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Acidity Constants of Some Tetrazole Compounds in Various Aqueous−Organic Solvent Media

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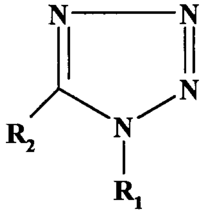
The acidity constants of some tetrazole compounds were determined pH-metrically at 25 °C and at the constant ionic strength $I = 0.1$ mol dm^{-3} (KNO_3) in pure water as well as in various aqueous mixtures having variable mole fractions (0.05−0.3) of organic solvents. The organic solvents used are methanol, ethanol, *N*,*N*-dimethylformamide, dimethyl sulfoxide, and acetone. Generally, the pK_a values increase with an increase in the content of the organic solvent. It was concluded that the major effects responsible for this behavior are, in addition to the electrostatic effect, the stabilization of the conjugate base by hydrogen-bonding interactions with solvent molecules and solvent basicity. Effect of molecular structure of tetrazoles on the pK_a values is discussed. Moreover, the thermodynamic functions (ΔH, $\Delta G°$, and $\Delta S°$) associated with the ionization process of investigated compounds in a pure aqueous medium are derived and their values are discussed.

Introduction

Tetrazole compounds have a wide range of pharmaceutical applications,[1] where they act as stimulants or sedatives on the central nervous system. These compounds have antiinflammatory, antilipemic, antimicrobial, and antiallergic activities.[2] Moreover, such compounds are useful as oxidizers and effective agents for regulating plant growth and as explosives and rocket propellants.[3] In addition, tetrazole compounds have a significant role in medicinal chemical research.[4] *N*-Unsubstituted tetrazoles are moderately strong NH acids, where pK_a values of tetrazoles lie in the range of −0.8 to about 6 depending on the electronic properties of the substituent at position 5 of the tetrazole ring.[5−8] A reliable correlation between the basicity and acidity for such compounds was established.[9−11] Nevertheless, there is no study in the literature concerning the medium effects or thermodynamic studies on the acid ionization constants of such compounds. Therefore, with continuation of our studies concerning solvent effects on the ionization processes of such biologically important compounds,[12−14] the acidity constants of 1,2,3,4-tetrazole (**I**), 5-amino-1,2,3,4-tetrazole (**II**), and 5-mercapto-1-methyltetrazole (**III**) have been determined pH-metrically at 25 °C and at the constant ionic strength $I = 0.1$ mol dm^{-3} (KNO_3) in aqueous solutions containing varying mole fractions (0.05−0.30) of organic solvents with different properties.



I $R_1 = R_2 = H$

II $R_1 = H, R_2 = NH_2$

III $R_1 = CH_3, R_2 = SH$

The organic media used are amphiprotic (methanol and ethanol), dipolar aprotic [*N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO)], and low basic aprotic (acetone) solvents. The acid ionization constants are explained in relation to both the proportion and nature of the organic solvent. The effect of the molecular structure of the compounds on the pK_a values is also discussed. Further, the changes in thermodynamic functions (ΔH, $\Delta G°$, and $\Delta S°$) associated with the ionization processes of the subjected compounds in a pure aqueous medium have been determined and discussed.

Experimental Section

Materials and Solutions. The tetrazole compounds used were purchased from Sigma and Aldrich. The purity for these compounds exceeds 99.5% and it was verified by the TLC method. The organic solvents used were of high purity (spectrograde products) and were distilled before use by standard methods.[15] All other chemicals were A.R. grade.

Stock solution (0.10 mol dm^{-3}) of each tetrazole compound was prepared by dissolving a known mass in the appropriate volume of CO_2-free doubly distilled water. Carbonate-free KOH solution (≈0.2 mol dm^{-3}) was prepared by dissolving the appropriate mass in CO_2-free doubly distilled water and standardized before use by a standard solution of potassium hydrogen phthalate. A stock solution of nitric acid (≈0.1 mol dm^{-3}) was prepared and used after standardization. The ionic strength (0.1 mol dm^{-3}) was maintained by using a solution of KNO_3 as a supporting electrolyte. More dilute solutions were prepared by accurate dilution.

Procedure. The following two solutions were prepared (total volume 25 cm^3) and titrated individually against the carbonate-free KOH solution: (a) HNO_3 [(8.0−10.0) × 10^{-3} mol dm^{-3})]; (b) solution (a) in the presence of 4.0 × 10^{-3} mol dm^{-3} of each tetrazole compound and containing different mole fractions (0.05−0.30) of the organic solvent used. A solution of (1.0 mol dm^{-3}) KNO_3 was used to attain

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a constant ionic strength for the two solutions. A water thermostat Fischer Scientific Isotemp Refrigerated Circulator Model 9000 (temperature uncertainity ±0.1 °C) was used to obtain the desired temperature. The titrations were carried out in an inert atmosphere where nitrogen gas was bubbled through the titrated solutions. The titration was repeated at least three times (40 points for each) at each mole fraction of a solvent.

pH measurements were performed by means of a Metrohm automatic titrator model SM 702 with a combined pH glass electrode equipped with a magnetic stirrer (Switzerland). The accuracy of the instrument was ±0.001 pH unit. The instrument was calibrated using aqueous standard buffers of pH 4.00 (phthalate buffer) and 9.20 (borate buffer). Because the ionic strength of the test solution is constant, the hydrogen ion activity can be expressed in terms of concentration. So the electrode system was calibrated in an aqueous medium in terms of hydrogen ion concentration instead of activities.[16] This calibration was required for the calculation of acidity constants in pure water. Thus, to account for the differences in acidity, basicity, relative permittivity, and ion activities for an aqueous mixture relative to pure water, the pH values in the former medium were corrected depending on the method described by Douhéret,[17] where the meter reading pH_R obtained in a partially aqueous medium differs by an amount δ from the corrected reading pH*:

$$pH^* = pH_R - \delta \tag{1}$$

Values of δ for the various proportions of each organic solvent were determined as recommended.[17]

The titration curve corresponding to solution (b) show only one inflection point denoting that only one proton is titrated. This inflection is consistent with the following acid−base equilibrium:

$$AH \Leftrightarrow A^- + H^+ \tag{2}$$

The pK_a values were determined by adopting the Irving−Rossotti technique,[18,19] which has been fully described previously,[12−14] using two different methods (the average value and linear plot methods). All calculations were performed using a computer program based on unweighted linear least-squares fits.

Results and Discussion

Medium Effects on the Acidity Constants. The mean pK_a values at 25 °C along with the error obtained by applying the least-squares fits are listed in Table 1. The previously reported[20] pK_a value for 1,2,3,4-tetrazole and pK_{a2} value for 5-amino-1,2,3,4-tetrazole in a pure aqueous medium are reproduced in this study. However, the differences in the pK_a values from those reported in the literature, using the same method, could be attributed to the different experimental conditions (temperature and ionic strength). The first acid ionization constant value (pK_{a1}) of 5-amino-1,2,3,4-tetrazole is very low (1.76);[20] therefore, it could not be determined under the experimental conditions used in this study. Moreover, the pK_a value for 5-mercapto-1-methyltetrazole is reported for the first time.

The data cited in Table 1 clearly reveal that both the proportion and the nature of the organic solvent have a conspicuous influence on the acid ionization constant values of the studied compounds. Generally, increasing the mole fraction of the organic solvent in the medium leads to a decrease in the acid ionization constant for each compound.

Table 1. Mean pK_a Values for Tetrazole Compounds (I−III)[a] in Different Water (1) + Organic Solvent (2) Media at 25 °C and at the Constant Ionic Strength I = 0.1 mol dm^{-3} (KNO_3)

			pK_a values[a]		
x_2[b]	$(\epsilon_r)_m$	$\{1/(\epsilon_r)_m\}\ 10^2$	**I**	**II**	**III**
0.00	78.40	1.28	4.70 ± 0.03 (4.90)[19]	5.95 ± 0.02 (6.07)[19]	3.28 ± 0.04
			Methanol		
0.05	76.11	1.31	4.72 ± 0.02	5.98 ± 0.02	3.30 ± 0.03
0.10	73.82	1.36	4.72 ± 0.02	6.05 ± 0.03	3.34 ± 0.02
0.15	71.53	1.40	4.74 ± 0.01	6.11 ± 0.01	3.38 ± 0.05
0.20	69.24	1.44	4.80 ± 0.02	6.15 ± 0.03	3.47 ± 0.03
0.25	66.95	1.49	4.83 ± 0.03	6.19 ± 0.02	3.55 ± 0.03
0.30	64.66	1.55	4.90 ± 0.04	6.32 ± 0.04	3.61 ± 0.04
			Ethanol		
0.05	75.69	1.32	4.74 ± 0.02	6.00 ± 0.02	3.33 ± 0.02
0.10	72.99	1.37	4.76 ± 0.04	6.08 ± 0.02	3.40 ± 0.01
0.15	70.29	1.42	4.80 ± 0.03	6.13 ± 0.03	3.47 ± 0.03
0.20	67.58	1.48	4.85 ± 0.03	6.21 ± 0.02	3.52 ± 0.05
0.25	64.88	1.54	4.89 ± 0.04	6.26 ± 0.04	3.58 ± 0.03
0.30	62.17	1.61	4.92 ± 0.06	6.38 ± 0.03	3.66 ± 0.02
			DMSO		
0.05	76.81	1.30	4.71± 0.04	5.96± 0.02	3.29 ± 0.02
0.10	75.22	1.33	4.73± 0.02	6.03 ± 0.03	3.33 ± 0.01
0.15	73.63	1.36	4.75 ± 0.04	6.09 ± 0.04	3.39 ± 0.04
0.20	72.04	1.39	4.79 ± 0.03	6.13 ± 0.02	3.43 ± 0.03
0.25	70.45	1.42	4.83 ± 0.04	6.16 ± 0.04	3.49 ± 0.03
0.30	68.86	1.45	4.86 ± 0.02	6.21 ± 0.03	3.53 ± 0.04
			DMF		
0.05	76.31	1.31	4.70 ± 0.02	5.95± 0.02	3.29 ± 0.05
0.10	74.23	1.35	4.72 ± 0.03	6.00 ± 0.03	3.32 ± 0.03
0.15	72.15	1.39	4.74 ± 0.04	6.08 ± 0.03	3.37 ± 0.04
0.20	70.06	1.43	4.78 ± 0.03	6.12± 0.02	3.41 ± 0.01
0.25	67.98	1.47	4.80 ± 0.02	6.16 ± 0.04	3.47 ± 0.02
0.30	65.89	1.52	4.82 ± 0.04	6.19 ± 0.03	3.49 ± 0.03
			Acetone		
0.05	75.53	1.32	4.78 ± 0.06	6.08 ± 0.03	3.34 ± 0.04
0.10	74.16	1.35	4.80 ± 0.05	6.16 ± 0.02	3.43 ± 0.03
0.15	72.04	1.39	4.84 ± 0.03	6.23 ± 0.03	3.50 ± 0.04
0.20	69.92	1.43	4.89 ± 0.06	6.28 ± 0.04	3.54 ± 0.04
0.25	67.80	1.47	4.92 ± 0.04	6.32 ± 0.03	3.63 ± 0.02
0.30	65.68	1.52	4.95 ± 0.03	6.39 ± 0.04	3.69 ± 0.05

[a] **I−III** refer to 1,2,3,4-tetrazole, 5-amino-1,2,3,4-tetrazole, and 5-mercapto-1-methyltetrazole, respectively. [b] x is the mole fraction of the solvent.

The acid ionization constant in a pure aqueous medium ($K_{a(w)}$) is related to that in a partially aqueous medium ($K_{a(s)}$) by the relation[21]

$$K_{a(w)} = K_{a(s)}(\gamma_{A^-}\gamma_{H^+}/\gamma_{HA}) \tag{3}$$

where γ is the activity coefficient of the respective species in a partially aqueous medium relative to that in pure water. The electrostatic effect resulting from the change in the relative permittivity of the medium operates on the activity coefficient of any charged species.[21] Thus, one can expect that increasing the content of the organic solvent in the medium will increase the activity coefficient of both the H^+ and conjugate base A^-. Consequently, according to eq 3, increasing the mole fraction of the organic solvent should decrease the acid ionization constant (i.e., pK_a is high). This is consistent with the results reported in Table 1. However, methanol and DMF have approximately similar relative permittivity (32.6 and 36.0, respectively)[21] so that the electrostatic effects in aqueous solutions

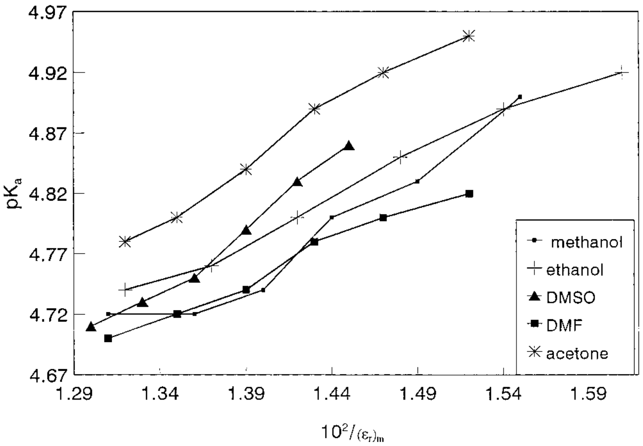

Figure 1. Variation of pK$_a$ value of 1,2,3,4-tetrazole (**I**) with $1/(\epsilon_r)_m$ of the medium in various water + organic solvent media at 25 °C and at the constant ionic strength $I = 0.10$ mol dm^{-3} (KNO$_3$).

containing the same mole fraction of these two solvents should be virtually identical. (i.e., pK$_a$ values for a compound in such solutions should be the same.) However, the data obtained indicate that all compounds are more acidic in the aqueous mixtures of DMF than in that of methanol. Also, though ethanol and acetone have comparable relative permittivity (24.3 and 20.7, respectively),[21] the ionization process of each compound is more pronounced in the presence of ethanol than in the presence of acetone, where the medium contains the same mole fraction of each. This indicates that the acid ionization constants of tetrazole compounds obtained in various aqueous mixture media, though governed by the electrostatic effect, are strongly influenced by other solvent effects. This conclusion is further substantiated by the obtained nonlinear plots of pK$_a$ values against the reciprocal of the relative permittivity $(\epsilon_r)_m$ of the medium (cf. Figure 1), according to the relationship,[22] which relates the variation of pK$_a$ values to the relative permittivity of the medium. The relative permittivity of the medium $(\epsilon_r)_m$ is obtained from the relation (cf. Table 1):

$$(\epsilon_r)_m = \epsilon_1 x_1 + \epsilon_2 x_2 \tag{4}$$

It was recognized that solvent effects such as hydrogen bonding and solvent basicity as well as dispersion forces and proton−solvent interactions exert a profound influence on the ionization process of weak acids in the presence of organic solvents.[21] The effective density of dispersion centers in each organic solvent used is higher than that in pure water.[23] Accordingly, one can expect a higher stabilization of the conjugate base A$^-$ of each compound by the dispersion forces, which are established between the delocalized oscillator dipole of the conjugate base and the localized oscillator dipole of the solvent. Furthermore, the proton is expected to be highly stabilized in aqueous mixtures by its interaction with organic solvent and water molecules (proton−solvent interaction) compared with water molecules alone in pure water.[23] Consequently, both A$^-$ and H$^+$ will be highly stabilized upon increasing of the mole fraction of the organic solvent in the aqueous medium; that is, γ_{A^-} and γ_{H^+} are decreased. Thus, in the light of eq 3, the acid ionization constant of the studied tetrazoles would increase (pK$_a$ decreases) with increasing organic solvent content in the medium. However, this is not the case, as is evident from the data cited in Table 1. Therefore, one can conclude that both the dispersion forces and proton−solvent interaction effects do not have a significant role in the ionization process of the studied tetrazole compounds.

On the other hand, water molecules are characterized by a high tendency to donate hydrogen bonds compared with other solvent molecules.[24] Therefore, the conjugate base A$^-$ is expected to be less stabilized by hydrogen-bonding interaction with solvent molecules as the mole fraction of an organic solvent is increased (i.e., γ_{A^-} increases). This will tend to increase the pK$_a$ values of all compounds as eq 3 implies. Accordingly, the observed increase in the pK$_a$ values of the compounds upon increasing mole fraction of the solvents in aqueous mixtures can be ascribed, in addition to the electrostatic effect, to the hydrogen-bonding interaction between the conjugate base A$^-$ and the organic solvent molecules.

The results given in Table 1 indicate that the variation of pK$_a$ values in the media containing the same mole fraction of alcohol or acetone appears to be in the order methanol < ethanol < acetone. This is presumably due to the decrease in the tendency of the solvent to develop a hydrogen bond to the ionic form A$^-$ upon going from methanol to acetone.[23] This was deduced from the fact that acetone is characterized by a very weak tendency to develop hydrogen bonds to a solute than alcohols.[21,24,25] Further, the tendency of alcohol to associate with solutes through hydrogen bond decreases with an increase in the molecular weight of alcohol.[25] Moreover, acetone is considered to be a very weak basic solvent compared with ethanol or methanol.[21,26] Therefore, the stabilization of the proton, by developing a hydrogen bond from solvent molecule to the hydrogen, will tend to decrease upon increasing of the mole fraction of acetone in the medium. Accordingly, the activity coefficient of H$^+$ is increased, that is, a high pK$_a$ value. This behavior emphasizes that the differences in stabilization of the conjugate base A$^-$ and hydrogen ion H$^+$ by a hydrogen bond play a vital role in the ionization process of the compounds studied. On the other hand, methanol, ethanol, and acetone are characterized by low basicity compared to water;[21] therefore, the proton becomes less stabilized in the presence of these solvents in the aqueous medium. Thus, increasing the mole fractions of these solvents in the medium will result in an increase in the activity coefficient of the proton, thereby causing a decrease in the ionization constant (i.e., a high pK$_a$ value) as indicated by eq 3. Accordingly, one can suggest that changing the medium basicity, by increasing the mole fraction of methanol, ethanol, or acetone, is an additional factor affecting the ionization process of the investigated compounds in aqueous mixtures of these organic solvents.

However, the results reported in Table 1 reveal that the acidity ionization process of the subjected compounds is more pronounced in the media containing the poorer hydrogen bond donor solvents DMF and DMSO than in the media of other solvents, where the mole fraction of the solvents is the same. This behavior can be ascribed to the high basic character of DMF and DMSO compared to other solvents; that is, both DMF and DMSO solvents have higher hydrogen bond accepting abilities. This is expected to lead to the construction of a stronger hydrogen bond acceptor from the un-ionized solute (AH) by which the ionization is promoted (i.e., low pK$_a$ value).

Therefore, one can conclude that the hydrogen-bonding interaction and the change in the basicity of the medium, in addition to the electrostatic effect, have a profound effect on the ionization process of the studied compounds in aqueous mixtures of methanol, ethanol, acetone, DMF, and DMSO.

Table 2. Thermodynamic Functions Associated with the Ionization Process of Tetrazole Compounds (I−III) in a Pure Aqueous Medium at the Constant Ionic Strength $I = 0.10$ mol dm^{-3} (KNO_3)

	pK_a values/°C					ΔH	$\Delta G^{\circ\,b}$	$\Delta S^{\circ\,b}$
compd^a	5	15	25	35	45	kJ mol^{-1}	kJ mol^{-1}	J mol^{-1} K^{-1}
I	4.92	4.78	4.70	4.64	4.57	14.32	26.81	−41.91
II	6.12	6.02	5.95	5.84	5.74	15.89	33.94	−60.57
III	3.43	3.36	3.28	3.20	3.14	12.54	18.71	−20.70

[a] **I**−**III** refer to 1,2,3,4-tetrazole, 5-amino-1,2,3,4-tetrazole, and 5-mercapto-1-methyltetrazole, respectively. [b] Values calculated at 25 °C.

Effect of Molecular Structure on the Acidity Constant. The pK_a values reported in Table 1 for studied tetrazole compounds in different media reveal the lower acidity of 5-amino-1,2,3,4-tetrazole (compound **II**). The lower acidity of this compound can be attributed to the high electron density at the aromatic system as a result of the electron donor character of the substituent amino group, therefore, stronger bonding of the proton to the heterocyclic nitrogen atom, affording a lower acidity constant for this compound. On the other hand, the data in Table 1 indicate high acidity of 5-mercapto-1-methyltetrazole (compound **III**). The obtained pK_a value (3.28) for this compound in an aqueous medium runs in the magnitude of pK_a values (3.04−3.12) that are published[6] for 1-phenyl-5-mercaptotetrazole and some 1-aryl-5-mercaptotetrazoles having a similar ring structure. It was reported that 1-phenyl-5-mercaptotetrazole exists mainly in the thione structure.[2,6,27] Therefore, this suggests the capability of 5-mercapto-1-methyltetrazole (compound **III**) being in the thione structure having the electron-withdrawing C=S group, which decreases the electron density on the tetrazole ring. Consequently, the bond between the hydrogen atom and the heterocyclic nitrogen atom is weakened, leading to easier ionization, that is, a low pK_a value. This can be substantiated by the low value of ΔH for compound **III** (12.54 kJ mol^{-1}), indicating the ionization of this compound requires a small amount of energy relative to other compounds **II** and **I** (cf. Table 2).

Thermodynamic Parameters of the Ionization Process. The thermodynamic parameters (ΔH, ΔG°, and ΔS°) associated with the ionization process are estimated. For this purpose, the acidity constants (K_a) in a pure aqueous medium at the constant ionic strength $I = 0.1$ mol dm^{-3} KNO_3 within the temperature range 5−45 °C were determined. According to the van't Hoff relationship, by plotting log K_a at different temperatures vs $1/T$ (Figure 2) and equating the gradient with $-\Delta H/19.15$, the values of the enthalpy change (ΔH) was determined. The standard free energy (ΔG°) and entropy (ΔS°) changes are also calculated at 25 °C. The pK_a values along with the thermodynamic functions are collected in Table 2. The results in this table indicate that the acid ionization constant values increase as the temperature is increased. This is consistent with the endothermic nature of the ionization process. The obtained pK_a and therefore ΔG° values of the investigated compounds increase in the order **II** > **I** > **III**. This is in agreement with the higher tendency of the ionization of **III** compared with those of other compounds. The value of enthalpy change ΔH connected to the acid ionization process for the subjected compounds runs in the same above sequence, that is, **II** > **I** > **III**. This behavior reveals that the ionization of compound **II** requires a relatively great amount of energy relative to that of compound **I** or **III**. The negative sign of ΔS° values for all compounds is taken as a criterion for the presence of intermolecular hydrogen bonding in aqueous media[28] resulting from the greater degree of orientation of water molecules in an aqueous medium on ionization. This indicates that hydrogen bonds formed between tetrazole compounds and solvent have a profound effect on the ionization process in aqueous media. This substantiates the conclusion that hydrogen-bonding interaction plays an important role in the ionization process of such compounds.

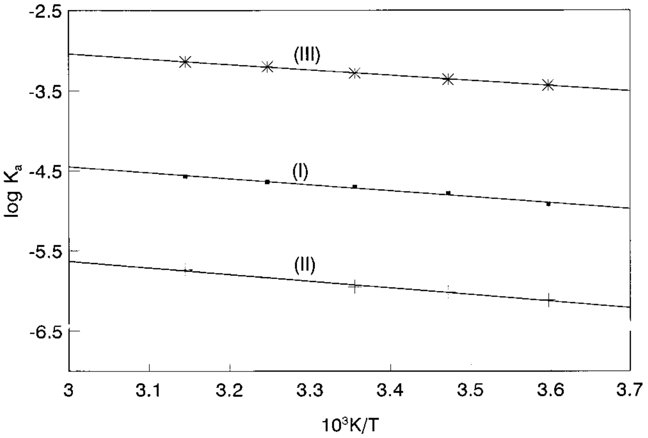

Figure 2. Plots of log K_a values against $1/T$ for the studied compounds 1,2,3,4-tetrazole (**I**), 5-amino-1,2,3,4-tetrazole (**II**), and 5-mercapto-1-methyltetrazole (**III**) in a pure aqueous medium and at the constant ionic strength $I = 0.10$ mol dm^{-3} (KNO_3).

Literature Cited

(1) Gilchrist, T. L. *Heterocyclic Chemistry*, 2nd ed.; John Wiley & Sons: New York, 1992.

(2) Katritzky, A. R.; Rees, C. W. *Comprehensive Heterocyclic Chemistry*; Pergamon Press: Oxford, 1984.

(3) John, E. O.; Kirchmeier, R. L.; Shreeve, J. M. Reactions of 5-(Perfluoro-alkyl)tetrazolates with Cyanogen, Nitrosyl, and Cyanuric Chlorides. *Inorg. Chem.* **1989**, *28*, 4629−4633.

(4) Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V. *Comperhensive Heterocyclic Chemistry II*; Pergamon Press: Oxford, 1996.

(5) Ruelke, H.; Friedel, A.; Martin, E.; Kottke, K.; Graefe, I.; Kuehmstedt, H. Studies Concerning the Acidity and the Distribution Behavior of 1-Phenyl-5-mercaptotetrazole *Pharmazie* **1991**, *46*, 456−457.

(6) Ostrovskii, V. A.; Poplavskii, V. S.; Shcherbinin, M. B. Acid−Base Properties and the Structure of the 5-(-Dimethylaminoethyl)-tetrazole. *Russ. J. Org. Chem.* **1969**, *34*, 870−875.

(7) Ostrovskii, V. A.; Koren, A. O. Alkylation and Related Electrophilic Reactions at Endocyclic Nitrogen Atoms in the Chemistry of Tetrazoles. *Heterocycles* **2000**, *53*, 1421−1448.

(8) Ostrovskii, V. A.; Koldobskii, G. I.; Shirokova, N. P.; Poplavskii, V. S. Tetrazoles. 9. Acid−Base Properties of 5-Substituted Tetrazoles. *Khim. Geterotsikl. Soedin.* **1981**, 559−562. Poplavskii, V. S.; Ostrovskii, V. A.; Koldobskii, G. I. Tetrazoles. 13. Protonation of Tetrazolylacetic Acids. *Khim. Geterotsikl. Soedin.* **1982**, 1421−1425.

(9) Catalan, J.; Menendez, M.; Elguero, J. On the Relationship Between Basicity and Acidity in Azoles. *Bull. Soc. Chim. Fr.* **1985**, 30−33.

(10) Catalan, J.; De Paz, J. L. G.; Yanez, M.; Elguero, J. The Azoles: A Theoretical Study. *Chem. Scr.* **1984**, *24*, 84−91.

(11) Naumenko, V. N.; Gaponik, P. N.; Ivashkevich, O. A.; Andreeva, T. N. Assessment of N-alkyl and Alkenyltetrazole Basicity. *Dokl. Akad. Nauk BSSR* **1989**, *33*, 826−829.

(12) Boraei, A. A. A. Medium Effects on the Ionization Constants of Some Quinoline Derivatives. *Monatsh. Chem.* **1994**, *125*, 869−876.

(13) Boraei, A. A. A.; Ahmed, I. T.; Hamed, M. M. A. Acid Dissociation Constants of Some Mercaptobenzazoles in Aqueous−Organic Solvent Mixtures. *J. Chem. Eng. Data* **1996**, *41*, 787−790.

(14) Boraei, A. A. A. The Acid Ionization Constants of Some Thiazolidine Compounds: Medium Effects and Thermodynamic Studies. *Phosphorus, Sulfur Silicon* **1998**, *142*, 69−81.

(15) Vogel, A. I. *Textbook of Practical Organic Chemistry*, 4th ed.; Longman: London, 1986.

(16) May, P. M.; Williams, D. R. *Computational Methods for the Determination of Formation Constants*; Plenum Press: New York, 1985.

(17) Douhéret, G. The Dissociation of Organic Compounds in Aqueous Organic Media. I. Determination of the Liquid Junction Potential and the Effect of the Medium on the Hydrogen Ion in These Systems, and the Study of the Dissociation of Some Acid−Base Couples. *Bull. Soc. Chim. Fr.* **1967**, 1412−1419. Liquid Junction Potentials and Effects in Mixed Solvents (Water-Dipolar Aprotic Solvent). Application to the Standardization of the Glass-Calomel Electrodes System in These Mixtures. Dielectric Properties of These Mixtures. *Bull. Soc. Chim. Fr.* **1968**, 3122−3131.

(18) Irving, H.; Rossotti, H. S. Methods for Computing Successive Stability Constants from Experimental Formation Curves. *J. Chem. Soc.* **1953**, 3397−3405. Irving, H.; Rossotti, H. S. The Calculation of Formation Curves of Metal Complexes from pH-Titration Curves in Mixed Solvents. *J. Chem. Soc.* **1954**, 2904−2910.

(19) Rossotti, H. S. *The Study of Ionic Equilibria. An Introduction*; Longman: London, 1978; Chapter 1.

(20) Dean, J. A. *Lange's Handbook of Chemistry*, 14th ed.; McGraw-Hill: New York, 1992.

(21) Coetzee, J. F.; Ritchie, C. D. *Solute−Solvent Interaction*; Marcel Dekker Ltd.: New York, 1969.

(22) Denison, J. T.; Ramsey, J. B. The Free Energy and Entropy of Dissociation of Some Perchlorates in Ethylene Chloride and Ethylidene Chloride. *J. Am. Chem. Soc.* **1955**, *77*, 2615−2621.

(23) Mahmoud, M. R.; Abdel-Hamid, R.; Idriss, K. A. Medium Effect on the Ionization Constants of Some Hydroxy Derivatives of 1-Ethyl-2-Styryl-pyridinium and -Quinolinium Iodides. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 574−578.

(24) Franks, F.; Ives, D. J. G. Structural Properties of Alcohols-Water Mixtures. *Q. Rev.* **1966**, *20*, 1−44.

(25) Alfenaar, M.; De Ligny, C. L. Activity Coefficients of Individual Ions. *Rec. Trav. Chim. Pays-Bas* **1967**, *86*, 929−951.

(26) Huheey, J. E. *Inorganic Chemistry: Principles of Structure and Reactivity*, 3rd ed.; Harber & Row: New York, 1983.

(27) Lieber, E.; Ramachandran, J. Isomeric 5-(Substituted)aminothia-Triazole and 1-Substituted-Tetrazolinethiones. *Can. J. Chem.* **1959**, *37*, 101−109. Brzerinski, B.; Grech, E.; Malaiski, Z.; Soberyk, L. Tautomerism of 1-Methyltetrazolylthion. *Pol. J. Chem.* **1994**, *68* (2), 261−267.

(28) Masoud, M. S.; Abou Ali, S. A.; Ali, G. Y.; El-Dessouky, M. A. Substituent Effects on the Dissociation Constants and the Strength of the Hydrogen Bond in Some Azo Cresol Componds. *J. Chem. Eng. Data* **1983**, *28*, 297−300.

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