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PROTOLYTIC EQUILIBRIUM OF CERTAIN ANNELATED AZOLOAZINES

A. P. Volovodenko[1], R. E. Trifonov[1], P. V. Plekhanov[2], G. L. Rusinov[2], D. G. Beresnev[2], and V. A. Ostrovskii[1]

The first and second protonations of annelated azoloazines have been investigated quantitatively in aqueous solution. Compounds investigated were pyrazolo[1,5-a]pyrimidine (pK_{BH^+} 0.03±0.02, $pK_{BH^{2+}}$ -7.87±0.30), 1,2,4-triazolo[4,3-b]-1,2,4-triazine (pK_{BH^+} -0.04±0.02, $pK_{BH^{2+}}$ -8.00±0.10), 1,2,4-triazolo[1,5-a]pyrimidine (pK_{BH^+} 0.21±0.03, $pK_{BH^{2+}}$ -9.00±0.09) and its 6R derivatives (R = NO_2, Br, Cl). The annelated azoloazines studied are weaker bases than their unannelated analogs. According to quantum chemical calculations (AM1), protonation of these heterocycles may occur both at the azole and the azine fragments of the molecule.

Keywords: annelated azoloazines, basicity, protonation, prototropic tautomerism.

Annelated azoloazines are bicyclic systems with certain heteroatoms present in both the azole and azine fragments. Progress in the chemistry of annelated azoloazines has been caused by their widespread use in medicine and coordination chemistry. Purine and its derivatives are the most important components of nucleic acids [1]. Azoloazine fragments enter into the structure of many biologically active substances, including medicinal preparations with a wide spectrum of action [2-4]. Azoloazines form stable complexes with various metal ions, which makes them promising as corrosion inhibitors and in systems for industrial purification of waste waters [5,6]. Benzannelated azoloazines are interesting subjects for the investigation of such fundamental properties of heterocyclic compounds as tautomerism, aromaticity, etc. [7,8]. The ability to display acidic and basic properties mainly determines the biological activity, the efficiency of complex formation, and also certain other chemical and physicochemical properties of heterocycles. The acid–base properties of azoloazines have generally not been investigated. The exceptions are the purines and pteridines [1,9,10].

The protolytic equilibria of certain compounds were investigated in aqueous sulfuric acid solutions by the spectrophotometric method in the present work. Compounds investigated were pyrazolo[1,5-*a*]pyrimidine (**1**), 1,2,4-triazolo[4,3-*b*]-1,2,4-triazine (**2**), and also unsubstituted 1,2,4-triazolo[1,5-*a*]pyrimidine (**3**) and its derivatives 6-nitro- (**4**), 6-bromo- (**5**), and 6-chloro-1,2,4-triazolo[1,5-a]pyrimidine (**6**). Basicity constants (pK_{BH^+}) were determined for the neutral molecules **1-6** and also for the monoprotonated forms ($pK_{BH^{2+}}$) of the unsubstituted heterocycles **1-3**. A theoretical analysis of the azoloazines was carried out in addition to the experimental investigation. The enthalpy of formation of the free bases **1-6**, and also of the various tautomeric forms of the mono- and dications, were calculated by the AM1 method. The proton affinity (*PA*) in the gas phase was calculated for the free bases and for the corresponding cations taking into consideration the formation of the thermodynamically most stable mono- and diprotonated forms.

[1] St. Petersburg State Technological Institute, St Petersburg 198013, Russia; e-mail: trifonov@actor.ru.
[2] Institute of Organic Synthesis, Urals Branch, Russian Academy of Sciences (RAN), Ekaterinburg 620219, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 816-824, June, 2000. Original article submitted March 23, 2000.

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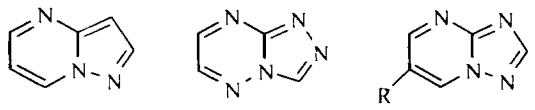
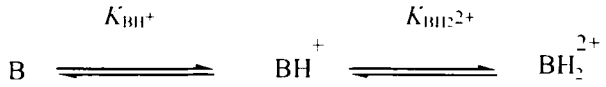


1 **2** **3-6**

3 R = H; **4** R = NO_2; **5** R = Br; **6** R = Cl

Protonation of the free bases **1-6** and the corresponding monocations is reflected in the electronic absorption spectra [11].

The special feature of the azoloazines as bases is the presence of several nonequivalent centers of basicity in the azole and azine fragments of the molecule. Because of this the possibility of not only mono- but also diprotonation must be considered.



When protonating azoloazines **1-6** it is possible to form from 2 to 4 different tautomeric forms of the monocations and 2 to 6 forms of the dications. This complicates significantly the interpretation of the protonation picture.

Two to three absorption bands were observed in the electronic spectra (Table 1) irrespective of the form in solution of heterocycles **1-6**. This is characteristic of annelated systems [9,12]. The picture of the change of electronic spectra on mono- and diprotonation was unique for each compound studied. The introduction of NO_2, Br, and Cl substituents into position 6 of triazolopyrimidine **3** leads to a bathochromic shift of the absorption bands of the bases and of the protonated forms. This effect is particularly marked for the nitro derivative.

The dependence of the molar extinction coefficient ε at λ_{anal} on the acidity function H_0 for the heterocycles **1-6** has the S-shaped form typical of protolytic processes (Fig. 1). The dependence of ε on H_0 for the unsubstituted heterocycles **1-3** has a more complex character, two jumps were observed in different regions of acidity. The latter are caused by the first and second protonations of the heterocyclic base.

In the case of the nitro and halo triazolo-pyrimidines **4-6** the second protonation failed to be recorded spectrally in the practical range of acidity. This is explained by the electron-withdrawing character of the substituents.

TABLE 1. The UV Characteristics of the Free Bases of Mono- and Dications of Annelated Heterocycles **1-6**

Compound	λ^{B}_{max} (ε^{B}_{max})	$\lambda^{BH^+}_{max}$ ($\varepsilon^{BH^+}_{max}$)	$\lambda^{BH^{2+}}_{max}$ ($\varepsilon^{BH^{2+}}_{max}$)
1	225 (42000), H_2SO_4 (pH 1)	230 (31000), 291 (3730), 56.9% H_2SO_4 (H_0 -4.15)	228 (38000), 95.7% H_2SO_4 (H_0 -9.90)
2	207 (16200), 260 (3000), 310 (2000), H_2SO_4 (pH 1)	~200 (~15000), 253 (3800), 393 (300), 64.5% H_2SO_4 (H_0 -5.05)	250 (6300), 95.7% H_2SO_4 (H_0 -9.90)
3	~200 (~15000), 272 (3750), ethanol (pH 7)	~200 (~15000), 258 (4100), 64.5% H_2SO_4 (H_0 -5.05)	270 (6200), 110% oleum (H_0 -13.03)
4	240 (3750), 345 (4900), buffer solution H_3PO_4 (pH 2.26)	223 (10300), 73.33% H_2SO_4 (H_0 -6.31)	
5	218 (31000), 290 (4000), buffer solution H_3PO_4 (pH 2.26)	215 (27000), 50.75% H_2SO_4 (H_0 -3.45)	
6	215 (14000), 290 (1200), buffer solution H_3PO_4 (pH 2.26)	210 (11600), 73.33% H_2SO_4 (H_0 -6.31)	

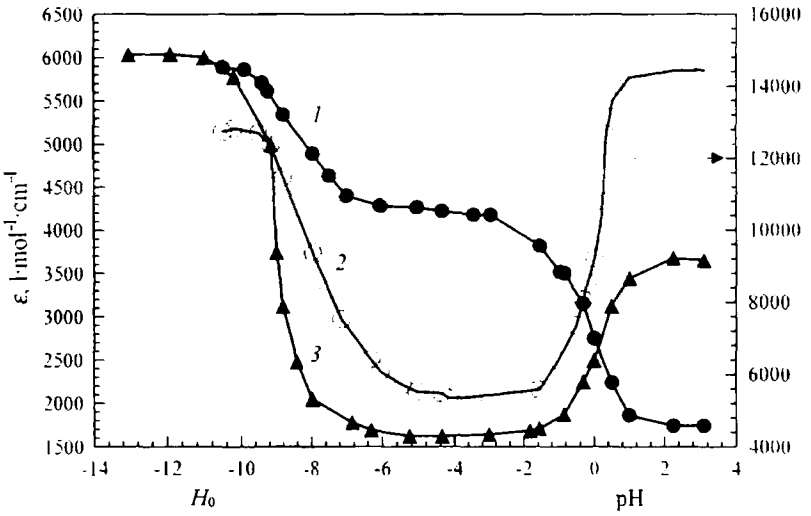


Fig. 1. Dependence of the molar extinction coefficient of compounds on the acidity of the medium: compound **1** is on curve 1; compound **3** on curve 2; compound **4** on curve 3.

The values of pK_{BH^+} and $pK_{BH^{2+}}$, obtained from the dependence of ε on pH or H_0 at analytical wavelengths (Table 2), were calculated by the Yates–McClelland method [13]. All the heterocycles investigated are weak bases. Annelation reduces significantly the basicity of both the azine and the azole rings of the condensed system (pK_{BH^+} of pyrimidine, pyrazole, and 1,2,4-triazole is 2.48, 1.23, and 2.45 [9,14] respectively), which does not contradict known data [14-16].

The difference between the first and second protonation constants of the unsubstituted pyrazolopyrimidine (**1**), triazolotriazine (**2**), and triazolopyrimidine (**3**) is very large and is 8-9 orders of magnitude. We note that a similar picture was also reported previously for unannelated azines [17].

It is interesting to evaluate the influence of the number of nitrogen atoms in the condensed system on the basicity of the azoloazines. As is seen from Table 2 the values of the basicity constants of heterocycles **1-3** differ insignificantly among themselves. Consequently the increase in the number of nitrogen atoms in the system does not show up in its basicity.

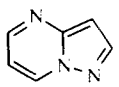
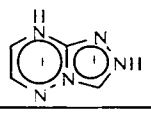
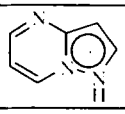
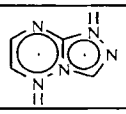
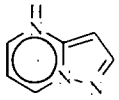
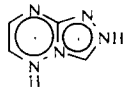
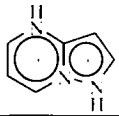
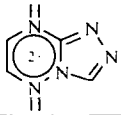
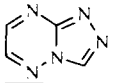
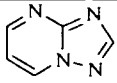
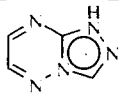
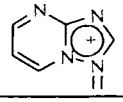
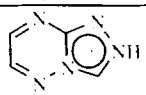
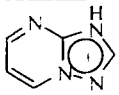
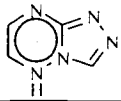
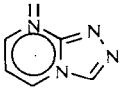
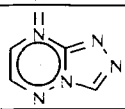
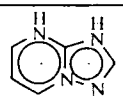
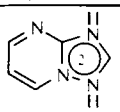
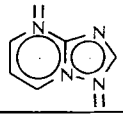
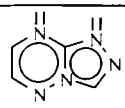
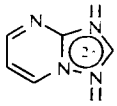
The effect of the substituent in position 6 of the triazolopyrimidines **3-6** on basicity (Table 2) is significantly less than in the case of the unannelated heterocycles [9,14,18]. We were failed to develop any correlation relationships between the values of the basicity constants (pK_{BH^+}) and the electronic constants of substituents. For example, the correlation coefficient r for the relationship of pK_{BH^+} and σ did not exceed 0.85.

TABLE 2. Basicity Constants (pK_{BH^+}, $pK_{BH^{2+}}$) for Compounds **1-6***

Compound	First protonation				Second protonation			
	pK_{BH^+}	$x(m)$	r	n	$pK_{BH^{2+}}$	$x(m)$	r	n
1	0.03±0.02	0.81±0.02	0.98	5	-7.87±0.30	0.55±0.1	0.98	5
2	-0.04±0.02	0.99±0.03	0.97	6	-8.00±0.10	1.1±0.2	0.99	5
3	0.21±0.03	0.84±0.02	0.98	5	-9.00±0.09	1.13±0.1	0.99	6
4	-1.52±0.04	0.66±0.07	0.99	5				
5	-0.19±0.03	0.86±0.02	0.97	6				
6	-0.85±0.05	0.94±0.04	0.97	6				

* $\lg I = -x \cdot pH + pK'_{BH^+}$, $pK_{BH^+} = pK'_{BH^+} / x$; $\lg I = -m \cdot H_0 + pK'_{BH^+}$, $pK_{BH^+} = pK'_{BH^+} / m$.

TABLE 3. Values of the Enthalpy of Formation of the Free Bases and Conjugate Acids of Heterocyclic Compounds **1-6**, Calculated by the AM1 Semi-empirical Method

No.	Compound	ΔH_f, kcal/mole	No.	Compound	ΔH_f, kcal/mole
1a		110.74	**2h**		586.22
1b		272.96	**2i**		608.81
1c		267.31	**2j**		608.47
1d		542.62	**2k**		622.55
2a		152.57	**3a**		126.54*
2b		316.33	**3b**		296.59*[2]
2c		319.10	**3c**		276.90*[3]
2d		346.11	**3d**		287.58*[4]
2e		326.04	**3e**		544.69
2f		602.78	**3f**		638.86
2g		596.36	**3g**		555.46

* For free bases of 6-substituted 1,2,4-triazolo[1,5-*a*]pyrimidines, ΔH_f, kcal/mole: **4a** – 133.99; **5a** – 132.62; **6a** – 121.47.

*[2] For 1H$^+$ cations of 6-substituted 1,2,4-triazolo[1,5-*a*]pyrimidines ΔH_f, kcal/mole: **4b** – 317.37; **5b** – 305.89; **6b** – 294.18.

*[3] For 3H$^+$ cations of 6-substituted 1,2,4-triazolo[1,5-*a*]pyrimidines ΔH_f, kcal/mole: **4c** – 297.97; **5c** – 286.32; **6c** – 274.77.

*[4] For 4H$^+$ cations of 6-substituted 1,2,4-triazolo[1,5-*a*]pyrimidines ΔH_f, kcal/mole: **4d** – 309.13; **5d** – 297.62; **6d** – 286.81.

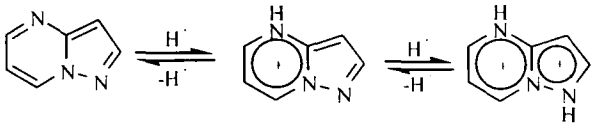
The solvation coefficients (x, m) in the Yates–McClelland equation for the heterocycles **2-6** studied in the majority of cases lie within acceptable limits, which indicates the applicability of the Hammett acidity function for describing the first and second protonation of these compounds [11,19]. The exception was pyrazolopyrimidine **1**, for which the values of the solvation coefficients for the first and especially for the second protonation were significantly less than one (Table 2). It is possible that this is connected with the change in protonation center on going over to heterocycle **1**.

The enthalpies of formation of the free bases, and also of the possible tautomeric forms of the corresponding conjugate acids, viz. the mono- and dications of heterocycles **1-6**, were calculated by us using the semiempirical AM1 method for additional interpretation of the experimental data (Table 3). Selection of the AM1 method was because of its good applicability to calculations on the thermodynamic parameters of aromatic nitrogen-containing heterocycles [20,21]. It is seen from Table 3 that the thermodynamic stability of the tautomeric forms of the conjugate acids of **1-6** differ significantly.

The results obtained enabled the most probable protonation schemes for the annelated heterocycles **1-6** to be drawn up.

Pyrazolo[1,5-*a*]pyrimidine (1). On protonating pyrazolopyrimidine **1** it is possible to form two tautomeric forms of the monocation **1b,c** (Table 3) and only one form of the dication **1d**. According to the data of Table 3, the monocation **1c** is the most stable and is more stable than form **1b** by more than 5 kcal/mole. Consequently it might be expected that the center of protonation of pyrazolopyrimidine will be the nitrogen atom of the pyrimidine portion of the molecule (Scheme 1).

Scheme 1

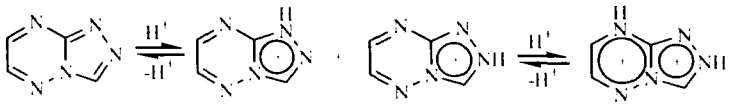


1a **1b** **1d**

As is known unannelated pyrazole (pK_{BH^+} 2.48 [14]) is more basic than pyrimidine (pK_{BH^+} 1.23 [17]), but probably annelation reduces the basicity of the pyrazole portion more significantly than that of the pyrimidine portion.

1,2,4-Triazolo[4,3-*b*]-1,2,4-triazine. Triazolotriazine **2a** has four nonequivalent basic centers. The protonation scheme of this heterocycle is fairly complex. Theoretically it is possible to form four monocations **2b-e** and six dications **2f-k** (Table 3). Thermodynamically the most stable are the monocation **2b** and the dication **2h** (Scheme 2).

Scheme 2

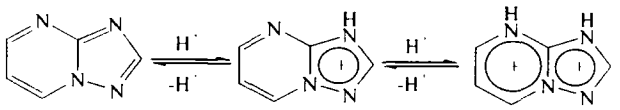


2a **2b** **2c** **2h**

In difference to pyrazolopyrimidine **1a** the first protonation of triazolotriazine **2a** is predominantly in the azole portion of the molecule. We note that the thermodynamic stability of the 1H$^+$ (**1b**) and 2H$^+$ cations (**2c**) differ insignificantly (less than 3 kcal/mole). It might be expected that both forms will be present in solution. Protonation of the azine portion is energetically 10 kcal/mole less favored. On second protonation the dications **2g** and **2h** are the most stable. Cation **2h** is more stable than cation **2g** by 10 kcal/mole, which is caused evidently by destabilization of cation **2g** by mutual repulsion of NH fragments.

1,2,4-Triazolo[1,5-*a*]pyrimidines. Protonation of triazolopyrimidines occurs predominantly at the 3 position of the heterocycle (triazole portion) with the formation of monocations **3c-6c** (Scheme 3). The cations **3b-6b** are destabilized due to the effect of a "pyrrole" type nitrogen atom at position 8. As in the case of the triazolotriazine, protonation of triazolopyrimidines at the azine portion with the formation of cations **3d-6d** is less probable. The second protonation of heterocycles **3-6** occurs in the pyrimidine portion with the formation of the dications **3e-6e**. We note that the mutual repulsion of the two NH fragments of dications **3e-6e** proves to have a less destabilizing action than one "pyrrole" nitrogen atom.

Scheme 3



3a **3c** **3e**

The presence of substituents in position 6 of the triazolopyrimidine ring is not shown in the principal protonation scheme.

In view of Schemes 1-3 values were calculated for the proton affinity in the gas phase (*PA*, *PA*$^{+}$) of the corresponding bases and monocations (Table 4).

The values of *PA* and *PA*$^{+}$ were calculated from the equation: $PA = \Delta H(H^{+}) + \Delta H_{B} - \Delta H_{BH^{+}}$, where $\Delta H(H^{+})$ = 314.9 kcal/mole (AM1), ΔH_{B}, and $\Delta H_{BH^{+}}$ are the enthalpies of formation of proton, base, and protonated form respectively [22].

As is known, good correlation dependencies were found between the values of $pK_{BH^{+}}$ and the values of *PA* for azoles and azines [15,23,24]. However, there were no similar quantitative correlations for the condensed heterocycles studied in the present work. This is due to several factors. Primarily, the protonation of annelated heterocyclic free bases and their monocations in solution may not lead to any particular form of conjugate acid but to an equilibrium mixture of tautomers. Secondly, intermolecular effects acquire a principal importance on protonation of annelated heterocycles.

The following general conclusion may be drawn from the investigations carried out. The behavior of annelated azoloazines in acid media are unique for each series of heterocycles, as was shown by us in the example of compounds **1-6**. The character of the solvation of the free bases and of the corresponding conjugate acids was different, which was expressed in the values of the solvation coefficients (x, m) [25]. The latter may be caused by the presence of different centers of protonation and diprotonation in the compounds investigated. For pyrazolopyrimidine **1** the first protonation occurs at a nitrogen atom of the azine portion, but for triazolotriazine **2** and triazolo-pyrimidines **3-6** it occurs in the azole portion. Probably the absence of generalizing rules of the "property–property" type for condensed heterocycles in difference to their unannelated analogs is caused in the same way. Evidently additional investigations are required for a final answer to the problems posed.

TABLE 4. Values of the Basicity Constants ($pK_{BH^{+}}$) and Proton Affinity in the Gas Phase (*PA*, *PA*$^{+}$, kcal/mole) Calculated for the Formation of the Most Stable Forms of the Conjugate Acids of Heterocycles **1-6**

No.	$pK_{BH^{+}}$	*PA*	*PA*$^{+}$	No.	$pK_{BH^{+}}$	*PA*	*PA*$^{+}$
1	0.3	158.34	39.58	**4**	-1.52	150.95	
2	-0.04	151.14	45.01	**5**	-0.19	161.20	
3	0.21	164.54	47.11	**6**	-0.85	161.60	

EXPERIMENTAL

The UV absorption spectra were recorded on a Perkin-Elmer Lambda 40 spectrophotometer. The concentration of sulfuric acid in aqueous solutions was determined by potentiometric titration with a precision of ±0.2 wt.%. Values of the acidity function H_0 were taken from [26]. Aqueous buffer solutions of ionic strength μ 0.01 prepared according to [27] were used when studying basicity. The model heterocycles **1**, **3-6** were synthesized and purified by known methods for pyrazolo[1,5-*a*]pyrimidine **1** [28]; triazolo[1,5-*a*]pyrimidine **3** [29]; 6-nitrotriazolo[1,5-*a*]pyrimidine **4** [30]; 6-bromo- and 6-chlorotriazolo[1,5-*a*]pyrimidines **5** and **6** [31]. The properties of the compounds obtained corresponded with literature data [28-31]. Triazolo[4,3-*b*]triazine **2** was synthesized by an improved method given in [32].

Triazolo[4,3-*b*]triazine (2). Conc. HCl (0.4 ml) was added to a solution of glyoxal (1.56 ml, 10.6 mmol) and 3,4-diamino-1,2,4-triazole hydriodide (2 g, 8.8 mmol) in water (10 ml) and the mixture was stirred at 60°C for 40 min. The solvent was distilled off in vacuum at a temperature below 60°C. The residue was treated many times with ethyl acetate. Yield 0.56 g (52%); mp 163-164°C (mp 165-166°C according to [33]). ^{1}H NMR spectrum (DMSO-d_6, 100 MHz, δ, ppm): 8.75 (2H, s, $CH_{triazine}$); 9.70 (1H, s, $CH_{triazole}$). Found, %: C 40.06; H 2.59; N 57.77. $C_4H_3N_5$. Calculated, %: C 39.67; H 2.50; N 57.83.

Calculations by the AM1 method were carried out with the MOPAC program [34].

REFERENCES

1. T. Eicher and S. Hauptmann, *The Chemistry of Heterocycles: Thieme Organic Chemistry Monograph Series*, Thieme, Stuttgart (1995).
2. A. Kleemann, J. Engel, B. Kutscher, and D. Reichert, *Pharmaceutical Substances. Version 1.0*, Thieme, Stuttgart (1999).
3. A. S. Dudyrev and V. V. Bogdanov (editors), *Promising Directions in Chemistry and Chemical Technology* [in Russian], Khimiya, Leningrad (1990).
4. A. F. Pozharskii and A. T. Soldatenkov, *Molecules–Rings* [in Russian], Khimiya, Moscow (1993).
5. M. A. Romero, J. M. Salas, M. Quiros, M. P. Sanchez, J. Molina, J. Elbahraoui, and R. Faure, *J. Mol. Struct.*, **354**, 189 (1995).
6. S. B. Sanni, J. M. M. Smits, P. T. Beurskens, J. G. Haasnoot, J. Schild, and A. T. H. Lenstra, *J. Crystallogr. Spectrosc. Res.*, **16**, 823 (1986).
7. A. R. Katritzky, M. Karelson, and N. Malhotra, *Heterocycles*, **32**, 127 (1991).
8. A. R. Katritzky, M. Karelson, and P. A. Harris, *Heterocycles*, **32**, 329 (1991).
9. A. R. Katritzky (editor), *Physical Methods in Heterocyclic Chemistry*, Academic Press, New York (1963).
10. V. I. Ivanskii, *Chemistry of Heterocyclic Compounds* [in Russian], Vysshaya Shkola, Moscow (1978).
11. V. A. Ostrovskii and G. I. Koldobskii, *Weak Organic Bases* [in Russian], Izd. Leningrad Gosudarst. Univ., Leningrad (1990).
12. R. H. Abu-Eittah, M. M. Hamed, A. Nigm, A. El-Azhary, *Int. J. Quantum Chem.*, **28**, No. 6, Part 1, 731 (1985).
13. R. E. Trifonov, N. I. Rtishchev, and V. A. Ostrovskii, *Spectrochim. Acta, Part A*, **52**, No. 14, 1878 (1996).
14. J. Catalan, J. L. M. Abboud, and J. Elguero, *Adv. Heterocycl. Chem.*, **41**, 187 (1987).
15. J. Catalan, R. M. Claramunt, J. Elguero, J. Laynez, M. Menendez, F. Anvia, J. H. Quian, M. Taagepera, and R. W. Taft, *J. Am. Chem. Soc.*, **110**, 4105 (1988).
16. J. A. Zoltewicz and L. W. Deady, *Adv. Heterocycl. Chem.*, **22**, 71 (1978).
17. T. L. Gilchrist, *Heterocyclic Chemistry*, 3rd *Edit.*, Longmans, London (1947).
18. F. Gago, J. Alvarez-Builla, and J. Elguero, *J. Chromatogr.*, **449**, No. 1, 95 (1988).
19. Yu. L. Khaldna, *Usp. Khim.*, **49**, No. 7, 1174 (1980).
20. A. A. Shaffer and S. G. Wierschke, *J. Comput. Chem.*, **14**, No. 1, 75 (1993).
21. V. K. Turchaniniov and S. V. Eroshchenko, *J. Mol. Struct. (Theochem)*, **85**, 371 (1992).

22. M. I. Kabachnik, *Usp. Khim.*, **48**, No. 9, 1523 (1979).
23. R. E. Trifonov, Author's Abstract of Dissertation for Candidate of Chemical Sciences, Saint Petersburg (1998).
24. V. A. Ostrovskii, G. B. Erusalimskii, and M. B. Shcherbinin, *Zh. Org. Khim.*, **29**, No. 7, 1297 (1993).
25. J. Catalan, M. Sanchez-Cabezudo, J. L. G. De Paz, and J. Elguero, *J. Mol. Struct. (Theochem)*, **166**, No. 2, 415 (1988).
26. R. A. Cox and K. Yates, *Can. J. Chem.*, **61**, 2225 (1983).
27. D. D. Perrin, *Austral. J. Chem.*, **16**, 572 (1963).
28. G. Mühmel, R. Hanke, and E. Breitmaier, *Synthesis*, No. 8, 673 (1982).
29. M. Kuenstlinger and E. Breitmaier, *Synthesis*, No. 1, 44 (1983).
30. V. L. Rusinov, I. Ya. Postovskii, A. Yu. Petrov, E. O. Sidorov, and Yu. A. Azev, *Khim. Geterotsikl. Soedin.*, No. 11, 1854 (1981).
31. Y. Makisumi, *Chem. Pharm. Bull.*, **9**, 808 (1961).
32. F. G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, 1221 (1972).
33. J. Daunis, H. Lopez, and G. Maury, *J. Org. Chem.*, **42**, 1018 (1977).
34. J. J. P. Stewart, *MOPAC 6.0, QCPE Program 455*, Bloomington, IN (1990).