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Synthesis and Spectrophotometric Study of Some New Azo dyes derived from Metoclopramide.

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ABSTRACT

This study involves the preparation of four azodyes 2-(Metoclopramide azo)- imidazole(L1), 2-(Metoclopramide azo)phenylephrine (L2) , 2-(Metoclopramide azo) oxindol (L3) and 2-(Metoclopramide azo)-4,5-diphenyl imidazole(L4). They have been described by C.H.N. , I.R. and Visible spectroscopic techniques. The acid-base properties were studied at different pH values (0.67-12) , then the ionization and protonation constants were determined.

Keywords : Metoclopramide, Azodyes , Ionization & Protonation constants and Spectral studies

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INTRODUCTION

Metoclopramide,4-amino-5-chloro-2-methoxy-N-(2-diethyl-ami-no-ethyl) benzamide is a white or almost white,odorless, crystalline powder (m.p. about 185°C) very soluble in water, alcohol freely, partially insoluble in ether,it is a dopamine- receptor antagonist, an antiemetic and a stimulant of upper gastroin-testinal motility and it is used for the management of gastrointestinal mo-tility disorders and gastrointestinal reflux[1,2].The visible spectrophotometric methods are the most analytical methods used for metoclopramide determination using different reagent including dibenzoylmethane[3], benzoylacetone[4], αnaphthol[5], diazotizedp-nitroaniline[6].

It has been by the reaction of with 4-dimethylaminobenzaldehyde to produce a yellow dye[7] Other methods include HPLC[8],titrimetric[9], and flow injection method[10]. The study of azo dyes with interesting physical and spectrophotometric properties have been active area of research diction .Azodyes are weak acids or weak bases of very important class of chemical compounds containing a heterocyclic moieties which have attracted the attention of many researchers in recent years. widely used in many practical applications such as photochromic materials, colorants, non-linear optics, sensors and indicators[11], so that it is used in the development of a simple spectrophotometric method for the determination of metaclopramide. The method has been satisfactorily applied to the determination of metaclopramide hydrochloride in dosage forms. The present work involves the synthesis of new azodye derived from Metoclopramide. Spectrophotometric studied on the dye were carried out like acid-base properties at different pH values , solvent effect of polar and non-polar solvents .

EXPERIMENTAL

Double distilled water , solvents (for spectral use) and all chemicals of highest purity were used.

Apparatus and materials

Visible absorption spectra were recorded by using PD-303 UV.,V.spectrophotometer , FT-IR-8400S spectrophotometer (Shimadzw) College of Educationfor Pure Science Basrah university ,pH-meter (H.Jurgons Co. Beremen,L. Puls Munchen 15), Heraus CHN Pro apparatus, Petrochemical Institute (Iran), Bunchi B190K for melting point measurement ,accurate balance E-Mette Weender (Land Strasse) 94-108.

Diazotization

0.005mole of Metoclopramide of weight 1.680g. was dissolved in 1.8ml concentrated hydrochloric acid , then 10 ml of distilled water to each salt forming .The solutions were cooled to 0 – 5 Co in ice-bath . 5 ml of sodium nitrite 0.38g. was then added drop wise with stirring continued to each solution to produce diazonium salt.

Preparation of dyes $L_1 – L_4$

0.005 mole of each imidazole ,phenylephrine, oxindole and 4,5-diphenyl imidazole , of weights 0.340, 1.018 , 0.665 and 1.1 g. respectively were dissolved in 50 ml alkaline ethanol . These solutions were added to the above diazonium salt solutions to forming sodium forms of the dyes L_1 – L_4 . The dyes solutions neutralized to the hydrogen forms by adding diluted hydrochloric acid by aid of pH paper . The precipitates were filtered off and twice recrystallized from 1:1ethanol : methanol mixture .

Solutions

A stock solution of (1×10^{-3} M) of each L_1 , L_2 , L_3 and L_4 dyes were prepared by dissolving an accurately weighed amount of the compounds in the required volume of ethanol , more dilute solutions were obtained by accurate dilution. Universal pH (2-12) and Acetate pH(0.67-2) buffer solutions[12]were prepared.

Procedure

Acid–Base studies [13],to study the effect of pH values on the absorption spectra on the dyes (L_1–L_4) and to

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determine the protonation and ionization constants , a series of buffer solutions (acetate and universal) were prepared with different pH values (0.67–12)with concentrations of dyes are ($0.8x10^{-4}$-0.2×10^{-4})M, the absorbance of these solutions was recorded at range of (310–580 nm) using a cell of 1cm length and buffer solution as a blank solution . By the aid of half height method the constants were calculated. For solvent effect studies, a series of solutions of dyes (L_1–L_4) were prepared of concentration of ($0.8x10^{-4}$-0.2×10^{-4})M in Ethanol,H_2O,Methanol, Dichloroethane, Dioxane, Dimethylformamid (DMF) and Dimethyl sulfoxide (DMSO).The absorbance of these solutions were recorded at range of (310 – 560 nm) using cell of 1cm length and using a solvent as a blank solution .

RESULTS AND DISCUSSION

C.H.N analysis of prepared dyes were illustrated in (Table 1)

Table 1: Elemental analysis data for synthesized dyes

N%		H%		C%		Chemical formal	simple
Found	Calc	Found	Calc	Found	Calc		
21.64	22.19	5.78	6.07	60.35	60.94	$C_{17}H_{23}N_6O_2Cl$	L_1
14.36	14.65	6.25	6.69	58.11	57.82	$C_{23}H_{32}N_5O_4Cl$	L_2
16.24	15.78	5.98	5.85	58.87	59.55	$C_{22}H_{26}N_5O_3Cl$	L_3
15.52	15.8	5.56	5.83	65.31	65.62	$C_{29}H_{31}N_6O_2Cl$	L_4

IR Analysis

Table (2) shows the famous IR frequencies of important bands of functional groups frequencies as seen in Figure (1).

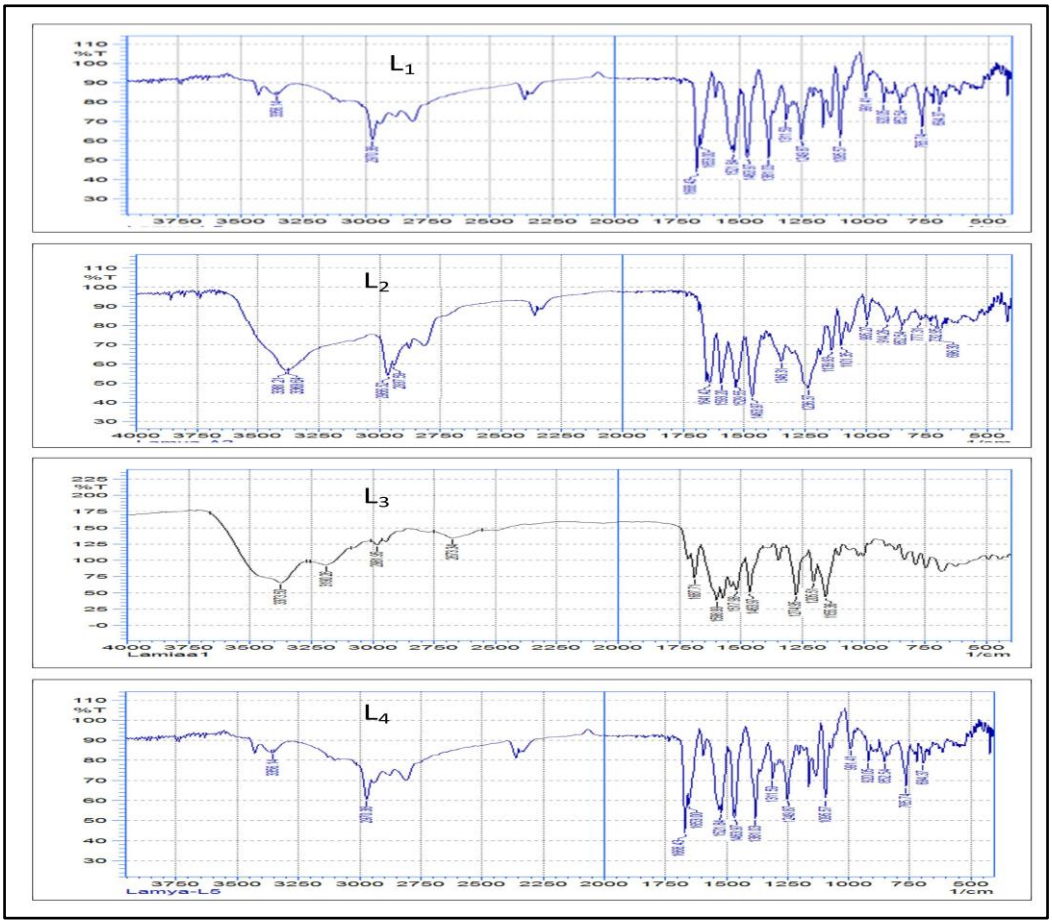

Fig 1: IR spectra of the azodyes L_1–L_4

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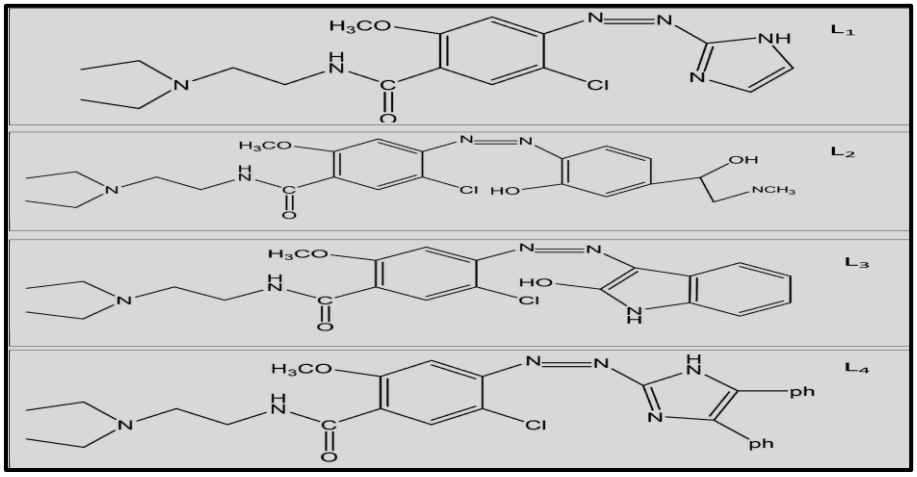
Table 2: The famous IR frequencies of important bands of azo dyes L_1–L_4

υN=N	υC=C	υC=N	υC=O	υH-N	υOH	simple
1521.84m	1463.97m	1653.00s	1668.43	3356.14w.b		L_1
1529.55s	1463.97s		1641.42s	3369.64int	3381.21s.b	L_2
1517.98m	1463.97m		1678.71m	3190.26w.b	3373.50s.b	L_3
1533.14m	1463.97	1602.35m	1649.14s	3431.36w.b		L_4

b =bord s =strong m=med w=weak

From IR analysis , Elemental analysis (CHN) and literatures and scientific previous researches , the chemical formula of azo dyes L_1-L_4 was suggested (schemes 1).



Scheme 1

Acid- Base Properties

To see the effects of acidity and basicity of buffer solutions on the dyes and to calculate the ionization and protonation constants, a series of acetate and universal buffer solutions were prepared at different pH values [0.67-12] for each dye [14].The absorbance with concentrations of dyes are (0.8×10^{-4}-0.2×10^{-4})M, the absorbance of these solutions was recorded at range of (310–580 nm),using buffer solution of such pH value as a blank solution. For L_1(Figure 2), the spectra characterized by two wavelength maximum bands at 440nm in pH range (10-12) and range(360-400 nm) for the other pH range . The first which more intense bands due to ionized form (basic form , anionic form).And the second of pH range (< 10) related to protonation form (acidic form , cationic form).

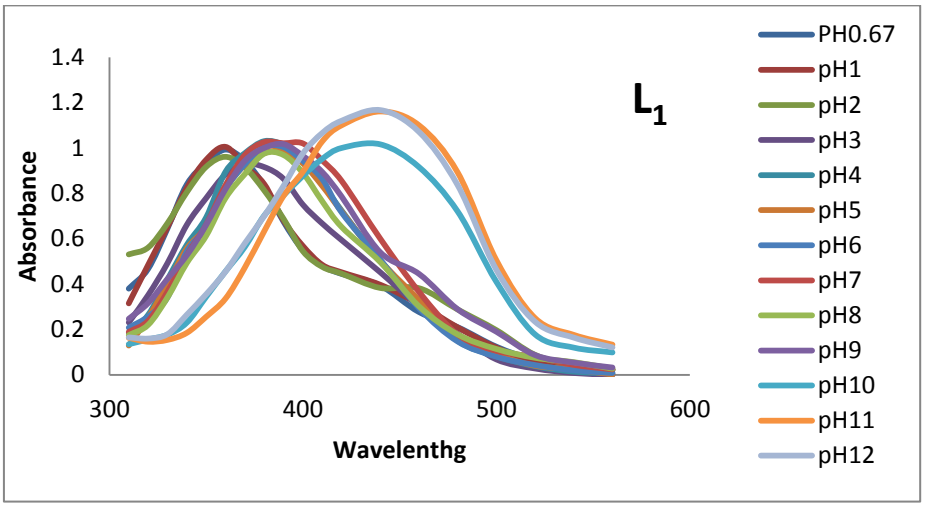


Fig 2: The electronic spectra of L_1 at different pH values

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For L_2 (Figure 3) , the spectra are also characterized by two maximum bands at 480 nm. in pH range (8 - 12) and at 350 nm. for the other pH range . The first which less intense bands at 480nm. , due to ionized form (pH > 8), and the second of more intense at 350 nm. of pH range (< 7) related to protonation form.

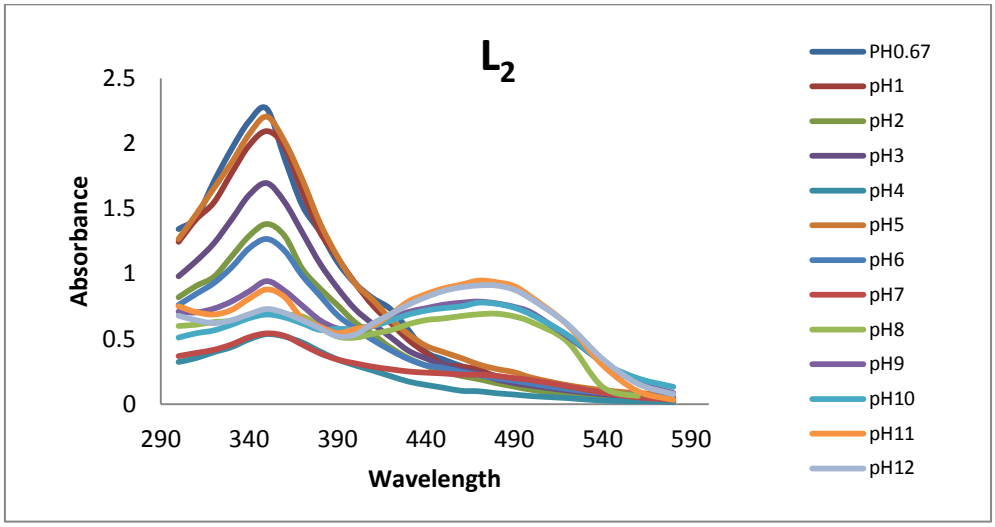

Fig 3: The electronic spectra of L_2 at different pH values

For L_3 (Figure 4), at max. wavelength range (370-390nm.) of acidic medium, this due to protonation. And the other wavelength max. in alkaline medium at 470 nm

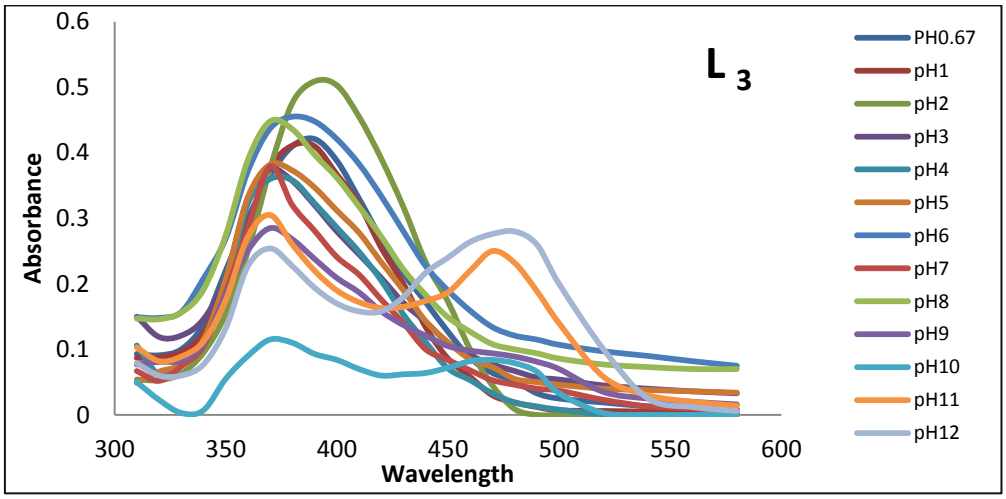

Fig 4 : The electronic spectra of L_3 at different pH values

For L_4(Figure 5), the spectra characterized by two wavelength maximum bands at 510nm in pH range (8-12) and range(460-470 nm) for the other pH range . The first which more intense bands due to ionized form (basic form , anionic form).And the second of pH range (< 8) related to protonation form (acidic form , cationic form).

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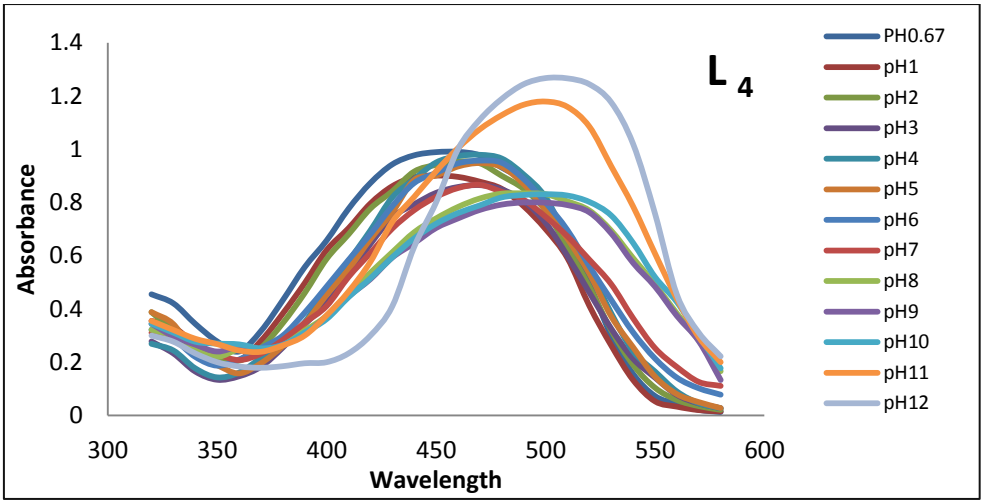

Fig 5 : The electronic spectra of L_3 at different pH values

The ionization and protonation constants were calculated (Table 3) by the aid of Figures(2-5), the absorbance – pH curves were plotted (Figure 6). From Absorbance–pH curve (Figure 6 for L_1–L_4) and by the aid of height method the pK values were obtained by the relation[15] :

pK = pH (at A1/2) where
A1/2 = (AL+ Amin.) / 2

Where AL and Amin are limiting and minimum absorbance's respectively.

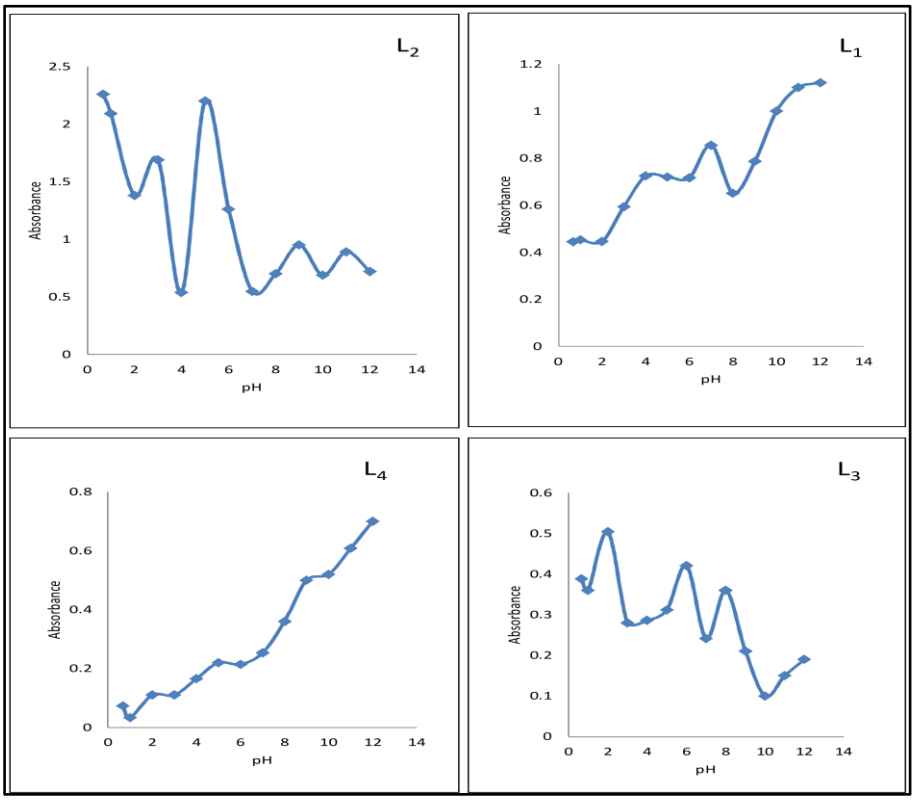

Fig 6: pH – Absorbance curve for dyes L_1 –L_4

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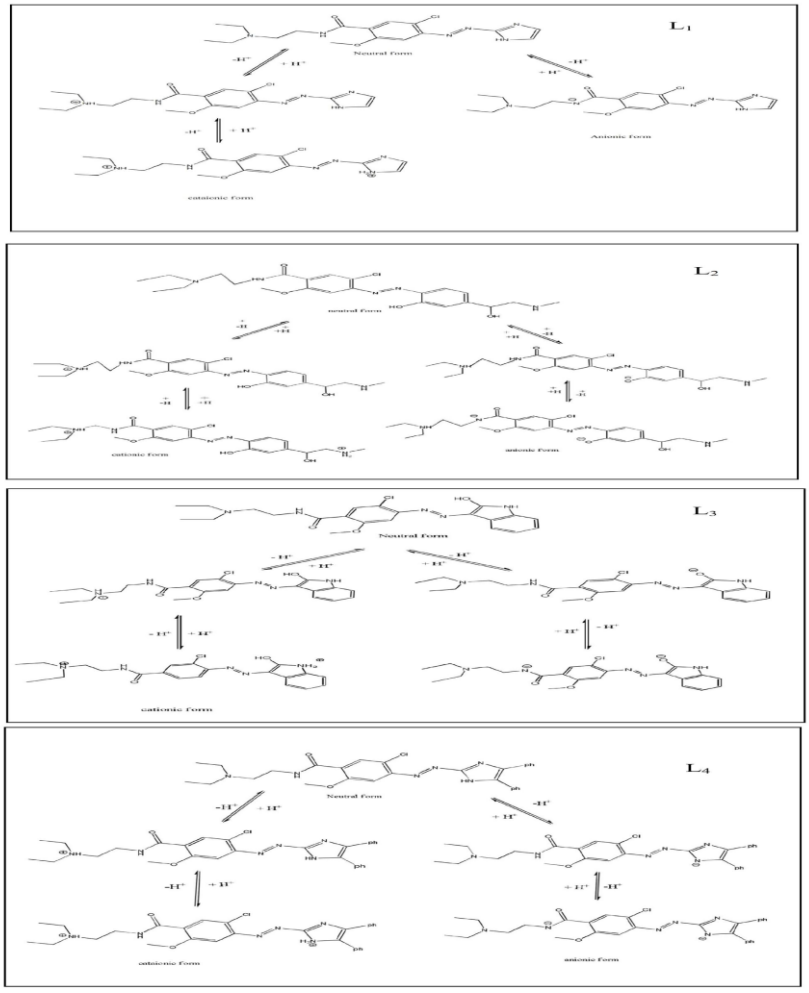
Table 3 : The protonation (pKp) and ionization (pKa) constants of azodyes L_1-L4

pK_{a2}	$A_{1/2}$	pK_{a1}	$A_{1/2}$	Pk_{P2}	$A_{1/2}$	Pk_{P1}	$A_{1/2}$	λ (nm)	Dyes
		9.4	0.875	2.4	0.585	6.3	0.78	420	L_1
10.5	0.789	7.9	0.748	2.6	1.535	4.5	1.368	350	L_2
10.6	0.140	7.6	0.3	1.4	0.432	5.4	0.353	400	L_3
10.9	0.603	8.2	0.357	1.7	0.071	4.1	0.168	550	L_4

From Figures.6 the mechanism of the ionization and protonation of each dye can be suggested (schemes 2).



schemes 2

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