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Novel Heterocyclic Quinone as Typical Alternative Precursors In the Synthesis of Mono (Tri) Methine Cyanine Dyes

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ABSTRACT

Novel unsymmetrical condensed heterocyclic quinone dyes and related mono(tri)-methine cyanine analogous incorporating thiazolo/oxazolo [2,3-b] -benzo(pyrido) oxazino/ benzoxazino -[2`,3`-b`] heterocyclic quinone;N-phenyl oxazolo/ pyrazolo-[2,3-b] benzoxazino [2`,3`-b`] heterocyclic quinone moieties were prepared. The new synthesized heterocyclic quinone cyanine dyes and relative intermediates were identified and structurally characterized by elemental and spectral analyses. The visible absorption spectra, solvato/media-chromic behaviors of some selected dyes were investigated in some organic solvents and different pH aqueous solutions. The spectral shifts were discussed in relation to molecular structure and in terms of medium effects.

Keywords: Synthesis; Heterocyclic Quinone; Mono/Tri-methine Cyanine Dyes; Absorption spectra; Solvatochromic Behavior; Acid-Base properties.

Introduction

Little attention has been focused on the use of condensed heterocyclic quinone in the synthesis of methine cyanine dyes. Cyanine dyes have found various applications in different fields, they used as potential sensitizers for photodynamic therapeutic therapy agents [1,2], as Laser disc media [3,4], as optical recording material[5], as analytical reagents over a wide pH range [6,7] and used in sensitizing

[1]This Article was Extracted from M.M.GOMAA Ph.D Thesis, Award the degree under my supervisor Chemistry Department, Faculty of Science, Aswan University (2001) & for fifth memory of Spirit Late Dr. R.M.BU ELHAMD

the silver halide microcrystals in photographic films [8,9]. As an extension to our group work on the synthesis and studies of cyanine dyes incorporating heterocyclic quinone [10-18] some new unsymmetrical 2(4) and/or 2(2)– monomethine cyanine dyes (7a-g,8&10) and tri- or meso- substituted tri-methine cyanine dyes (12a-f) incorporating thia(oxa)zolo-[2,3-b] benz(pyrid) oxazine [2`,3`-b`] heterocyclic quinone, N- phenyl pyrazolo- [2,3-b] oxazino-1,4-benzoxazino [2`,3`-b`]benzo-5,12-dione moieties have been synthesized to study the photo stability of heterocyclic quinone cyanine dyes to make them suitable for various applications.

RESULTS AND DISCUSSION

SYNTHESIS

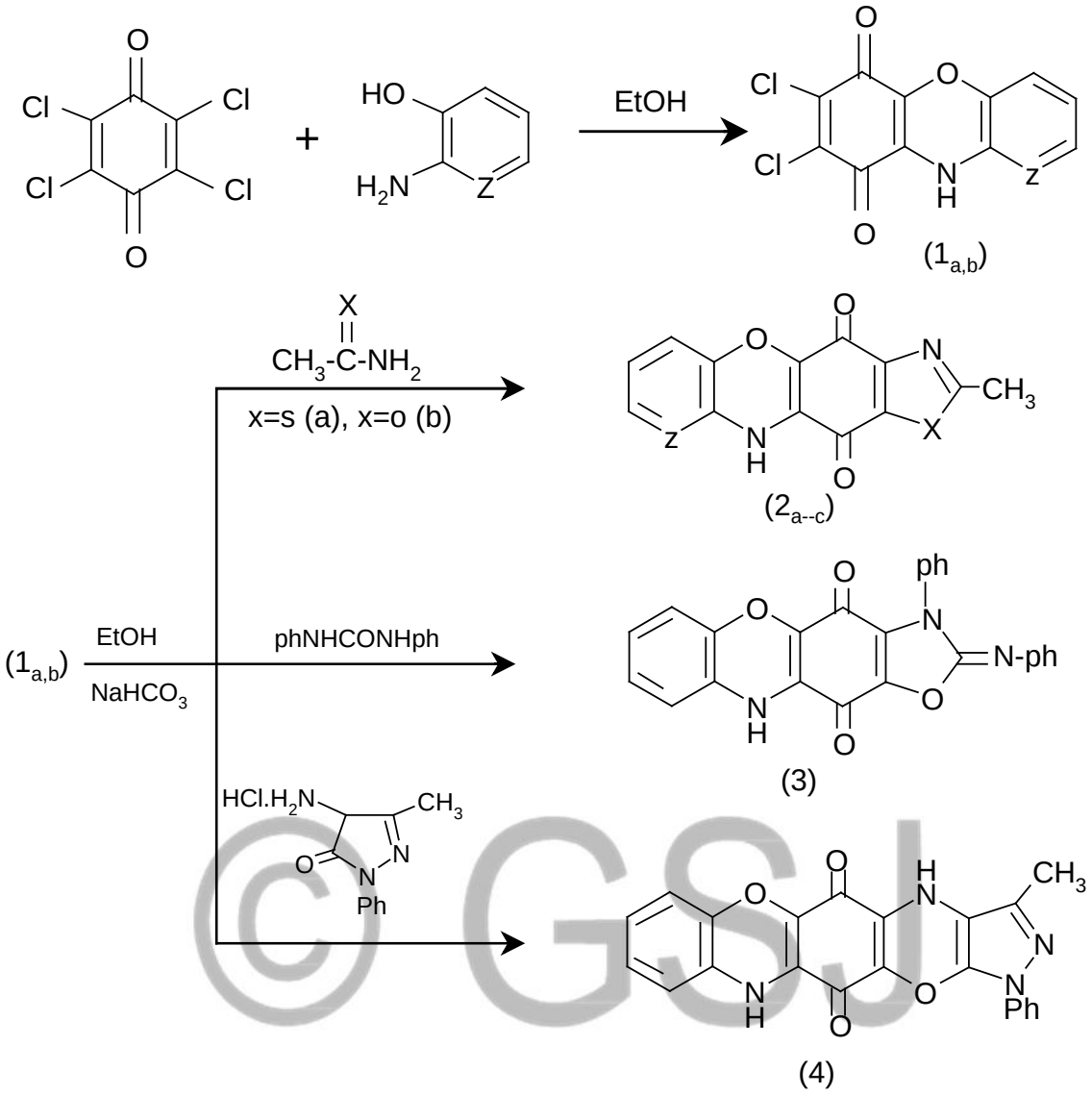
Reaction of chloranil with o- amino phenol/ 2-amino-3-hydroxy pyridine in absolute ethanol resulted in the formation of 7,8-dichloro benz(pyrid)oxazine- 6, 9-dione ($1_{a, b}$). The interaction of equimolar amounts of (1_a) and thioacetamide, acetamide, diphenyl urea and/or 4- amino 3- methyl -1- phenyl pyrazol-5-one hydrochloride or equimolar amounts of (1_b) and thioacetamide in the presence of saturated $NaHCO_3$ solution following prospective reference **[19]** resulted in formation of 2- methyl thia(oxa)zolo [2, 3-b]; benz(pyrid) oxazino- [2, 3-b]–4,11– dione (2_{a-c}); 2- phenyl imino-N- phenyl oxazolo[2,3-b], benzo-xazino [2`,3`-b`] -4,11- dione (3) and/or 3- methyl-N- phenyl pyrazolo [2,3-b]- oxazino-/ benzoxazino- [2`,3`-b`]– 5,12 – dione **(4). Scheme (1).**

Selective quaternization of 2-methyl thiazolo/oxazolo [2,3-b] benzo(pyrido)- oxazino [2`,3`-b`]-4,11- dione **(2a-c)** and 3-methyl-N- phenyl pyrazolo [2,3-b]- oxazino-/ benzoxazino-[2`,3`-b`]-5,12 - dione (4) using ethyl iodide through a sealed tube at 140°c in the presence of ethanol resulted in key intermediate namely as 2-methyl thiazolo/oxazolo [2,3-b] benzo(pyrido) oxazino-[2`,3`-b`]-4,11-dione -3- ium ethiodide salts (5a-c) and 3-methyl -N- phenyl- pyrazolo[2,3-b]oxazino-/benzoxazino-[2`,3`-b`]-5,12-dione-2-ium ethiodide salt **(6)** respectively. The solubility of **(5_{a-c} & 6)** in conc. H_2SO_4 liberates iodine vapor on warming. Meanwhile, acid hydrolysis of 2-phenyl imino-N- phenyl oxazolo [2, 3-b] benzoxazine- [2`,3`-b`]-4,11-dione **(3)** using conc. $H_2SO_4$ resulted in other key intermediate compound namely as 2- oxo N-phenyl oxazolo [2, 3-b] benzoxazine-[2`,3`-b`]- 4, 11- dione **(9). Scheme (2).**

Interaction of equimolar ratio of **(5a-c &6)** and 1-ethyl pyridinium (quinolinium and/or isoquinolinium) iodide salts under basic catalysis resulted in the formation of the corresponding thiazolo/oxazolo [2,3-b] benzo(pyrido) oxazino-[2`,3`-b`]-4,11-dione-mono-2(4,1) methine -; N-phenyl pyrazolo [2,3-b] oxazino- / benzoxazine-[2`,3`-b`]–

5,12-dione-mono-3(4)- methine cyanine dyes **(7a-g & 8).** Meanwhile, the interaction of equimolar amount of **(9)** and 2-methyl quinoline –2-ium ethiodide salt under the same previous condition afforded the corresponding N-phenyl oxazolo-[2,3-b]benzoxazino[2`,3`-b`]-4,11- dione-mono-2(2)- methine cyanine dye **(10). Scheme (2).** Thiazolo/oxazolo [2,3-b] benzoxazino-[2`,3`-b`]-4,11-dione-tri- or meso-substituted tri-2 (2,4)-methine cyanine dyes **(12_{a-f})** were prepared through interaction of equimolar ratio of heterocyclic quinone quaternary salts ($5_{a,b}$) and triethyl-orthoformate, acetamide, and / or benzamide under acetic anhydride or piperidine catalyses following reference [20] to afford an intermediate **(11_{a-d}).** Such compounds are soluble in concentrated sulphuric acid liberating iodine vapor on warming. Further interaction of the latter intermediate heterocyclic quinone quaternary moieties **(11_{a-d})** and 2(4)-metho heterocyclic quaternary salts ,in equimolar ratio, under thermal piperidine catalysis afforded thiazolo/oxazolo [2,3-b] benzoxazino-[2`,3`-b`]-4,11-dione-tri or meso- substituted tri-2 (2,4)-methine cyanine dyes **(12_{a-f}). Scheme (3).**

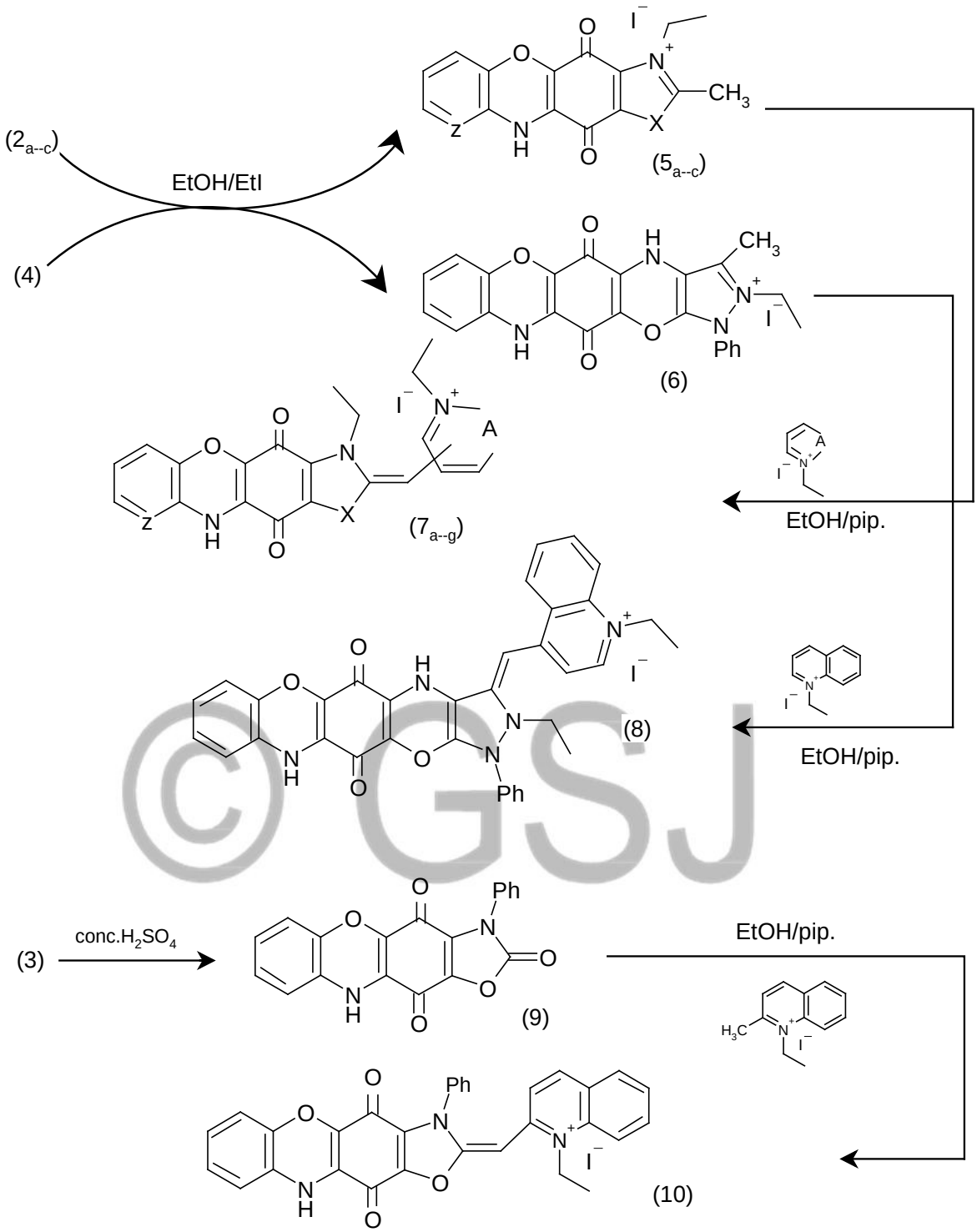
The structure of **($1_{a,b}$, 2_{a-c}, 3, 4, 5_{a-c}, 6 & 9)** was confirmed by elemental analysis, IR[21], ^{1}H-NMR and Mass spectra[22], **Table (1).** The structure of thiazolo/oxazolo [2,3-b] benzo(pyrido) oxazino-[2`,3`-b`]-4,11-dione- mono-2 (4,1)- methine cyanine dyes (7a-g); N-phenyl pyrazolo [2,3-b] oxazino- / benz-oxazine-[2`,3`-b`]–5,12-dione-mono-3(4)- methine cyanine dye **(8)** and N-phenyl oxazolo- [2,3-b] benzoxazino[2`,3`-b`]-4,11-dione-mono-2(2)-methine cyanine dye **(10)** was confirmed by elemental analysis, IR **[21],** $^1$H-NMR and Mass spectra **[22], Table (2A).** The structure of **($11_{a-d}$)** and thiazolo/oxazolo [2,3-b] benzoxazino-[2`,3`-b`]-4,11-dione-tri- or meso- substituted tri-2 (2,4)-methine cyanine dyes **(12_{a-f})** was confirmed by elemental analysis, IR [21], ^{1}H-NMR and Mass spectra [22],**Table (2B).** Thiazolo/oxazolo [2, 3-b] benzoxazino-[2`,3`-b`]-4,11-dione- tri or meso substituted tri-2 (2,4)- methine cyanine dyes **(12_{a-f})** are highly colored compounds ranging from dark brown / deep violet (blue). They are partially soluble in non polar solvent, fairly soluble in polar solvents with pale and intense greenish fluorescence depending upon solvents polarity. They are soluble in concentrated sulphuric acid liberate iodine vapor on warming. Their ethanolic solutions turned yellow or became colorless on acidification and restore their permanent color on basification.



($1_{a,b}$): Z=CH (a); N (b).

(2_{a--c}): Z=CH, X=S (a); Z=CH, X=O (b)& Z=N, X=S (C).

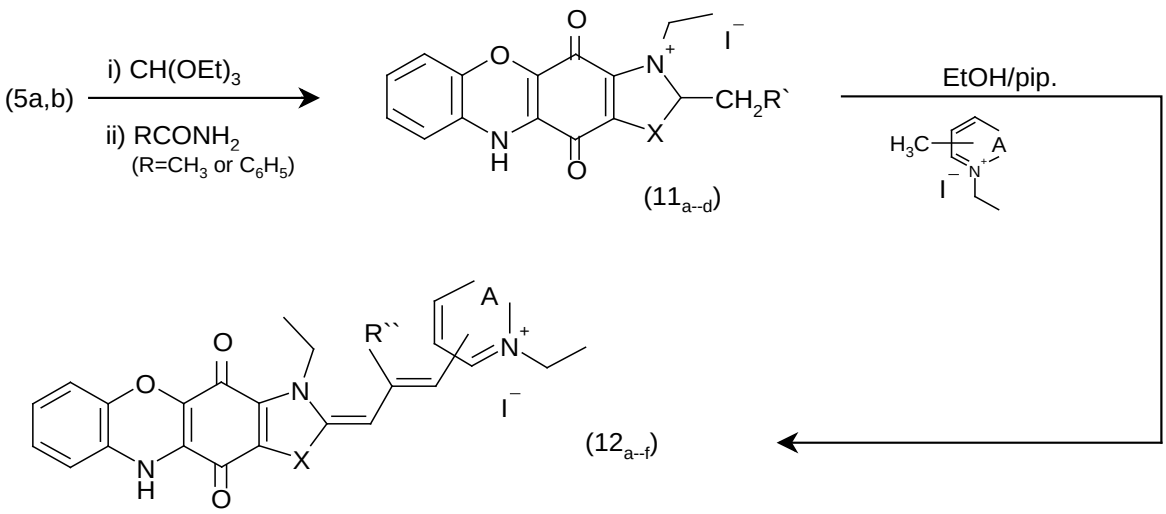
Scheme(1)



(2_{a--c}),(5_{a--c}) : Z=CH, X=S (a); Z=CH, X=O (b)& Z=N, X=S (C).

(7_{a--g}) : Z=CH, X=S, A=N-ethyl pyridin-4-ium iodide (a),
: Z=CH, X=S, A=N-ethyl quinolin-4-ium iodide (b),
: Z=CH, X=S, A=2-ethyl isoquinolin-1-ium iodide (c),
: Z=CH, X=O, A=N-ethyl pyridin-4-ium iodide (d),
: Z=CH, X=O, A=N-ethyl quinolin-4-ium iodide (e).
: Z=CH, X=O, A=2-ethyl isoquinolin-1-ium iodide (f) &
: Z=N, X=S, A=N-ethyl quinolin-4-ium iodide (g).

Scheme(2)



(11_{a--d}): X=S, R`=$CH(OEt)_2$ (a); X=O, R`=$CH(OEt)_2$ (b); X=S, R`=$COCH_3$ (cX=S, R`=COC_6H_5 (d).

(12_{a--f}): X=S, R``=H, A=N-ethyl pyridin-2-ium iodide (a),
X=S, R``=H, A=N-ethyl quinolin-2-ium iodide (b),
X=S, R``=H, A=N-ethyl pyridin-4-ium iodide (c),
X=S, R``=CH_3, A=N-ethyl quinolin-2-ium iodide (d),
X=S, R``=C_6H_5, A=N-ethyl quinolin-2-ium iodide (e)&
X=O, R``=H, A=N-ethyl quinolin-2-ium iodide (f).

Scheme(3)

Colour and absorption spectra of synthesized heterocyclic quinone mono (tri)-methine cyanine dyes (7a-g, 8, 10 & 12a-f).

They are colored compounds ranging from buff /black crystals. They are partially soluble in non polar solvents exhibit color solutions brown/dark crystals and easily soluble in polar solvents exhibit color solutions brownish red/black with slight or strong fluorescence depending upon solvent used. Their ethanolic solutions turned pale or colorless on acidification, while their permanent color restore on basification. They are highly colored compounds ranging from brownish- red to intense violet. They are partially soluble in non polar solvents, easily soluble in polar organic solvents accompanied with pale greenish-red fluorescence which is solvent dependent. They are soluble in concentrated sulphuric acid liberate iodine vapor on warming. Their ethanolic solutions gave permanent color in alkaline medium which became yellow or colorless on acidification.

The absorption spectral data (λ_{max} and ε_{max} values) of the newly synthesized thiazolo/oxazolo [2,3-b] benzo(pyrido)oxazino-[2`,3`-b`]-4,11-dione- mono-2 (4,1)-methine; N-phenyl pyrazolo [2,3-b] oxazino- / benzoxazine-[2`,3`-b`]–5,12-dione-mono-3(4)-methine and N-phenyl oxazolo-[2,3-b]benz- oxazino [2`,3`-b`]- 4,11-dione-mono-2(2)- methine cyanine dyes **(7a-g, 8 & 10)** are listed in **Table (3)..** The visible absorption spectra of such dyes exhibit various absorption bands located in the visible region and batho- (hypso) chromically shifted depending upon the heterocyclic quaternary residue **(A),** their linkage position, substituent (X,Z) and the type of fused heterocyclic quinone . Thus, substituting A=N-ethyl pyridin-4-ium iodide in **(7a, d)** with A=N-ethyl quinolin-4-ium iodide in **(7b,e)** gives a bathochromic shift of 8-47 nm with the appearance of new absorption bands located at λ_{max} =460 nm for the dye **(7b)** and at λ_{max} =330 nm for the dye **(7e)** respectively **(Table 3).** This can be attributed to the more extensive π-delocalization within quinolin-2-ium moiety. Changing the linkage position of the quinolinium residue from 4-ium in dyes ($7_{b,e}$) to 1-ium in dyes **($7_{c,f}$)** resulted in hypsochromic shift of 8-30 nm (Table 3).This is due to the decreasing of π-delocalization of heterocyclic quaternary isoquinolin-1-ium ethiodide. Substituting (Z=CH) in dye **(7_b)** by (Z=N) in dye **(7_g)** causes hypsochromic shift by 85 nm. It was obvious that monomethine cyanine dyes incorporating thiaheterocyclic nuclei **(X=S, $7_{a,b,c}$)** showed absorption bands bathochromically shifted than those incorporating oxaheterocyclic analogue (X=O, $7_{d,e,f}$). This is due to the inductive electron donating character of sulphur more than oxygen, consequently causes an easier charge transfer towards heterocyclic quaternary salts as electron sink **Table (3).** On comparison between monomethine cyanine dye incorporating N-phenyl oxazole nucleus attached to benzoxazinoquinone heterocyclic nuclei **(10)** with dye incorporate N-ethyl oxazole analogue **(7e),** it was obvious that the former dye **(10)** exhibit strong bathochromic shifted by 125-187nm than those of the later dye **(7e)., Table (3)..** This is attributed to high delocalization of π-phenyl electrons to pathway of dye electrons. Meanwhile, monomethine cyanine dye incorporating N-phenyl pyrazolo [2,3-b] oxazine nucleus attached to benz oxazino quinone heterocyclic nuclei (8) give bathochromic shift by 127nm than those incorporate N-ethyl oxazole analogous **(7e). Table (3)..** This is due to the more extensive π-delocalization within N-phenyl pyrazolo[2,3-b] oxazine nucleus.

The absorption spectra of thiazolo/oxazolo [2,3-b] benzoxazino-[2`,3`-b`]-4,11-dione-tri or meso substituted tri-2 (2,4)-methine cyanine dyes **(12_{a-f})** in 95% ethanol showed absorption bands undergo batho (hypso) chromically shifted depending upon the heterocyclic quaternary residue (A), their linkage position, substituent's (X) and (R``). Thus, substituting A=N-ethyl pyridin-2-ium iodide in **(12_a)** with A=N-ethyl quinolin-2-ium iodide in **(12_b)** gives a bathochromic shift of 20-60nm concomitant with increasing in number of the absorption bands (appearance of new absorption bands located at λ_{max} =660 nm for **(12_b**) **(Table 3),** This is due to the more extensive π-delocalization within the molecule and an easier charge transfer from (N or S) as electron source to the terminal quinolin-2-ium salt as electron sink via conjugated polymethine group. Additionally, changing the linkage position from 2-ium ethiodide in dye **(12_a)** [A = 1-ethyl pyridin-2-ium ethiodide] to 4-ium in dye **(12_c)** [A = 1-ethyl pyridine-4-ium ethiodide] resulted in bathochromic shift of 2-5nm than **(12_a).** This is due to the increasing of an extension conjugation of 4-linkage pyridine moiety rather than 2-linkage analogous, **Table (3).**

Substituting (R=H) in dye **(12_b)** by electron donating group (R=CH_3) in dye **(12_d)** causes highly bathochromic shift by 30nm than **(12_b).** This is due to the positive inductive effect of methyl group (more electron donating) causes an increase of charge transfer towards electron sink via conjugated polymethine group, **Table (3).** Meanwhile, substituting (R=H) in dye **(12_b)** by (R = C_6H_5) in dye **(12_e)** resulted in hypsochromically shifted by 80nm than **(12_b)** with the appearance of new absorption bands located at λ_{max} =500nm, 555nm **(12_e)** . This can be attributed to the difficult charge transfer towards electron sink via conjugated polymethine group and sharing of phenyl π-electrons with polymethine pathway, **Table (3)..** Finally, substituting (X=S) in dye **(12_b)** by (X=O) in dye **(12_f)** causes hypsochromically shifted by 10nm than **(12_b).** This is due to the highly electro negativity of oxygen atom, consequently causes difficult charge transfer towards heterocyclic quaternary salts (electron sink), **Table (3).**

Solvatochromic behaviors of some selected synthesized quinone mono (tri)-methine cyanine dyes (7b & 12d).

Absorption spectra of some selected heterocyclic compounds and their related cyanine dyes may be influenced by surrounding medium and that solvent can bring about a change in the position, intensity and shape of absorption bands due to their

color changes in organic solvents. This bands shifting is due to change in the π - π^* and n - π^* transition energy. Solvatochromism is caused by differ initial solvation of the ground and first excited state of the light absorbing molecule or its chromophore. Thus, an increasing solvent polarity, the ground state molecule is better stabilized by solvation than the molecule in the excited state; negative solvatochromism will result, or vice versa, better stabilization of the molecule in the first excited state relative to that in the ground state with increasing solvent polarity will lead to positive solvatochromism. To an extension to our work [20, 23], the solvatochromic behavior of some selected cyanine dyes was studied to correlate the effect of structure on molecular orbital energy levels. Thus, the electronic absorption spectra and solvatochromic behavior of some selected synthesized heterocyclic compounds and related mono (tri) methine cyanine dyes **(7b &12d)**, in the wavelength range 350 – 700nm, have been studied in different dielectric constant solvents (Viz, H_2O (78.54), DMF (36.70), EtOH (24.3), MeOH (33.0), $CHCl_3$ (4.806), acetone (21.01), CCl_4 (2.238) and C_6H6 or dioxane (2.22, 7.209). **Table (4).** It is clear from data that λ_{max} of the intramolecular charge transfer band exhibits a marked red shift on transfer from nonpolar to polar solvents (positive solvatochromism). This indicates that the polar excited states of these cyanine dyes are stabilized by polarization interaction forces as the polarizability of the solvent is increased. The unexpected blue shift observed in the λ_{max} of such cyanine dyes in ethanol and water may be due to strong electrostatic interaction [H- bonding] of solvent that cause hypsochromic shift of λ_{max}. The electronic absorption spectra of mono (tri)-methine cyanine dye **(7b &12d)** in pure non-polar solvents displaying bands with λ_{max} in the range 560-590nm **(7b)** and 400-685 nm(12d). Meanwhile, in polar solvents the λ_{max} values increases to some extent to the range 575-600 nm **(7b)** and 407-700 nm **(12d)**. A fine isopiestic point was obtained for such dyes indicating the existence of equilibrium between the solvated complex and the free solute molecule. The unexpected blue shift observed in the λ_{max} of such dyes **(7b & 12d)** in ethanol and water may be due to strong electrostatic interactions hydrogen bonding of solvent that cause a hypsochromic shift of λ_{max} . The monomethine cyanine dye **(7b)** is absorbed the fundamental light absorption (blue-red) as it has got absorption values in the range 430-600 nm, **Table (4).** This might be suggested to be used as photo sensitizer in most polar and non polar organic solvents in the (blue-red) light regions. Meanwhile, the trimethine

cyanine dye **(12d)** is absorbed the fundamental light absorption (red-violet) as it has got absorption values in the range 407-700 nm, **Table (4).** This might be suggested to be used as photo sensitizers in most polar and non polar organic solvents in the (red-violet) light regions.

Acid-Base Properties of some selected synthesized quinone mono-(tri)-methine cyanine dyes (7b&12d).

The ethanolic solutions of some selected synthesized quinone mono (tri)-methine cyanine dyes **(7b & 12d)** give a permanent color in basic medium which is discharged on acidification. This promoted us to study their spectral behavior in different aqueous universal buffer solutions (pH range: 1.5-11.5) in order to ensure optimal pH in the application of such dyes as photo sensitizers. The effectiveness of the dyes as photo sensitizers increases when they are present in the ionic forms (non protonated form) which have higher planarity [24]. The electronic absorption spectra of cyanine dyes **7b and 12d**, were taken as examples of relative series, in universal buffer solutions, showed in low pH values undergo a hypsochromic color change due to the protonation of the carbonyl group or thiazole ring and/or benzoxazine ring (heterocyclic moiety). In such cases, the interaction is inhibited and the intramolecular charge transfer (CT) between the heterocyclic moiety of dyes (donor) and heterocyclic acceptor nitrogen atoms(quinolinium ethiodide) does not absorb energy in the visible region, and long wavelength CT band disappears. On the other hand, the resulted bathochromic shift as the pH of the medium increases is due to that the protonated dyes become deprotonated**, Table (5A).** The spectrophotometric determination of dissociation and protonation constants (pk_a) values of such dyes **(7b, 12d)** can be utilized through the variation of the absorbance with pH values [25,26]. The pka values of dyes, taken as examples (7b, 12d), depends upon the linkage position and number of methine group, **Table (5B) & Fig.(1)**. Thus, it was suggested that the dye **(7b)** has more acidic character than **(12d).** This is due to the increasing number of methine group in dye **(12d)** causes the high planarity.

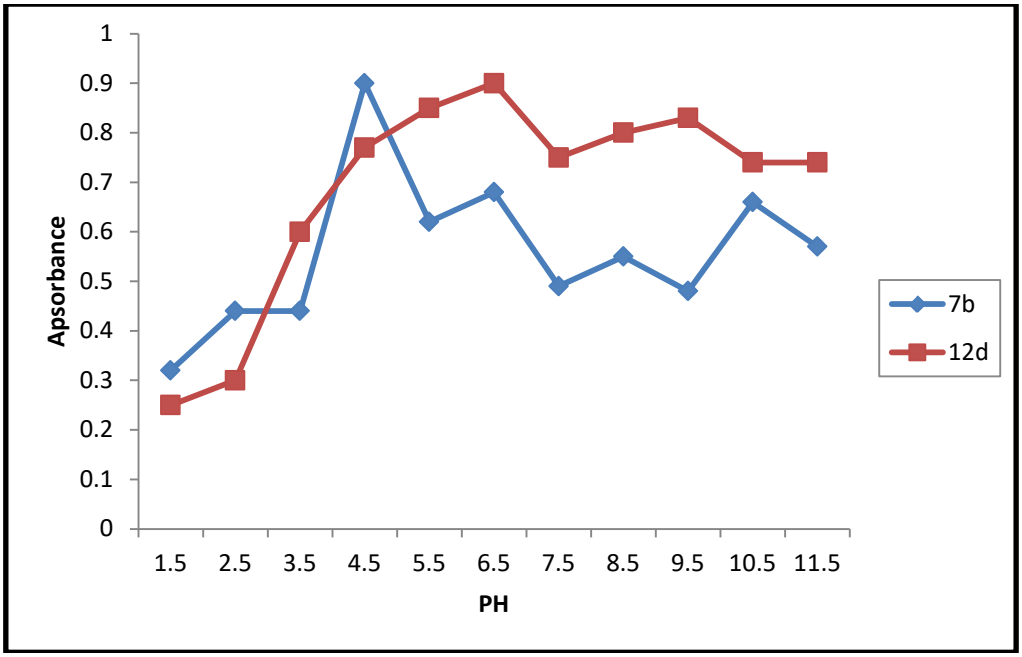


Fig.(1): pk_a values of monomethine cyanine dye (7b) and trimethine cyanine dye (12d)

CONCLUSION

New condensed unsymmetrical quinone heterocyclic cyanine dyes were prepared. The absorption spectra of the synthesized cyanine dyes were investigated in ethanol and the spectral shifts are discussed in terms of medium effects. It appears that the absorption spectral bands of the prepared cyanine dyes underwent bathochromic and/or hypsochromic shifts according to the heterocyclic quaternary residue (A), their linkage position, substituent (X,Z) and the type of fused heterocyclic quinone. The solvatochromic behaviors of selected dyes (7b & 12d) indicates that the polar excited states of these cyanine dyes are stabilized by polarization interaction forces as the polarizability of the solvent is increased (positive solvatochromism). The acid-base properties of some selected dyes indicated that these dyes are useful for photo sensitizers in both acid and base medium. The pk_a values determined suggested that the monomethine cyanine dyes have more acidic character than trimethine cyanine dyes analogous.

EXPERIMENTAL

Melting points were recorded on a Galenkanp melting point apparatus and are uncorrected. Microanalyses were carried out at the Micro analytical center at Cairo University. Infrared spectra were recorded in potassium bromide on a Perkin-Elmer

127B Infrared spectrophotometer. ^{1}H NMR spectra were recorded in deuterated DMSO-d6 on a Varian Gemini 200 NMR spectrometer. Mass spectra were recorded on HpMs 6988 spectrometer and electron-impact (EI). Visible spectra (300- 700 nm) were recorded on a Shimadzu UV/visible 160-A spectrophotometer at Aswan Faculty of Science. All reagents and solvents were obtained from Aldrich Chemical Company (Milwaukee, WI, USA).

Synthesis of 7, 8- dichloro benzo (pyrido) oxazine - 6, 9- dione (1a,b):

Equimolar amounts of chloranil and o.amino phenol /2 – amino –3- hydroxy pyridine (0.01 mole) were refluxed using absolute ethanol as solvent for 6-8 hours, filtered hot, concentrated and cooled, the products (1a,b) were precipitated on dilution with water and crystallized from ethanol, **Table (1).**

Synthesis of 2-methyl thiazolo/oxazolo [2,3-b]; benzo(pyrido) oxazino- [2`,3`-b`]-4,11- dione (2a-c); 2-( phenyl imino) -3-N-phenyl oxazolo [2,3-b]-benzoxazino [2`,3`-b`] -4,11- dione (3) and/or 3-methyl-N- phenyl pyrazolo- [2,3-b] oxazino-/ benzoxazino-[2`,3`-b`]-5,12 - dione (4).

Such compounds were prepared in a way similar to that described in reference [19] through the interaction of equimolar amounts of ($1_{a,b}$; 0.01 mole) and thioacetamide, acetamide, diphenyl urea and/or 4- amino -3- methyl -1- phenyl pyrazol-5-one hydrochloride (0.01 mole) using saturated solution of sodium bicarbonate and reflux for 3-5 hours, filtered hot, concentrated, cooled and acidified, the precipitated products were filtered off after dilution with water and crystallized from the suitable solvents, Table (1).

Synthesis of 2-methyl thiazolo/oxazolo [2,3-b] benzo(pyrido) oxazino- [2`,3`-b`]-4,11-dione -3- ium ethiodide salts and 3-methyl -N- phenyl- pyrazolo[2,3-b]oxazino-/benzoxazino-[2`,3`-b`]-5,12-dione-2-ium ethiodide salt (5a-c) and (6):

Excess amount of ethyl iodide were added to the selected compounds (2a-c & 4), the reaction mixture was refluxed for 3-5 hours in a sealed tube at 140°C on a water bath. The precipitated formed was washed by ether, triturated with ethanol by refluxing, filtered hot, concentrated and cooled. The precipitated products were separated, collected and crystallized from ethanol to give (5a-c& 6), **Table (1).**

Synthesis of thiazolo/oxazolo [2,3-b] benzo(pyrido)oxazino-[2`,3`-b`]-4,11-dione- and/or N-phenyl pyrazolo [2,3-b] oxazino- / benzoxazine- [2`,3`-b`]–5,12-dione- mono-2 (4,1) [3 (4)]- methine cyanine dyes (7a-g) and (8):

An ethanolic solution of equimolar amount of (5a-c, 6), (0.01 mole) and 1-ethyl pyridinium (quinolinium and/or isoquinolinium) iodide salts (0.01 mole) were refluxed for 9 hours in the presence of piperidine (3-5 drops), filtered hot, concentrated and acidified with acetic acid. The precipitated products after dilution with water filtered off and crystallized from ethanol to give (7a-g& 8). The results are listed in **Table (2A).**

Synthesis of 2-oxo-N- phenyl oxazolo-[2,3-b]benzoxazino[2`,3`-b`]-4, 11- dione (9):

2-Phenyl imino-N- phenyl oxazolo [2, 3-b] benzoxazine- [2`,3`-b`]-4,11-dione compound (3) and conc. H_2SO_4 (5N) was heated to boiling under reflux tell there was no more evaluation of ammonia, the solution was concentrated and allowed to cool. The residue was dissolved in minimum volume of distilled water and basified with NaOH (5N), the precipitated was filtered off and crystallized from ethanol to give compound (9). The results:(9): Yield 65%; m.p. 200 ^oC, Anal. Cald. for $C_{19}H_{10}N_2O_5$ (346): C, 65.90; H, 2.89; N, 8.09. Found: C, 65.88; H, 2.79; N, 8.20. Ms: m/z= 347.

Synthesis of N-phenyl oxazolo-[2,3-b]benzoxazino[2`,3`-b`]- 4,11- dione mono-2(2)- methine cyanine dyes (10).

An ethanolic solution of intermediate compound (9, 0.01 mole) was refluxed with quinaldine ethiodide (0.01 mole) for 10 hours under the same previous condition to give dye (10). The result is listed in **Table (2A).**

Synthesis of benzo condensed biheterocyclic quinone tri- or meso-substituted tri- methine cyanine dyes (12a-f):

Synthesis of intermediate heterocyclic quinone (11_{a-d}):

Equimolar amounts of the heterocyclic quaternary salts ($5_{a,b}$, 0.01 mole) were refluxed with triethylorthoformate, acetamide, and/or benzamide (0.01 mole) under acetic anhydride or piperidine catalyses following reference [20] procedure to give compounds (11_{a-d}). **Table (2B).**

Synthesis of tri or meso- substituted trimethine cyanine dyes (12_{a-f}):

An ethanolic solution of equimolar amounts of (11_{a-d}, 0.01 mole) and 2(4)- metho heterocyclic quaternary salts were refluxed in the presence of few drops of piperidine for 9-12 hours. The reaction mixture was filtered hot from unreacted materials, concentrated, cooled and acidified with acetic acid. The precipitated products after dilution with water were collected and crystallized from the suitable solvent to give (12_{a-f}) . The results are listed in **Table (2B).**

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Table (1): Characterization data for starting compounds ($1_{a,b}$, 2_{a-c}, 3, 4, 5_{a-c}, 6):

Compd. no.	Mol. formula (mol. wt.)	Calcd. %, Found % C	H	N	Yield %	m.p., ^oC	IR((ν^{KBr} max.), cm^{-1}	^{1}H-NMR ($CDCl_3$) δ, ppm, Assignment	M^+
1a	$C_{12}H_5NO_3Cl_2$ (281)	51.24 51.00	1.77 1.55	4.98 4.80	80	210	1721cm^{-1}(C = O quinone), 1457-1500 cm^{-1}(C = C), 2921cm^{-1} (NH)&1112cm^{-1} (C-O -C cyclic).	7.0 - 8.0 (m, 4H, Ar-H)& 6.3 (s, 1H, NH).	282
1b	$C_{11}H_4N_2O_3Cl_2$ (282)	46.81 46.99	1.42 1.53	9.93 9.99	65	200			282
2a	$C_{14}H_8N_2O_3S$ (284)	59.15 59.35	2.81 2.66	9.85 9.60	65	260	1721cm^{-1} (C = O quinone), 1457 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH) &1023-1114 cm^{-1} (C-O -C cyclic; thiazole C-S-C).	7.4 – 8.0 (m, 4H, Ar-H), 7.2 (s, 1H, NH)& 2.5– 4.0 (S, 3H, CH_3-thiazole).	285
2b	$C_{14}H_8N_2O_4$ (268)	62.68 62.48	2.98 3.00	10.44 10.60	70	> 300	1720cm^{-1} (C = O quinone), 1460 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH) &1020–1100 cm^{-1} (C-O -C cyclic; oxazole C-O-C).	7.2 – 8.0 (m, 4H, Ar-H), 7.1 (s, 1H, NH)& 2.1 – 3.9 (S, 3H, CH_3-oxazole).	268
2c	$C_{13}H_7N_3O_3S$ (285)	54.74 54.81	2.46 2.22	14.74 14.63	73	230			286
3	$C_{25}H_{15}N_3O_4$ (421)	71.26 70.93	3.56 3.63	9.98 9.75	65	200			423
4	$C_{22}H_{14}N_4O_4$ (398)	66.33 66.21	3.52 3.32	14.07 14.30	75	165			399
5a	$C_{16}H_{13}N_2O_3SI$ (440)	43.63 43.40	2.95 2.70	6.36 6.10	65	255	1721cm^{-1} (C = O quinone), 1457 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarter-nary salt) &1023-1114 cm^{-1} (C-O -C cyclic; thiazole C-S-C).	6.0 – 8.0 (m, 5H, Ar-H+ NH), 3.0 - 4.0 (t, 3H, CH_3 of ethiodide), 2.0 - 3.0 (q, 2H, CH_2 of N^+ - CH_2), 1.0–1.9 (S, 3H, CH_3-thiazole).	441

5b	$C_{16}H_{13}N_2O_4I$ (424)	45.28 45.10	3.06 3.20	6.60 6.40	70	260	1720cm^{-1} (C = O quinone), 1460 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarter nary salt) &1020–1100 cm^{-1} (C-O -C cyclic; oxazole C-O-C).	6.1– 8.0 (m, 5H, Ar-H+ NH), 3.1 - 4.0 (t, 3H, CH_3 of ethiodide), 2.0 - 3.0 (q, 2H, CH_2 of N^+ - CH_2), 1.0–1.8 (S, 3H, CH_3-oxazole).	425
5c	$C_{15}H_{12}N_3O_3SI$ (441)	40.82 40.69	2.72 2.85	9.52 9.44	70	210			443
6	$C_{24}H_{19}N_4O_4I$ (554)	51.99 52.15	3.43 3.23	10.11 10.31	60	160			555

Table (2A): Characterization data for monomethine cyanine dyes (7_{a-g}, 8&10).

Compd. no.	Mol. formula (mol. wt.)	Calcd. %, Found %			Yield %	m.p., ^oC	IR((ν^{KBr} max.), cm^{-1}	^{1}H-NMR ($CDCl_3$)	M^+
		C	H	N				δ, ppm, Assignment	
7a	$C_{23}H_{20}N_3O_3SI$ (545)	50.64 50.69	3.66 3.69	7.70 7.90	65	190			546
7b	$C_{27}H_{22}N_3O_3SI$ (595)	54.45 54.65	3.69 3.49	7.05 7.22	60	140	1721cm^{-1} (C = O quinone), 1457 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarter-nary salt),1023-1114 cm^{-1} (C-O -C cyclic; thiazole C-S-C)& 3500 – 3700 cm^{-1} (ν stretching –CH of mono-methine).	6.0 - 8.4 [m,12H, (10 Ar-H + 1 NH + 1H (=CH)], 2.2 - 2.8 (q, 2H, CH_3*CH_2 joined to immonium salt), 3.2 - 3.8 (t, 3H, CH_3 of ethiodide), 1.6 - 2.6 (t, 3H, CH_3 of N-ethyl group) 0.8-1.4 (q, 2H, CH_3*CH_2 of N-ethyl).	597
7c	$C_{27}H_{22}N_3O_3SI$ (595)	54.45 54.35	3.69 3.90	7.05 7.15	75	160			596
7d	$C_{23}H_{20}N_3O_4I$ (529)	52.17 52.37	3.70 3.78	7.93 7.99	70	> 300			530

7e	$C_{27}H_{22}N_3O_4I$ (579)	55.95 55.75	3.79 3.59	7.25 7.45	70	> 300	1720cm^{-1} (C = O quinone), 1460 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarter nary salt),1020–1100 cm^{-1} (C-O -C cyclic; oxazole C-O-C))& 3500 – 3700 cm^{-1} (ν stretching –CH of mono-methine)..		580
7f	$C_{27}H_{22}N_3O_4I$ (579)	55.95 56.03	3.79 3.92	7.25 7.15	65	> 300			581
7g	$C_{26}H_{21}N_4O_3SI$ (596)	52.34 52.00	3.52 3.45	9.39 9.52	77	240			597
8	$C_{35}H_{28}N_5O_4I$ (709)	59.23 59.50	3.94 3.90	9.87 9.90	70	240			710
10	$C_{31}H_{22}N_3O_4I$ (627)	59.33 59.13	3.51 3.33	6.70 6.55	85	175	1720cm^{-1} (C = O quinone), 1460 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarter nary salt),1020–1100 cm^{-1} (C-O -C cyclic; oxazole C-O-C))& 3500 – 3700 cm^{-1} (ν stretching –CH of mono-methine)..	6.6-8.0 [m, 17H, (15 $H_{arom.}$+NH+=CH)], 3.2-3.8 (t, 3H, CH_3 of ethyl iodide), 2.2-2.8 (q, 2H, $CH_2 - N^{\oplus}$)	629

Table (2B): Characterization data for the intermediate and tri- / meso- substituted tri-methine cyanine dyes (11_{a-d} & 12_{a-f}).

Compd. no.	Mol. formula (mol. wt.)	Calcd. %, Found % C	H	N	Yield %	m.p., ^{o}C	IR((ν^{KBr} max.), cm^{-1}	^{1}H-NMR ($CDCl_3$) δ, ppm, Assignment	M^{+}
11a	$C_{21}H_{23}N_2O_5SI$ (542)	46.49 46.30	4.24 4.20	5.17 5.40	75	140	1721cm^{-1} (C = O quinone), 1457 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarternary salt),1023-1114 cm^{-1} (C-O -C cyclic; thiazole C-S-C) and 1083-1210 cm^{-1} ($(OEt)_2$- acyclic ether).		543
11b	$C_{21}H_{23}N_2O_6I$ (526)	47.90 48.30	4.37 4.33	5.32 5.03	80	300	1720cm^{-1} (C = O quinone), 1460 –1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N-quarternary salt) &1020–1100 cm^{-1} (C-O -C cyclic; oxazole C-O-C) and 1083-1210 cm^{-1} ($(OEt)_2$- acyclic ether).		528
11c	$C_{18}H_{15}N_2O_4SI$ (482)	44.81 44.60	3.11 3.00	5.81 5.60	70	160			483
11d	$C_{23}H_{17}N_2O_4SI$ (544)	50.74 50.55	3.13 3.01	5.15 5.35	69	170		7.2 – 8.0 ppm (m, 11H, 9Harom. + 2H of CH_2 group), 6.0 – 6.5 ppm (S, 1H, NH), 4.0 – 3.0 ppm (q, 2H, CH_2 joined to immonium salt and 3.0 – 2.0 ppm (t, 3H, CH_3 group of ethiodide).	545
12a	$C_{25}H_{22}N_3O_3SI$ (571)	52.53 52.59	3.85 3.90	7.35 7.45	75	280			572

12b	$C_{29}H_{24}N_3O_3SI$ (621)	56.03 56.22	3.86 3.80	6.76 6.96	80	>300	1721cm^{-1} (C = O quinone), 1457 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarternary salt),1023-1114 cm^{-1} (C-O -C cyclic; thiazole C-S-C) &1363 cm^{-1} (CH = CH-CH =).		623
12c	$C_{25}H_{22}N_3O_3SI$ (571)	52.53 52.56	3.85 3.92	7.35 7.50	70	290			571
12d	$C_{30}H_{26}N_3O_3SI$ (635)	56.69 56.58	4.09 4.11	6.61 6.93	65	>300			636
12e	$C_{35}H_{28}N_3O_3SI$ (697)	60.25 60.50	4.01 4.40	6.03 6.15	70	240	1721cm^{-1} (C = O quinone), 1457 – 1500 cm^{-1} (C = C), 2921cm^{-1} (NH, N- quarternary salt), 1023-1114 cm^{-1} (C-O -C cyclic; thiazole C-S-C) & 1363 cm^{-1} (CH = CH-CH =).	6.2-8.5 [m, 18H, (15H$_{arom.}$ + 2H polymethine + NH)], 4.0-4.5 (t, 3H, CH_3 joined to immonium salt), 3.0-3.5 (q, 2H, CH_2 of ethiodide), 2.5 (t, 3H, CH_3 of ethyl group) ,& 1.6 (q, 2H, CH_2 of ethyl group)	699
12f	$C_{29}H_{24}N_3O_4I$ (605)	57.52 57.66	3.97 4.24	6.94 6.90	75	>300			606

Table (3): Absorption spectra of mono(tri)methine cyanine dyes (7_{a-g}, 8, 10& 12_{a-f})

λ_{max} (nm)/ ε_{max} (mol^{-1} cm^2)						
Monomethine cyanine dyes (7_{a-g})						
7_a	7_b	7_c	7_d	7_e	7_f	7_g
513 (6.600)	560 (9.600)	530 (4.400)	500 (12.800)	508 (14.800)	500 (17.600)	--
--	460 (12.600)	--	465 (12.200)	465 (18.000)	465 (17.000)	--
425 (15.200)	430 (14.000)	427 (15.200)	410 (12.200)	415 (12.600)	427 (16.200)	475 (16.800)
--	--	--	--	--	360 (12.400)	--
--	--	--	--	330 (1.720)	320 (17.600)	--
Monomethine cyanine dyes (8& 10)						
8	10					
635 (2.400)	695 (2.000)					
--	580 (13.200)					
--	540 (10.800)					
465 (9.600)	--					
435 (10.800)	--					
Trimethine cyanine dyes (12_{a-f})						
12a	12b	12c	12d	12e	12f	
--	660 (2.400)	--	690 (3.200)	--	650 (4.400)	
--	570 (5.400)	--	595 (12.800)	580 (11.200)	585 (14.600)	
510 (6.000)	--	512 (6.800)	560 (11.400)	555 (10.800)	555 (13.400)	
--	--	--	--	500 (10.000)	500 (9.000)	
445 (8.000)	470 (7.800)	450 (14.000)	--	430 (17.600)	--	
415 (9.600)	435 (8.800)	--	400 (9.600)	415 (17.600)	--	

Table (4): Absorption spectra of selected newly synthesized benzo condensed biheterocyclic quinone monosubstituted methine cyanine dye (7b) and benzo condensed biheterocyclic quinone-2(2)-trimethine cyanine dye (12d) in different organic solvents:

Compound No.	EtOH		Water		$CHCl_3$		Dioxane		DMF		Acetone		CH_3OH		Iso propyl alc.		C_6H_6	
	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max	λ_{max}	$\varepsilon \times 10^3$ max
7_b	560	(9600)	550	(1100)	600	(1240)	590	(1100)	600	(1220)	590	(1200)	595	(4600)	592	(8000)	590	(1300)
	460	(12600)	-	-	575	(11400)	560	(11600)	570	(11000)	550	(10000)	565	(8000)	558	(7400)	560	(11800)
	430	(14000)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
12_d	690	(3200)	700	(2000)	700	(2000)	700	(3000)	695	(4200)	685	(8000)	695	(3800)	590Sh	(4000)	685	(3000)
	595	(12800)	580	(12000)	600	(7000)	615	(10000)	600	(14200)	595	(15000)	595	(15000)	595	(14600)	585	(13600)
	560	(11400)	548	(11000)	570	(6000)	583	(12000)	570	(12600)	555	(14000)	560	(14000)	562	(13000)	-	-
	400	(9600)	400Sh	(1100)	407Sh	(7400)	400Sh	(11000)	400	(11000)	400	(13600)	400	(13600)	400	(11100)	400	(11100)

Table (5A): Absorption values and the variation of absorbance in λ_{max} characteristic for selected newly synthesized quinone monomethine cyanine dye (7b) and trimethine cyanine dye (12d) in different universal buffer solutions.

Compound No.		7b			12d		
		λ_{max}	$\varepsilon_{max} \times 10^3$	Absorbance	λ_{max}	$\varepsilon_{max} \times 10^3$	Absorbance
In 95% ethanol		560 460 430	(9600) (12600) (14000)		690 595 560 400	(3200) (12800) (11400) (9600)	
Universal Buffers	*1.5*	- 462 -	- (6800) -	0.32	- - - -	- - - -	0.25
	2.5	- 458 -	- (9200) -	0.44	- 580Sh - -	- (1200) - -	0.30
	3.5	- 460 -	- (8600) -	0.44	- 590 550	- (2200) (1800)	0.60

					-	-	
	4.5	- 463 -	- (1800) -	0.90	- 600 550 -	- (3000) (2600) -	0.77
	5.5	- 460 -	- (1040) -	0.62	- 600 560 -	- (3000) (2600) -	0.85
	6.5	- 463 -	- (1380) -	0.68	- 600 550 -	- (3600) (3000) -	0.90
	7.5	- 460 -	- (1000) -	0.49	- 600 550 -	- (3000) (2600) -	0.75
	8.5	- 460 -	- (1100) -	0.55	- 600 560 -	- (3200) (2800) -	0.80
	9.5	- 460 -	- (9600) -	0.48	- 595 550 -	- (3400) (2600) -	0.83
	10.5	- 460 -	- (1320) -	0.66	- 595 550 -	- (2400) (2200) -	0.74
	11.5	- 460 -	- (1140) -	0.57	- 595 550 -	- (2400) (2200) -	0.74

Table (5B): Comparison between colors absorbed of Selected quinone monomethine cyanine dye (7b) and trimethine cyanine dye (12d) in EtOH, universal buffer solutions and their optimal pH or pk_a values.

Compound No.	Color Absorbed in				pH ≥	pk_a
	EtOH		Universal Buffer			
	λ_{max}	Colour	λ_{max}	Colour		
7b	560	Yellow	460	Blue	1.5	3.5, 5.1, 9.5
	460	green				3,4,6,8,10
	430	violet-blue				
12d	690	Red	600	Orange	8.5	8
	595	Orange				4,7,9,10
	560	Yellow green				
	400	Violet				