

The potentiometric and spectrophotometric determination of dissociation constants for some 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives¹

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Abstract

In order to establish the dissociation constants of organic compounds, the spectrophotometric and potentiometric methods are the most precise and useful ones. Comparing the results, we used both methods for three derivatives of 2-mercapto-5-*R*-amino-1,3,4-thiadiazole. For the pK_a determination by the spectrophotometric method we measured the ratio between the concentration of dissociated and undissociated forms. The ratio was calculated from spectral data. The potentiometric method for pK_a consists of measuring the pH values within a potentiometric titration with 0.1 M NaOH. The results proved a very low acid character of the derivatives. The pK_a values were influenced by the properties of the amino group substituents, and the results confirm the theoretical considerations. The study confirms the thion-thiolic tautometry of the 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives and their property of being ligands for the coordination of the cations of some representative and transitional metals, with application in the preconcentration, in the detection and the quantitative determination of polluting and toxic cations in environmental analysis. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

The 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives (which are the products from the cyclization of derivatives of bistiourea) have been

subject to extensive research for more than 4 decades, within the Department of Analytical Chemistry of the Faculty of Pharmacy in Cluj-Napoca. The derivatives were used as analytical reagents for preconcentration, separation, detection and quantitative determination of some representative and transitional heavy metals such as Pb^{2+} , Hg^{2+} , Cd^{2+} , Ag^+ , Cu^{2+} , Bi^{3+} , Co^{2+} , Ni^{2+} [1–3].

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In order to determine precisely the structure and the properties of the reactives studied, to evaluate the low acid character of these compounds and to evidentiate the thion-thiolic tautometry in solution in some experimental conditions, this paper proposed to determinate the dissociation constants, the pK_a values, respectively. By means of these determinations it is possible to explain the property of ligand for mercapto-5 *R*-amino-1,3,4-thiadiazole derivatives in the coordination of the above mentioned cations.

The thion-thiolic tautometry of these derivatives in hydroalcoholic solutions, according to the pH of the environment, can be represented as following (Fig. 1).

The thion-thiolic tautometry was studied by UV spectrometry methods, by enthalpic titration and, in this study by the potentiometric and spectrophotometric determination of the pK_a .

2. The enthalpic titration

The enthalpic titration was carried out with a solution of 0.1 M NaOH, using our own installation. The enthalpic constant Q of the titration cell (a Dewar container), was calculated, according to the reaction:

$$Q = N_m \frac{\Delta H}{\Delta T_Q} = 0.34205 \text{ Kcal/}^\circ\text{C}$$

Q , the enthalpimetric constant of the cell;

N_m , the number of the moles of the product of reaction formed;

ΔT_Q , the total temperature variation at the neutralization of 250 ml 0.01 M HCl with 1 M NaOH;

$\Delta H = \Delta H^0$, 13.4 Kcal mol⁻¹.

The 2-mercapto-5 *R*-amino-1,3,4-thiadiazole derivatives are organic compounds with a low acid character, which dissociate in only one level. In Fig. 2 the enthalpimetric titration curve of 2 MATD (a hydroalcoholic solution 50%) with a solution of 0.1 M NaOH is presented. As we can observe, the inclination of the curve changes at only one point, which corresponds to the neutralisation of the -SH group in the reactives.

In order to eliminate the secondary thermic

effects, due to mixing two ligands with apparently different temperatures, and also due to the mixing in itself, were passed from rectangular coordinates to oblique ones. Transformation equations were used that led to a titration curve which shows only the thermic effect due to the neutralisation reaction. Within this context we also calculated the heat of neutralisation.

The equation of transformation of experimental data in oblique coordinates and the relation for calculating the heat of neutralisation are as follows:

$X = x\sqrt{1-p^2}$ where, X and Y are oblique coordinates, x and y are rectangular coordinates

$Y = y - px$ where p is the inclination of the last point of the curve, ΔH is the neutralization heat of the sample of reactive

$\Delta H = \frac{Q}{N_m} \cdot \Delta T$ where ΔT is the temperature variation during the titration, Q and N have above mentioned significance

The very low acid character of the 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives was evidenced by the ionisation of the thiolic group at the dilution of reactives in alkaline hydroxides, when the equilibrium moves towards the enolised form. As a consequence, the derivatives in our study behave like very weak acids. In order to prove this characteristic, the dissociation constant, and the pK_a values were determined by means of potentiometric and spectrophotometric methods, respectively [4–9].

3. The potentiometric determination of dissociation constants for the 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives

Even though the reactives taken into consideration are very weak acids, they can be potentiometrically treated with a titrated solution of NaOH. The reaction of potentiometric titration is the following (Fig. 3).

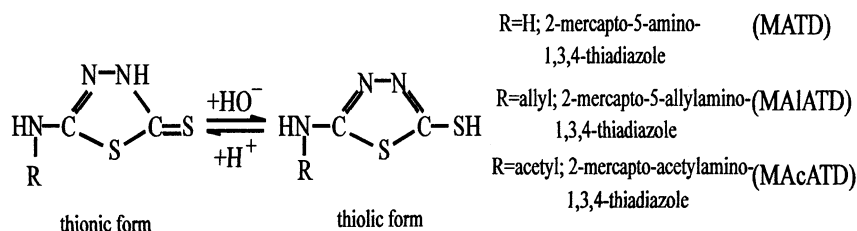


Fig. 1. The thion-thiolic tautomerism of 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives.

The pK_a values were calculated according to the relation:

$$pK_a = \text{pH}_{1/2} + \log \frac{[\text{HA}]}{[\text{NaOH}]} - \log f_{\text{HA}}$$

$\text{pH}_{1/2}$ is the pH of the solution at the inflexion point of the titration curve, [HA] represents the molar concentration of the reactive, [NaOH] is the molar concentration of NaOH and f_{HA} the coefficient of activity

3.1. Material and method

We worked with a Chemcadet pH-meter. The solutions of reactives with a well known titre in

concentrations 0.5×10^{-2} ; 10^{-2} and 2×10^{-2} M were titrated with 0.1 M NaOH in the presence of a constant ionic strength realised with a solution of 0.1 M KNO_3 .

Fig. 4 presents this titration curve and the second derivative for potentiometric titration of MATD with 0.1 M NaOH and Table 1 presents the experimental data, and the pK_a values obtained, respectively.

The value of the $\text{pH}_{1/2}$ can be graphically determined; it is the value corresponding to the inflexion point of the curve. The value of the $\text{pH}_{1/2}$ was also calculated by the Hoesteller and Roberts method, and corresponds to the inflexion point of the curve.

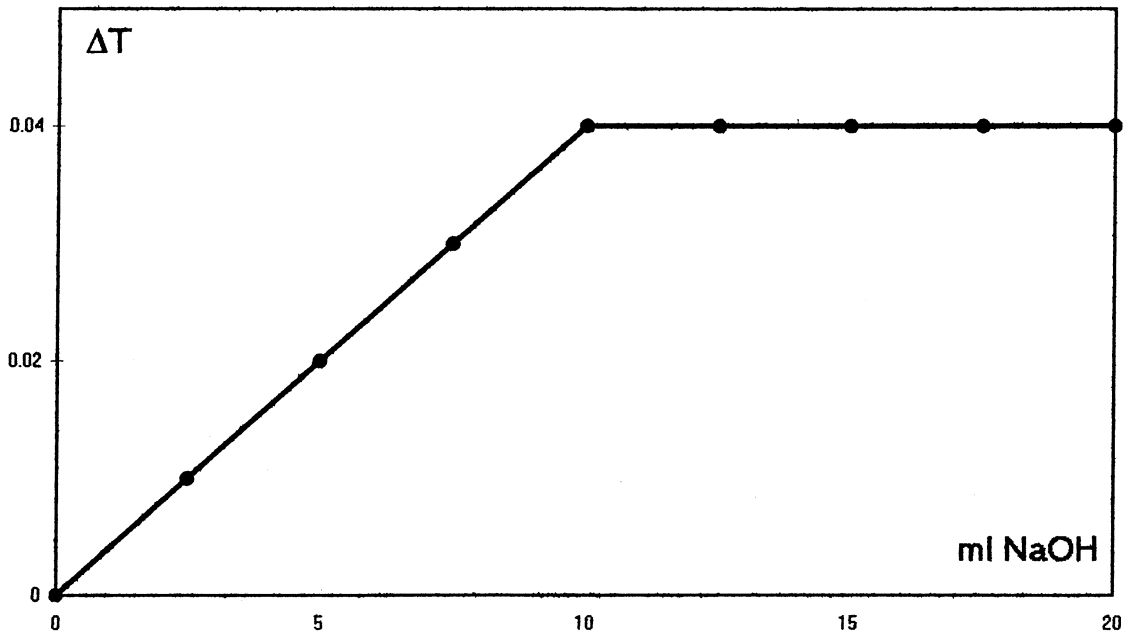


Fig. 2. The enthalpimetric titration curve of 30 ml $3 \cdot 10^{-2}$ M MATD with a solution of 10^{-1} M NaOH.

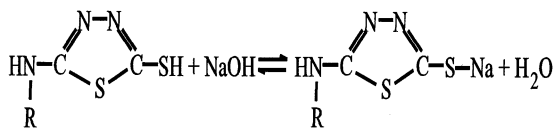


Fig. 3. The reaction of potentiometric titration of 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives with NaOH.

4. The spectrophotometric determination of the dissociation constants of 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives

In parallel, we determined by the spectrophotometric method the pK_a values of the reactives taken into consideration, since the optical density of the solutions changes according to the pH. In order to assess the pK_a we have to determine the ratio between the concentrations of the dissociated and nondissociated forms at certain pH values; this ratio is calculated from spectral data. We calculated the pK_a using the relation:

$$pK_a = \text{pH} - \log f - \log \frac{\varepsilon - \varepsilon_A}{\varepsilon_B - \varepsilon}$$

where ε_A is the molar absorbance of the dissociated reactive in an acid environment; ε_B , the molar absorbance of the anion A^- in a basic environment; ε , the molar absorbance of the mixture ($HA + A^-$) at an intermediary pH values and f , the coefficient of activity of the anion A^- of the reactive in solution.

4.1. Materials and methods

We used an Ultrospec III UV-VIS spectrophotometer (Pharmacia LKB, UK) that registered the values of the absorbance in the range 260–360 nm. In order to provide acid environment ($\text{pH} \approx 1.5$) we used 0.1 M HCl; for the basic environment we used 0.1 M NaOH ($\text{pH} \approx 12$) and for the intermediary one we used a 0.05 M $\text{Na}_2\text{B}_4\text{O}_7/0.1$ M HCl buffer ($\text{pH} \approx 7.5-9.5$). The pH values were checked up with a Chemcadet pH-meter. The alcoholic solutions of the ligands had a concentration of 10^{-5} M.

For the spectrophotometric determinations of the pK_a were need to determine the ratio $\varepsilon - \varepsilon_A / \varepsilon_B - \varepsilon$ at different wavelengths in the range in which the basic and acid forms are far enough

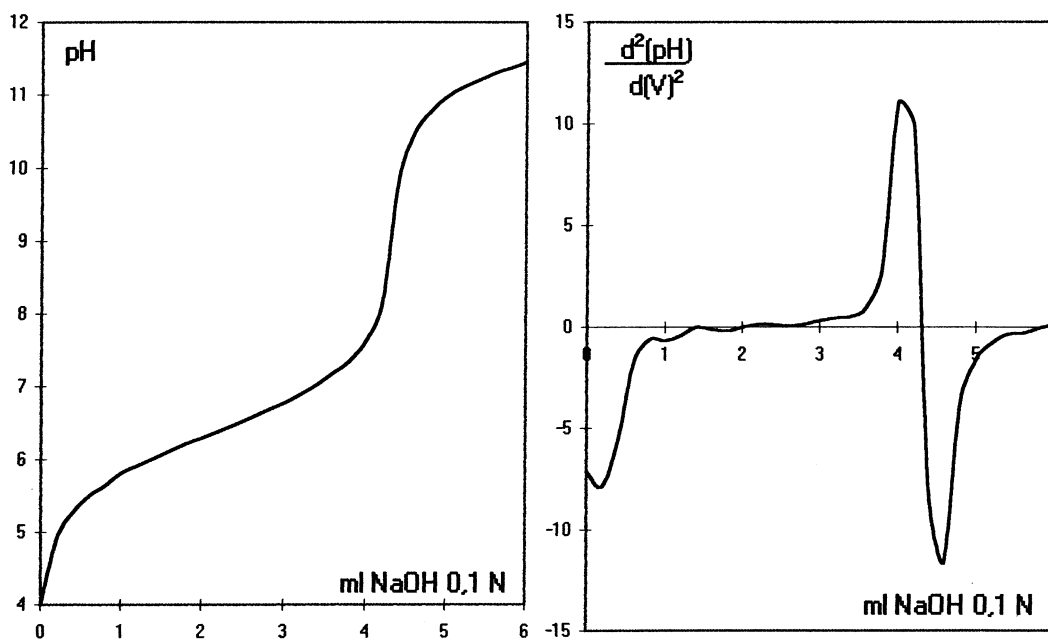


Fig. 4. The potentiometric titration curve and the second derivatives of 40 ml 10^{-2} M MATD with 10^{-1} M NaOH.

Table 1
The potentiometric determination of dissociation constants

Reactives	C_R	C_{NaOH}	$-\log C_R/C_{NaOH}$	$\log f$	pH 1/2	pK_a
MATD						
					9.49	8.945
					9.44	8.895
	2×10^{-2} M	10^{-1} M	-0.7	-0.155	9.27	8.725
					9.24	8.695
					9.22	8.675
					9.75	8.9
					9.68	8.83
	1×10^{-2} M	10^{-1} M	-1.005	-0.155	9.53	8.68
					9.82	8.97
					9.84	8.99
					10.18	9.035
					9.99	8.845
	0.5×10^{-2} M	10^{-1} M	-1.3	-0.155	9.8	8.655
					9.86	8.715
					9.95	8.805
MAIATD						
					9.32	8.77
					9.18	8.63
	2×10^{-2} M	10^{-1} M	-0.71	-0.155	9.22	8.67
					9.14	8.59
					9.08	8.53
					9.42	8.59
					9.54	8.7
	1×10^{-2} M	10^{-1} M	-0.99	-0.155	9.55	8.71
					9.78	8.95
					9.56	8.72
					9.62	8.49
					9.86	8.73
	0.5×10^{-2} M	10^{-1} M	-1.29	-0.155	9.78	8.65
					9.86	8.73
					9.68	8.55
MAcATD						
					8.98	8.425
					8.91	8.355
	2×10^{-2} M	10^{-1} M	-0.71	-0.155	8.93	8.375
					8.86	8.305
					9.035	8.48
					9.355	8.52
					9.3	8.465
	1×10^{-2} M	10^{-1} M	-0.99	-0.155	9.15	8.315
					9.32	8.485
					9.31	8.475
					9.47	8.355
					9.6	8.485
	0.5×10^{-2} M	10^{-1} M	-1.27	-0.155	9.49	8.375
					9.59	8.475
					9.53	8.415

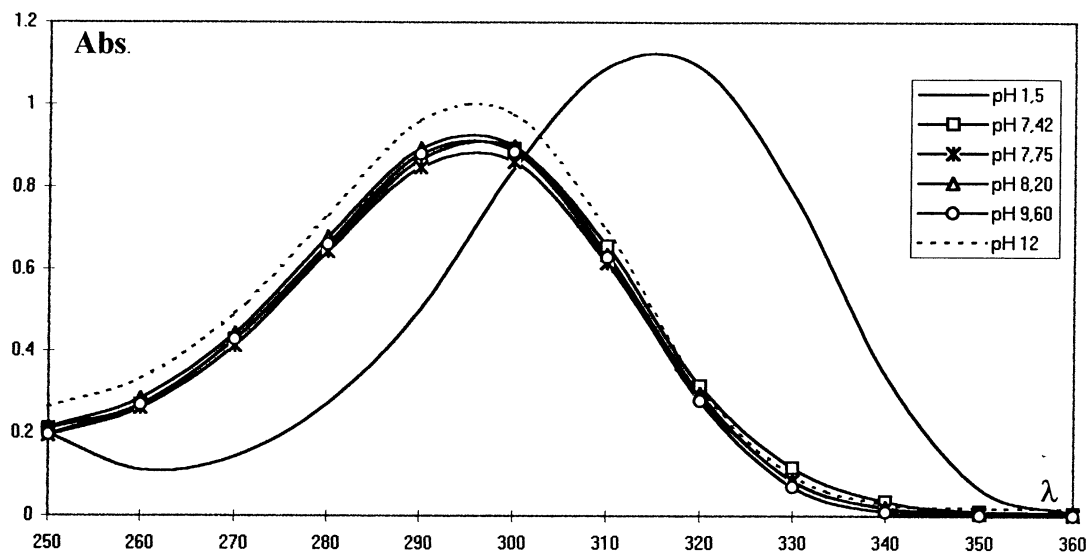


Fig. 5. The absorption curves in UV of MAIATD at the different pH values.

Table 2

The experimental data and the pK_a values calculated for MAIATD

pH	$(\epsilon - \epsilon_A)/(\epsilon_B - \epsilon)$				pK_a			
	λ	7.72	8.07	8.62	9.11	7.72	8.07	8.62
270	4.597	3.506	6.229	4.597	8.764	8.881	8.632	8.764
271	4.806	4.143	7.571	4.538	8.744	8.809	8.547	8.769
272	4.734	4.027	7.341	5.554	8.751	8.821	8.560	8.681
273	4.672	4.000	7.261	5.552	8.757	8.824	8.565	8.682
274	3.618	3.194	5.524	4.203	8.868	8.922	8.684	8.803
275	4.325	3.767	10.389	5.119	8.790	8.850	8.409	8.717
276	6.482	4.986	8.311	7.551	8.614	8.728	8.506	8.548
277	4.378	3.793	6.875	5.582	8.785	8.847	8.589	8.679
278	5.141	3.688	6.927	5.141	8.715	8.859	8.585	8.715
279	5.135	3.830	6.828	5.486	8.715	8.843	8.592	8.687
280	4.872	4.264	7.808	5.543	8.738	8.796	8.534	8.682
281	4.639	4.143	7.509	5.783	8.760	8.809	8.550	8.664
282	4.793	3.948	7.190	5.985	8.745	8.830	8.569	8.649
283	4.593	4.010	7.589	5.775	8.764	8.823	8.546	8.664
284	3.835	3.407	5.468	4.724	8.842	8.894	8.688	8.752
285	4.800	3.607	6.250	5.163	8.745	8.869	8.630	8.713
286	4.263	3.237	7.333	4.556	8.796	8.916	8.561	8.767
287	4.575	3.409	6.132	5.467	8.766	8.893	8.638	8.688
288	4.300	3.676	5.718	4.747	8.793	8.861	8.669	8.750
289	4.098	3.467	6.106	4.937	8.813	8.886	8.640	8.733
290	3.842	3.035	5.765	4.610	8.841	8.944	8.665	8.762
				pK_a	8.767	8.853	8.589	8.708
				pK_a average	8.729			

from one another (and the Lambert–Beer law is respected), in the range 275–290 nm.

Fig. 5 shows, as an example, the absorption curves in UV of MAIATD, and Table 2 shows the experimental data and the pK_a values for the same derivative. Table 3 presents the pK_a values for the derivatives of 2-mercapto-5-*R*-amino-1,3,4-thiadiazole studied; the statistic calculation confirmed the accuracy of the method, and the standard deviation was within the limits accepted by the validation norms.

5. Results and discussion

According to the experimental results the acid character of the derivatives taken into consideration increases according to the following order:



One can notice that the radicals of the amino group of the reactives modify the acid character of the whole molecule. The pK_a values for MATD and MAIATD are comparable, but MATD has a lower acid character (the unsubstitutable amino group increases the basic character). As for the MAcATD, there is a increase in the acid character and a decrease in the pK_a value, respectively. This fact can be explained by the decrease of the basic character of the amine which is substituted and by the influence of the acetyl radical which contributes to the intensification of the effect of $p-\pi$ conjugation upon the whole molecule. The increase in the acidity can be explained by the intensification of the deficit of electrodes, a fact which favours the hydrogen moving from the atom of nitrogen to the advantage of the reactions

Table 3
Comparison between spectrophotometric and potentiometric method

Reactives	Statistical parameters	Spectrophotometry				Potentiometry			
MATD	pK_a average	9.058	9.017	8.885	8.875	8.787	8.874	8.811	
	n	21	21	21	21	5	5	5	
	t	2.09	2.09	2.09	2.09	2.78	2.78	2.78	
	SD	0.045	0.045	0.077	0.080	0.124	0.125	0.146	
	$t.s.n^{-1/2}$	0.020	0.020	0.035	0.036	0.154	0.155	0.181	
	pK_a	9.058 ± 0.020	9.017 ± 0.020	8.885 ± 0.035	8.875 ± 0.036	8.787 ± 0.154	8.874 ± 0.155	8.811 ± 0.181	
		$pK_a = 8.95 \pm 0.147$ (SD = 0.09)				$pK_a = 8.824 \pm 0.111$ (SD = 0.045)			
MAIATD	pK_a average	8.766	8.852	8.588	8.708	8.638	8.734	8.630	
	n	21	21	21	21	5	5	5	
	t	2.09	2.09	2.09	2.09	2.78	2.78	2.78	
	SD	0.053	0.049	0.066	0.056	0.09	0.132	0.108	
	$t.s.n^{-1/2}$	0.024	0.022	0.030	0.025	0.112	0.163	0.133	
	pK_a	8.766 ± 0.024	8.852 ± 0.022	8.588 ± 0.030	8.708 ± 0.025	8.638 ± 0.112	8.734 ± 0.163	8.630 ± 0.133	
		$pK_a = 8.729 \pm 0.176$ (SD = 0.110)				$pK_a = 8.667 \pm 0.143$ (SD = 0.058)			
MAcATD	pK_a average	8.673	8.512	8.552	8.401	8.388	8.452	8.421	
	n	16	16	16	16	5	5	5	
	t	2.13	2.13	2.13	2.13	2.7	2.78	2.78	
	SD	0.165	0.157	0.176	0.198	0.067	0.079	0.058	
	$t.s.n^{-1/2}$	0.088	0.083	0.093	0.105	0.083	0.098	0.072	
	pK_a	8.673 ± 0.088	8.512 ± 0.083	8.552 ± 0.076	8.401 ± 0.105	8.388 ± 0.083	8.452 ± 0.098	8.421 ± 0.072	
		$pK_a = 8.535 \pm 0.178$ (SD = 0.112)				$pK_a = 8.420 \pm 0.079$ (SD = 0.032)			

that suppose the existence of a thiolic form. We notice that the differences between the pK_a values within the series of compounds used as analytic reactivities are small; we can conclude that, as the molecule is complex, the pK_a values measure the global effect, as results of all chemical interactions in the molecule. Also, due to this methods, there is new evidence that confirms the existence of the thion-thiolic tautometry, proving that in an alkaline environment, the tautomer equilibrium moves towards the thiolic form, in which the ligands participate at the formation of compounds with different metallic ions.

6. Conclusions

The reactivities studied present a thion-thiolic tautometry (keto-enolic) and behave like monoacids. By enthalpimetric titration was highlighted the thion-thiolic tautometry manifested in solution and the heat of neutralization was calculated.

The pK_a values of the 2-mercapto-5-*R*-amino-1,3,4-thiadiazole derivatives were determined by potentiometric titration and by spectrophotometry in UV.

The pK_a values determined by two methods are similar; the precision of each method is good, which is proved by the statistic calculation.

On the basis of these data we can explain more correctly the property of ligand of the derivatives of 2-mercapto-5-*R*-amino-1,3,4-thiadiazole and their usage in the preconcentration, the separation, the detection and the quantitative determination of heavy metals, with applications in the protection of the environment.

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