Spectrometric study on the triazolium ylides

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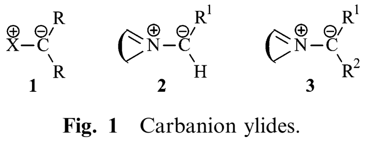
The pK_a values of triazolium ylides represent a quantitative parameter for the estimation of their stability. In the case of tautomeric triazolium ylides the differences in pK_a values correspond to the differences in theoretical ΔH or ΔE values. The experimental values of pK_a were obtained using a spectrometric method that involves the titration of triazolium salts.

Carbanion ylides are zwitterionic compounds in which a carbanion is covalently bonded to a positively charged heteroatom **1** (Fig. 1). In this paper we make reference to cycloimmoniium ylides only.[1,2] The positive nitrogen atom belongs to an azaheterocycle. The cycloimmoniuin ylides can be classified as monosubstituted carbanions **2** and disubstituted carbanions **3**, depending on the carbanion nature.[3] Cycloiommonium ylides have interesting properties for use as analytical reagents[4,5] or semi-conducting materials[6] as well as biological activity.[7,8] But their most known application is as intermediates in various heterocyclic syntheses of new classes of azaheterocyclic compounds.[9,10]

Up to date, a few distributed cycloimmonium ylides have been have been measured as crystals, by X-ray diffraction. This is not possible for the less stable monosubstituted cycloimmonium ylides. Otherwise, both semi-empirical and *ab inito* calculations have found the planar structures of monosubstituted ylides as more stable conformers.[11] It is considered[12] from the thermodynamic point of view that these monosubstituted systems are stable but their high reactivity renders them experimentally unstable.

All cycloimmonium ylides are strongly colored products. The electronic band in the visible is ascribed to an intramolecular charge transfer.[13] In the UV these ylides have a bigger number of bands ($n-\pi^*$). The visible band shifts are hypsochromic when passing from non-planar to polar solvents and from non-protic to protic solvents.[14] The protonation reaction of cycloimmonium ylides, and especially its reversibility, makes these compounds acid-base indicators.[4] The specific color of cycloimmonium ylides allows the elaboration of new colorimetric methods for the determination of acid chloride, anhydrides, isocyanates and isothiocyanates.[3,15]



1 **2** **3**

Fig. 1 Carbanion ylides.

In this paper we develop a spectrometric study on the passage of triazolium salts to the corresponding ylides and also on the tautomeric equilibrium of triazolium ylides in aqueous solution. Based on this study the experimental values of their pK_as were evaluated.

Experimental

All chemicals used were analytical reagent grade. Solutions of NaOH (1 mol L^{-1}) and HCl (1 mol L^{-1}) were prepared from standard Merck products by diluting with distilled water. Solutions of 10^{-3} mol L^{-1} were obtained by dissolving the exactly weighted amount of recrystallized triazolium salts in distilled water. The syntheses of the used triazolium salts are given in ref. 16. The pH of the solutions were measured using a LPH430T pH-meter having a glass saturated calomel combined electrode. Adsorbance measurements were carried out by a Lambda 2S Perkin–Elmer UV-VIS spectrometer in a 1 cm quartz cell.

pK_a determination

For the pK_a determinations we adopted the Lachmann and Polster procedure.[17] The concentrated solutions of NaOH or HCl used in the titrations were added in small volumes with a micropipette titration. The error dilution is less than 0.06% (0.5 mL) for a titration. The titration spectra were recorded for every pH measurement.

In every case two opposite titrations have been performed: salt → ylide and ylide → salt, using NaOH and HCl, respectively. The evaluation of the apparent pK_a values has been

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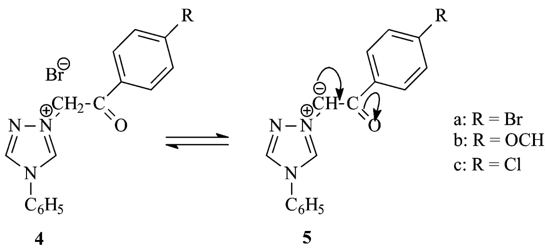


Scheme 1 Generation of monosubstituted ylides **5**.

calculated using the Henderson–Hasselbach equation adapted for spectrometric titrations[18]

$$pK_a = pH - \log\frac{A_{max} - A}{A - A_{min}}$$

where A_{max} is the maximal absorbance of the conjugated acid or conjugated base function in the titration, A_{min} is the minimal absorbance of the same conjugated form, and A represents the average of all recorded absorbances due to the conjugated form.

Results and discussions

The colorless 1,4-disubstituted triazol-1-ium bromides **4**, in the presence of NaOH, give the colored corresponding 4-phenyl 1,2,4-triazol-1-ium phenacylides **5**, as the single possible monosubstituted triazolium ylides (Scheme 1). We recall that the salts **4** are obtained starting from 1-phenyl-l,3,4-triazole and ω-bromoacetophenones.[16a] As an example, in Fig. 2 we present the variation of the absorbance during the titration of the salt **4a** with aqueous NaOH solution. The analogous curves with a single isobestic point have been obtained for the other two salts, **4b** and **4c**. We notice that for the compounds **4a**, **4b** and **4c**, no spectral modifications were observed in acidic media (pH range 2.50–5.00).

In Table 1 are given the calculated pK_a values, the used pH range and the recorded wave lengths λ, corresponding to the maximum absorbances and isobestic points. We could consider the values of pK_a as a measure of the ylide stability. The delocalization of the ylide negative charge (C^-) over the entire carbanion is one of the most important stabilizing factors for this type of compounds.[19] The increase of substituant constants: $\sigma_{Cl}(0.22) < \sigma_{Br}(0.23) < \sigma_{OCH3}(0.27)^{20}$ is found in the increase of the pK_a values as followed: pK_a **4c** < pK_a **4a** < pK_a **4b**. For these three studied triazolium ylides, the decrease of the thermodynamical stability is thus as follows: **4c** > **4a** > **4b**.

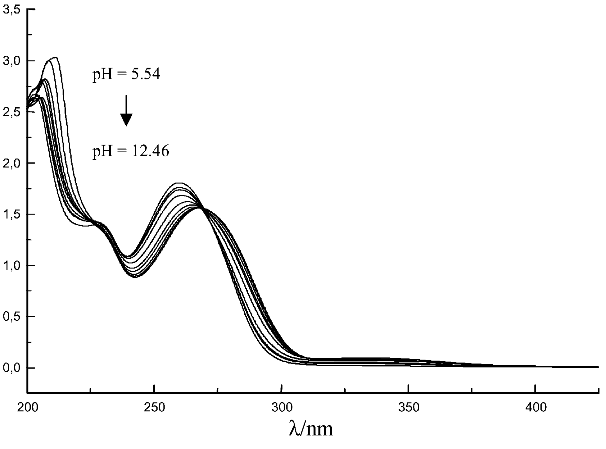


Fig. 2 Spectral evolution of compound **4a** recorded in the pH range 5.54–12.46.

Table 1 pK_a values at 25 °C with pH range, λ for isobestic point and used absorbances

Product	pK_{a_1}	pK_{a_2}	pH range	$\lambda_{ip1}{}^a$	$\lambda_{ip2}{}^a$	$\lambda_{max1}{}^a$	$\lambda_{max2}{}^a$
4a	10.96	–	12.5–2.5	271	–	262	–
4b	11.51	–	12.5–2.5	265	–	272	–
4c	10.91	–	12.5–2.5	265	–	270	–
6a	10.95	12.28	12.5–2.5	232	265	250	316
6b	10.86	12.19	12.5–2.5	232	268	252	336
6c	9.23	11.07	12.5–2.5	248	278	268	315

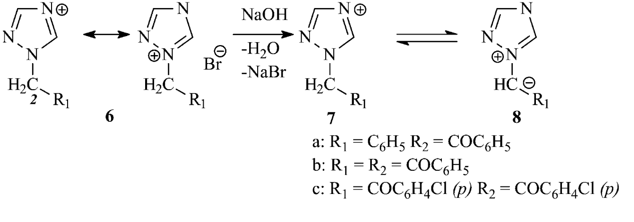
[a] λ_{ip} wavelength of isosbestic points, λ_{max} wavelength maximum of absorbances.

A very interesting aspect can be notice by analyzing the analytical data in Table 1, consecrated this time to the titration of the triazolium salts **6** with NaOH solution (Scheme 2). In fact, the 1,2,4-triazolium salts **6**, obtained in this case from 1,2,4-triazole and two successive treatments with benzyl chloride and ω-bromoacetophenone (**6a**) or twice with ω-bromoacetophenone (**6b**) or 4-chloro-ω-bromoacetophenone (**6c**)[16b,c] give two corresponding tautomeric 1,2,4-triazolium ylides, **7** and **8**.

The existence of such an equilibrium has been proven previously both by NMR-spectroscopy and by synthesis.[21,22] In reaction with picryl chloride each tautomeric form gives the corresponding disubstituted triazolium ylide. In Fig. 3 is given the variation of the absorbance during the titration of the salt **6a** with aqueous NaOH solution. Analogous curves have been obtained for the titration of the two other salts **6b** and **6c**, always with two isobestic points. The assignments of the absorbances to each tautomeric form is very difficult. Using some theoretical data concerning the mobility of the methylenic hydrogens in salts **6** and the stability of tautomeric forms **7** and **8**, we tried to determine the more abundant ylidic tautomeric form in the first step of dehydrohalogenation (**6** → **7** ⇌ **8**).

The numerical data in Tables 2 and 3 have been obtained using the semi-empirical AM1 and PM3 procedures in Cache Library[23] and the *ab initio* RHF/6-3lG method in Spartan package.[24] Briefly, in the AM1 and PM3 procedures, the most stable conformation of every salt **6** was found by a multiconformational search developed on the level of all single bounds of the involved systems as in previous papers.[25] Next, the most stable conformer was subjected to a new geometry optimization. The selection of the most stable conformer was based on ΔH (heat of formation) and E_t (total energy). Only the most stable conformer found by AM1 has been submitted to a geometry optimization by the 6-31G procedure. Finally, for each salt **6**, the three obtained geometries corresponding to each theoretical method, AM1, PM3 and 6-3lG, have been compared. No significant structural differences have been observed.

In reality, it is very difficult to evaluate the mobility of the hydrogens H(1) and H(2) in the two different methylenic group of the salt **6** by the values of the total atomic charges. For



Scheme 2 Tautomeric equilibrium of ylides **7** and **8**.

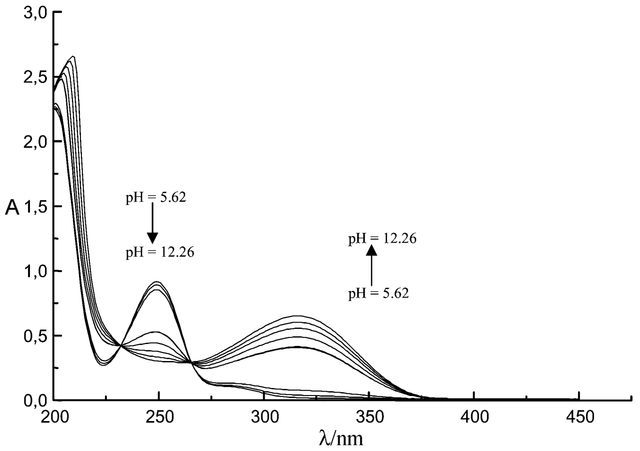


Fig. 3 Spectra evolution of compound **6a** recorded in the pH range 5.62–12.26.

example, from the Mulliken charges calculated by the 6-31G procedure the H(2) hydrogen is more acidic in salt **6b** and less acidic, in salt **6c** (Table 2). The calculated charges by the semi-empirical AM1 and PM3 procedures find as more acidic the H(2) hydrogens in salts **6b** and **6c**. The opposite result could be observed by the calculated charges (Mulliken and electrostatic) in the case of salt **6a**. This is why we extended our theoretical investigations on the stability of the tautomeric forms **7** and **8**.

In Table 3 are given the total energies (kJ mol^{-1}) calculated by the same three methods, AM1, PM3 and 6-31G, and also the solvation energy (kcal mol^{-1}) by AM1/H$_2$O for all three pairs of tautomeric forms **7** and **8**. Indeed, all three theoretical procedures find the tautomeric ylidic structures **7** as more stable, see lower E_t. Also, from the values of the solvation energies the same tautomeric forms **7** are favored. In each titration, the first pK_{a_1},value is connected to formation of the first ylidic tautomeric form **7**, while the second pK_{a_2} value corresponds to formation of the tautomeric ylidic form **8**. The difference between pK_{a_1} and pK_{a_2} in every pair of tautomeric ylides could be taken in consideration as a measure of the difference in their stabilities. Always, the form **7** is more stable than its corresponding tautomeric form **8**.

We consider that the knowledge of the concentrations of tautomeric ylidic forms at equilibrium has a dominant role in establishing the ratio of final synthetic products that involve these ylides as intermediates. For example, in the reaction with picryl chloride all triazolium ylides presented in this paper give the corresponding carbanion disubstituted triazolium ylides, which by an electrocyclization reaction lead to triazoloisoindoles.[16] Two different isoindoles, corresponding to each tautomeric form, have been obtained. The analytical procedure described in this paper permits us to prove the formation of two tautomeric forms at the choice of the base which generates these forms in its corresponding triazolium salt.

Table 2 Charges (a.u.) of methylenic hydrogens in the salts **6**

		H(1)		H(2)	
Salt	Method	Mulliken	Electrostatic	Mulliken	Electrostatic
6a	AMI	0.160	0.163	0.159	0.166
	PM3	0.121	0.135	0.120	0.109
	6-31G	0.264	0.267	0.256	0.264
6b	AM1	0.156	0.153	0.175	0.182
	PM3	0.123	0.099	0.130	0.192
	6-31G	0.269	0.270	0.277	0.280
6c	AM1	0.156	0.157	0.176	0.181
	PM3	0.122	0.148	0.143	0.198
	6-31G	0.278	0.271	0.271	0.272

Table 3 Total E_t (kJ mol^{-1}) and solvation E_t (kcal mol^{-1}) energies of the tautomeric forms of **7** and **8**

Ylide	Method	E_t	E_s
7a	AM1	−320254.39	
	PM3	−291629.70	
	6-31G	−2338367.44	
	AM1/H$_2$O	–	−9.805
8a	AM1	−320225.05	
	PM3	−291594.96	
	6-31G	−2338233.54	
	AM1/H$_2$O	–	−8.468
7b	AM1	−363526.92	
	PM3	−331373.28	
	6-31G	−2634345.30	
	AM1/H$_2$0		−13.158
8b	AM1	−363521.92	
	PM3	−331370.10	
	6-31G	−2634337.43	
	AM1/H$_2$0		−11.950
7c	AM1	−433015.57	
	PM3	−389535.59	
	6-31G	−5044021.33	
	AMI/H$_2$0		−13.050
8a	AMI	−433015.57	
	PM3	−389535.59	
	6-31G	−5044021.33	
	AM1/H$_2$0		−11.639

Conclusions

The pK_a values of 4-phenyl-l,2,4-triazol-l-ium phenacylide **5**, represent a measure of their stability. A good relationship between σ and pK_{a1} has been verified.

The difference between pK_{a_1} and pK_{a_2} values of phenacyltriazoliumphenacylides **7** and **8** could be taken as a measure of the difference in their thermodynamical stabilities.

In our opinion, the presented pH-meter titration procedure coupled with electronic absorption spectra seems to be the most accurate method to determine pK_a values in this class of zwitterionic compounds that is the cycloimmonium ylides.

References

1 A. W. Johnson, *Ylide Chemistry*, Academic Press, New York, 1966.
2 I. Zugravescu and M. Petrovanu, *N-Ylide Chemistry*, McGraw Hill, New York, 1976.
3 G. Surpateanu, J. P. Catteau, P. Karafiloglou and A. Lablache-Combier, *Tetrahedron*, 1976, **32**, 2647.
4 G. Surpateanu and E. Rucinschi, *Chem. Anal. (Warsaw)*, 1974, **19**, 493.
5 G. Surpateanu, N. Foca and J. Zugravescu, *An. Stiint. Univ Al. I. Cuza. Iasi, Sect. 1a–c*, 1973, **19**, 39.
6 G. Surpateanu, V. Stefan, E. Rucinschi and I. Zugravescu, *Phys. Status Solidi A*, 1970, **3**, 147.
7 M. Goldberg, *Arch. Int. Pharmacodyn. Ther.*, 1970, **186**, 287.
8 J. Bermudes, C. S. Fake, G. F. Joiner, K. A. Joiner, F. D. King, W. D. Miner and G. J. Sanger, *J. Med. Chem.*, 1990, **33**, 1924.
9 G. Surpateanu and A. Lablache-Combier, *Heterocycles*, 1984, **22**, 2079.
10 Y. Karzazi and G. Surpateanu, *Heterocycles*, 1999, **51**, 863.
11 P. Woisel, G. G. Surpateanu and G. Surpateanu, *Targets Heterocycl. Syst.*, 2001, **5**, 261.
12 J. P. Cheng, B. Lin, Y. Zhao, Y. Sun, X. M. Zhang and Y. Lu, *J. Org. Chem.*, 1999, **64**, 604.
13 (*a*) E. M. Kosover, *J. Am. Chem. Soc.*, 1958, **80**, 3253; (*b*) E. M. Kosover, *J. Am. Chem. Soc.*, 1958, **80**, 326l; (*c*) E. M. Kosover,

J. Am. Chem. Soc., 1958, **80**, 3267; (*d*) E. M. Kosover and B. G. Ramsey, *J. Am. Chem. Soc.*, 1959, **81**, 856.

14 G. Surpateanu and D. Dorohoi, *An. Stiint. Univ. Al. I. Cuza Iasi, Sect. 1a–c*, 1977, **23**, 99.

15 (*a*) G. Surpateanu, N. Foca, E. Rucinschi and I. Zugravescu, *An. Stiint. Univ. Al. I. Cuza Iasi, Sect. 1a–c*, 1973, **19**, 33; (*b*) G. Surpateanu, N. Foca, F. Rucinschi and I. Zugravescu, *An. Stiint. Univ. Al. I. Cuza Iasi, Sect. 1a–c*, 1973, **19**, 3l(*Chem. Abstr.*, 1973, **79**, 142 698p).

16 (*a*) G. G. Surpateanu, G. Vergoten, A. Elass and G. Surpateanu, *Heterocycles*, 1999, **51**, 2213; (*b*) P. Woisel, M. L. Lehaire and G. Surpateanu, *Tetrahedron*, 2000, **56**, 377; (*c*) P. Woisel, G. Surpateanu, F. Delattre and M. Bria, *Eur. J. Org. Chem.*, 2001, 1407

17 H. Lachmann and J. Polster, *Spectrometrische Titrationen*, Vieweg, Wienbaden, 1982.

18 H. H. Perkampus, *UV-VIS Spectrometry and Its Applications*, Springer-Verlag, Berlin, 1992, pp. 132–142.

19 Y. Karzazi and G. Surpateanu, *J. Mol. Struct.*, 1999, **510**, 197.

20 L. Hansch and A. Leo, *Substituent Constants for Correlation Analysis in Chemistry and Biology*, Wiley, New York, 1979.

21 A. Couture, A. Lablache-Combier, P. Grandclaudon and G. Surpateanu, *Heterocycles*, 1990, **31**, 2111.

22 G. Surpateanu, N. C. Lungu, N. Avarvari, A. Lablache-Combier, P. Grandclaudon and A. Couture, *J. Chem. Phys.*, 1994, **91**, 1648.

23 CaChe Library, Oxford Molecular Group Inc., 1998.

24 Spartan Pro 1.0.8, Wavefunction, Inc., 200l.

25 (*a*) G. G. Surpateanu, G. Vergoten and G. Surpateanu, *J. Mol. Struct.*, 2000, **526**, l43; (*b*) G. G. Surpateanu, G. Vergoten and G. Surpateanu, *J. Mol. Struct.*, 2001, **559**, 263.