STUDIES ON THE SYNTHESIS OF CONJUCTED FIVE-SIX BIHETEROCYCLIC CYANINE DYE SERIES

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SUMMARY: Synthesis of new types of pyrazolo (4,3-d)-benzoxazine/quinoxaline cyanine dyes covering dimethine, mono (di)-cationic styryl, azastyryl and merocyanines were achieved by interaction of 3-methyl-l-phenyl pyrazolo (4,3-d)-benzoxazine/quinoxaline with active carbonyl components. The newly synthesized dyes were identified by spectral data.

Key Word: Heterocyclic dye series.

INTRODUCTION

Cyanine dyes incorporating condensed benzoxazine/quinoxaline which despite its importance received little attention. The only known compounds of these dyes is the dimethine (1, 2) and apocyanines (3) which are prepared in this laboratory. In this respect, the use of biheterocyclic systems may be of special interest (4-13) as this may offer a chance for the preparation of cyanine dyes of high photosensitization. The compounds under discussion contained the asymmetrical pyrazolo (4,3-d) benzoxazine/quinoxaline system as a main entity of all molecules.

RESULTS AND DISCUSSION

Interaction of 4-bromo-3-methyl-1-phenyl pyrazolo-5-(one) with hydroxy (amino) aromatic amines in the presence of ethanol and acid (base) catalysis, proceeds through enolization of the former and the evolution of a molecule each of hydrogen bromide and water (14), achieve a new biheterocyclic compound (IIa, b). This biheterocyclic compound was classified as five-six fused heterocyclic (14) namely as 4H-3-methyl-1-phenyl pyrazolo (4,3-d)-benzoxazine/quinoxaline (II, a, X=0; b, X=NH).

The structure of (IIa, b) was confirmed by elemental analysis, IR and H^1n.m.r spectral data (15), (Table 4).

Selective SeO_2 oxidation of (IIa, b) to give the corresponding 3-carboxaldehyde (IIIa, b) and quaternization gave the corresponding 3-carboxaldehyde-2yl-salt (IV); the 3-carboxaldehyde derivatives (IIIa, b; IV) leads to the synthesis of the desired mono (di)-cationic dimethine cyanines. Thus, the reaction of (IIIa, b) and / or their 2-ethiodide (IV) with methyl quaternary salts in the presence of piperidine gave the corresponding asymmetrical mono (di)-cationic dimethine cyanines (Va-e) (Scheme 1).

The structure of compounds (IIIa, b; IV; Va-e) were confirmed by elemental analysis (Table 1), IR and H^1n.m.r spectral data (15) (Table 4).

The dimethine cyanines (Va-e) were highly colored compounds (reddish-violet to intense-violet) fairly soluble in polar organic solvents and in conc. H_2SO_4 liberating iodine vapor on heating. Their ethanolic solution gave violet color in alkali medium which discharged on acidification.

The visible spectra of asymmetrical mono(di)-cationic dimethine cyanines (Va-e) in 95% ethanol exhibited absorption bands which become bathochramically or hypsochromically shifted according to the type of quaternary heterocyclic residue (A), or the nature of benzoxazine/quinoxaline moieties and/or the nature of attached

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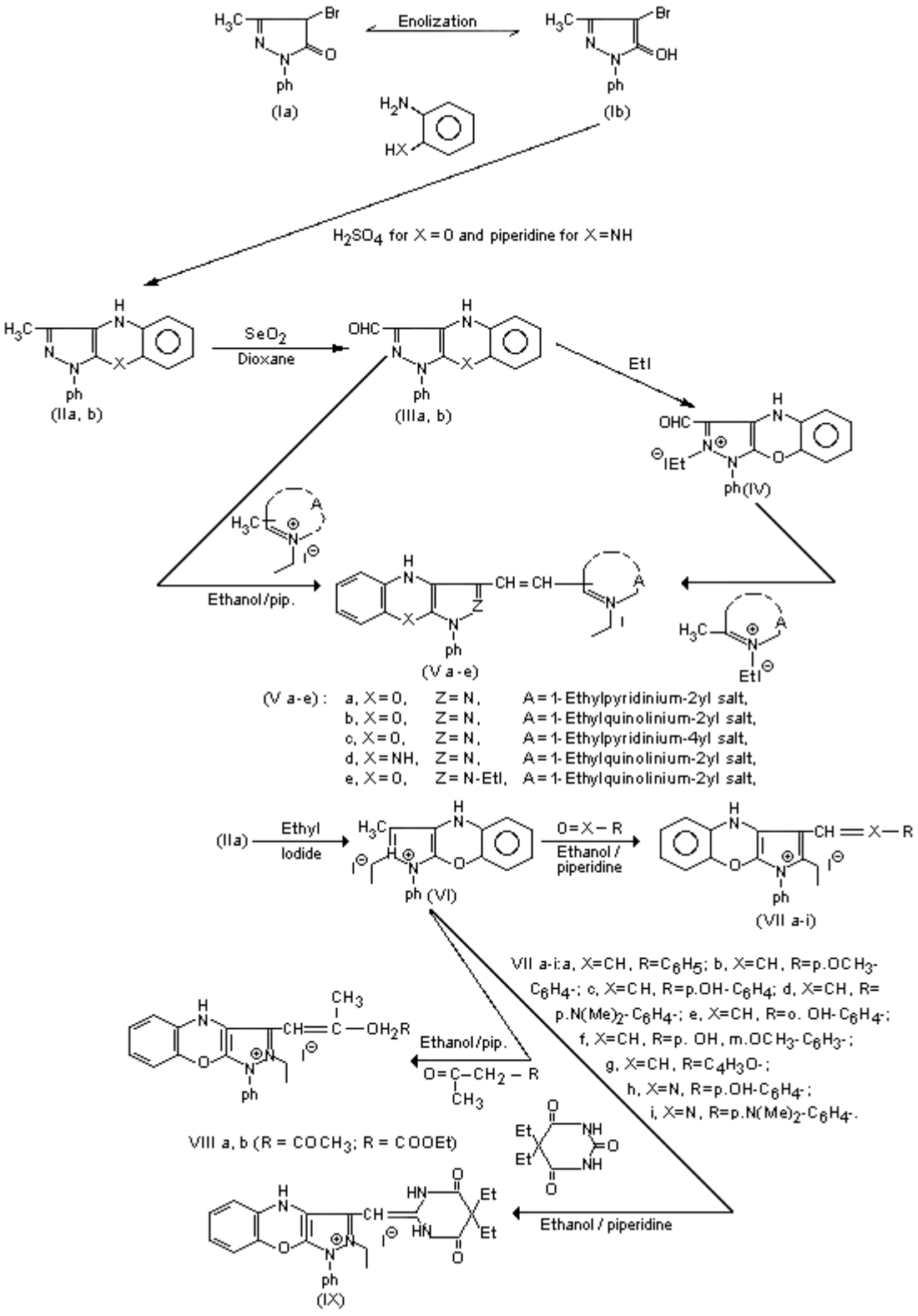
Scheme 1


Enolization
(Ia)
(Ib)
H2SO4 for X = O and piperidine for X=NH
(IIa, b)
SeO2
Dioxane
(IIIa, b)
EtI
ph(IV)
Ethanol/pip.
(V a-e)
(V a-e) : a, X=O, Z=N, A=1-Ethylpyridinium-2yl salt,
b, X=O, Z=N, A=1-Ethylquinolinium-2yl salt,
c, X=O, Z=N, A=1-Ethylpyridinium-4yl salt,
d, X=NH, Z=N, A=1-Ethylquinolinium-2yl salt,
e, X=O, Z=N-Etl, A=1-Ethylquinolinium-2yl salt,
(IIa)
Ethyl Iodide
(VI)
Ethanol / piperidine
(VII a-i)
VII a-i:a, X=CH, R=C6H5; b, X=CH, R=p.OCH3-C6H4-; c, X=CH, R=p.OH-C6H4; d, X=CH, R=p.N(Me)2-C6H4-; e, X=CH, R=o. OH-C6H4-; f, X=CH, R=p. OH, m.OCH3-C6H3-; g, X=CH, R=C4H3O-; h, X=N, R=p.OH-C6H4-; i, X=N, R=p.N(Me)2-C6H4-.
Ethanol/pip.
VIII a, b (R = COCH3; R = COOEt)
Ethanol / piperidine
(IX)

pyrazolo condensed with the benzoxazine nuclei. The behavior of such dyes in the visible spectra is a expected; dye incorporating quinoline (Vb) is more red shifted than those of pyridine moieties (Va, c). Also, the pyrazolo (4,3-d)-oxazine monocationic dimethine cyanine (Vb) is more red shifted than those of pyrazolo-(4,3-d)-quinoxaline analogous having the same quaternary heterocyclic residue (A). On the other hand, substituting the pyrazolo (4,3-d)-benzoxazine by pyrazolium-2-yl-salt moiety in the cyanine molecule of the same quaternary heterocyclic residue, the absorption bands become blue shifted (Table 1).

Quaternization of (IIa) using ethyl iodide to give the corresponding pyrazolo (4,3-d) benzoxazinium-2yl-salt (IV) leads to the synthesis of the desired asymmetrical styryl and azastyryl cyanines (VIIa-i). Thus, interaction of equimolar ratio of (IV) and different benz. (heterocyclic)-aldehydes and/or nitroso derivatives in the presence of piperidine as catalyst and ethanol as solvent afford the corresponding 4H-1-phenyl pyrazolo (4,3-d)-benzoxazinium-2-yl-salt-3(2)-styryl (azastyryl) cyanine dyes (VIIa-i) (Scheme 1).

The structure of compounds (VI; VIIa-i) were established by elemental analysis (Table 2), IR and H^1n.m.r spectral data (15), (Table 4).

The asymmetrical 3-styryl (azastyryl)-cyanines (VIIa-i) were colored compounds (reddish to deep-brown), fairly soluble in polar organic solvents and in conc. H_2SO_4 liberating iodine vapor on heating. Their ethanolic solution gave yellow color in acidic medium turned into reddish-brown on basification with alkali hydroxide.

The visible absorption spectra of 3-styryl (azastyryl)-cyanines (VIIa-i) in 95% ethanol showed absorption bands, whose molar absorbitivity was influenced by aryl electron donating substituents. Thus, in this connection it has to be pointed out that the auxochromic groups of oxygen and nitrogen atoms causes remarkable high absorbitivity. This may be attributed to the partial mixing of the lone pair orbitals of oxygen or nitrogen with the π-system of the heterocyclic ring leading to a modified set of energy levels and this moves the bond intensity to high absorbitivity. On substituting the phenyl group in dye (VIIa) by furanyl group in dye (VIIg), the absorption bands become red shifted (Table 2).

A comparison of the absorption of 3-styryl with 3-azastyryl having the same aryl substituent, showed that the former dyes are more bathochromically shifted (Table 2). This is due to the presence of azomethine group which causes antagonistic effect.

Interaction of equimolar ratios of (VI) and carbonyl component such as acetylacetone, ethylacetoacetate or diethylacetoacetate or diethylbarbituric acid in the presence of piperidine as basic catalyst and ethanol as solvent achieved the corresponding a cyclic or cyclic merocyanines (VIIIa, b; IX).

The structure of compounds (VIIa, b; IX) were confirmed by elemental analysis (Table 3), IR and H^1n.m.r spectral data (15), (Table 4).

The acyclic or cyclic merocyanines (VIIIa, b; IX) were

Table 1: Characterization of mono-(di) cationic dimethine cyanine dyes (Va-e).

Comp. No.	Color	m.p (°C)	Yield (%)	Mol. formula (M.wt)	Analysis % Calcd. (Found)			Absorption spectra in 95% ethanol		
					C	H	N	λ nm.	A (ε mol^{-1}	cm^{-1})
Va	Deep-brown	245	90	$C_{24}H_{21}N_4OI$ (508)	56.69 (56.53)	4.13 (4.43)	11.02 (10.92)	590, 505, 430	0.108 0.318 0.3	(1080) (3180) (3000)
Vb	Blue	207	85	$C_{27}H_{23}N_4OI$ (546)	59.34 (59.13)	4.21 (4.43)	10.26 (10.10)	690, 582, 500	0.135 0.64 0.68	(1350) (6400) (6800)
Vc	Deep-brown	230	70	$C_{24}H_{21}N_4OI$ (508)	56.69 (56.81)	4.13 (4.55)	11.02 (11.10)	597, 502, 475	0.158 0.468 0.43	(1580) (4680) (4300)
Vd	Violet	175	80	$C_{27}H_{24}N_5I$ (545)	59.45 (59.62)	4.40 (4.72)	12.84 (12.52)	690, 580, 495	0.22 0.7 1.22	(2200) (7000) (12200)
Ve	Deep-violet	223	75	$C_{30}H_{28}N_4OI_2$ (714)	50.42 (50.40)	3.92 (3.14)	7.84 (7.71)	655, 595, 560, 515	0.27 0.467 0.562 0.45	(2700) (4670) (5620) (4500)

Table 2: Characterization of styryl and azastyryl cyanine dyes (VII a-i).

Comp. No.	Color	m.p (°C)	Yield (%)	Mol. formula (M.wt)	Analysis % Calcd. (Found)			Absorption spectra in 95% ethanol		
					C	H	N	λ nm.	A (ε mol^{-1}	cm^{-1})
VII a	Pale-brown	175	91	$C_{25}H_{22}N_3OI$ (507)	59.17 (59.41)	4.34 (4.11)	8.28 (8.81)	506, 472	0.27 0.29	(2700) (2900)
VII b	Reddish brown.	170	93	$C_{26}H_{24}N_3O_2I$ (537)	58.1 (57.75)	4.47 (4.23)	7.82 (7.91)	506, 474, 350	0.31 0.31 0.66	(3100) (3100) (6600)
VII c	Brown	160	94	$C_{25}H_{22}N_3O_2I$ (523)	57.36 (57.70)	4.21 (4.28)	8.03 (7.89)	509, 471, 330	0.35 0.419 0.63	(3500) (4190) (6300)
VII d	Deep-brown brown	105	96	$C_{27}H_{27}N_4OI$ (550)	58.91 (59.11)	4.91 (5.05)	10.18 (10.32)	505, 475, 342	0.55 0.52 0.25	(5500) (5200) (2500)
VII e	Reddish-brown	179	80	$C_{25}H_{22}N_3O_2I$ (523)	57.36 (57.21)	4.21 (4.81)	8.03 (8.12)	505, 475, 340	0.287 0.28 0.48	(2870) (2800) (4800)
VII f	Deep-brown	185	78	$C_{26}H_{24}N_3O_3I$ (553)	56.42 (56.62)	4.34 (4.03)	7.59 (7.33)	505, 475, 350	0.37 0.35 0.56	(3700) (3500) (5600)
VII g	Deep-brown	70	98	$C_{23}H_{20}H_3O_2I$ (497)	55.53 (55.12)	4.02 (3.89)	8.45 (8.31)	520, 432	1.25 1.45	(12500) (14500)
VII h	Pale-brown	180	89	$C_{24}H_{21}N_4O_2I$ (524)	54.96 (55.11)	4.01 (3.85)	10.69 (10.42)	505, 470	0.42 0.40	(4200) (4000)
VII i	Deep-brown	170	92	$C_{26}H_{26}N_5OI$ (551)	56.62 (56.51)	4.72 (4.43)	12.70 (12.68)	505, 440	0.37 0.44	(3700) (4400)

Table 3: Characterization of merocyanines (VIIIa, b; IX).

Comp. No.	Color	m.p (°C)	Yield (%)	Mol. formula (M.wt)	Analysis % Calcd. (Found)			Absorption spectra in 95 % ethanol		
					C	H	N	λ nm.	A (ε mol^{-1}	cm^{-1})
VIII a	Reddish brown	147	96	$C_{23}H_{24}N_3O_2I$ (501)	55.09 (55.21)	4.79 (4.55)	8.38 (8.42)	505 440	1.818 1.80	(18180) (18000)
VIII b	Reddish brown	149	85	$C_{24}H_{26}N_3O_3I$ (531)	45.24 (54.42)	4.896 (5.02)	7.91 (7.79)	502, 415	0.678 0.458	(6780) (4580)
IX	Deep-reddish brown	190	93	$C_{26}H_{28}N_5O_3I$ (585)	53.33 (53.53)	4.79 (4.65)	11.97 (11.90)	500, 432	0.35 0.39	(35.00) (3900)

colored compounds (reddish to deep brown), fairly soluble in polar organic solvents and in conc. H_2SO_4 liberating iodine vapor on heating.

The visible absorption spectra of acyclic merocyanines (VIIIa, b) in 95% ethanol showed absorption bands which influenced by the type of (R) group attached. Thus, aclclic merocyanine (VIIIa, R=$COCH_3$) showed absorption bands more red shifted than those of their analogus (VIIIb, R=COOET) (Table 3).

A comparison of absorption spectra of acyclic merocyanine (VIIIa) with cyclic merocyanine (IX), reveals that acyclic merocyanine (VIIIa) is more bathochromically shifted than those of cyclic merocyanine (IX) (Table 3).

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr on a PYE-Unicam SP 1100 Infrared spectrophotometer. Absorption spectra in the visible region (300-800) were recorded on a SHIADZU. UV. vis. 240 recording spectrophotometer. The H^1n.m.r spectra were determined with TNM-PMX 60 NMR spectrometer JEOI.

Synthesis of 3-methyl-1-phenyl pyrazolo (4,3-d)-benzoxazine (quinoxaline) (IIa, b) (14)

Equimolar ratios of 4-brome-3-methyl-1-phenyl pyrazolo-5 (one) (I), and o-aminophenol or o-phenylenediamine (0,01 mol) were dissolved in 30 ml ethanol to which (1 ml) conc. H_2SO_4 was added in case of o-aminophenol and piperidine (3-5 drops) in case of o-phenylenediamine. The reaction mixture was refluxed for 3-5 hrs to attained a dark color. It was filtered while hot, concentrated, and the products precipitated by dilution with water.

The precipitated products were crystallized from aq.-methanol to give the titled compounds (IIa,b). Comp. IIa; X=0, Brown cryst., m.p. 165°C; yield 85%; Anal. data for $C_{16}H_{13}N_3O$,

Calcd C, 73.00; H, 4.94; N, 15.97

Found C, 73.08; H, 4.75; N, 16.01

IIb; X=NH, reddish-brown cryst., m.p. 105°C; yield 65%; Anal. data for $C_{16}H_{14}N_4$,

Calcd.: C, 73.28; H, 5.34; N, 21.37

Found. : C, 73.38 ; H, 5.30 ; N, 21.41

Synthesis of 4H-1-phenyl pyrazolo (4,3-d)-benzoxazine/quinoxaline-3-carboxaldehyde (IIIa, b)

A mixture of (IIa, b; 0.01 mol.) and selenium dioxide (0.01 mol.) was dissolved in dioxane (20 ml.) and the solution refluxed for 7-9 hrs. The deposited selenium metal was filtered off and the filtrate concentrated and cooled. The precipitated product was crystallized from dioxan to give (IIIa, b).

IIIa; X=0; deep brown cryst.; m.p. 195°C; yield 70%; Anal.

Table 4: IR and H^1n.m.r spectral data of starting materials and five-six biheterocyclic cyanine dye compounds.

Comp. No.	IR (γ^{KBr}_{max} cm^{-1})(15)		H^1n.m.r (CDC_1) ppm (15)	
IIa.	760-710	(ν-mono-& di-sub. benz.)	7.9-7.1	(m, 9H, arom -H)
	1660	(ν- C = N)	4.3	(s, IH, NH)
	1250	(ν- COC cyclic)	1.7	(s, 3H, CH_3-)
	3450	(ν- NH gp.)		
IIIa	770-710	(ν-mono-& di-sub. benz.)	8-7.1	(m, 9H, arom -H)
	1665	(ν- C = N)	9.7	(s, IH, CHO)
	1245	(ν- COC cyclic)	4.3	(s, IH, NH)
	3450	(ν- NH gp.)		
	1700	(ν-CHO)		
IV	770-710	(ν-mono-& di-sub. benz.)	9.8	(s, IH, CHO)
	1245	(ν- COC cyclic)	8-7.2	(m, 9H, arom -H)
	2440	(ν- NH gp.)	4.4	(s, IH, NH)
	1700	(ν-CHO)	4.1	(t, 2H, CH_2I)
	2980	(ν-ethiodide)	3.3	(q, 3H, CH_3I)
Vb	1250	(ν- COC cyclic)	8-6.9	(m, 17H, arom. +hetero. + CH=CH syst.)
	3450	(ν- NH gp.)	4.4	(s, 1H, NH)
	2980	(ν-ethiodide)	4.1	(t, 2H, CH_2I)
	3040	(ν- CH=CH)	3.3	(q, 3H, CH_3I)
VI	1230	(ν- COC cyclic)	8-7.1	(m, 9H, arom -H)
	3450	(ν- NH gp.)	4.4	(s, IH, NH)
	2984	(ν-ethiodide)	3.8	(t, 2H, CH_2I)
	760-695	(ν-mono-& di-sub. benz.)	3.1	(q, 3H, CH_3I)
			1.7	(s, 3H, CH_3-)
VIIa	770-710	(ν-mono-& di-sub. benz.)	8-6.8	(m, 16H, arom. + CH=CH system)
	3450	(ν- NH gp.)	4.5	(s, IH, NH)
	2980	(ν-ethiodide)	4.1	(t, 2H, CH_2I)
	3050	(ν- CH=CH)	3.3	(q, 34, CH_3I)
IX	3450-3430	(ν- NH gps.)	8-6.8	(m, 9H, arom. -H)
	1380	(ν- =CH)	5.9	(s, IH=CH)
	1715	(ν- C=O)	4.8	(s, 3H, 3NH)
	1250	(ν- COC cyclic)	4.1	(t, 2H, CH_2I)
	2980	(ν-ethiodide)	1.3	(q, 3H, CH_3I)
			1.8	(t, 4H, 2 CH_2-)
			1.3	(q, 6H, CH_3-)

data for $C_{16}H_{11}N_3O_2$,

Calcd.: C, 69.31; H, 3.97; N, 15.16

Found: C, 69.98; H, 4.30; N, 14.99

IIIb; X=NH; greenish-black cryst.; m.p. 95°C; yield 57%; Anal. data for $C_{16}H_{12}N_4O$,

Calcd.: C, 69.56; H, 4.35; N, 20.29

Found: C, 69.45; H, 4.11; N, 20.63

Synthesis of 4H-1-phenyl pyrazolo (4,3-d)-benzoxazine/quinoxaline-2yl-salt-3-carboxaldehyde (IV)

A pure sample of (IIIa; 0.5 gm.) was suspended in excess of ethyl iodide (5 ml) and heated on water bath for 3-5 hrs in sealed tube. The products (IV) were collected, washed with ether and crystallized from ethanol. The result is listed as follow:

IV; X=O; brown cryst.; m.p. 217°C; yield 40%; Anal. data for $C_{18}H_{16}N_3O_2I$,

Calcd.: C, 49.88; H, 3.70; N, 9.70

Found: C, 50.01; H, 3.33; N, 9.25

Synthesis of asymmetrical 1-phenyl pyrazolo (4,3-d)-benzoxazine/quinoxaline-3-[2(4)]-mono(di)-cationic dimethine cyanine dyes (Va-e)

Equimolar amounts of (IIIa, b) or (IV) and the appropriate quaternary salt (α-picoline, γ-picoline or quinaldine; 0.01 mol.) were dissolved in ethanol (30 ml) and piperidine (2 ml) was added. The reaction mixture was refluxed for 5-7 hrs, filtrated while hot, concentrated, cooled, acidified with acetic acid and diluted with water. The precipitated products were crystallized from aqueous ethanol to give (Va-e) (Table 1).

Synthesis of 3-methyl-1-phenyl pyrazolo (4,3-d)-benzoxazinium/quinoxalinium-2-yl-salt (VI)

A pure sample of (IIa) was converted to (VI) by the same procedure as used to convert (IIIa) to (IV).

VI; X=0; brown crystal; m.p. 210°C; yield 86%; Anal. data for $C_{18}H_{18}N_3OI$,

Calcd.; C, 51.55; H, 4.30; N, 10.03

Found: C, 51.73; H, 4.42; N, 10.18

Synthesis of 1-phenyl pyazolo (4,3-d)-benzoxazinium/quinoxalinium-2-yl-salt styryl (azastyry)-cyanines (VIIa-i)

Equimolor ratios of (VI; 0.01 mol.) and aromatic (heterocycle)-aldehydes or nitroso phenol (amines) 0.01 mol.) were dissolved in 20 ml ethanol to which 3-5 drops piperidine was added. The reaction mixture was refluxed for 3-10 hrs depending upon the aldehyde or nitroso compounds used. The reaction mixture was filtered while hot, concentrated, cooled, acidified (AcOH), and diluted with water, the precipitated products were identified as titled cyanines (VIIa-i). The results are summarized in (Table 2).

Synthesis of 1-phenyl pyrazolo (4,3-d)-benzoxazine-3-acyclic/cyclic merocyanine dyes (VIIIa, b; IX)

Acyclic merocyanines: These two representive examples were prepared by interaction of the quaternary salt (VI, I mol.) with acetylacetone or ethylacetoacetate (1 mol.) in presence of ethanol and a few drops of piperidine. The reaction mixture was refluxed for 60-90 mins, the product collected washed several times with ethanol and crystallized from aqueous ethanol (Table 3).

Cyclic merocyanines: This was prepared by interaction (VI, I mol.) with diethylbarbituric acid (1 mol.) in presence of ethanol and piperidine. The mixture was refluxed for 140 mins, the product (IX) was collected, washed with ethanol and then crystallized from ethanol to give reddish-brown needles (Table 3).

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