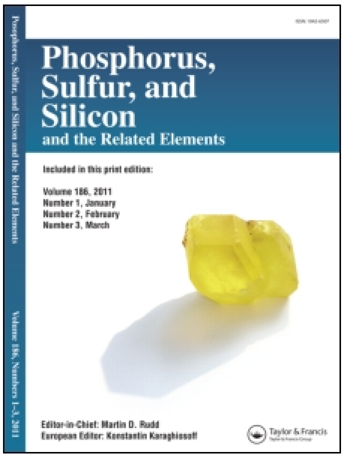

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Synthesis and Tautomeric Structure of 7-Arylhydrazono-7H-[1,2,4]Triazolo[3,4-b][1,3,4]Thiadiazines

Mosselhi A. N. Mosselhi[a]; Magda A. Abdallah[a]; Yassin F. Mohamed[a]; Ahmad S. Shawali[a]
[a] Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt

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SYNTHESIS AND TAUTOMERIC STRUCTURE OF 7-ARYLHYDRAZONO-7H-[1,2,4]TRIAZOLO[3,4-b]-[1,3,4]THIADIAZINES

Mosselhi A. N. Mosselhi, Magda A. Abdallah,
*Yassin F. Mohamed, and Ahmad S. Shawali**
Department of Chemistry, Faculty of Science,
University of Cairo, Giza, Egypt

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*Two synthetic approaches were developed for the title compounds **8a–g** via coupling of diazotized anilines with 7-acetyl-6-methyl-3-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **7**, and reaction of N-aryl 2-oxopropanehydrazonoyl chlorides **9** with 4-amino-3-mercapto-5-phenyl-1,2,4-triazole **1**. The tautomeric structures of **8** were elucidated by their spectral analyses and correlation of their acid dissociation constants with Hammett equation.*

Keywords: 1,2,4-triazole-3-thione; [1,2,4]triazolo[3,4-b][1,3,4]thiadiazines; hydrazonoyl halides; tautomerism; thiohydrazonates

INTRODUCTION

In spite of the enormous body of literature dealing with the chemistry of [1,2,4]triazolo[3,4-b]thiadiazine derivatives, nothing has been reported about the arylazo derivatives of such ring system. This is surprising in terms of the wide range of biological activities reported for various [1,2,4]triazolo[3,4-b]thiadiazine derivatives against gram negative bacteria,[1] gram positive bacteria,[2] antiinflammatory activity,[3] and the well known industrial and pharmaceutical uses of arylazo compounds. In light of these considerations, it was thought interesting to explore the synthesis of a series of the hitherto unknown 3-phenyl-6-methyl-7-arylazo-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines. In continuation of previous studies on reactions of azolethiones 2-4 (Chart 1) with hydrazonoylhalides and the synthesis of arylazo heterocycles,[4–8] we envisaged that the title compounds or their arylazo

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Address correspondence to Ahmad S. Shawali, Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt.

tautomers could be prepared directly from 5-substituted-4-amino-3-mercapto-1,2,4-triazole **1**. Herein, we report full details of two alternative convenient approaches for synthesis of the target compounds **8** and elucidation of their tautomeric structures as they can exist in one or more of the three tautomeric forms **8A–C** (Scheme 1).

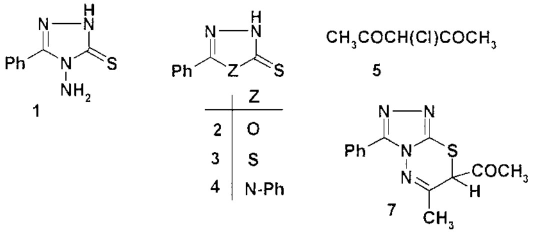
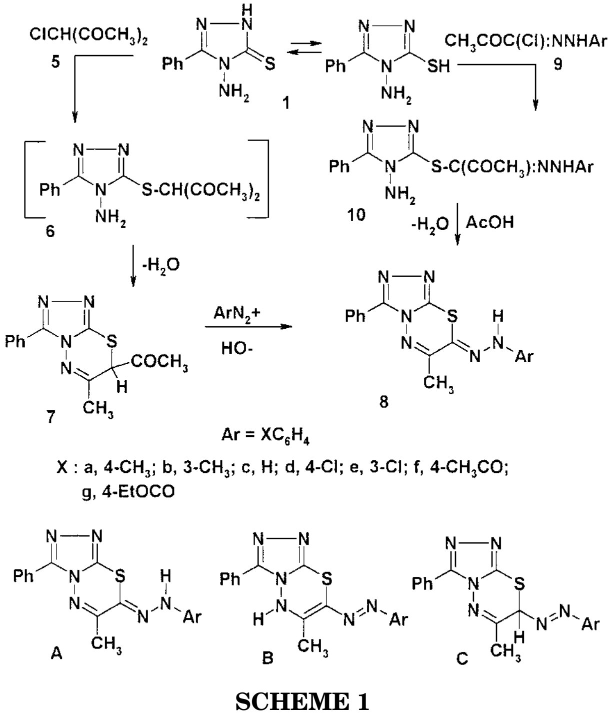


CHART 1



SCHEME 1

RESULTS AND DISCUSSION

The starting 4-amino-3-mercapto-5-phenyl-1,2,4-triazole **1** and 3-chloro-2,4-pentanedione **5** used in this study were prepared as previously described.[9,10] Treatment of **1** with 3-chloro-2,4-pentanedione **5** in ethanolic potassium hydroxide yielded 7-acetyl-6-methyl-(7H)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **7**, probably via cyclization of the initially formed substitution intermediate, namely 3-[(4-amino-5-phenyl-4H-1,2,4-triazol-3-yl)thio]-2,4-pentanedione **6** (Scheme 1). The structure of the isolated product **7** was elucidated on the basis of its spectral data (mass, IR, ^{1}H NMR) and microanalyses. For example, its PMR spectrum revealed characteristic signals at δ 2.39 (s, 3H), 2.45 (s, 3H), 4.20 (s, 1H), 7.26–8.02 (m, 5H).

Reaction of **7** with diazotized anilines in ethanol in the presence of sodium acetate, yielded products that were identified as 7-arylazo-6-methyl-3-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines **8** in overall good yields via Japp-Klingemann reaction[29] (Scheme 1). The structure of the isolated products was deducted on the basis of their spectral (MS, IR and ^{1}H NMR) and elemental analysis data in addition to their alternate synthesis outlined below. For example, their IR spectra revealed the absence of the acetyl carbonyl group and they showed NH absorption in the region 3160–3190 cm^{-1}. Also, their ^{1}H NMR spectra revealed the absence of the signal of CH_3CO protons which is present in the spectrum of **7**. Moreover they exhibit a hydrazone NH proton signal in the region δ 10.1–10.6 which is extinguished by addition of deuterium oxide (Table I).

The structure of the products **8** have been further established by their alternate synthesis. Thus, reaction of **1** with each of N-aryl 2-oxopropanehydrazonoyl chlorides **9a–g** in ethanol in the presence of sodium ethoxide in a 1:1 molar ratio at room temperature afforded in each case a single product identical in all respects (m.p., IR, PMR, MS) with the respective **8**. The direct formation of **8** from **1** and **9** indicates that the initially formed substitution products, namely the thiohydrazonates **10** (Scheme 1) underwent in situ dehydrative cyclization, under the employed reaction conditions, to give **8** as the end products. The intermediacy of **10** was confirmed by their isolation and conversion into **8**. For example, in our hands when the reaction of **1** with **9** was carried out in benzene in the presence of triethylamine at room temperature, the respective thiohydrazonates **10a–f** were obtained, respectively, in 85–90% yield. When the latter esters were refluxed in glacial acetic acid, they were converted into the corresponding triazolothiadiazine derivatives **8** (Scheme 1). The structures of the thiohydrazonates **10a–f** were evidenced by their mass spectra and other spectral data (see Experimental section). For example, the mass spectra of the isolated products **10a–f** revealed in each case a peak at m/z 192 corresponding to the thiol **1** cleaved from the molecular ions. The mass spectra of both aryl and heteroaryl thiohydrazonates were reported to be characterized by

TABLE I Spectral Data of Triazolothiadiazines **8** and the Thiohydrazonates **10**

Compd	IR(KBr), ν (cm^{-1})	^{1}H NMR (CDCl$_3$), δ
8a	3180 (NH)	2.24 (s, 3H), 2.51 (s, 3H), 7.10–8.09 (m, 9H), 10.21 (s, 1H).
8b	3191 (NH)	2.30 (s, 3H), 2.51 (s, 3H), 6.79–8.10 (m, 9H), 10.19 (s, 1H).
8c	3168 (NH)	2.51 (s, 3H), 7.36–8.07 (m, 10H), 10.40 (s, 1H).
8d	3168 (NH)	2.51 (s, 3H), 7.34–8.08 (m, 9H), 10.37 (s, 1H).
8e	3165 (NH)	2.47 (s, 3H), 6.98–8.10 (m, 9H), 10.37 (s, 1H).
8f	3155 (NH), 1672 (CO)	2.50 (s, 6H), 7.4–8.07 (m, 9H), 10.62 (s, 1H).
8g	3170 (NH), 1703 (CO)	1.31 (t, 3H), 2.5 (s, 3H), 4.28 (q, 2H), 7.41–8.08 (m, 9H), 10.59 (s, 1H).
10a	3120, 3272 (NH), 1643 (CO)	2.33 (s, 3H), 2.48 (s, 3H), 5.74 (s, 2H), 7.15–8.1 (m, 9H), 10.42 (s, 1H).
10b	3317, 3247, 3209 (NH), 1666 (CO)	2.33 (s, 3H), 3.32 (s, 3H), 6.31 (s, 2H), 6.87–8.03 (m, 9H), 10.93 (s, 1H).
10c	3161, 3273 (NH), 1662 (CO)	2.48 (s, 3H), 5.75 (s, 2H), 7.11–8.18 (m, 10H), 10.52 (s, 1H).
10d	3278, 4141 (NH), 1664 (CO)	2.4 (s, 3H), 5.7 (s, 2H), 7.2–7.4 (m, 9H), 10.7 (s, 1H).
10e	3317, 3248, 3209 (NH), 1666 (CO)	3.34 (s, 3H), 6.32 (s, 2H), 7.09–8.04 (m, 9H), 11.12 (s, 1H).
10f	3240, 3163 (NH), 1651 (CO)	1.77 (s, 3H), 3.3 (s, 3H), 6.72 (s, 2H), 7.23–8.04 (m, 9H), 9.89 (s, 1H).

the loss of the elements of the corresponding arenethiol and heteroaryl thiol from their molecular ions, respectively.[11]

Next, the tautomerism of **8** was examined. As shown in Scheme 1, the products **8** can have one or more of the three possible tautomeric structures namely the iminohydrazone, the azo-enamine and the CH-azo forms, **A–C** respectively. Of these forms, structure **A** seems to be the form of choice as it is consistent with their electronic absorption and ^{1}H NMR spectra. For example, like typical hydrazones,[12,13] the electronic absorption spectra of **8** in dioxane revealed in each case three absorption bands in the regions 385–370, 300–280, and 250–240 nm (Table II) and the spectra of the unsubstituted derivative **8c**, taken as a representative example of the series prepared, in different solvents exihibit little, if there is any, solvent dependence (Table II). On the basis of such absorption patterns, it can be concluded that the studied compounds **8** have in solution one tautomeric form namely the hydrazone tautomer **A**. Such a conclusion is substantiated by the spectra of **8c** at different pH's. In acid medium, the spectrum revealed a maximum (band-A) in

TABLE II Electronic Absorption Spectra and Acidity Constants (pK$_a$'s) of 7H-3-phenyl-6-methyl-7-arylhydrazono[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazines, **8**

Compd	λ_{max} (log ε) (dioxane) f[a]	pK$_a$ (±s)[b]	σ_X^-
8a	379 (4.41), 288 (4.24), 248 (4.37)	9.62 ± 0.03	−0.17
8b	376 (4.39), 291 (4.22), 250 (4.37)	9.18 ± 0.06	−0.07
8c	374 (4.40), 288 (4.29), 248 (4.35)	9.14 ± 0.05	0.00
8d	375 (4.38), 290 (4.26), 249 (4.30)	8.65 ± 0.05	0.23
8e	372 (4.47), 290 (4.35), 251 (4.42)	8.09 ± 0.03	0.37
8f	376 (4.51), 296 (4.35), 246 (4.29)	7.48 ± 0.07	0.68
8g	379 (4.46), 303 (4.23), 242 (4.17)	6.83 ± 0.05	0.84

[a] f λ_{max} (log ε) of **8c** in different solvents: Ethanol: 381 (4.43), 291 (4.29), 249 (4.37); Chloroform: 374 (4.36), 289 (4.19), 251 (4.32): Acetonitrile: 372 (4.38), 288 (4.25), 250 (4.94); Cyclohexane: 381 (4.44), 287 (4.33), 250 (4.43).

[b] ±s, standard deviation.

the region 350–420 nm, whereas in alkaline medium it exhibits another maximum (band-B) in the region 470–530 nm. As the pH increases, the intensity of band-A decreases and simultaneously that of band-B increases and one isobestic point is recorded indicating the presence of an equilibrium between the hydrazone form and its anion. This spectral behavior, while characteristic of a simple one-stage protolytic equilibrium, is also similar to that reported for typical hydrazones.[12]

This conclusion was also evidenced by the ^{1}H NMR spectra of the studied compounds **8**. Thus, while the latter spectra showed hydrazone NH proton signal in the region δ 10.2–10.6 (Table I), they revealed the absence of signals at δ 11.69[27] and δ 5.27[28] which are characteristic for the NH and CH protons of the azo-enamine and CH-azo forms **B** and **C** respectively.

To provide further evidence for the assignment of structure **A** for the products **8**, their acid dissociation constants, pK$_a$'s, were determined and their correlation by Hammett equation was tested.[12,14–18] The acid dissociation constants for the series **8a–g** were determined potentiometrically at 25°C in 80% dioxane-water mixture (v/v). In all determinations the ionic strength was kept constant at 0.1. From the pH-titrant volume data, the acid dissociation constants of the compounds studied were calculated (see Experimental section) and the results are summarized in Table II.

When these pK$_a$ values were plotted against Hammett substituent constants σ_X, all the substituents fall on the correlation line except the substituents with -R effect, namely the p-Ac and p-EtOCO groups which are capable of direct interaction with the negatively charged reaction site. However, when the pK_a data were plotted versus σ_X^- constants, a better correlation was obtained. The equation of the regression line obtained is:

$$pK_a = 9.13 - 2.63\sigma_X^-; \; r = 0.990; s = \pm 0.10$$

This excellent correlation indicates that the parameter r^- in the Yukawa-Tsuno equation: $pK_a = pK_a^O + \rho[\sigma_X + r^-(\sigma_X^- - \sigma_X)]$, and which gives the contribution of the resonance effect of the substituent varied, is close to unity for the series **8a–g** studied.[19]

The foregoing linear correlation between pK_a values and σ_X^- constants and the values of ρ and r^- found provide further evidence that the studied compounds **8** exist predominantly in the hydrazone form **A**. This is because the values of ρ (2.63) and $r^- = 1.00$ are similar to those reported for ionization of phenols ($\rho = 2.67$; $r^- = 1.00$) (20, 21) and anilinium ions ($\rho = 2.77$; $r^- = 1.00$) (22) in 50% ethanol-water mixture. If either form **B** or **C** were the predominant form for the studied compounds, the ρ values would have been less than 2.0 and will be similar to that reported for ionization of 2-arylazophenols ($\rho = 1.223$; $r^- = 0.286$),[20] since the bridge between the substituent and the reaction site in such forms **B** and **C** is longer than in **A**. Thus, it is not unreasonable to conclude that the observed linear correlation of the dissociation constants with Hammett equation indicates that the tautomeric form **A** prevails under the conditions of the measurement of pK_a's.

EXPERIMENTAL

Melting points were determined on a Gallenkamp electrothermal apparatus and are uncorrected. Elemental analyses were performed by the Microanalytical Laboratory (Cairo University, Giza, Egypt). IR spectra were recorded on Fourier Transform and Pye Unicam SP 300 infrared spectrophotometers. ^1H NMR spectra were recorded on a Varian Gemini 200 spectrometer in deuterated chloroform with use of tetramethylsilane as an internal standard. Electronic absorption spectra were recorded on Pye-Unicam AR55 and Cary spectrophotometers. Mass spectra were obtained on a GCMS-OQ 1000-EX Varian Mat 711 and SSQ 7000 spectrometers. The reagents 4-amino-5-phenyl-1,2,4-triazole-3-thione **1**[10] and 3-chloro-2,4-pentanedione **5**[9] were prepared by literature methods.

N-Aryl 2-oxopropanehydrazonoyl Chlorides, 9

The hydrazonoyl chlorides **9a–g** were prepared by coupling of 3-chloro-2,4-pentanedione **5** with diazotized anilines as previously described.[23,24] The physical constants of the known compounds **9a–e** are similar to those reported in literature. Those of the new derivatives **9f** and **9g** are as follows.

Compound 9f: Yield 85%; m.p. 184°C (EtOH); υ (cm^{-1}) 3227 (NH), 1693, 1654 (CO). ^{1}H NMR δ 2.49 (s, 3H), 2.53 (s, 3H), 7.51–7.99 (m, 4H), 11.01 (s. 1H). Anal. Calcd. for $C_{11}H_{11}ClN_2O_2$ (238.6): C, 55.36; H, 4.65; N, 11.74. Found: C, 55.5; H, 4.4; N, 11.9%.

Compound 9g: Yield 80%, m.p. 170°C (EtOH), υ (cm^{-1}) 3242 (NH), 1697, 1700 (CO); ^{1}H NMR δ 1.24 (t, 3H), 4.18 (q, 2H), 2.44 (s, 3H), 7.22–7.89 (m, 4H), 9.59 (s, 1H). Anal. Calcd. for $C_{12}H_{13}ClN_2O_3$ (268.7): C, 53.64; H, 4.88; N, 10.43; Found: C, 53.3; H, 4.7, N, 10.2%.

Synthesis of 7H-3-phenyl-6-methyl-7-acetyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine 7

To a solution of **1** (1.92 g, 0.01 mol) in ethanol was added an aqueous solution of potassium hydroxide (0.75 mL, 75%) and the mixture was warmed for 10 min at 80°C and cooled. To the resulting clear solution was added 3-chloro-2,4-pentanedione **5** (1.2 mL, 0.01 mol) dropwise while stirring the reaction mixture. After the addition of **5** was completed, the mixture was stirred for further 18 h at room temperature. The solid that precipitated was filtered off, washed with water, dried, and finally crystallized from benzene to give pure **7** in 65% yield, m.p. 142–143°C; ν(cm^{-1}) 1705 (CO): ^{1}H NMR δ 2.39 (s, 3H), 2.40 (s, 3H), 4.24 (s, 1H), 7.26–8.11 (m, 5H). Anal. Calcd. for $C_{13}H_{12}N_4OS$: C, 57.34; H 4.44; N, 20.57; Found: C, 57.1: H, 4.7; N, 20.3%.

Synthesis of Thiohydrazonate Esters 10

To a mixture of equimolar quantities of the hydrazonoyl chloride **9** and triazolthione **1** (10 mmol each) in dry benzene (40 mL) was added triethylamine (1.4 mL, 10 mmol). The mixture was stirred for 15 h at room temperature, then the excess solvent was distilled under reduced pressure. The solid left was collected and crystallized from ethanol to give **10** in 92% yield. The physical constants of the latter products are given in Table III.

TABLE III Physical Constants of [1,2,4]triazolo[3,4-b][1,3,4]thiadiazines **8** and Thiohydrazonate esters **10**

Compd	Yield (%)	m.p.°C[a]	Molecular formula	Anal. Calcd./Found C%	H%	N%
8a	76	252	$C_{18}H_{16}N_6S$	62.05	4.63	24.12
			(348.4)	62.3	4.2	23.8
8b	85	270-2	$C_{18}H_{16}N_6S$	62.05	4.63	24.12
			(348.4)	62.4	4.4	24.2
8c	85	300	$C_{17}H_{14}N_6S$	61.06	4.22	25.13
			(334.4)	61.1	4.1	24.9
8d	80	276	$C_{17}H_{13}ClN_6S$	55.36	3.55	22.78
			(368.8)	55.6	3.4	22.9
8e	90	290	$C_{17}H_{13}ClN_6S$	55.36	3.55	22.78
			(368.8)	55.2	3.4	22.8
8f	86	280	$C_{19}H_{16}N_6OS$	60.62	4.28	22.32
			(376.4)	60.9	4.5	22.1
8g	89	300	$C_{20}H_{18}N_6O_2S$	59.10	4.46	20.68
			(406.4)	58.9	4.5	20.6
10a	85	180	$C_{18}H_{18}N_6OS$	59.00	4.95	22.93
			(366.4)	59.0	4.8	22.8
10b	85	182	$C_{18}H_{18}N_6OS$	59.02	4.92	22.95
			(366)	59.0	4.8	22.8
10c	91	165	$C_{17}H_{16}N_6OS$	57.94	4.58	23.85
			(352.4)	57.8	4.5	23.6
10d	85	178	$C_{17}H_{15}ClN_6OS$	52.78	3.91	21.72
			(386)	52.6	3.9	21.5
10e	88	192	$C_{17}H_{15}ClN_6OS$	52.78	3.91	21.72
			(386)	52.7	3.9	21.6
10f	92	184	$C_{19}H_{18}N_6O_2S$	57.85	4.60	21.31
			(394)	58.0	4.6	21.0

[a] Solvent of crystallization is dioxane.

Synthesis of 7H-3,6-disubstituted 7-Arylhydrazono-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines 8

Method A: To a solution of 7H-3-phenyl-6-methyl-7-acetyl-[1,2,4] triazolo[3,4-b][1,3,4]thiadiazine **7** (10 mmol) in ethanol (40 mL) was added sodium acetate trihydrate (1.36 g) and the mixture was cooled to 0–5°C in an ice bath. To the resulting cold solution was added portionwise a cold solution of the appropriate diazonium salt, prepared by diazotizing the appropriate aniline derivative (10 mmol) dissolved in hydrochloric acid (6 ml, 6 M) with a solution of sodium nitrite (0.7 g, 10 mmol) in water (10 mL). After the addition of the diazonium salt was completed, the mixture was stirred for further 30 min in the ice bath. The solid precipitated during this period was filtered off, washed with water, dried, and crystallized from dioxane to give pure **8**. The physical constants of the compounds **8a–g** prepared are listed in Table III.

Method B: To a stirred solution of 4-amino-5-phenyl-1,2,4-triazole-3-thione **1** (10 mmol) in ethanolic sodium ethoxide solution, prepared by adding sodium metal (0.23 g, 10 mmol) to absolute ethanol (20 mL), was added the appropriate hydrazonoyl chloride **9** (10 mmol). The mixture was stirred for 15 h at room temperature. The solid that precipitated was collected by filtration and crystallized from dioxane to give the respective pure **8**. The products isolated proved identical in all respects with those obtained above by method A.

Method C: A solution of the appropriate thiohydrazonate **10** (2 mmol) in acetic acid (10 mL) was heated under reflux for 1 h and cooled. The solid that precipitated was filtered off, washed with water, and finally crystallized from dioxane to give the respective **8**. The physical constants of the products prepared are identical to those obtained above.

pK_a Determination: The acid dissociation constants of the compounds **8a–g** were determined potentiometrically in 80% dioxane-water mixture at 25 ± 0.1°C and ionic strength (KNO_3) of 0.1. An Orion 420A pH-meter fitted with combined glass electrode type 518635 was employed for measurement of pH values. The instrument was accurate to ±0.01 pH unit. It was calibrated using two standard Beckman buffer solutions of pH 4.01 and 7.00. The pH meter reading (B) recorded in dioxane-water solution was converted to hydrogen ion concentration $[H^+]$ by means of the widely relation of van Uitert and Haas[25] namely: $-\log [H^+] = B + \log U_H$, where $\log U_H$ is the correction factor for the solvent composition and ionic strength used for which B is read. The value of $\log U_H$ was found to be 0.48.

The experimental procedure followed in the determination of pK_a values and their calculations, by the method of least squares, from the titrant volume—pH data using the relation:

$$pK_a = pH_i - \log V_i/(V_c - V_i)$$

where pH_i is the corrected pH value of the solution when the volume of the added titrant is V_i and V_c is the volume of the titrant at the equivalence point, as previously described.[26] The pK_a values obtained were reproducible to within ±0.02 pK_a unit. The results are summarized in Table II.

REFERENCES

[1] B. S. Holla and B. Kalluraya, *Indian J. Chem.*, **27(B),** 683 (1988).

[2] N. F. Eweiss and A. A. Bahajaj, *J. Heterocycl. Chem.*, **24,** 1173 (1987).

[3] G. Mazzone, F. Bonina, R. Pignatello, A. M. Panico, A. Caruso, M. G. Leone, M. Amico-Roxas, and G. Blantino, *Farmaco Ed. Sci.*, **44,** 933 (1989).

[4] C. Parkanyi, A. O. Abdelhamid, and A. S. Shawali, *J. Heterocycl. Chem.*, **21,** 521 (1984).

[5] M. A. N. Mosselhi, M. A. Abdallah, S. M. Riyadh, A. E. Harhash, and A. S. Shawali, *J. Prakt. Chem.*, **340,** 160 (1998).

[6] M. A. Abdallah, M. A. N. Mosselhi, I. M. Abbas, A. A. Fahmi, and A. S. Shawali, *J. Chem. Research (S)*, 370 (1995).

[7] I. M. Abbas, M. A. Abdallah, M. A. Mosselhi, S. Z. Mohamed, and A. S. Shawali, *J. Chem. Research (S)*, 308 (1994).

[8] P. Frohberg, M. Wiese, and P. Nuhn, *Arch. Pharm. Pharm. Med. Chem.*, **330,** 47 (1997).

[9] M. Suzuki and M. Nagawa, *J. Pharm. Soc. Jpn.*, **75,** 394 (1955).

[10] J. R. Reid and N. D. Heindel, *J. Heterocycl. Chem.*, **13,** 925 (1976).

[11] A. J. Elliott, P. D. Callaghan, M. S. Gibson, and S. T. Nemeth, *Can. J. Chem.*, **53,** 1484 (1975).

[12] A. S. Shawali, N. M. S. Harb, and K. O. Badahdah, *J. Heterocycl. Chem.*, **22,** 1397 (1985).

[13] R. Jones, A. J. Ryan, S. Stemhell, and S. E. Wright, *Tetrahedron*, **19,** 1497 (1963).

[14] D. A. Charistos, G. V. Vagenas, I. C. Tzavellas, C. A. Tsderidis, and N. A. Rodios, *J. Heterocycl. Chem.*, **31,** 1593 (1994).

[15] A. S. Shawali, I. M. Abbas, M. A. Abdallah, and A. A. Fahmi, *Indian J. Chem.*, **29B,** 1012 (1990).

[16] A. S. Shawali, M. S. Rizk, A. O. Abdelhamid, M. A. Abdallah, C. Parkanyi, and M. E. Wojciechowska, *Heterocycles*, **20,** 2211 (1983).

[17] A. S. Shawali, H. M. Hassaneen, and M. A. Hanna, *Heterocycles*, **15,** 697 (1981).

[18] A. E. Elhilaly, A. S. Shawali, and M. A. Madkour, *Inorganica Chim. Acta*, **36,** 179 (1979).

[19] Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Jpn.*, **32,** 971 (1959).

[20] Y. Yukawa, J. I. Bata, and Y. Yukawa, *Bull. Chem. Soc. Jpn.*, **32,** 960 (1959).

[21] J. Socha, J. Horska, and M. Vecera, *Collect. Czech. Chem. Commun.*, **34,** 2982 (1969).

[22] G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, **17,** 1176, 1183 (1934).

[23] M. I. Shevchuk and A. V. Dombrovskii, *Zh. Obshch. Khim.*, **33,** 1135 (1963).

[24] M. I. Shevchuk and A. V. Dombravskii, *Chem. Abstr.*, **59,** 9921g (1963).

[25] L. G. van Uitert and C. G. Haas, *J. Am. Chem. Soc.*, **75,** 451 (1953).

[26] A. Albert and E. P. Serjeant, *The Determination of Ionization Constants* (Chapman and Hall Ltd., London, 1971), pp. 9–39.

[27] Y. Kurasawa, R. Miyashita, A. Takada, H. S. Kim, and Y. Okamoto, *J. Heterocycl. Chem.*, **32,** 671 (1995).

[28] J. G. Schantl and P. Hebeisen, *Tetrahedron*, **46,** 393 (1990).

[29] R. R. Phillip, Organic Reactions, R. Adams, Ed., John Wiley & Sons, New York, Vol. 10, Chap. 2, p. 143 (1959).