Fused Five Membered Heterocyclic Amino Acids As An alternative Precursors in Phytopigment Cyanine like Synthesis

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ABSTRACT:

4-Acetyl-3-methyl-1-phenyl pyrazolin-5-imine **(1b)** undergoes multi step processes (selective quaternization & hydration) with chloroacetic acid in saturated sodium bicarbonate solution to achieve 1-Chloroacetyl-3, 4-dimethyl-1-phenyl-pyrrolo [2, 3-b] pyrazolo-2-carboxylic acid-2, 5-dicarboxy methylene chlorides **(18)**. Such compound under acidic conditions afforded N-acetyl-3, 4-dimethyl-1-phenyl-pyrrolo [2, 3-b] pyrazolo-2-carboxylic acid-2, 5-dicarboxymethylene chlorides **(19)**. Piperidine catalyzed of the later **(19)** achieved 1[H] -3, 4-dimethyl-pyrrolo [2, 3-c] pyrazolium-2-carboxylic acid-2-carboxymethylene hydroxide salt **(20)** which on interaction with N-methyl heterocyclic quaternary salts under piperidine catalysis afforded 3,4-dimethyl-1-phenyl-Pyrrolo-[2,3-c]-pyrazol -5-carboxylate zero- 6-[4(1)]-methine cyanine phyto pigment like **(21a-c).** The latter **20** subjected to condense with 4-acetyl-3-methyl-1-phenyl pyrazol-5-one (**1a)** under piperidine catalysis to give 6-[1-(3-methyl-1-phenyl-5-one-pyrazol-4-yl) ethyl]-3,4-dimethyl -1-phenyl- Pyrrolo-[2,3-c]-pyrazol-5-carboxylate **(22).** The reaction of 3,4-dimethyl-1-phenyl-Pyrrolo-[2,3-c]-pyrazol-5-carboxylate **(20)** with aromatic aldehyde and/or acetophenone derivatives under thermal piperidine catalysis afforded 3,4-dimethyl-1-phenyl-Pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid-6[1]-aryl-ethyl derivatives **(23a-g).** Further reaction of **(23a-g)** and N-methyl heterocyclic quaternary salts under thermal piperidine catalysis afforded 3,4-dimethyl-1-phenyl-Pyrrolo-[2,3-c]-pyrazol-5-carboxylic acid meso-substituted aryl aza tri –6[2(4)]-methine cyanine Phytopigment like **(24a-e).** The new synthesized cyanine dyes were identified by elemental & spectral analyses, The UV-visible absorption spectra of some selected dyes was investigated in pure organic solvents, as well as in aqueous universal buffer solutions.

Key Words: N-bridgehead Heterocyclic phytopigment like, synthesis, spectral, Solvato-(Media)-chromic Behaviour.

1. INTRODUCTION

Heterocyclic acids serve a central role in biology and chemistry being the fundamental constituents of proteins and mediators of nitrogen metabolism and provide raw material for a large number of biologically important primary and secondary metabolites**. [1]** The number of naturally occurring amino acids has grown substantially from 20 amino acids normally found in proteins to over 700. **[2].** In addition, there has been a tremendous surge of interest in preparation of relatively in accessible unnatural amino acids whose potential biological properties and general synthetic utilities are just beginning to be realized. Of the methods presently available, those derived from Electrophilic glycine equivalents are worth mentioning. **[3]** In the course of cyclization reactions of different-diketones with hydrazine derivatives achieved heterocyclic Carboxylic acids **[4]** which considered as inhibitors of rat liver alcohol dehydrogenase **(6) [4].** 2-Carboxy-3-methyl pyrrolo [2,3] naphth-4,9-dione-1[4(1)] mono aza- -substituted trimethine and 3-methyl-1-phenyl pyrrolo[3,4-d] pyrazolino phytopigment like were prepared by and were prepared by **[6,7].**

2. RESULTS AND DISCUSSIONS

2.1 SYNTHESIS

4-Acetyl-3-methyl-1-phenyl-pyrazolin-5-imine **(1b)** undergoes selective quaternization and hydration as a multi step processes with chloroacetic acid in saturated sodium bicarbonate solution to achieve 1-chloroacetyl-3, 4-dimethyl-1-phenyl-pyrrolo[2,3-b]pyrazolo-2-carboxylic acid-2, 5-dicarboxy methylene chlorides **(18)** via the formation 4-acetyl-1-chloroacetyl-3, 4-dimethyl-1-phenyl-pyrrolo [2, 3-b] pyrazol-ium-2-carboxylic acid-2, 5-dicarboxy methylene -ammonium chloride salt as intermediate **(17)** which under basic conditions achieved ring closure product **(18).** The reaction was suggested to proceed through dehydro halogenated (-HCl) process **(17)** followed by dehydration (-H_2O) process to give **(18)**. Such compound under acidic conditions afforded N-acetyl-3, 4-dimethyl-1-phenyl-pyrrolo [2, 3-b] pyrazolo-2-carboxylic acid-2, 5-dicarboxymethylene chlorides (**19)**. Meanwhile,

piperidine catalyzed of the later compound achieved, via hydrolysis process, 1[H] -3, 4-dimethyl-pyrrolo [2, 3-c] pyrazolium-2-carboxylic acid-2-carboxymethylene hydroxide salt **(20). Scheme (1A).**
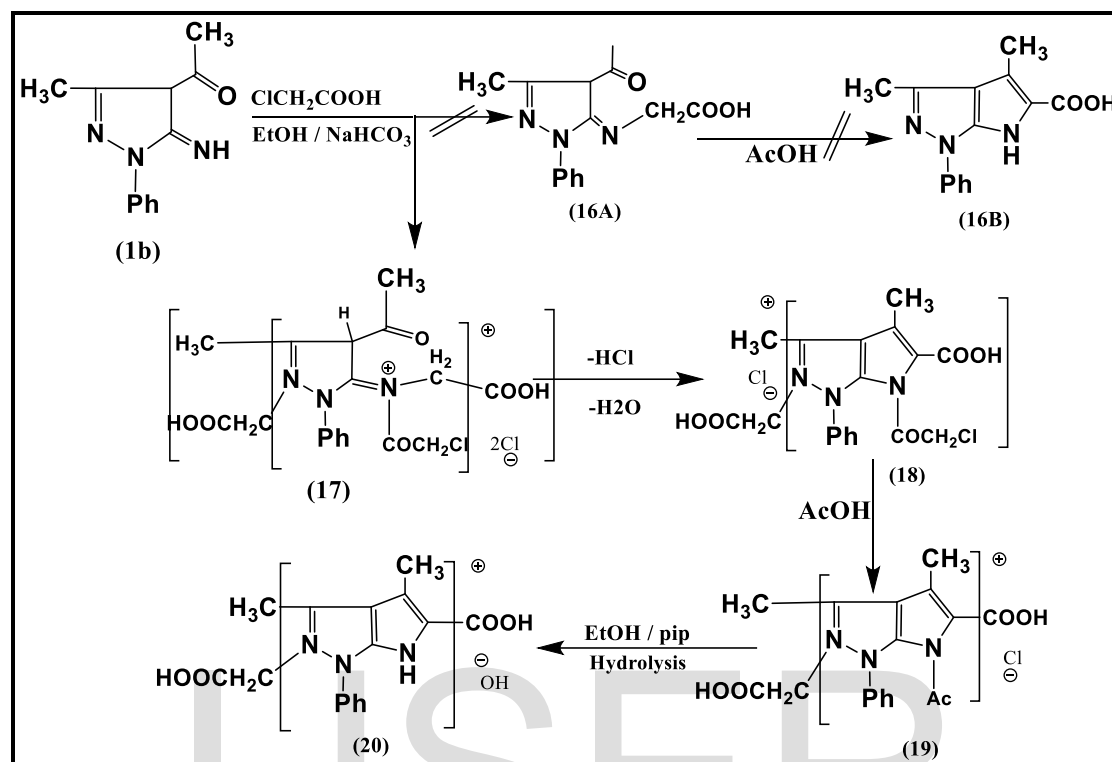
Scheme (1A)

Reaction of equimolar ratios of **(20)** with N-methyl heterocyclic quaternary salts (pyridinium, quinolinium and isoquinolinium) iodide under piperidine/ethanol conditions afforded the corresponding 3,4-dimethyl-1-phenyl- Pyrrolo-[2,3-c]-pyrazol-5-carboxylate zero- 6-[4(1)]-methine cyanine phytopigment like **(21a-c).** This reaction was suggested to proceed through the oxidative elimination reaction for secondary amino group in **(20)** with active hydrogen of heterocyclic quaternary salts followed by rearrangement with dehydro-halogenated (-HI) process to give **(21a-c), Scheme (1B).** The latter **(20)** subjected to condense with 4-acetyl-3-methyl-1-phenyl pyrazol-5-one (**1a**) under piperidine/ethanol conditions to give 6-[1-(3-methyl-1-phenyl-5-one-pyrazol-4-yl)ethyl]-3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazole-5-carboxylate **(22).** This reaction was suggested to proceed through the nucleophilic addition reaction between secondary amino group in compound **(20)** and carbonyl group in 4-acetyl-3-methyl-1-phenyl pyrazol-5-one (**1a**) involving a dehydration ($-H_2O$) process to give (**22), Scheme (1B).** Our approaches are extended to the synthesis of 3,4-dimethyl-1-phenyl- Pyrrolo-

[2,3-c]-pyrazole-5-carboxylic acid-6[1]- aryl-methinyl (ethyl) derivatives **(23a-g)** through the reaction of 3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazole-5-carboxylate **(20)** with aromatic aldehyde and/or acetophenone derivatives, in equimolar ratios, under thermal piperidine catalysis gave **(23a-g).** This reaction was suggested to proceed through the nucleophilic addition reaction between secondary amino group in compound **(20)** and carbonyl group in aromatic aldehyde or acetophenone derivatives involving a dehydration (-H$_2$O) process to give **(23a-g)**, **Scheme (1B)**. Further reaction of 3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid-6[1]-aryl-ethyl derivatives **(23a-g)** and N-methyl heterocyclic quaternary iodide salts (pyridine, quinoline and isoquinoline) ,in equimolar ratios, under thermal piperidine catalysis to afford 3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazol-5-carboxylic acid meso-substituted aryl Aza Tri –6[2(4)]-Methine Cyanine Phyto pigment like **(24a-e).** This reaction was suggested to proceed via the nucleophilic substitution reaction of methyl group in **(23e-g)** with active hydrogen of heterocyclic quaternary iodide salts involving oxidative elimination followed by rearrangement with dehydro-halogenated process to give **(24a-e), Scheme (1B).** On treatment of latter with conc. sulphuric acid, iodine vapor was not liberated on warming. The strongly acidic form **(Zwitterions character)** of N-heterocyclic α-carboxylic acid was considered as direct initial attempts for heterocyclic phyto pigment like synthesis, since N-bridge head heterocyclic characterized with high site reactivity susceptible to be attack either by carbon nucleophiles /electrophiles in substitution /addition reactions.
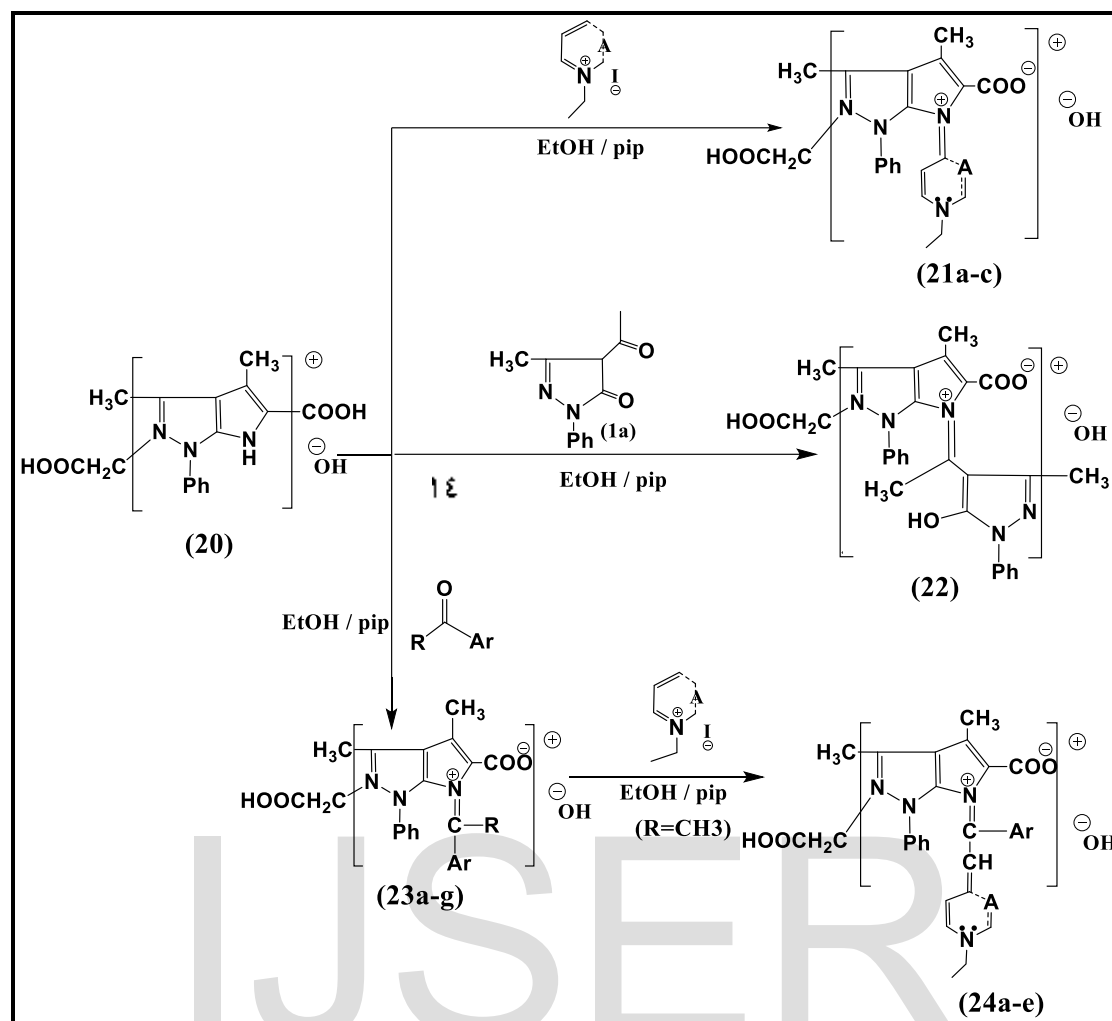
Scheme (1B)

(21a-c): A=quinolin-4-ium salt **(a)**; A=isoquinolin-1-ium salt **(b)**; A=pyridin-4-ium salt **(c)**; **(23a-g):** R=H, Ar= benzaldehyde **(a)**; R=H, Ar= p-N-dimethyl benzaldehyde **(b)**;R=H, Ar= m-Nitro-benzaldehyde **(c)**.R=H, Ar= p-OH-benzaldehyde **(d)**.R=CH_3, Ar= acetophenone **(e)**; R=CH_3, Ar= P-Nitro-acetophenone **(f)**;R=CH_3, Ar= p-methoxy-acetophenone **(g)**.**(24a-e):** Ar= p-Nitro-acetophenone, A=quinolin-4-ium salt **(a)**; Ar= p-Nitro-acetophenone, A=quinolin-1-ium salt **(b)**; Ar= p-Nitro-acetophenone, A=pyridin-4- ium salt **(c)**;Ar=p-methoxy-acetophenone,A=quinolin-4-ium-salt**(d)**; Ar= acetophenone, A=quinolin-4-ium salt **(e)**;

2.2. SPECTRAL ANALYSIS

The structure of (**18,19** & **20)** were characterized and identified by elemental and spectral analysis, (IR,^{1}H-NMR and Mass spectral data). Thus, IR (ν^{KBr} cm^{-1}) of (**18,19** & **20)** showed in addition to the general absorption bands at 1497 cm^{-1} (C=N), 1592 cm^{-1} (C=C), 3400 cm^{-1} (OH), **[9]**, ^{1}H-NMR (CD$_3$OD, 250

MHz) spectra of (**18,19 & 20**) showed in addition to the general single and multiple signals at δ 1.19-1.29 (s, CH_3, of pyrazol), 3.1(s,3H,CH_3 of pyrolo), 6.4 (s,1H,OH), 7.25-7.90 (m, 13H, Ar +Het) **[8,9].** The structure **(18)** was considered most likely based on mass spectrum resulted in M+ peak and base peak at m/e=425 which in agreement with the structure **[10].** The structure **(19)** was considered most likely based on mass spectrum resulted in M+3 peak and base peak at m/e=394 which in agreement with the structure, **[10].** The structure **(20)** was consider most likely based on mass spectrum resulted in M+1 peak and base peak at m/e=331 which in agreement with the structure **[10],** Mass spectra of (**18,19 & 20**) reveals a molecular ion $[M]^+$ peaks at m/z =425,and base peak at m/z =215 for (**18),** molecular ion $[M+3]^+$ peaks at m/z =394,and base peak at m/z =215 for (**19),** molecular ion $[M+1)]^+$ peaks at m/z =331,and base peak at m/z =214 for **20,** **[10].**, IR (ν^{KBr} cm^{-1}) of (**21a,22,23b, f,24a, d**) showed general absorption bands at 1497 cm^{-1} (C=N), 1592 cm^{-1} (C=C), 3400 cm^{-1} (OH), **[9]**, ^{1}H-NMR (CD_3OD, 250 MHz) spectra of (**21a,22,23b, f,24a, d**) showed the general single and multiple signals at δ 1.19-1.29 (s, CH_3, of pyrazol), 3.1(s,3H,CH3 of pyrolo), 6.4 (s,1H,OH), 7.25-7.90 (m, 13H, Ar +Het) **[8,9],**

2.3. COLOUR &SPECTRAL BEHAVIOUR

Zero methine cyanine phyto pigments like **(21a-c, 22, 23a-g, 24a-e)** are easily soluble in polar organic solvents and concentrated sulphuric acid from which iodine vapor was not liberated on warming. In 95%ethanol possess (dark brown to reddish brown), in colour. Their ethanolic solutions exhibited permanent coloured in basic media which reversibly discharged on acidification **Table (2,3).** The absorption spectra of zero methine cyanine phytopigment like **(21a-c,22, 23a-g, 24a-e)** in 95% ethanol consists of different absorption bands, their position and molar extinction coefficient being influenced by the type of heterocyclic quaternary residue **(A),** Thus, the absorption spectra of **(21a)** (A=quinolin-4- ium ethiodide) exhibit (λ_{max} 487nm; ε_{max} 8836 $mol^{-1}cm^2$). Substituting in **(21c)**, (A= pyridin-4-ium ethiodide), exhibit (λ_{max} = 449 nm.ε_{max}= 3731 $_{mol}^{-1}cm^2$) causes bathochromic shift due to the more extensive π-delocalization or conjugation. Changing the linkage position of quinoline residue from 4-ium in dye **(21a)** [A= quinolin-4- ium ethiodide] to 1-

ium in dye **(21b)** [A= quinolin-1-ium ethiodide] resulted in bathochromic shift in absorption band exhibited (λ_{max} 473nm; ε_{max} 2734 mol^{-1}cm^2. On comparison of the absorption spectra between dyes **(21a-c** & **22)**, a bathochromic shift in absorption band was exhibited **(22**, λ_{max} = 406,505nm. ε_{max} = 12567,9439 mol^{-1}cm^2). This is due to an increase in electron donating of 3-methyl-1-phenyl-5-one-pyrazol substituted than heterocyclic quaternary residue **(A)** as electron sink .On the other hand, The absorption spectra of aza styryl cyanine phyto pigments **(23a-g)** in 95% ethanol consists of different absorption bands, their position and molar extinction coefficient being influenced by the nature of aryl substituents **(R)** and **(Ar)**, Thus, the absorption spectra of **(23a)** (R=H, Ar= benzaldehyde) exhibit (λ_{max} 374nm; ε_{max} 28836 mol^{-1}cm^2). Substituting in **(23b)**, (R=H, Ar= p-N-dimethyl benzaldehyde), exhibit (λ_{max} = 414, 484 nm.ε_{max}= 37870 $_{mol}$$^{-1}$cm^2) resulted in bathochromic shift. This is due to the more electron donating   character of N-dimethyl group. Changing the linkage position of [Ar= benzaldehyde] in dye **(23a)** to [Ar= m-Nitro-benzaldehyde] in dye **(23c)** resulted in hypsochromic shift in absorption band exhibited (λ_{max} 390nm; ε_{max} 13429 mol^{-1}cm^2. This is due to the more electron withdrawing character of the NO$_2$ group. Also, substituting of [Ar= benzaldehyde] in dye **(23a)** to [Ar= p-OH benzaldehyde] in dye **(23d)** resulted in bathochromic shift in absorption band exhibited (λ_{max} 409nm; ε_{max} 12522 mol^{-1}cm^2. This is due to the more electron donating character of the hydroxyl group. Additionally, substituting of [R=H, Ar= benzaldehyde] in dye (**23a)** to [R=CH$_3$, Ar= acetophenone] in dye **(23e)** resulted in bathochromic shift in absorption band exhibited (λ_{max} 548nm; ε_{max} 5794 mol^{-1}cm^2. This is due to the hyper conjugation and electron donating character of the methyl group. On other hand, substituted (**23e)** [Ar= acetophenone] by [Ar= p-Nitro-acetophenone] in dye **(23f)** resulted in hypsochromic shift in absorption band exhibited (λ_{max} 400nm; ε_{max} 10023 mol^{-1}cm^2. This is due to the more electron withdrawing character of the NO$_2$ group. Also, substituting of [Ar= acetophenone] in dye (**23e)** by [Ar= p-OCH$_3$ acetophenone] in dye **(23g)** resulted in bathochromic shift in absorption band exhibited (λ_{max} 551nm; ε_{max} 4365 mol^{-1}cm^2. This is due to the more electron donating character of methoxy group. **Table (2,3).**.Similarly, The absorption spectra of substituted aza trimethine cyanine phyto pigments like **(24a-e)** in 95% ethanol consists of different absorption

bands, their position and molar extinction coefficient being influenced by the type of heterocyclic quaternary residue **(A),** nature of aryl substituents **(Ar),** Thus, the absorption spectra of **(24a)** (Ar= p-Nitro-acetophenone, A=quinolin-4- ium ethiodide) exhibit (λ_{max} 460nm; ε_{max} 14818 mol^{-1}cm^2). Substituting of (Ar= p-Nitro-acetophenone, A= pyridin-4-ium ethiodide) in **(24c)**, exhibit (λ_{max} = 450 nm.ε_{max}= 14749 mol^{-1}cm^2) causes hypsochromic shift due to the more extensive π-delocalization or conjugation. Changing the linkage position of quinoline residue from 4-ium in dye **(24a)** [A= quinolin-4- ium ethiodide] to 1-ium in dye **(24b)** [A= quinolin-1-ium ethiodide] resulted in hypsochromic shift in absorption band exhibited (λ_{max} 455nm; ε_{max} 3368 mol^{-1}cm^2.   On other hand, substituted **(24a)** [Ar= p-Nitro-acetophenone] by [Ar= p-methoxy acetophenone] in dye **(24d)** resulted in bathochromic shift in absorption band exhibited (λ_{max} 479nm; ε_{max} 9181 mol^{-1}cm^2. This is due to the more electron donating character of methoxy group. Also, substituted (**24a**) [Ar= p-Nitro-acetophenone] by [Ar= acetophenone] in dye **(24e)** resulted in bathochromic shift in absorption band exhibited (λ_{max} 470nm; ε_{max} 11374 mol^{-1}cm^2. This is due to the more electron withdrawing character of the NO$_2$ group. **Table (3).**

2.4. SOLVATOCHROMIC BEHAVIOUR

The absorption spectra of 3,4-Dimethyl-1-phenyl- pyrrolo-[2,3-c]-pyrazole -5-carboxylic acid zero- 6-[4(1)]-methine phyto pigment cyanine dyes like, 6-[1-(3-methyl-1-phenyl-5-one-pyrazol-4-yl) ethyl]-3,4-dimethyl -1-phenyl- pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid**,** 3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazol-5-carboxylic acid-6[1]- aryl-methinyl (ethyl) derivatives **(21a,c, 22, 23b,c,e,f),** in the wavelength range 250-700 nm, have been studied in different organic solvents (H$_2$O, DMF, EtOH, MeOH, acetone, CCl$_4$, CHCl$_3$, and C$_6$H$_6$) **[11]** respectively. The colour changes of such dyes with solvents having different polarities are presented in **Tables (2, 3).** This is constructed with the intention to illustrate the solvatochromic behaviour of the dyes (λ_{max} and ε_{max}) values of the intramolecular charge transfer bands are given in **Tables (1)**. These dyes are showed positive solvatochromism with increased solvent polarity which depend on the structure and type of dye. This indicates that the polar excited states of such cyanine phyto pigments like are stabilized

by polarization interaction forces as the polarizability of the solvent is increased. This behaviour occurs as a result of electrostatic interactions of the distributed cationic charges with the dipoles of the solvated molecules which lead to formation of specific solvated forms of dyes. The absorption spectra of dyes in ethanol are characterized by the presence of one or two essential bands which reflects the presence of intermolecular charge transfer [**12).** This intermolecular charge transfer had arisen from transferring the electron lone pair of nitrogen atoms of the heterocyclic ring system towards positively charged residue along the conjugated chain between both. The relevant data in **Tables (1)** as well as the representing graphs disclosed that these electronic charge transfer bands exhibit a hypsochromic shifts in ethanol relative to DMF, CHCl$_3$, and CCl$_4$. These shifts can be attributed to the bathochromic shift occurred in DMF relative to ethanol is mainly a result of an increase in solvent polarity due to increasing the dielectric constant of the former, **Tables (1).** The hypsochromic shifts appeared in ethanol relative to CHCl3, and CCl$_4$ is generated from the solute-solvent interaction through intermolecular hydrogen bonding between ethanol and lone pair of electrons within the heterocyclic ring system. Otherwise, this decreases the mobility of the electron cloud over the conjugated pathway towards the positively charged center, **Table (1).** It was worth mentioning that the intermolecular hydrogen bonding between CHCl$_3$ molecules and lone pair nitrogen electrons of heterocyclic ring system is difficult due to the sterric hindrance of three bulk chlorines. Moreover, solute solvent interactions in cases of CHCl$_3$, and CCl$_4$ generated a residual negative charge on heterocyclic ring nitrogen atoms of the system which intern facilitated electronic charge transfer to positively charged centre and this explain the bathochromic shifts in these solvents relative to ethanol, **Table (1).** The unexpected hypsochromic shifts in the absorption spectral maxima in water relative to ethanol and its lower extinction coefficients were mainly ascribed to an ease of interactions of water molecules, through intermolecular hydrogen bonding with lone pair of heterocyclic nitrogen electrons ring system, through intermolecular hydrogen bonding, which intern preclude charge transfer from heterocyclic ring system to positively charged residue along the conjugated bridge, **Table (1,2,3,4).** In point view of light absorption, it was obvious that most of the previous

selected cyanine phyto pigments like, **(5a,c-g, 10a,b,d,e, 14a,c-e, 15a,c,d,e, 21a,c, 22, 23b,c,e,f, 24a,c,d, 27a,b,d, 28 & 30b,d,e)** are absorbed the fundamental light absorption (violet-red) as they have got absorption values in the range 350-660 nm **Tables (1,2,3,4) [13]**. The selected cyanine phyto pigments like might be suggested to be used as photosensitizers in most polar and non polar organic solvents in the (violet-red). Thus, it was obvious that **(5a,c-g, 21a,c)** absorbed green-blue light in EtOH, acetone, benzene, $CHCl_3$, CCl_4 and MeOH λ_{max} = 340-385 nm extended and improved to the absorption of green light in DMF and acetone λ_{max} = 440-495 nm. Dyes **(14a,c-e, 15a,c,d,e)** absorbed green-blue light in EtOH, acetone, benzene, $CHCl_3$, CCl_4 and MeOH λ_{max} = 300-350 nm extended and improved to the absorption of green light in DMF and acetone λ_{max} = 400-480 nm. Also, **(22, 23c,e, 10a,b,d,e, 27a,b,d, 30b,d,e)** absorbed near violet light in EtOH, benzene, $CHCl_3$, CCl_4 and MeOH λ_{max} = 360-420 nm extended and improved to the absorption of green light in DMF and acetone λ_{max} = 520-575 nm. Dye **(28)** absorbed blue light in EtOH, benzene, $CHCl_3$, CCl_4 and MeOH λ_{max} = 450-470 nm extended and improved to the absorption of blue-green light in DMF and acetone λ_{max} = 500 nm. Dye **(23f)** absorbed violet light in EtOH, benzene, $CHCl_3$, CCl_4 and MeOH, λ_{max} 380-400 nm extended and improved to the absorption of blue light in DMF and acetone λ_{max} = 470-490 nm. Finally, **(23b, 24a, c, d),** absorbed blue-green light in EtOH, benzene, $CHCl_3$, CCl_4 and MeOH λ_{max} = 330-375 nm extended and improved to the absorption of red light DMF and acetone λ_{max} =450-520 nm. The solution of some selected synthesized 3,4-dimethyl-1-phenyl- Pyrrolo-[2,3-c]-pyrazole -5-carboxylic acid zero- 6-[4(1)]-methine cyanine phytopigment like**,** 3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid-6[1]- aryl-methinyl (ethyl) derivatives**,** 3,4-dimethyl-1-phenyl-pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid meso-substituted di–6[4(1)]-methine

2.5. MEDIACHROMIC BEHAVIOUR

Phytopigment cyanine dye like **(21a, c, 23b, and 24d)** gives a permanent colour in basic medium which is discharged on acidification. This promoted us to study their spectral behaviour in different aqueous universal buffer solution in order to ensure optimal pH in the application of such dyes as

photosensitizers and determine their pKa values too. The effectiveness of compounds as photosensitizers increases when they are present in the ionic forms (non protonated form) which have higher planarity **[16].** The absorption spectra of the selected cyanine dyes **(20, 21a,c, 23b, 24d, 27b,d and 30b,d,e)** in aqueous universal buffer solution of different values of pH (2.09,4.10,6.09,7,8.36, 10.38,11.98) show regular changes with increasing pH of the medium especially in the n-$\pi*$ and CT bands**, Table (2).** Also The electronic spectra of selected cyanine dyes in aqueous universal buffer solutions of varying pH values showed bathochromic shifts with an intensification of absorption bands at high pH values (alkaline media), otherwise, hypsochromic shifts with quenching the intensity of the absorption bands at low pH values (acidic media) were recorded. Moreover, increasing the pH values of the medium intensified the electronic charge transfer due to deprotonation which intern support heterocyclic lone pair's electrons of ring system and increase its mobility. In the other hand, decreasing pH values of medium interrupted the charge transfer due to protonation and intermolecular hydrogen bonding which intern preclude the availability of the lone pairs of the heterocyclic ring system. Several methods had been adopted for spectrophotometric estimation of the dissociation constants of weak acids; the variation of absorbance at settled wavelength could be utilized. Thus, on plotting the absorbance at settled wave number versus pH values, S-shaped curves were obtained. For all S-shaped curves, the horizontal portion to left corresponded to the acidic form of an indicator, while the upper portion to right corresponded to the basic form. Since the pKa value was defined as the pH value for which one half of the indicator (dye) is in basic form and the other half in an acidic form. This point, (pKa value), was determined by the intersection of the S-curve with horizontal line midway between the left and right segments, **Table (3).** The spectral behaviour of **(20, 21a,c, 23b, 24d)** in 95% ethanol and/or in aqueous universal buffer solution showed that these compounds absorbed blue light λ_{max} = 340-385 nm and near violet light extended to the green light λ_{max} = 440-495 nm. In acid medium (pH $\geq$ 2.09), such dyes undergo a hypsochromic colour change due to protonation of the heterocyclic nitrogen atom (oxygen) or heterocyclic quaternary nitrogen atom

salts [quinolin-2-/ pyridin-4- ium] salts and other non-quaternize N-methyl (quinoline-2-/pyridine-4. In such cases the intramolecular charge transfer (CT) between heterocyclic donor nitrogen (oxygen) and heterocyclic acceptor nitrogen atoms does not occur, and long wave length CT band disappears. A new short wave length band is observed, which could be assigned to a localized $\pi-\pi^*$ transition. On the other hand, the resulted bathochromic shift as the pH of the medium increases is due to that the protonated compounds becomes deprotonated and their mesomeric interaction with the rest of the molecule becomes high and consequently the CT interaction with the free base is facilitated, **Table (2)**. The pk_a values were obtained using the standard procedure **[15]**, the pKa values and spectral characteristics of the protonated forms of dyes are collected in Table 6. Thus, it was suggested that these dyes are sensitive as photosensitizers in both acidic and basic mediums. This may be due to presence of N-methyl quinolin-2-/ pyridin-4-linkage and other quinolin-2-/ pyridin-4-ium salts causing high planarity of the dye molecule.

3. EXPERIMENTAL

All melting points are uncorrected. Elemental analysis was carried out at the Micro analytical center (Cairo-University). IR (νKBr) spectra were determined with Perkin Elmer Infrared 127ß Spectrophotometer (Cairo-University). ^{1}H–NMR spectra were recorded with a Bruker AMX-250 spectrometer. Mass spectra were recorded on a HpMs 6988 spectrometer (Cairo University). The absorption spectra were recorded within the wavelength range (350-700) on 6405 UV/Visible recording spectrophotometer, Aswan-Faculty of Science. 4-Acetyl–3–methyl–1–phenyl pyrazol–5–one (imine) (1). 4-arylideno-3-methyl-1-phenyl pyrazol-5-one (imine) **(2a-f)** was carried out according to **[16]**,

Synthesis of N-Chloro-acetyl-3, 4-dimethyl-1-phenyl-pyrrolo[2, 3-b] pyrazol-2-carboxylic acid 2, 5-dicarboxymethylene chlorides (18).

An ethanolic solution of 4-acetyl–3–methyl–1–phenyl pyrazol–5–(imine) (0.01mol) and chloroacetic acid (0.01mol)) in the presence of saturated solution sodium bicarbonate was refluxed for 8 hrs. The reaction mixtures were filtrated from unreacted materials. The filtrate was concentrated, cooled and acidified with acetic acid. The precipitated product after dilution with water was separated, filtrated, crystallized from ethanol, and afforded (**18), 18:** m. p.

= 160 °C, yield = 71 %, colour = yellow, Molecular formula: $C_{18}H_{17}N_3O_5Cl_2$, M.wt = 425.5, Analysis % calculated (found): C = 50.72(50.78), H = 4.02(4.05), N = 9.86(9.91)

Synthesis of 1[H] -3, 4-dimethyl-pyrrolo [2, 3-c] pyrazolium-2-carboxylic acid-2-carboxymethylene hydroxide salt (20).

A weight amount of **(18)** (0.01 mol) was refluxed with acetic acid for 6 hours, concentrated, diluted with water,collected and recrystalised from acetic acid to give N-acetyl-3, 4-dimethyl-1-phenyl-pyrrolo [2, 3-b] pyrazolo-2-carboxylic acid-2, 5-dicarboxymethylene chlorides (**19),** and then the product refluxed with piperidine followed by EtOH extraction for 4 hours, The products were collected and recrystalised to give **(20), 19:** m. p. = 140°C, yield = 66 % , colour = Reddish brown, Molecular formula: $C_{18}H_{18}$ N_3O_5Cl, M.wt = 391.5, Analysis % calculated (found): C = 55.18(55.19),H = 4.63(4.68), N = 10.72(10.79). **20:** m.p. = 150°C, yield = 51 %, colour = Deep reddish brown, Molecular formula: $C_{16}H_{17}$ N_3O_5, M.wt = 331, Analysis % calculated (found):C = 58.01(58.04),H = 5.17(5.19),N = 12.68(12.71)

Synthesis of 3,4-dimethyl-1-phenyl- Pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid zero- 6- [4(1)]-methine cyanine dyes (21a-c).

Equimolar proportions **(20**, 0.01 mol) and (pyridin-4-ium, quinolin-4(1)-ium salts ,0.01 mol) were dissolved in ethanol (30 ml) and piperidine (3-5 drops) was added. The reaction mixtures were refluxed for about 7-9 hrs., filtered hot, concentrated and cooled and acidified with acetic acid. The precipetated solids after dilution with water were collected and crystallized from aqueous ethanol to give **(21a-c) Table (4).**

Synthesis of 6-[1-(3-methyl-1-phenyl-5-one-pyrazol-4-yl) ethyl]-3,4-dimethyl -1-phenyl- Pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid (22):

Equimolar proportions **(20,** 0.01 mol) and 4-acetyl-3-methyl-1-phenyl pyrazol-5-one (0.01 mol) were dissolved in ethanol (30 ml) to which piperidine was added.The reaction mixture was refluxed for about 6-8 hrs., filtered hot, concentrated and cooled and acidfied with acetic acid.The products after dilution with water were collected and recrystalised from aqueous ethanol**.** **(22):** m. p. = 210 °C, yield = 52 %, colour = violet Molecular formula: $C_{28}H_{27}N_5O_6$**,** M.wt = 529, Analysis % calculated (found): C= 63.51(63.58), H = 5.14(5.19), N = 13.23(13.27)

Synthesis of 3,4-dimethyl-1-phenyl- Pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid-6[1]- aryl-methinyl (ethyl)derivatives (23a-c).

Equimolar proportions **(20,** 0.01 mol) and aromatic aldehyde and/or acetophenone derivatives (0.01 mol) were dissolved in ethanol (30 ml) to which piperidine was added.The reaction mixture was refluxed for about 6-8 hrs., filtered hot, concentrated, cooled and acidfied with acetic acid.The products after dilution with water were collected and recrystalised from aqueous ethanol **Table (4).**

Synthesis of 3,4-dimethyl-1-phenyl- Pyrrolo-[2,3-c]-pyrazole-5-carboxylic acid meso-substituted di –6[4(1)]-methine phyto cyanine dye like (24a-c).

A Mixture of **(23a-c,** 0.01mol) and 2(4)-methyl (pyridin-2(4)-ium, quinolin-2-ium salts (0.01mol) were refluxed in ethanol for 8 hr, in the presence of few drops of piperidine. The reaction mixtures were filtrated from unreacted materials. The filtrate was concentrated, cooled and acidified with acetic acid. The precipitated products after dilution with water were separated, filtrated, crystallized from the suitable solvent **Table (4).**

Synthesis of compound 3-methyl-5-imino-1-phenyl pyrazolo 4-(N-acetyl-pyridin (quinolin)-1-ium iodide) (25a,b).

A Mixture of 4-acetyl-3-methyl-1-phenyl-5-imino pyrazolo (2.1 gm ,0.01 mol) , iodine (2.54 gm, 0.01 mol) and (α) picoline and /or quinlidine (1 ml).The reaction mixture was refluxed for 3 hours, and filtered, concentrated and cooled, the solid product was collected and crystallized from ethanol to give:

(25a): m. p. = 130 °C, yield = 85 %, colour = brown, Molecular formula: $C_{18}H_{19}N_4OI$, M.wt = 434, Analysis % calculated (found) : C = 49.77 (49.81), = 4.37 (4.41), N = 12.90 (12.94), (**25b):** m.p.= 180°C, yield = 89 %, colour = Deep reddish brown ,Molecular formula: $C_{22}H_{21}N_4OI$, M.wt = 484, Analysis % calculated (found): C = 54.54 (54.58), H = 4.33 (4.37),N = 11.57(11.59).

Synthesis of 1-acetyl-3`-methyl-1`-phenyl- pyrazolin-5-N-acetylimine-4`(2)-indolizine (benzoindolizine) (26a,b):

Mixture of **(25a,b,** 0.005 mol) with acetic anhydride (10 ml). was refluxed for 3 hours, and filtered, concentrated and cooled, the solid product was collected and crystallized from ethanol to give the two following compounds: **26a:** m. p.

= 165°C, yield = 85 % ,colour = black, Molecular formula = $C_{22}H_{21}N_4O_2I$ **,** M.wt = 500, Analysis % calculated (found) = C = 52.82 (52.86), H = 4.2 (4.25), N = 11.2 (11.22), **26b:** m.p.= 120°C, yield = 70 %, colour = yellowish brown, Molecular formula : $C_{26}H_{23}N_4O_2I$,M.wt = 550, Analysis % calculated (found) = C = 56.75 (56.78), H = 4.18 (4.19),N = 10.18 (10.19).

Solvatochromic and Acid -Base Properties:

The organic solvents were used of spectroscopic grade of purified according to the recommended methods **[17]**. The electronic absorption spectra of the studied dyes in different organic solvents were recorded within the wavelength (350-700 nm) on 6405 UV/Visible recording spectrophotometer using 1 cm cell. The stock solution of the dye was of the order 10^{-3} M. Solution of low molarities used in spectral measurements was obtained by accurate dilution.

I-preparation of dyes solution:

1-For studying the effect of pure solvents in the UV and visible range: Accurate volumes of the stock solution of the dyes were diluted to appropriate volume in order to obtain the required concentrations. The spectra were recorded immediately after mixing in order to eliminate as much as possible the effect of time. 2- For studying the   spectral behaviour in mixed solvents in the visible region: An accurate volume of the stock solution (10^{-3} M in ethanol) of the dyes were placed in 10 ml measuring flask containing the required volume of ethanol, then completed to the mark with the other solvent. 3- For studying the spectral behaviour in aqueous universal buffer solutions: An accurate volume of the stock solution was added to 5 ml of the buffer solution in 10 ml measuring flask, then completed to the mark with redistilled water. The pH of such solution was checked before spectral measurements.

2-Preparation of Universal Buffer Solution:

A modified buffer series derived from that of, **[18]** was prepared for use in the present investigation. The constituents are as follows:

a-A solution of 0.4 M of each phosphoric and acetic acid was prepared by accurate dilution of A. R. concentrated stock. b-A solution of 0.4 M of boric acid was obtained by dissolving the appropriate weight of the recrystallized acid in redistilled water. c-A stock acid mixture was prepared by mixing equal volumes of three acids in large bottle. The total molarity of the acid was thus maintained at 0.4 M A series of buffer solutions with pH values ranging from

(2.09-11.98) was prepared as recommended by **[18]**. This was done by mixing 150 ml of the acid mixture in a 250 ml measuring flask with the appropriate volume of 1.0 M NaOH and completed to the mark with redistilled water. This modification was performed in order to keep the ionic strength constant at all pH‚ s mixed with different proporations of organic solvents used. The pH's of the buffer solutions were checked using Orion pH-meter model (60, A), accurate to $\pm$ 0.005 pH units, at 25 °C.

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Table (1): Values of absorption (nm) and extinction coefficients (mol^{-1}cm^{-1}) of

(20, 21a) in aqueous universal buffer solution.

Comp	Universal buffer													
	2.09		4.10		6.09		7		8.36		10.38		11.98	
	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}
20	380	2952	440	2639	400	2610	380	2753	390	2705	380	2760	395	2743
21a	454	1980	465	3590	468	5912	460	3482	479	4822	473	4483	481	3631
	313	14521	315	16983	270	39576	243	37632	254	37633	256	39574	240	37622
	246	39572	251	36121	-	-	-	-	-	-	-	-	-	-

Table (2): Values of absorption (nm) and extinction coefficients ($mol^{-1}cm^{-1}$) of **(21c, 23b, 24d)** in aqueous universal buffer solution.

Comp	Universal buffer													
	2.09		4.10		6.09		7		8.36		10.38		11.98	
	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}
21c	449	3132	457	3211	463	2423	267	34620	473	1901	471	1644	479	2020
	323	29851	310	34621	299	37631	454	1032	296	39577	313	39575	291	39133
23b	221	39132	471	39110	436	29144	417	32230	414	26132	409	36122	412	39134
	487	4133	420	33112	358	27683	363	28533	361	22284	363	34621	422	34623
	304	22800	353	36121	-	-	-	-	251	31352	-	-	358	37635
24d	443	7122	438	13445	441	11348	446	10112	460	12935	470	14522	476	16211
	280	40000	313	33746	310	32633	243	35247	304	37634	312	33746	315	35243

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Table (3): The variation of absorbance in λ_{max} characteristic for each selected **20,21a 21c,23b, 24d** in different buffer solutions

Comp. No. pH	21a λ_{530}	21c λ_{510}	23b λ_{440}	24d λ_{530}
2.09	0.068	0.137	0.408	0.422
4.10	0.233	0.172	3.311	0.872
6.09	0.438	0.12	2.185	0.741
7	0.237	0.059	1.604	0.65
8.36	0.329	0.15	1.116	0.82
10.38	0.266	0.122	1.467	0.876
11.98	0.143	0.003	1.377	0.931
pKa	7.2	6.5	6.6	6.7
	10.5	7.3	-	7.2
	-	-	-	-

Table (4): Characterization data of phyto cyanine dye like **((21a-c,23a-g, 24a-e).**

Comp. No.	M.P. °C	Yield %	Colour	Mol.Formula (Mol.wt)	% Calcd. (Found)			Absorption spectra in EtOH, λ_{max} (nm) ε_{max} (cm^2mol^{-1})	
					C	H	N		
21a	95	38	Violet	$C_{26}H_{24}N_4O_5$ (472)	66.10 (66.14)	5.08 (5.09)	11.86 (11.89)	487	8836
21b	160	41	Pal red	$C_{27}H_{26}N_4O_5$ (486)	66.66 (66.69)	5.37 (5.38)	11.52 (11.59)	473	2734
21c	176	31	Buff	$C_{22}H_{22}N_4O_5$ (422)	69.36 (69.38)	5.20 (5.24)	16.18 (16.19)	449	3731
23a	130	28	Deep red	$C_{23}H_{21}N_3O_5$ (419)	73.47 (73.49)	4.96 (4.98)	12.24 (12.27)	374	28836
23b	140	46	Violet	$C_{25}H_{26}N_4O_5$ (462)	71.50 (71.55)	5.70 (5.73)	14.51 (14.54)	414 484	37870 36087
23c	80	57	Pal red	$C_{23}H_{20}N_4O_7$ (464)	64.95 (64.97)	4.12 (4.15)	14.43 (14.44)	390	13429
23d	115	62	Pal brown	$C_{23}H_{21}N_3O_6$ (435)	70.19 (70.21)	4.74 (4.77)	11.70 (11.74)	409	12522
23e	180	29	Deep red	$C_{24}H_{22}N_3O_5$ (433)	73.95 (73.99)	5.04 (5.08)	11.76 (11.78)	548	5794
23f	90	73	Violet	$C_{24}H_{22}N_4O_7$ (478)	65.67 (65.68)	4.48 (4.49)	13.93 (13.97)	400 -	10023 -
23g	150	48	Pal red	$C_{25}H_{25}N_3O_6$ (463)	71.32 (71.35)	5.43 (5.46)	10.85 (10.87)	551	4365
24a	120	48	Red	$C_{34}H_{29}N_5O_7$ (619)	70.72 (70.76)	4.60 (4.63)	12.89 (12.87)	460	14818
24b	280	42	Deep red	$C_{35}H_{31}N_5O_7$ (633)	71.10 (71.13)	4.85 (4.87)	12.57 (12.59)	455	3368
24c	78	36	Red	$C_{30}H_{27}N_5O_7$ (569)	68.15 (68.18)	4.67 (4.68)	14.20 (14.23)	450	14749
24d	98	64	Violet	$C_{35}H_{32}N_4O_6$ (604)	75 (75.11)	5.30 (5.32)	10.61 (10.63)	479	9181
24e	240	27	Pal red	$C_{34}H_{30}N_4O_5$ (574)	77.11 (77.16)	5.22 (5.27)	11.24 (11.28)	470	11374

Table (5): Values of absorption (nm) & extinction coefficients (mol^{-1}cm^{-1}) of

(21a,c,22,23b, 23b,c,e,f,24a,c,d in pure organic solvents

Comp No.	Water		DMF		C_6H_6		$CHCl_3$		**CCl_4**		Acetone		MeOH		
	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{ma}
21a	471	4244	497	2854	495	2975	489	1706	492	2854	495	7176	481	4516	48?
21c	473	2583	457	1586	444	1948	454	4381	436	2341	438	2099	440	3096	44?
22	511	4101	537	4474	404	6540	406	6540	401	6540	412	6167	404	6540	40?
	-	-	-	-	516	3986	524	4244	521	4962	519	4703	524	4244	50?
23b	406	36963	412	35332	414	33912	469	32643	412	35332	412	35182	409	37356	41?
	463	35956	460	32401	463	32522	334	35694	440	32643	468	34818	465	36208	48?
	361	39531	358	26903	331	27537	-	-	337	28051	361	35691	353	37990	-
23c	393	3489	414	3217	438	2975	412	5151	406	4123	420	3368	417	3489	39?
23e	32	3268	560	2666	543	2780	551	2293	554	1805	546	2780	540	3154	54?
23f	370	11149	390	11351	395	10475	400	10144	395	19192	390	12206	385	10590	40?
	-	-	485	5703	-	-	-	-	-	-	470	5342	-	-	
24a	465	11646	476	8967	473	6027	471	7930	468	5000	463	7296	464	11767	46?
24c	449	10157	446	7975	449	7746	440	8348	438	7975	473	5450	430	10759	45?
24d	457	10142	473	10386	476	10042	473	12941	476	10645	470	7373	468	8836	47?