uključenu u kiselo-baznu ravnotežu izračunate su teorijska totalna energija E_t , solvacijska energija E_s i UV-VIS elektronski prijelazi korištenjem metoda AM1, PM3, RHF/6-31G*, AM1/H₂O i ZINDO. Teorijski parametri potvrđuju eksperimentalne pK_a vrijednosti. Konstante kiselosti zajedno sa teorijskim energijama predstavljaju kritične parametre za postizanje dobrih iskorištenja u sintezama ilida iz odgovarajućih benzotriazolijevih soli.