Potentiometric study for Determination of $\overline{PKa}$ values for Schiff bases derived from 2- acetyl pyridine with heterocyclic amines

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Abstract

The project was started by synthesis of two Schiff bases from 2- acetyl pyridine with 4- amino pyrimidine and 4- amino pyridine by a standard method . The structures of these Schiff bases had confirmed by physical method , namely by using U.V-IR spectra and melting points .
The main aims of the study was the determination of two consecutive nitrilium ions ionization constants pK_1 and pK_2 for in each molecule simultaneously . The last was regarded an improvement in potentiometric method for determination of pKa in these molecules . Finaly factors govern , the pK_1 or pK_2 values in these Schiff base ,as structure of imines, temperature and mixed solvent of ethanol in the range (10_60) % in water were given and discussed.

Key words : Ionization constant , Schiff bases, Heterocyclic ketone and amine , potentiometry .

الخلاصة

ابتداء البحث بتحضير قاعدتي شيف من 2-اسيتايل بر يديين مع 4- امينو بريميدين و4- امينوبر بيدين وبطريقة قياسية .

تم إثبات الهيئتين التركيبيتين لقاعدتي شيف بالطريقة الفيزيائية وبالتحديد بأطياف U.V-IR ودرجات الانصهار .

الهدف الرئيسي للدراسة هو تعيين قيم ثوابت التأين المتعاقبة لايونات النتريليوم pK_1 وpK_2 في كل جريئة في آن واحد . الأخير يعتبر تطوير بالطريقة المجهادية في تعيين pKa في هذه الجزيئات . أخيرا أوضح البحث العوامل المؤثرة عل قيم pK_1 وpK_2 مثل الهيئات التركيبية , درجة الحرارة والمذيب المتمثل بالايثانول في المدى من (10-60)% والتي تمت مناقشتها.

الكلمات الدالة: ثابت التأين , قواعد شيف ,الكيتونات الحلقية غير المتجانسة ,الطريقة المجهادية .

Introduction

The chemistry of heterocyclic ketones and amines had faced a great deal of attention by many workers . This was for their applications in many fields .

Many workers had given a great deal of attention to the chemistry of imines during the last decades. These were in the direction of U.V(1-3) ,IR(4,5) ,NMR(6) and mass(6,7) spectra .

Schiff bases had used in different fields as antimicrobial(8) agents , fungicides(9), biomarkers(10) and of oxidative(11) stress in model diabetes mellitus .

During the lest years, potentiometric titration was applied successfully for the determination of pKa for amide(12) ,ary azo pyrimidine(13) , biochemical(14) and drugs(15) .

The present work deals with the determination of two pK_1 and pK_2 values for some heterocyclic imines derived from 2- acetyl pyridine with 4-amino pyrimidine and 4-amino pyridine, by using a developed potentiometric method . The study deals with influence of three factors affecting the acidities of imines such as type of structures , temperature and solvent .

The study illustrated how tertiary amino groups in imines were converted to nitrilium cation as a strong acid conjugate during potentiometric titration of imines under study with HCl titrant .

Experimental

2- acetyl pyridine,4-amino pyrimidine and 4-amino pyridine were supplied form Aldrich Chemical Company . They were used as supplied with out any further purification, Ethanol was bought from local market, Methyl 2-pyridyl ketonylidene 4-amino pyrimidine (I) and Methyl 2-pyridyl ketonylidene 4-amino pyridine (II) were prepared by standard method (4) i.e. by mixing(0.01) mole 2-acetyl pyridine with (0.01) mole 4-amino pyrimidine and 4-amino pyridine respectively. About (10) ml of ethanol was added to each mixture, followed by reflux for the mixture for about (1.5) hour, cooling and filtration of final products. Crude Schiff base (I) and (II) were recrystallized from ethanol, pure imines (I) and (II) having a melting points of (116) C° and (131-133) C° respectively.

Determination of pKa

Solutions required

1-(0.01)M of imine in 10% ethanol _water medium .

2-(0. 1)M of HCl .

Pipette (50) ml of 10^{-2} M of Schiff base (I) or (II) and placed in a special titration cell containing double layers , for circulation of water inside the cell .Water was pumped from thermostat at any temperature range between (10-60) C° .When the temperature of imine reached an equilibrium , addition of(0.2) ml successive quantity of (0.1) M HCl was done . The mixture was stirred with magnetic bar placed inside the cell after addition , followed by measurement of pH after addition . Titration was continued for seven times till (1.4) ml total volume of titrant added . Two pK_1 and pK_2 values for conjugate acids were determined . The first $pK_1$was estimated after addition of range (0.2-1) ml titrant .This represent half neutralization reaction . The second pK_2 was estimated at range volumes of (1.2-1.4) ml of titrant .The pKa values were calculated from Handerson Hassellbach equation(16,17) of the from :

$$\mathrm{pKa} = \mathrm{pH} + \log \frac{[\mathrm{HA}]}{[\mathrm{BH}^+]} \quad \text{.............(1)}$$

Instrumentations

1.Electrothermal melting point apparatus was used for measurement of melting point of imines.

2. FT IR spectrophotometer was used for measurement of IR spectra of solid imines by KBr disc method .

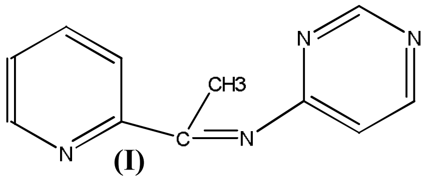
3.A computerized double beam Shimadzu 1601 for measurement of U.V spectra of imines solution.

4.A memmert thermostat manufactured by Searle company model L200, for fixation the temperature of imine solution.

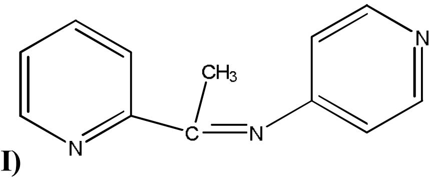
Water was pumped out from thermostat to cell using external water pump.

Results and discussion

The chemical structures of heterocyclic imines (I) and (II) were the following :



(I)



(II)

These imines (I) and (II) were resemble each other in their structures having 4 and 3 nitrogen atoms respectively . Theoretically could be regarded as a weak bases and combined easily with HCl titrant during potentiometric titration forming strong acid conjugates or nitrilium ions.

At the beginning of this investigation it was found of a great importance to confirm the structures of imines (I) and (II) by physical mean , namely , melting points, U.V and IR spectra.

The melting points of imines (I) and (II) having a values of (116) C^{o} and (131-133) C^{o} respectively . This means that degree of association or polymerization of (II)was greater than (I). This possibly happen by dipole-dipole association method(11).

The IR spectra and U.V spectra of imines (I) and (II) in ethanol shown Table (1) and showed the following absorption bonds :

Table(1) U.V-IR spectra of imines:

Imine No	U.V in ethanol (10^{-4}) M		IR wave number (cm^{-1})		
	λmax (nm)	ε max **Liter.mole^{-1}.cm^{-1}**	C-N	-C=N-	-C-H-
I	297	6100	1477.17(s)	1649.91(s)	3169.59(m)
II	268	3065	1435.73(s)	1649.31(s)	3075.86(m)

The U.V spectra of imines (I) and (II) showed a single absorption for each imine at optimum wavelengths λmax with molar extension coefficient vales greater than 1000 unit of Liter.mole^{-1}.cm^{-1} . This confirmed π—π^* transition(4) in each planer molecule .

The IR spectra showed the following stretching vibration as follows :

1.A strong absorptions for C-N tertiary amine in the range (1435.73-1477.17) cm^{-1} .

2. A strong stretching absorptions for -C=N- the azomethine linkages in the range (1649.31-1649.91) cm^{-1}.

3.A medium aromatic C-H group in the range(3075.86- 3169.59) cm^{-1}

These values of melting point , U.V and IR absorption bands confirmed(18) the chemical structures of imines under study .

Before starting pKa determination of imines (I) and (II) , it was found of a great importance to check the stability of imines when prepared in 10^{-2} M in 10% ethanol aqueous media .This was because some imines solutions under go a side reactions(6) as hydrolysis ,solvolysis …..etc in medium stated .This encourage the worker in this investigation to measure the conductance of imines 10^{-2} M solution for a period of 90 minutes as shown in Table (2)

Table (2): Conductance (ohm^{-1}) for 10^{-2} M imines (I) and (II) in 10% ethanol-water medium at different times .

Tim	Conductance (ohm^{-1})	
	I	II
0	8.85	91
5	8.89	89
10	8.81	88.1
15	8.72	88.1
20	8.72	88.1
25	8.71	88.1
30	8.75	88.5
35	8.79	89
40	8.8	89
45	8.8	89.1
50	8.8	89.5
55	8.8	89.9
60	8.85	90
65	8.85	90.1
70	8.89	90.5
75	8.91	90.5
80	8.95	90.9
85	9.0	91
90	9.0	91

Table (3): pK_1 and pK_2 for imines (I) in 10% ethanol and at different temperatures .

$T_{(k)}$	ml of HCl	pH	pKa	$\overline{pKa}$
298	0.2	4.08	4.995	3.899*
	0.4	3.72	4.271	
	0.6	3.50	3.803	
	0.8	3.30	3.383	
	1	3.17	3.046	
	1.2	3.07	2.722	2.499**
	1.4	2.94	2.275	
303	0.2	3.92	4.819	3.648*
	0.4	3.51	4.031	
	0.6	3.25	3.504	
	0.8	3.1	3.130	
	1	2.96	2.756	
	1.2	2.84	2.355	2.085**
	1.4	2.74	1.814	
313	0.2	3.76	4.636	3.435*
	0.4	3.35	3.837	
	0.6	3.10	3.311	
	0.8	2.92	2.876	
	1	2.81	2.517	
	1.2	2.78	2.160	1.92**
	1.4	2.70	1.680	
323	0.2	3.60	4.444	3.247*
	0.4	3.20	3.644	
	0.6	2.96	3.113	
	0.8	2.80	2.687	
	1	2.77	2.346	
	1.2	2.72	2.112	1.88**
	1.4	2.69	1.642	
333	0.2	3.53	4.356	3.122*
	0.4	3.10	3.508	
	0.6	2.86	2.962	
	0.8	2.68	2.472	
	1	2.70	2.312	
	1.2	2.65	1.937	1.528**
	1.4	2.60	1.118	

* pK_1

**pK_2

Table (4): pK$_1$ and pK$_2$ for imines (II) in 10% ethanol and at different temperatures

T$_{(k)}$	ml of HCl	pH	pKa	$\overline{\text{pKa}}$
298	0.2	9.17	10.131	9.271*
	0.4	9.02	9.625	
	0.6	8.87	9.241	
	0.8	8.70	8.876	
	1	8.48	8.481	
	1.2	8.20	8.024	7.492**
	1.4	7.80	7.800	
	1.8	7.61	6.652	
303	0.2	8.82	9.777	8.925*
	0.4	8.67	9.273	
	0.6	8.52	8.889	
	0.8	8.35	8.526	
	1	8.16	8.160	
	1.2	7.92	7.744	7.189**
	1.4	7.60	7.233	
	1.8	7.55	6.592	
313	0.2	8.48	9.436	8.579*
	0.4	8.33	8.933	
	0.6	8.16	8.529	
	0.8	8.01	8.186	
	1	7.81	7.810	
	1.2	7.57	7.394	6.876**
	1.4	7.30	6.933	
	1.8	7.26	6.302	
323	0.2	8.14	9.095	8.222*
	0.4	7.98	8.582	
	0.6	7.81	8.179	
	0.8	7.64	7.816	
	1	7.44	7.440	
	1.2	7.15	6.974	6.286**
	1.4	6.80	6.433	
	1.8	6.41	5.542	
333	0.2	8.02	8.975	8.118*
	0.4	7.87	8.472	
	0.6	7.71	8.079	
	0.8	7.54	7.716	
	1	7.35	7.350	
	1.2	7.00	6.824	6.046**
	1.4	6.35	5.983	
	1.8	6.29	5.332	

* pK$_1$
**pK$_2$

Table (2) showed a stability of conductance for 10^{-2} M imines solutions for the whole period of 90 minutes .A very small variation in conductance measurements were observed some times , due to voltage change in A.C current . The last as expected produced by fluctuation in the conductances and their values lie with in experimental errors .

The stable10^{-2} M imines solutions in 10% ethanol aqueous medium encourage the worker to deal with pKa determination of imines by potentiometric method .Hence the following division of results were thought to be necessary:-

1.Influence of structures on pK_1 and pK_2

Table(3,4) showed pK_1 and pK_2 values for imines (I) and (II) at fixed 10% ethanol aqueous medium and at different temperatures range between (20-60) C°. At these temperatures pK_1 and pK_2 values for imine (I) had a range of value (3.899-3.122) and (2.499-1.528) respectively. Similarly imine (II) had a range of pK_1 and pK_2 values (9.271-8.118) and (7.492-6.046) respectively .This means acidities of pK_1 and pK_2 in imine (I) were greater than imine (II). This agreed with the higher basicity of imine (I) as compared with imine (II). In other words they contained 4 and 3 nitrogen atoms in imines (I) and (II) respectively. This increased in basicity of imine (I) as compared with imine (II), gave a greater chance to imine(I)to react with protons of HCl titrant during potentiometric titration to produce higher concentrations of conjugated acids . This comes in agreement (16) with influence of structures of imines derived from benzoyl acetone and dimedone on their acidites, on their acidities.

2. Influence of temperatures on pK_1 and pK_2

Table(3)showed the influence of temperatures in the range (293-333) K on ionization constants pK_1 and pK_2 for nitrilium ions produced by reactions of basic Schiff bases (I) and (II) with HCl titrant, during potentiometric titration.

This facilitated the evaluation of thermodynamic parameters namely $\overline{\Delta G}, \overline{\Delta H}$ and $\overline{\Delta S}$ from standard (17) equations of the forms:-

$\Delta G = - RT \ln K_i$ ……….(2)

$i=1$ or 2

K_i =Ionization constant of nitrilium ion

$R=8.314\ J.mole^{-1}.K^{-1}$

T=Absolute temperature

All $\overline{\Delta G}$ values collected in Table (5) had a range of positive values between (20.7-51.5)kJ.$mole^{-1}$. This happed , because organic compounds contain covalent bondings and ionized with difficulty .

The variation of $\ln K_i$ with absolute temperature , encourage the worker in this investigation to evaluate the enthalpy $\overline{\Delta H}$ parameter for two ionization constants K_1 and K_2 from integrated Vant Hoff equation of the form :-

$\ln K = \text{constant} - \frac{\Delta H}{RT}$ ....(3)

The plots of $\ln K_1$or $\ln K_2$ of Versus T^{-1} imines (I) and (II)showed a four linear straight lines of correlation coefficients range (0.927-0.982) as in fig (1-2) for imines (I) and (II)respectively .The two positive signs of $\overline{\Delta H}$ thermodynamic parameter in each imine mean that ionization process occurred in an endothermic process . In any imine the second heat of ionization is greater than the first or $\Delta H_2 > \Delta H_1$. This was accepted and agreed in literature(19) since in second ionization reaction need more energy was required to perform the ionization reaction .

The change in entropy $\overline{\Delta S}$ accompanied ionization reaction in imines (I) and (II) were calculated from Gibbs equation (4) of the from :

$$\overline{\Delta G} = \overline{\Delta H} - T\overline{\Delta S} \quad ....(4)$$

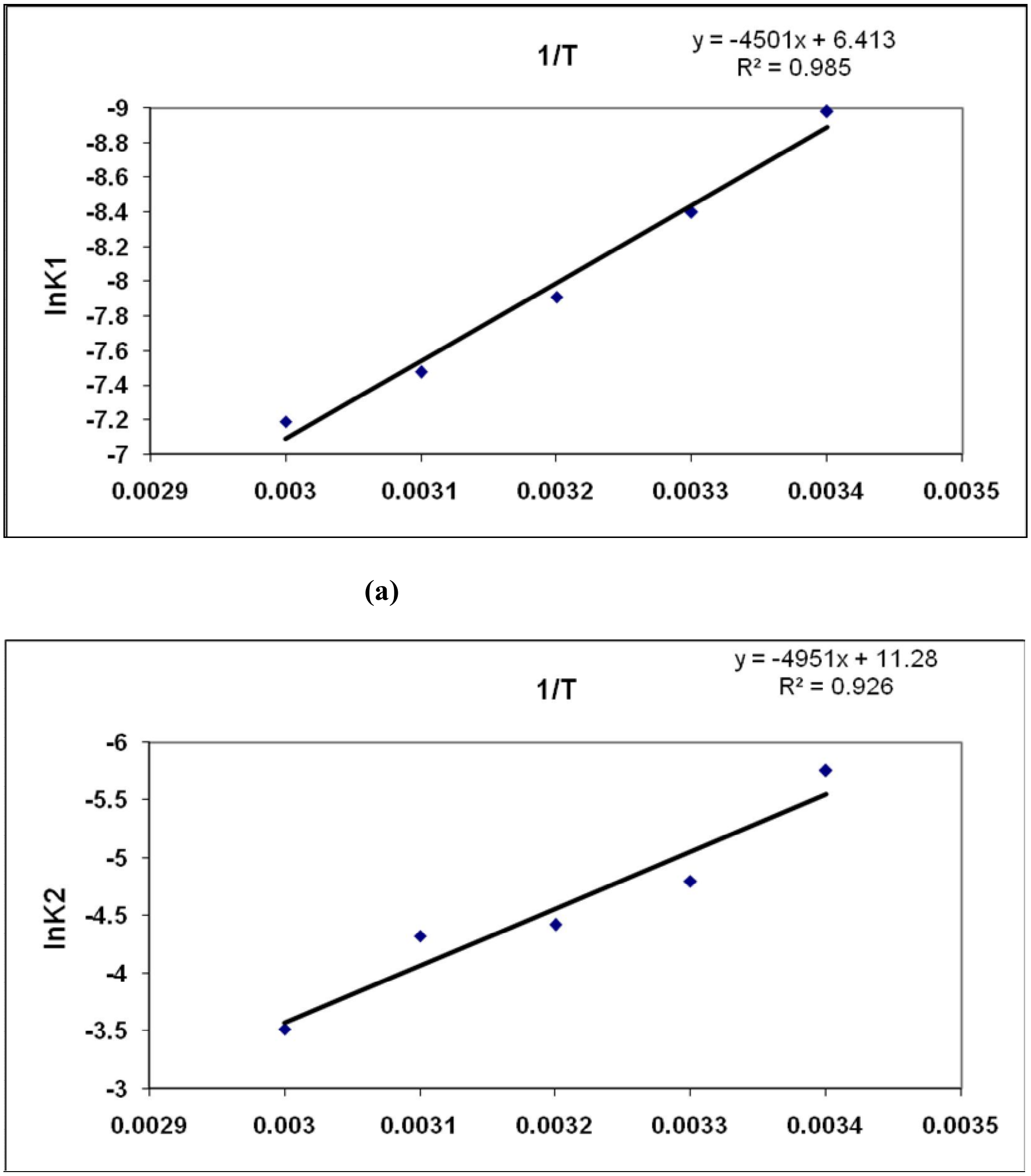
Table (5) showed a positive two $\overline{\Delta S}$ values for each imine. This positive sign stated mean that ionization reaction occurred by an increase in random i.e.

$S_2 > S_1$

S_2= entropy of product

S_1= entropy of reactant

Also in any imine ΔS_2 value was greater than ΔS_1 .These two last observations were in full agreement[(19)] with any ionization reactions having two ionization steps.



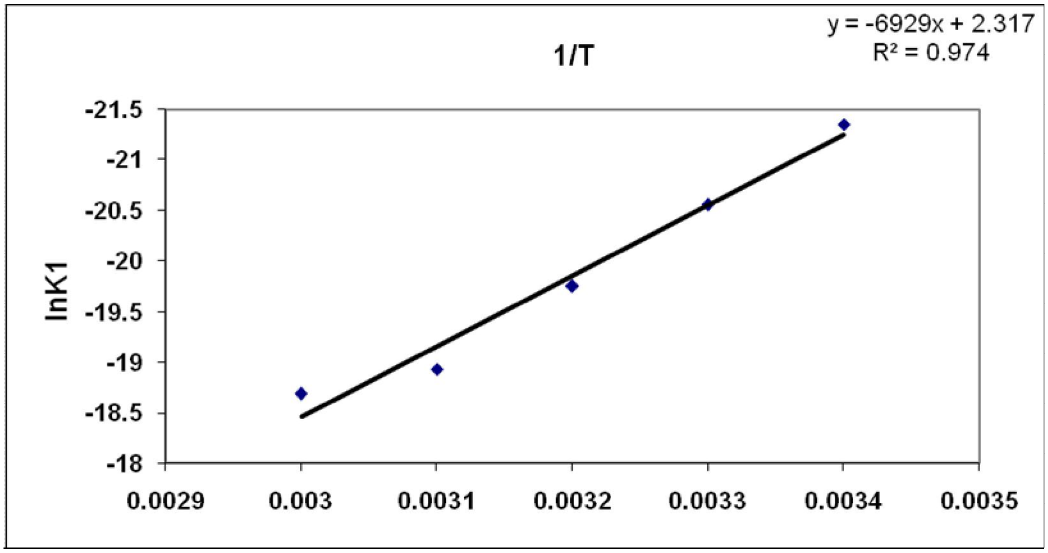
(a)

(b)

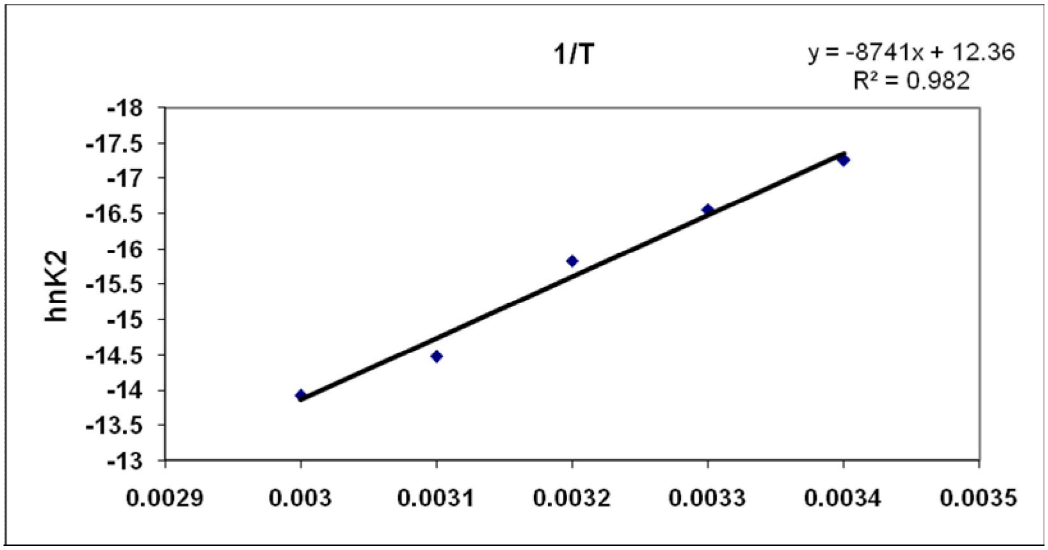
Fig(1): Vant Hoff plots for imine (I)

a- lnK_1 versus 1/T

b- lnK_2 versus 1/T



(a)



(b)

Fig(2): Vant Hoff plots for imine (II)
a- $\ln K_1$ versus 1/T
b- $\ln K_2$ versus 1/T

Table (5) Thermodynamic parameters $\overline{\Delta G}, \overline{\Delta H}$, $\overline{\Delta S}$ for ionization constants pK_1 and pK_2 in imines (I) and (II).

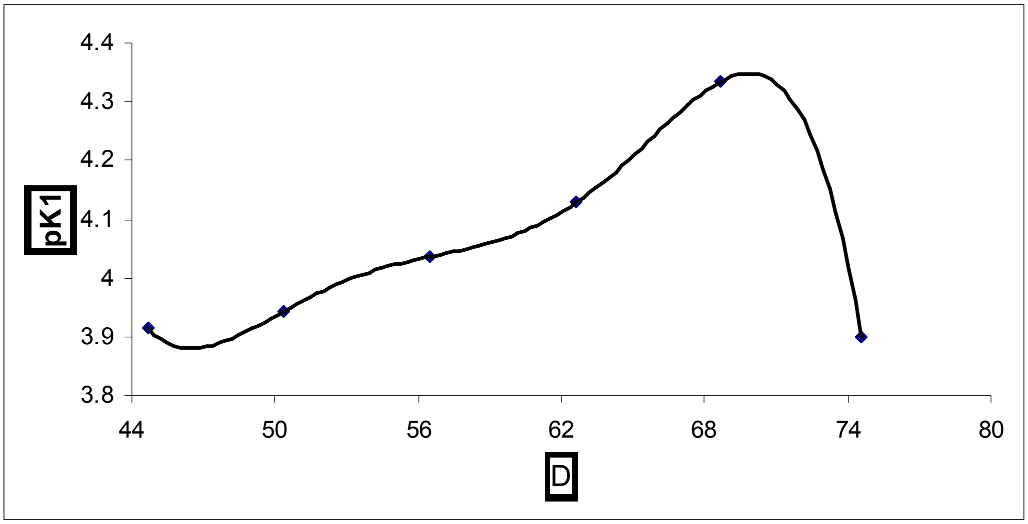
com NO.	Temp K	ln k	ΔH J.mol^{-1}	ΔG J.mol^{-1}	ΔS J.mol^{-1}.k^{-1}	$\overline{\Delta H}$	$\overline{\Delta G}$	$\overline{\Delta S}$
1*	293	-.8.978	37492.5	21870.4	53.32	37406.3	20717.9	53.32
	303	-8.399	37313.5	21158.3	53.32			
	313	-7.909	37269.9	20581.4	53.32			
	323	-7.476	37297.8	20076.2	53.32			
	333	-7.189	37657.9	19903.2	53.32			
1**	293	-5.754	41494.9	14016.8	93.78	41146.1	11792.4	93.78
	303	-4.801	40510.3	12094.4	93.78			
	313	-4.421	40858.4	11504.7	93.78			
	323	-4.322	41897.9	11606.4	93.78			
	333	-3.518	40969.2	9739.8	93.78			
2*	293	-21.347	57647.0	52001.3	19.27	57586.9	51557.4	19.27
	303	-20.551	57609.3	51770.9	19.27			
	313	-19.754	57436.5	51413.3	19.27			
	323	-18.932	57064.1	50840.4	19.27			
	333	-18.692	58177.5	51761.0	19.27			
2**	293	-17.251	72142.2	42023.5	102.79	72642.6	40467.9	102.79
	303	-16.555	72851.1	41704.4	102.79			
	313	-15.833	73376.5	41201.9	102.79			
	323	-14.474	72071.4	38868.8	102.70			
	333	-13.921	72771.7	38541.2	102.79			

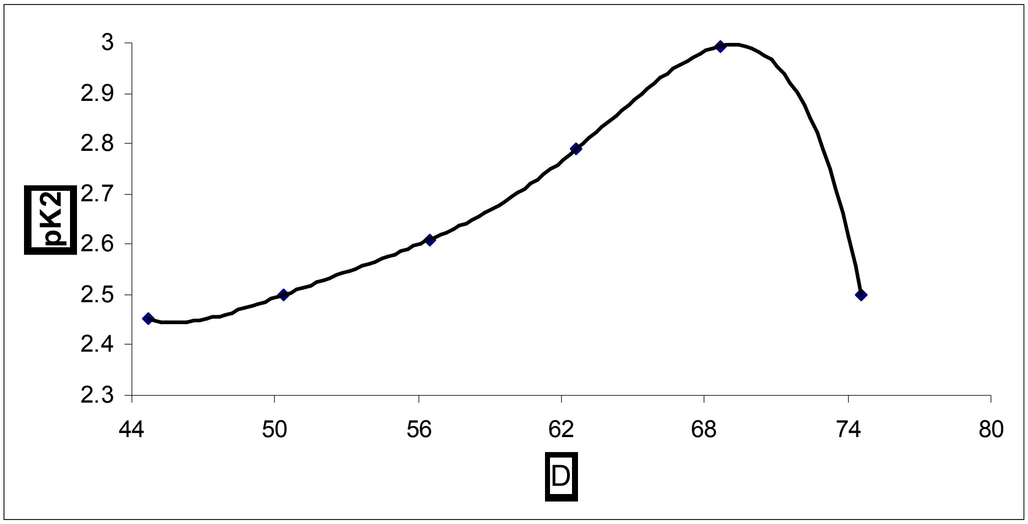
1*and 1** for pK_1 and pK_2 in imine (I).

2* and 2**for pK_1 and pK_2 in imine(II).

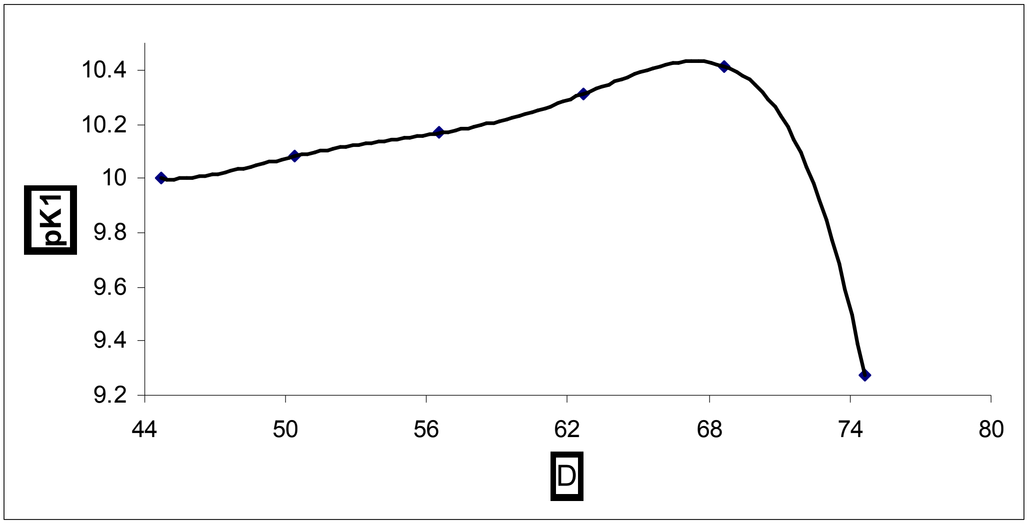
3.Influence of solvent on ionization constant

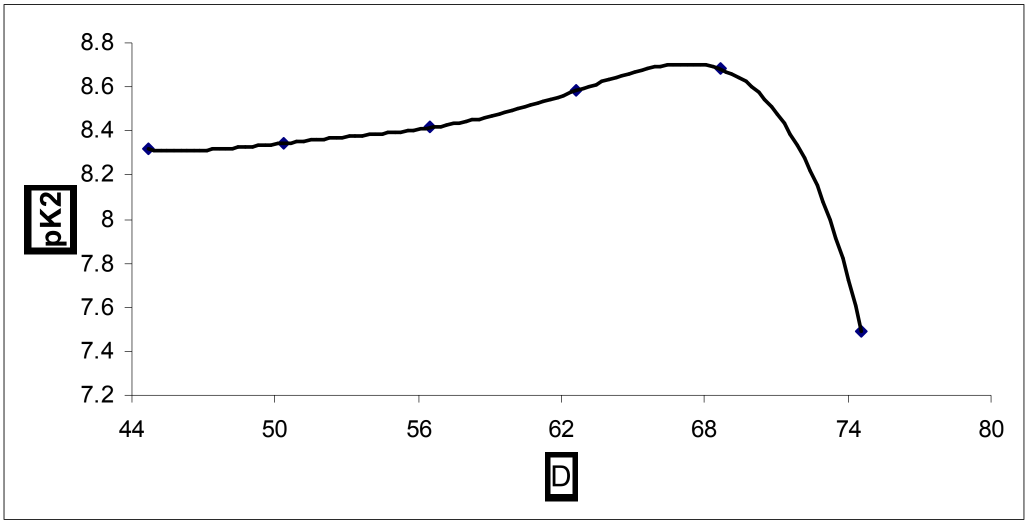
The percentages of ethanol in aqueous medium as a solvent were changed in a range (10-60)% . The ionization constants pK_1 and pK_2 for imines (I) and (II) were determined in six mixtures stated . The percentages of ethanol in water were converted in to dielectric constants (D) from literature(20) .A plots between pK_1 or pK_2 for each imine versus D as in fig. (3-4).These showed four graphs of bell shape . In other words a direct relation ship between pK_1 or pK_2 versus (D) , then suddenly converted in an inverse relation ship . This comes in agreement with earlier works(21,22).





Fig(3): The relation ship between pK_1 or pK_2 versus dielectric constant (D) of the media in imine I .





Fig(4): The relation ship between pK_1 or pK_2 versus dielectric constant (D) of the media in imine II.

Conclusions

1.Schiff bases 1 and 2 were prepared by standard method .Their structures were confirmed by physical method , using melting points and U.V-IR spectra .

2.Asimple ,fast and accurate potentiometric titration method was applied for the determination of pk_1 and Pk_2 ionization constants for nitrilium ions in imines 1-2.

3.pk_1 and Pk_2 were calculated from Handerson Hassellbach equation after addition of titrant HCl having maximum values of 1.0ml and 1.4 ml respectively.

4.The thermodynamic parameters calculated namely $\overline{\Delta G},\overline{\Delta H}$ and $\overline{\Delta S}$ show that ionization reaction of nitrilium ions were endothermic , non spontaneous and accompanied by an increase of random process.

5. $\Delta S_2 > \Delta S_1$ in any Schiff base (S) which agreed with ionization reaction of type (1-2) respectively :

$SH_2^{++} \longrightarrow S + 2H^+$ ....(1)
$SH^+ \longrightarrow S + H^+$ ....(2)

SH_2^{++} and SH^+ were called the double and mono nitrilium ions of any Schiff base produced during titration .

6.The relationship between pk_1 and Pk_2 versus D in any imine showed a bell shape ,as agreed with literature(16-17) .

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