Synthesis of Different Classes of Five / Five Membered Heterocyclic Cyanine Dyes: A Review Paper

H.A. Shindy*

Department of Chemistry, Faculty of Science at Aswan, South Valley University, Aswan, Egypt

Abstract: The paper reviews synthesis of different classes of biheterocyclic five/five membered heterocyclic cyanine dyes. In this review paper detailed synthesis steps for some of the biheterocyclic five/five membered cyanine dyes were represented by equations. The synthesis covers, monomethine cyanine dyes (simple cyanine dyes), aza-monomethine cyanine dyes, dimethine cyanine dyes, trimethine cyanine dyes (carbocyanine dyes), aza-trimethine cyanine dyes, tetramethine cyanine dyes, heptamethine cyanine dyes (tricarbocyanine dyes), styryl cyanine dyes (hemi cyanine dyes), aza-styryl cyanine dyes (aza-hemi cyanine dyes) and apocyanine dyes. In addition, in the introduction section we shed some light on the use and applications of cyanine dyes.

Keywords: Cyanine dyes, synthesis, five/five membered cyanine dyes, application of cyanine dyes, uses of cyanine dyes.

1. INTRODUCTION

Cyanine dyes [1-10] are a member of a class of highly colored organic compounds essentially used for increasing the range of wavelengths of light to which photographic emulsions are sensitive. A few members of the class are used in textile dyeing, but most of them are too easily destroyed by acids or by light therefore they are not to be satisfactory for this purpose. The silver salts in photographic films or plates are only affected by light of wavelengths at the range of 350 to 450 nanometres, which includes only a small part of the visible spectrum (about 400 to 700 nanometres). In 1873, [11] it was found that cyanine, a blue dye discovered in 1856, rendered the emulsion sensitive to a wider range of visibly colored light. Since then, related dyes have been developed [12] that sensitize the emulsions to all visible wavelengths and in the infrared region. Such sensitizers are especially useful in long-distance photography.

In addition, polymethine cyanine dyes represent linear conjugated molecules that exhibit numerous unique electronic and spectral properties which are useful for a broad area of applications connected with light conversion, e.g. spectral sensitization, initiation of polymerization, molecular probes in polymer science and biology, active and passive components for tunable lasers, nonlinear media exploiting excited - state absorption (ESA), etc [13]. Also, polymethine molecules serve as objects for developing new theoretical concepts and effective quantum-chemical models.

Besides, the recent research for NIR (near Infrared) polymethine dyes is due to various applications of the inexpensive solid - state diode lasers, generating light at about 800 nm. Fields of application currently under investigation are analytical ultra, trace determination of proteins by high-performance chromatography and laser fluorimetry, the localization and treatment of neoplasia in photopharmatherapy and particularly the optical data recording and reading systems (optical disks). The question has also been posed as to whether polymethine structures can serve as novel materials in non-linear optics capable of second - harmonic generation [14].

*Address correspondence to this author at the Department of Chemistry, Faculty of Science at Aswan, South Valley University, Aswan, Egypt; Tel: 0972322725; Fax: 0973480450; E-mail: hashindy2010@hotmail.com

2. SYNTHESIS

A series of methine cyanine dyes such as monomethine (3a-e), aza-methine (4a-c), trimethine (6a-i) and (8a-c) incorporating fused pyrazolo[3,4-d]oxazole nucleus were prepared [15], Scheme (**1**).

Substituents in scheme (**1**)

(1, 2, 3, 5): R=H(a), ρ.OCH_3 (b), ρ.NO_2(c), ρ.OH(d), ρ.Cl(e).
(4a-c): R=ρ.NO_2, 4.OH, Y=H(a); R=ρ.NO_2, 2.OH, Y=5,6-benzo (b);
R=ρ.NO_2, 2.OH, Y=3,4-benzo (c).
(6a-i) : R=H, A=C_4H_4-2-yl salt (a); R=H, A=C_4H_4-4-yl salt (b);
R=ρ.OCH_3, A=C_4H_4-2-yl salt (c); R=ρ.OCH_3, A=C_4H_4-4-yl salt(d);
R=ρ.NO_2, A= C_4H_4-2-yl salt (e); R=ρ.OH, A=C_4H_4-2-yl salt (f);
R=ρ.OH, A= C_4H_4-4-yl salt(g); R=ρ.Cl, A=C_4H_4-2-yl salt (h);
R=ρ.Cl, A=C_4H_4-4-yl salt (i).
(7a-c),(8a-c) : R=H (a), ρ.NO_2 (b), ρ.OH (c).

3,5-Dimethyl-1-phenyl-1H-pyrazolo[4,3-d][1,3]oxazole was prepared and oriented as starting material in the synthesis of some mono-, di-, and trimethine cyanine dyes [16], Scheme (**2**).

substituents in scheme (**2**)

(9a, b); (10a, b): X = N(a), $\overset{+}{N}$ - Et I^- (b).
(16a – c); (17a – c); (24a– c); (26a – c):
A =1-ethyl pyridinium-2-yl iodide (a);
A =1-ethyl quinolinium-2-yl iodide (b);
A =1-ethyl pyridinium-4-yl iodide (c).
(18a – c); (20a – c): A =1-ethyl pyridinium-4-yl iodide (a);
A =1-ethyl quinolinium-4-yl iodide (b);
A =2-ethyl isoquinolinium-1-yl iodide (c).

A number of photosensitizers, monomethine, dimethine, trimethine, styryl and mixed cyanine dyes incorporating pyrazolo / oxazole (thiazole) nuclei were prepared [17], Scheme (**3**).

Substituents in scheme (3)

(9a, b): X = N(a); $\overset{+}{N}$ - Et I^- (b).
(27a – d): X = N, Z = O (a); X = N, Z = S (b);
X = $\overset{+}{N}$ - Et I^-, Z = O (c); X = $\overset{+}{N}$ - Et I^-, Z = S (d).
(28a, b); (29a, b); (33a, b): Z =O (a); S (b).
(30a – d): Z = O, A =1-ethyl pyridinium-4-yl salt (a);
Z = O, A =1-ethyl quinolinium-4-yl salt (b);
Z = O, A =2-ethyl isoquinolinium-1-yl salt (c);
Z = S, A =1-ethyl quinolinium-4-yl salt (d).
(32a – d); (35a – d): Z = O, A =1-ethyl pyridinium-2-yl salt (a);
Z = O, A =1-ethyl quinolinium-2-yl salt (b);
Z = O, A =1-ethyl pyridinium-4-yl salt (c);

1875-6298/12 $58.00+.00

Z = S, A =1-ethyl quinolinium-2-yl salt (d).
(38a – e): Z = S, X = H (a); Z = S, X = OH (b); Z = S, X = NMe_2 (c); Z = S, X = Cl (d); Z = O, X = NMe_2 (e).
(39a, b): A = H, Ā =benzene (a); A = benzene, Ā = H (b).

5-Aryl-3-methyl-1-phenyl-pyrazolo[3,4-d]oxazoles were synthesized by Koraiem *et al.* [18] as starting material in the synthesis of some cationic di- and tetra- methine cyanine dyes, Scheme (**4**).

Substituents in scheme (**4**)

(41a – e); (42a – e); (43a – e): R = H (a), ρ.OCH_3 (b), ρ.NO_2 (c), ρ.OH (d), ρCl (e).
(44a –g), (45a – g): R = H, A = H-2-yl salt (a), R = H, A = C_4H_4-2-yl salt (b),
R = H, A = H-4-yl salt (c), R = ρ.OCH_3, A = C_4H_4-2-yl salt (d),
R = ρ.NO_2, A = C_4H_4-2-yl salt (e), R = ρ.OH, A = C_4H_4-2-yl salt (f),
R = ρ.Cl, A = C_4H_4-2-yl salt (g)
(46a – c): A = pyridine-2- (a); quinoline-2 (b); pyridine-4 (c).
(47a –e); (48a – e): R = H, X = H (a); R = H, X = ρ.OCH_3 (b);
R = H, X = ρ.NO_2 (c); R = ρ.OCH_3, X = H (d);
R = ρ.OCH_3, X = ρ.OCH_3 (e).

4,5-Dioxo-3-methyl-1-phenyl-pyrazoline is condensed with α-picoline-EtI, quinaldine-EtI or 2-methyl benzoxazole-EtI to form monomethine derivatives, which is then brominated and finally cyclocondensed with hydrazines or hydroxylamine to give apocyanine dyes [19], Scheme (**5**).

Substituents in scheme (**5**)

(50a – c); (51a – c); (52a – c); (53a – c); (54a – c):
A = 1-ethyl pyridinium-2-yl salt (a);
1-ethyl quinolinium-2-yl salt (b);
3-ethyl benzoxazolium-2-yl salt (c).

Dimethine, bis dimethine and tetramethine cyanine dyes derived from benzo [4,5-b; 4′,5′-b′] bis furo, thieno and pyrrolo-4,8-dione were prepared [20], Scheme (**6**).

Substituents in scheme (**6**)

(56a-c); (57a-c): X = O (a); S (b); NH (c).
(58a-e); (59a-e): X = O, A = 1-methyl pryidinium-2-yl salt (a);
X = O, A = 1-methyl quinolinium-2-yl salt (b);
X = O, A = 1-methyl pryidinium-4-yl salt (c);
X = S, A = 1-methyl quinolinium-2-yl salt (d);
X = NH, A = 1-methyl quinolinium-2-yl salt (e).
(60a-g); (61a-g): X = O, R = H (a); X = O, R = CH_3 (b);
X = O, R = C_6H_5 (c); X = O, R=C_6H_4-ρ-OCH_3 (d);
X=O, R=C_6H_4-ρ-NO_2 (e); X=S, R=CH_3 (f); X=NH, R=CH_3 (g).

A number of furo, thieno and pyrrolo[2,3-b]pyrazole cyanine dyes were synthesized [21], Scheme (**7**).

Substituents in scheme (**7**)

(56a - c); (62a - c); (63a - c), (65a - c) X = O (a); S (b); NH (c).
(64a - e) X = O, A = 1-methyl pyridinium-4-yl salt (a);
X = O, A = 1-methyl quinolinium-4-yl salt (b);
X = O, A = 2-methyl isoquinolinium-1-yl salt (c);
X = S, A = 1-methyl quinolinium-4-yl salt (d);
X = NH, A = 1-metyl quinolinium-4-yl salt (e).
(66a - c); (67a - c) X = O, A = 1-methyl pyridinium-2-yl salt (a);
X = O, A = 1-methyl quinolinium-2-yl salt (b);
X = O, A = 1-methyl pyridinium-4-yl salt (c);
X = S, A = 1-methyl quinolinium-2yl salt (d);
X = NH, A = 1-methyl quinolinium-2-yl salt (e).

A series of some photosensitizers dimethine, bis dimethine and tetramethine cyanine dyes containing furo, thieno and pyrrolo [2,3-*b*] pyrazole nucleus were prepared [22], Scheme (**8**).

Substituents in scheme (**8**)

(62a – c), (63a – c), (69a – c): X = O (a); X = S (b); X = NH (c).
(68a – h): X = O, Z = N, A = 1-methyl pyridinium-2-yl salt (a);
X = O, Z = N, A = 1-methyl quinolinium-2-yl salt (b);
X = O, Z = N, A = 1-methyl pyridinium-4-yl salt (c);
X = S, Z = N, A = 1-methyl quinolinium-2-yl salt (d);
X = NH, Z = N, A = 1-methyl quinolinium-2-yl salt (e);
X = O, Z = $^{\oplus}$N-$^{\ominus}$MeI, A = 1-methyl quinolinium-2-yl salt (f);
X = S, Z = $^{\oplus}$N-$^{\ominus}$MeI, A = 1-methyl quinolinium-2-yl salt (g);
X = NH, Z = $^{\oplus}$N-$^{\ominus}$MeI, A = 1-methyl quinolinium-2-yl salt (h).
(70a – e), (71a – e): X = O, A = 1-methyl pyridinium-4-yl salt (a);
X = O, A = 1-methyl quinolinium-4-yl salt (b);
X = O, A = 2-methyl isoquinolinium-1-yl salt (c);
X = S, A = 1-methyl quinolinium-4-yl salt (d);
X = NH, A = 1-methyl quinolinium-4-yl salt (e).
(72a – g), (73a – g): X = O, R = H (a); X = O, R = CH_3 (b); X = O, R = C_6H_5 (c);
X = O, R = C_6H_4-*ρ*-OCH_3 (d); X = O, R = R = C_6H_4-*ρ*-NO_2 (e);
X = S, R = CH_3 (f); X = NH, R = CH_3 (g).

2-Cyanomethylene(2-ethoxy carbonyl methylene)-4,5-dihydrothiazolo-[3,2a]oxazole (74a,b) were synthesized as starting material to prepare meso-substituted mono-, tri- and hepta- methine cyanine dyes [23], Scheme (**9**).

Substituents in scheme (**9**)

X = CN (a); COOEt (b).

Shindy synthesized a series of monomethine, dimethine, trimethine, styryl and aza-styryl cyanine dyes having naphthfuro[3,2-d] pyrazole nucleus [24], Scheme (**10**).

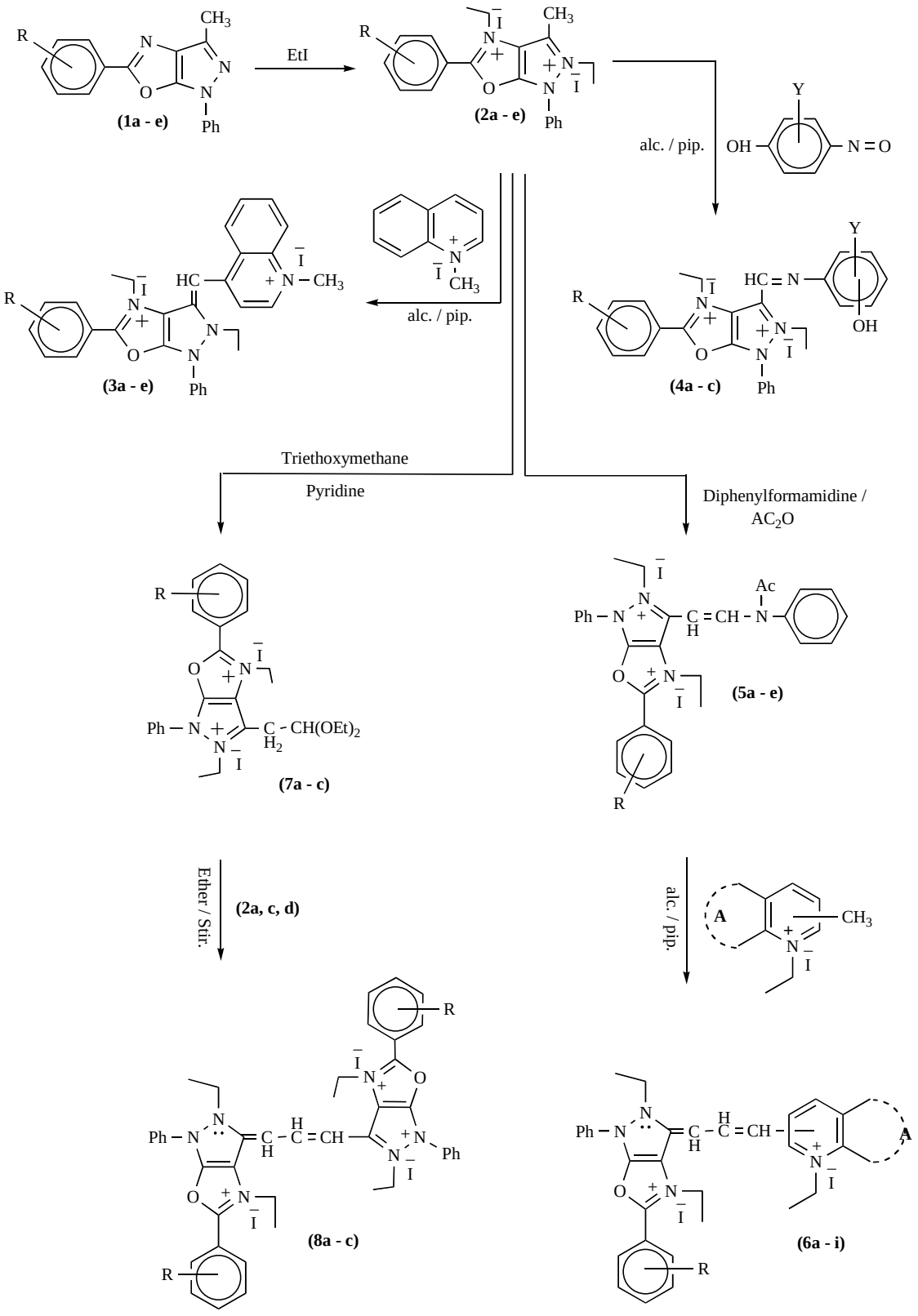
Substituents in scheme (**10**)

(85a – c): A = 1-methyl pyridinium-2-yl salt (a);
A = 1-methyl quinolinium-4-yl salt (b);
A = 2-methyl isoquinolinium-1-yl salt (c).
(87a – c); (89a – c): A = 1-methyl pyridinium-2-yl salt (a);
A = 1-methyl quinolinium-2-yl salt (b);
A = 1-methyl pyridinium-4-yl salt (c).
(90a – f): X = H (a); OH (b); OCH_3 (c); $N(CH_3)_2$ (d); NO2 (e); Cl (f).
(91a – c): Y = 4.OH (a); Y = 2.OH, 5,6-benzosubstituent (b);
Y = 2.OH, 3,4- benzosubstituent (c).

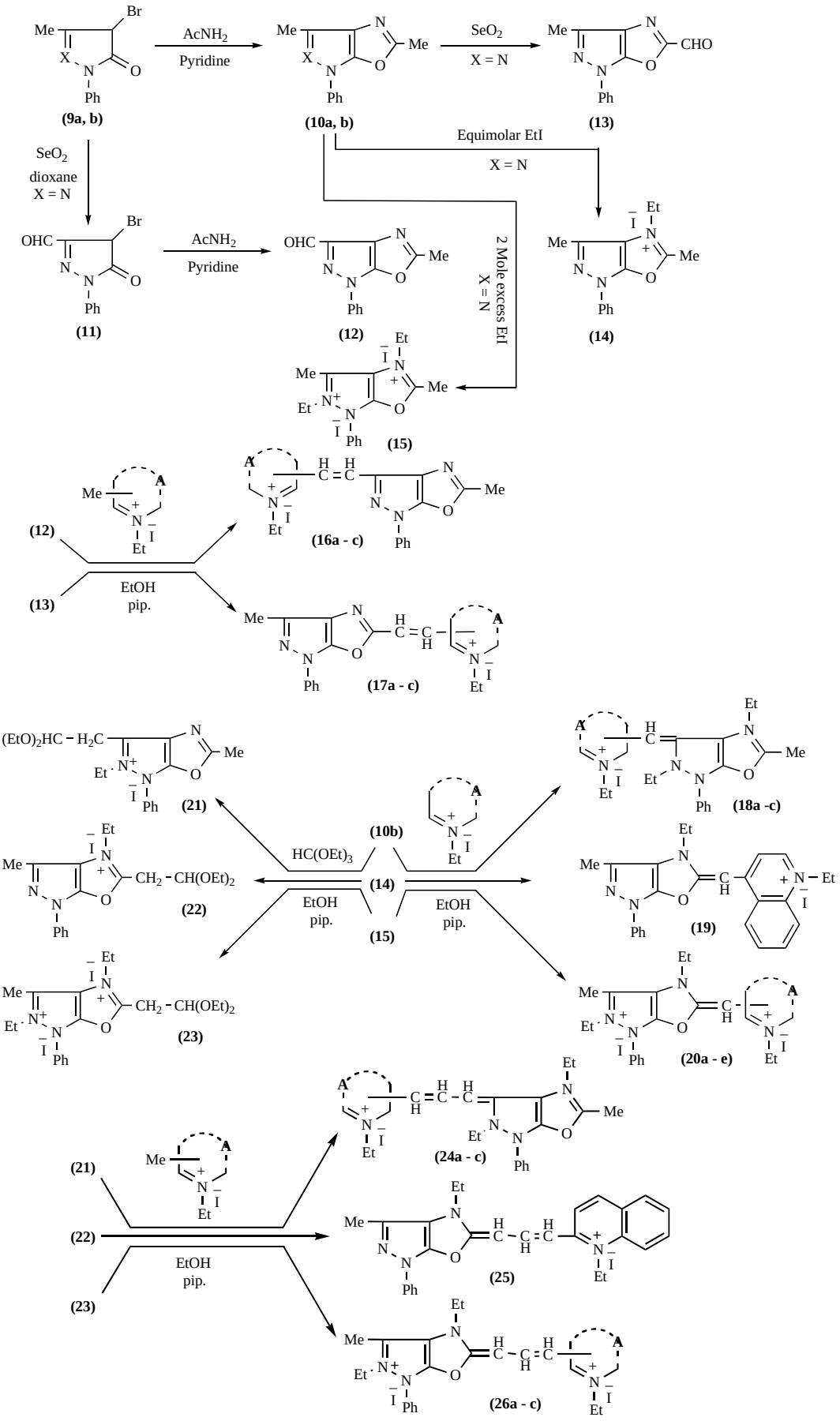
A number of monomethine cyanine, trimethine cyanine, substituted trimethine cyanine, aza-cyanine and mixed cyanine dyes having pyrazolo[4,5-d]oxazole nucleus were prepared by Shindy, *et al.* [25], Scheme (**11**).

Substituents in scheme (**11**)

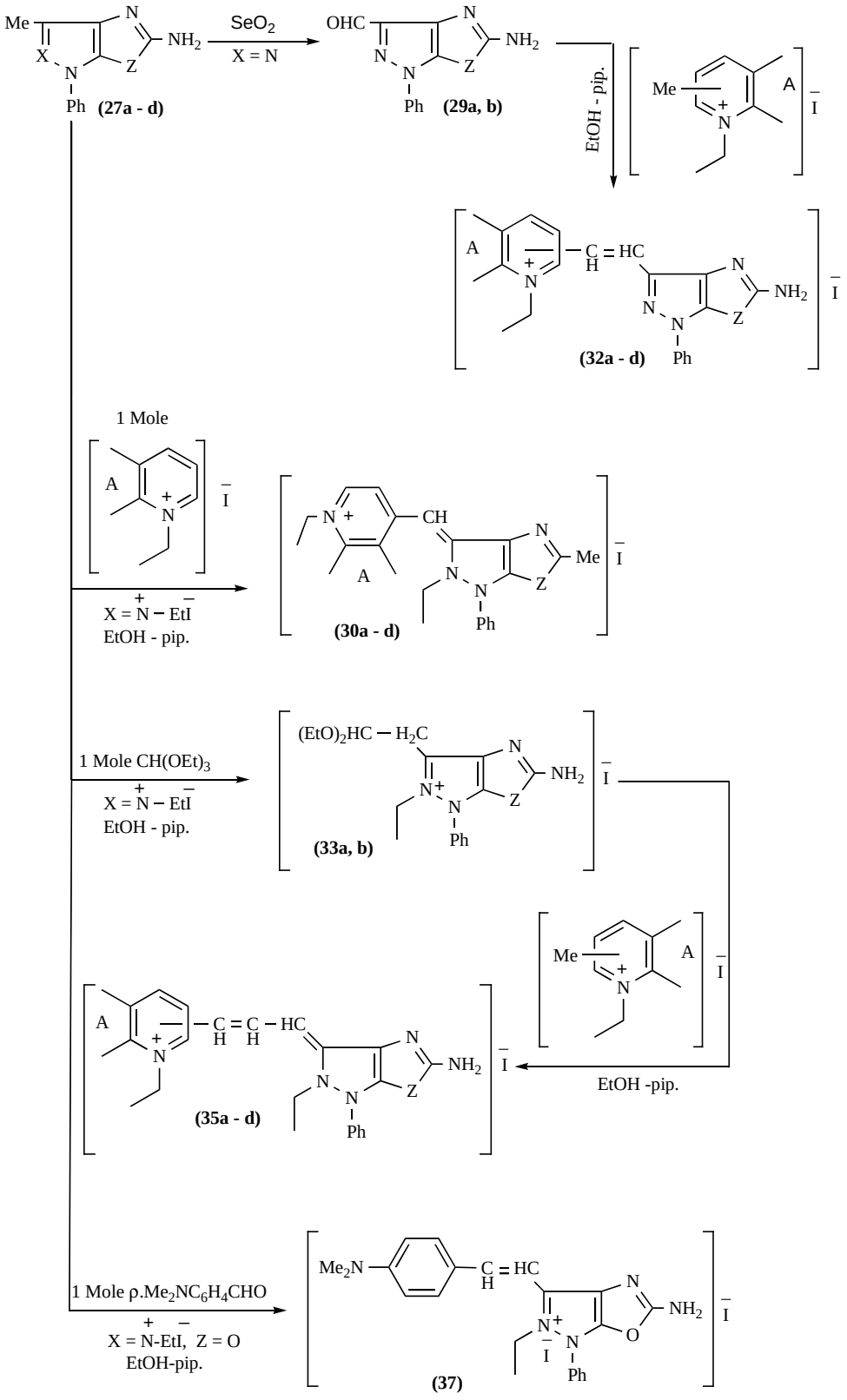
(95a – c), (98a – c): A = 1-ethyl-pyridinium-2-yl salt (a);
A = 1-ethyl-quinolinium-2-yl salt (b);
A = 1-ethyl-pyridinium-4-yl salt (c).
(96a – c): A = 1-ethyl-pyridinium-4-yl salt (a);
A = 1-ethyl-quinolinium-4-yl salt (b);
A = 2-ethyl-isoquinolinium-1-yl salt (c).
(99a – e), (100a – e): R = H (a); R = CH_3 (b); R = Ph (c);
R = Ph.OCH_3 (d); R = Ph.NO_2 (e).
(101a – c): R = 4-OH (a); R = 2-OH,5,6-benzosubstituent (b);
R = 2-OH,3,4-benzosubstituent (c).


EtI
(1a - e)
(2a - e)
alc. / pip.
(3a - e)
(4a - c)
Triethoxymethane
Pyridine
Diphenylformamidine /
AC2O
(7a - c)
(5a - e)
Ether / Stir.
(2a, c, d)
alc. / pip.
(8a - c)
(6a - i)

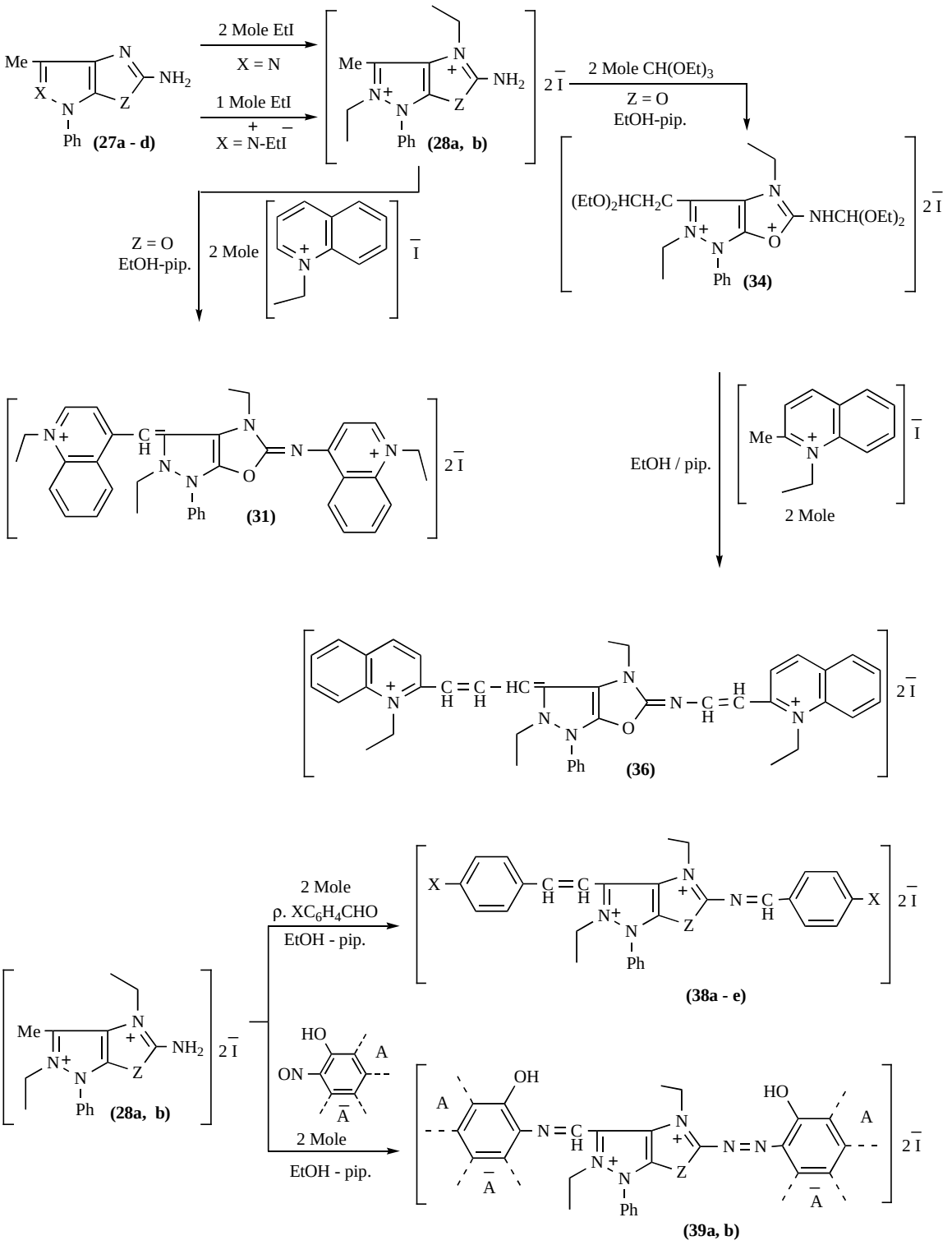
Scheme 1.


AcNH2
Pyridine
SeO2
X = N
dioxane
Equimolar EtI
2 Mole excess EtI
EtOH
pip.
HC(OEt)3
(9a, b)
(10a, b)
(11)
(12)
(13)
(14)
(15)
(16a - c)
(17a - c)
(18a -c)
(19)
(20a - e)
(21)
(22)
(23)
(24a - c)
(25)
(26a - c)

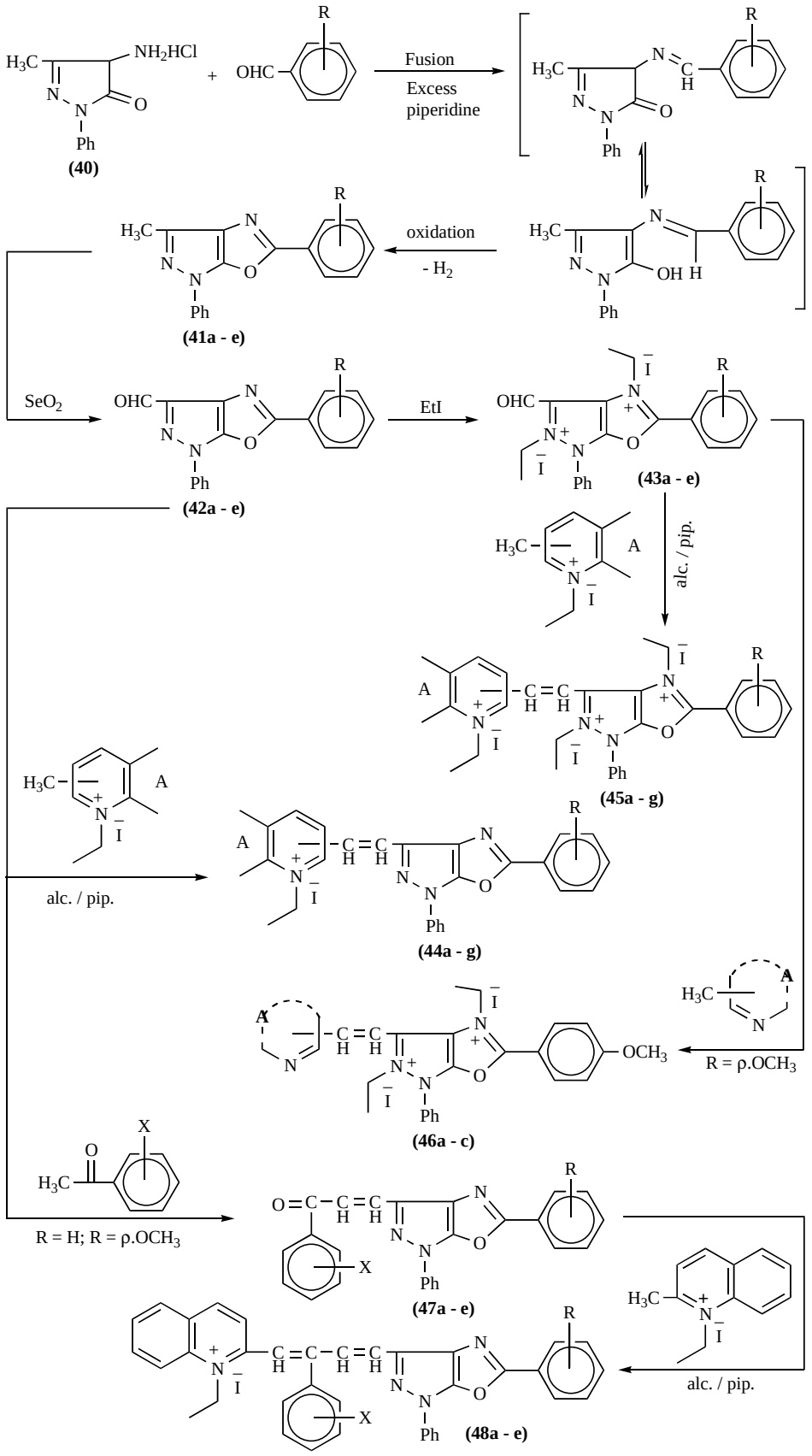
Scheme 2.


SeO2
X = N
(27a - d)
(29a, b)
EtOH - pip.
(32a - d)
1 Mole
X = N – EtI
EtOH - pip.
(30a - d)
1 Mole CH(OEt)3
X = N – EtI
EtOH - pip.
(33a, b)
EtOH -pip.
(35a - d)
1 Mole ρ.Me2NC6H4CHO
X = N-EtI, Z = O
EtOH-pip.
(37)

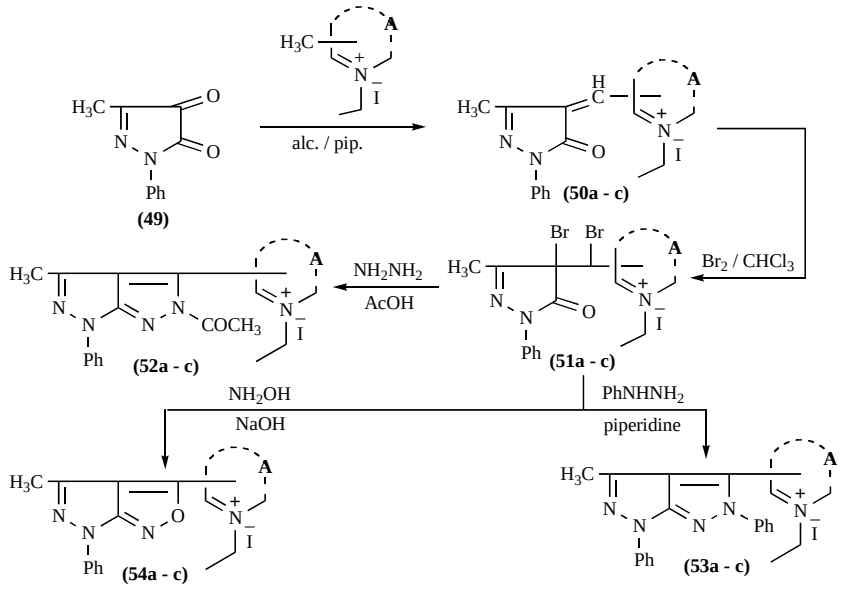
Scheme 3. Contd…



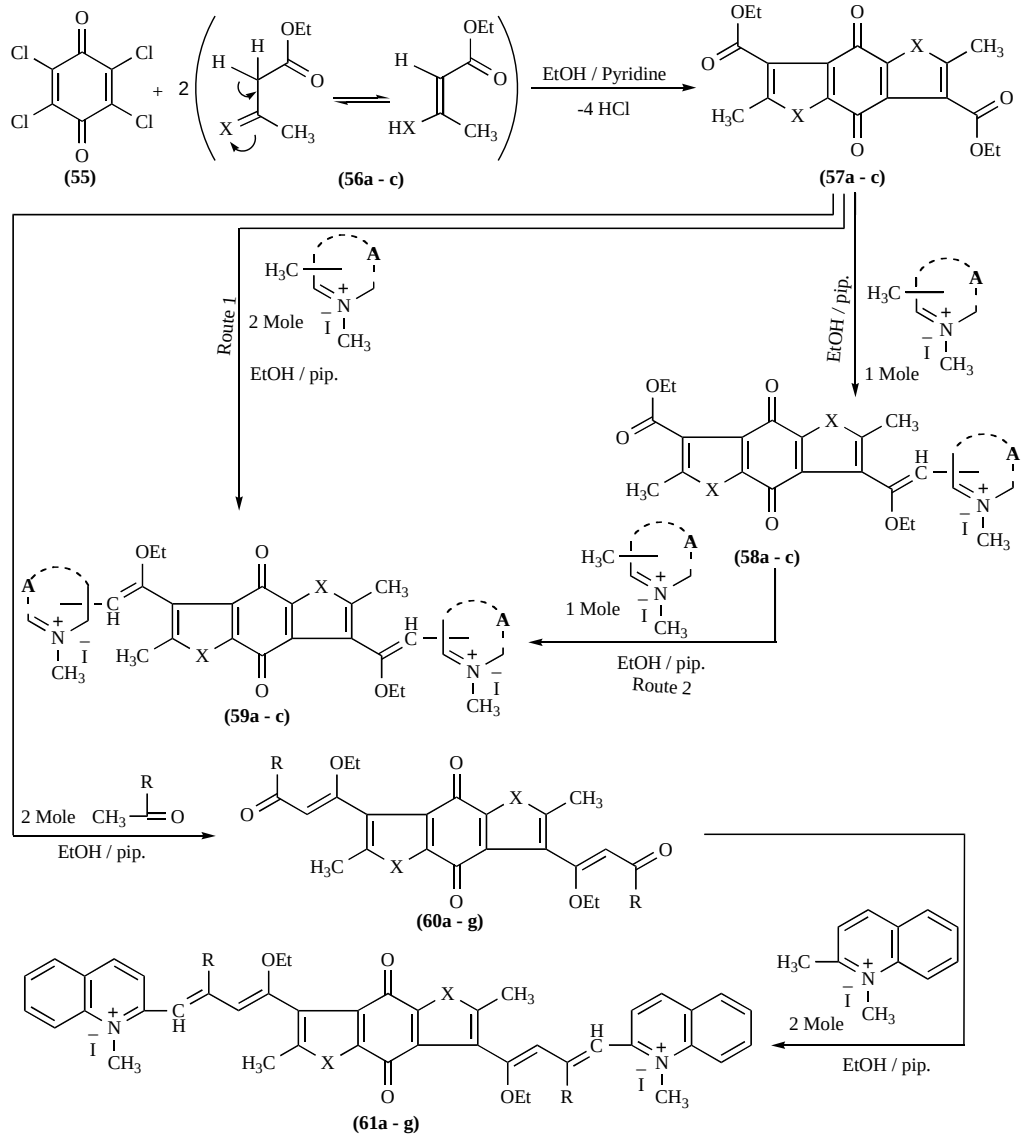
Scheme 3.


Fusion
Excess
piperidine
oxidation
- H2
SeO2
EtI
alc. / pip.
R = ρ.OCH3
R = H; R = ρ.OCH3
(40)
(41a - e)
(42a - e)
(43a - e)
(44a - g)
(45a - g)
(46a - c)
(47a - e)
(48a - e)

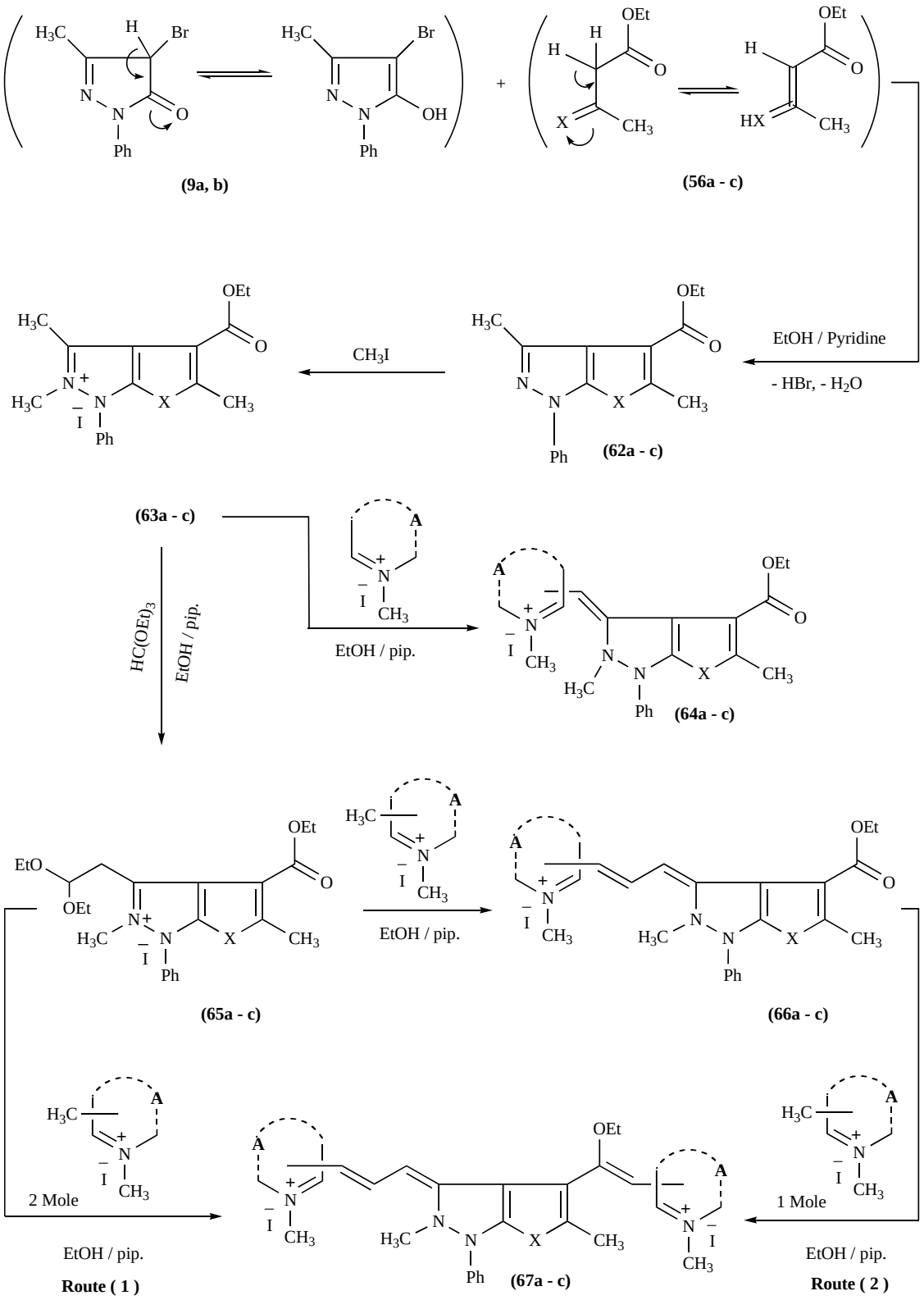
Scheme 4.



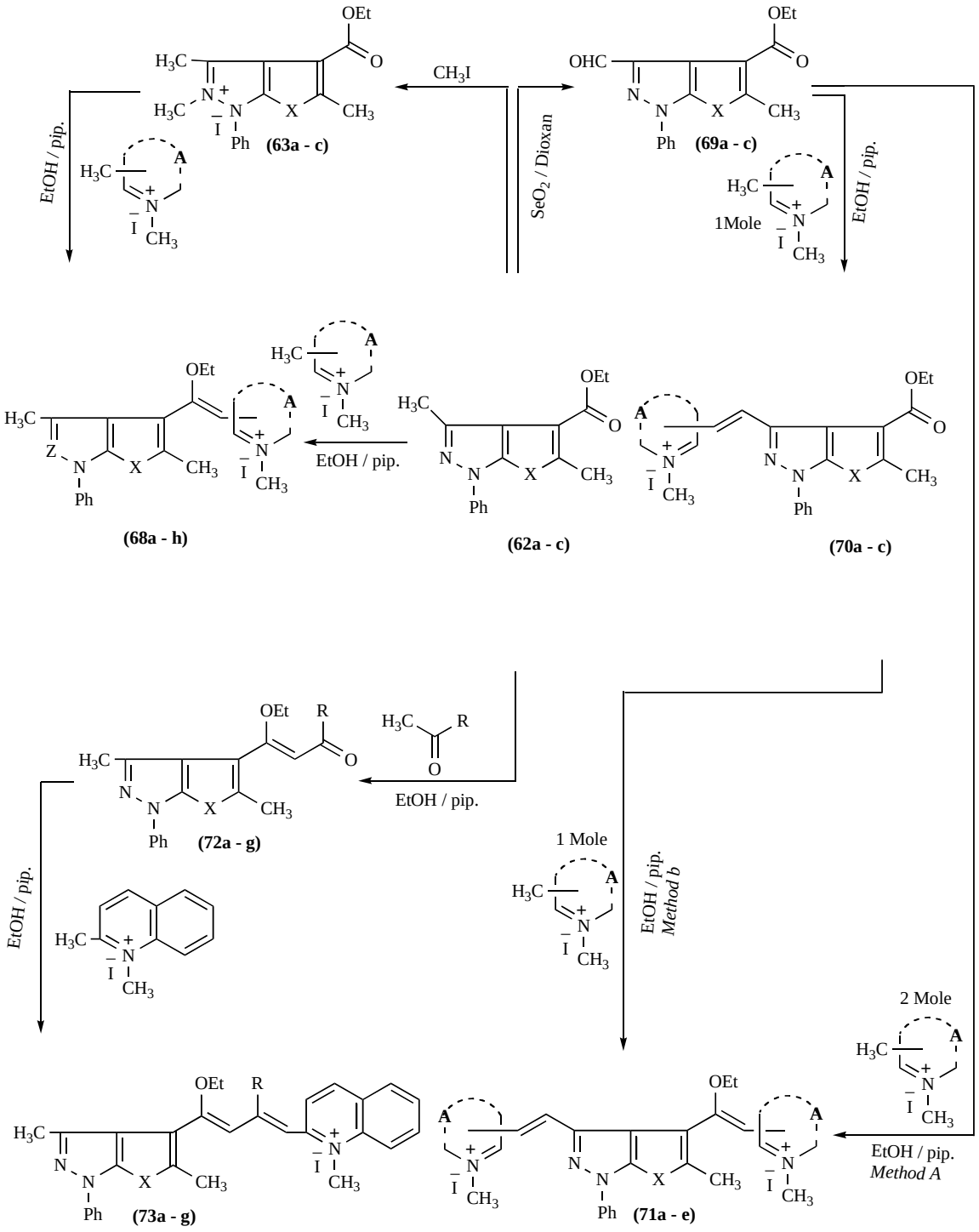
Scheme 5.



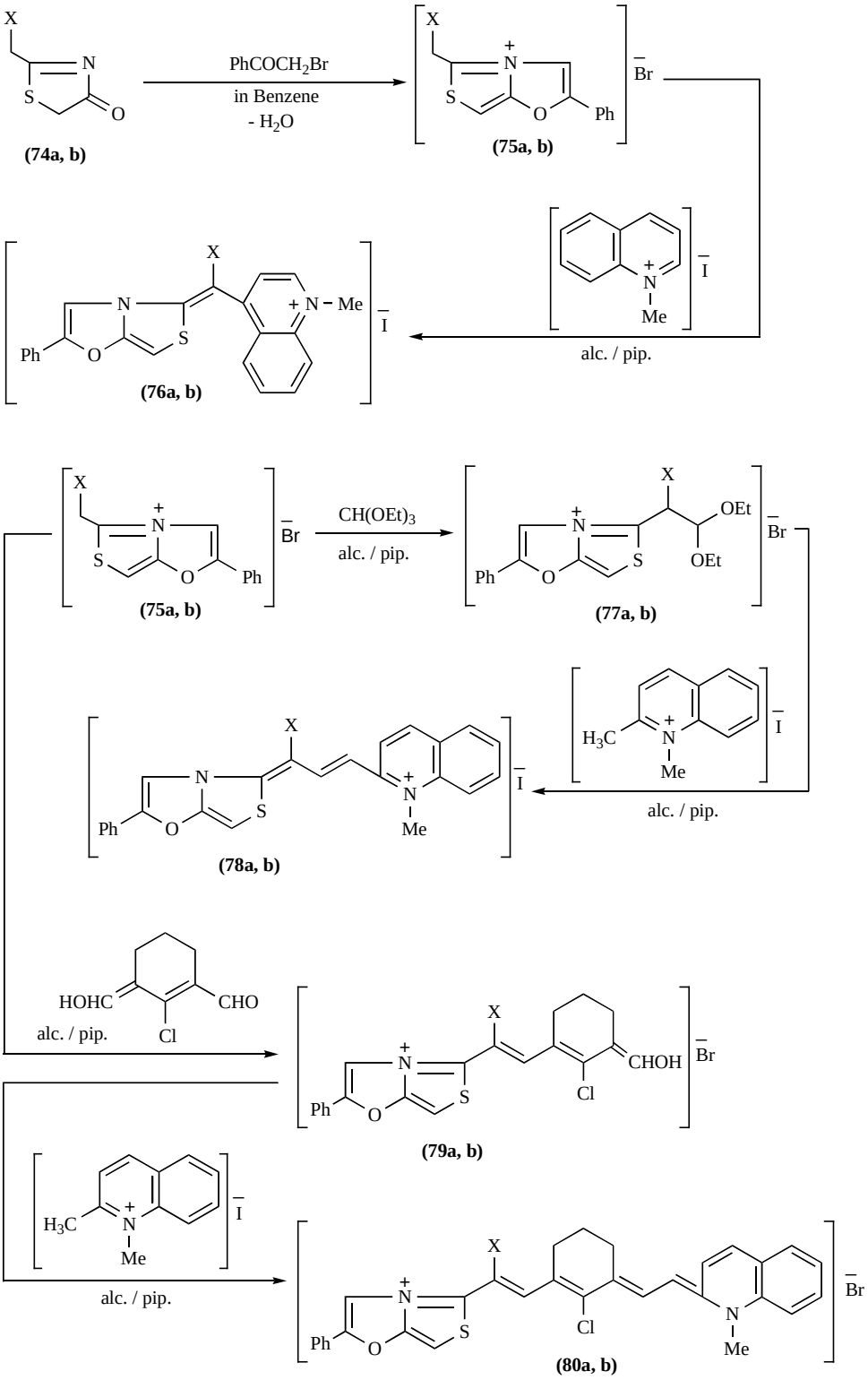
Scheme 6.


(9a, b)
(56a - c)
EtOH / Pyridine
- HBr, - H2O
(62a - c)
CH3I
(63a - c)
HC(OEt)3
EtOH / pip.
EtOH / pip.
(64a - c)
(65a - c)
EtOH / pip.
(66a - c)
2 Mole
1 Mole
EtOH / pip.
EtOH / pip.
Route (1)
Route (2)
(67a - c)

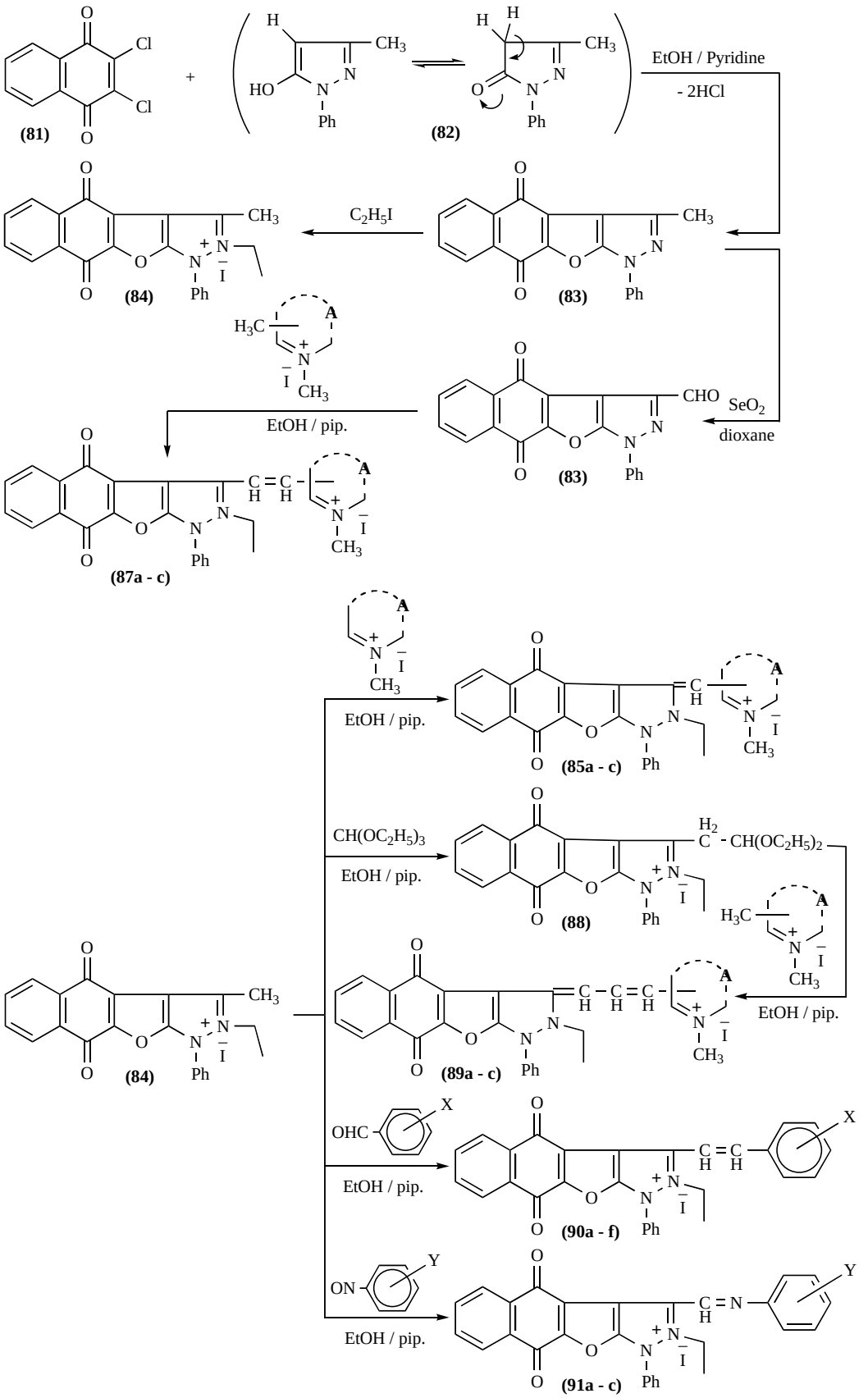
Scheme 7.


CH3I
SeO2 / Dioxan
EtOH / pip.
(63a - c)
(69a - c)
1Mole
(68a - h)
(62a - c)
(70a - c)
(72a - g)
1 Mole
EtOH / pip.
Method b
2 Mole
EtOH / pip.
Method A
(73a - g)
(71a - e)

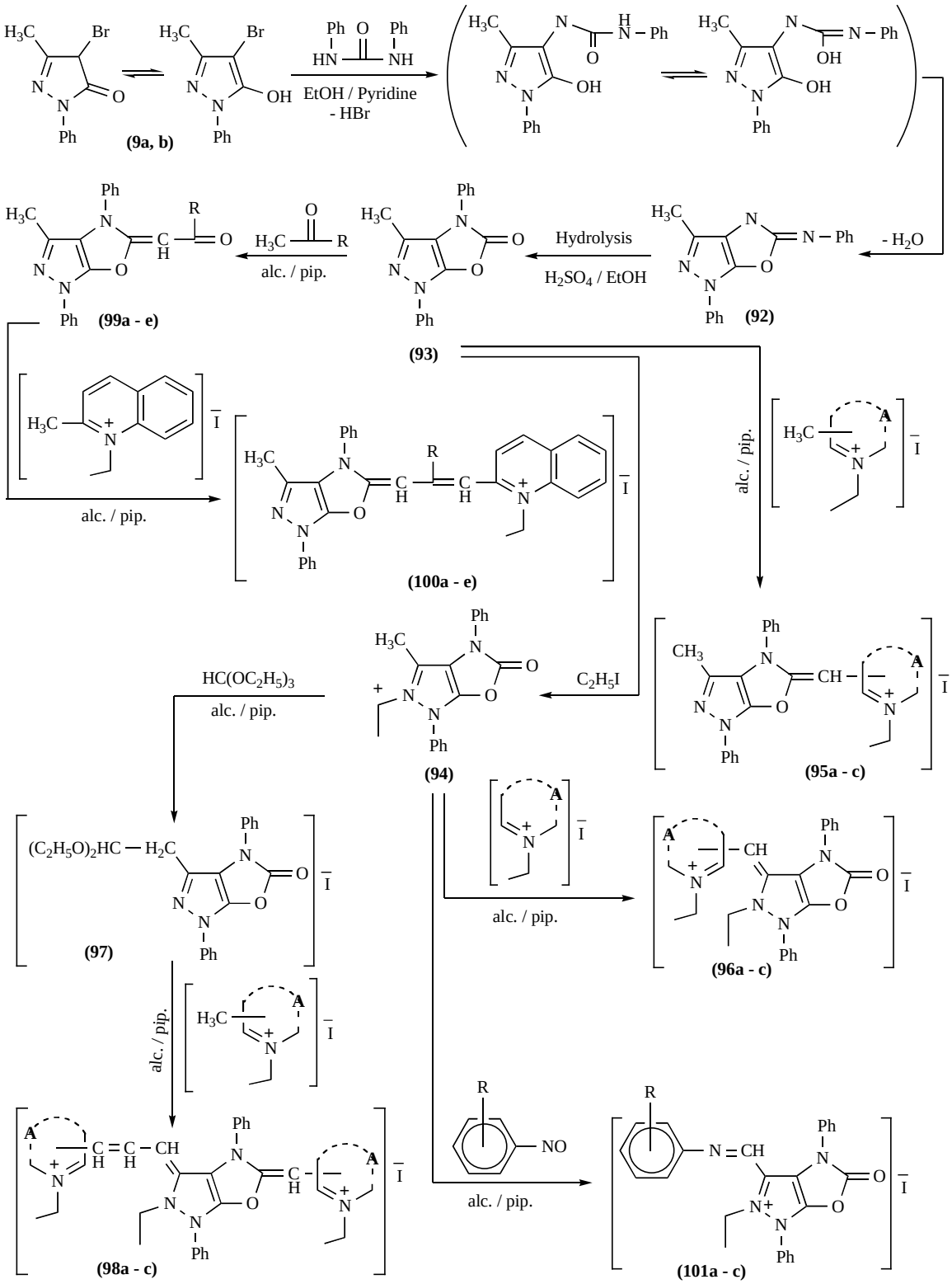
Scheme 8.


PhCOCH2Br
in Benzene
- H2O
(74a, b)
(75a, b)
(76a, b)
alc. / pip.
CH(OEt)3
alc. / pip.
(77a, b)
(78a, b)
alc. / pip.
HOHC
CHO
Cl
alc. / pip.
(79a, b)
alc. / pip.
(80a, b)

Scheme 9.


(81)
(82)
EtOH / Pyridine
- 2HCl
C_2H_5I
(84)
(83)
EtOH / pip.
SeO_2
dioxane
(87a - c)
(85a - c)
$CH(OC_2H_5)_3$
(88)
(89a - c)
(90a - f)
(91a - c)

Scheme 10.



Scheme 11.

ACKNOWLEDGEMENT

None declared.

CONFLICT OF INTEREST

None declared.

REFERENCES

[1] Jedrzejewska, B. and Rudnicki, A. The synthesis and spectroscopic investigation of dichromophoric hemicyanine dyes, *Dyes and pigments*, **2009**, *80*, 297-306.

[2] Abd El-Halim, S. T. and Awad, M. K. Solvatochromism, molecular and electronic structures of trans and cis isomers of typical styryl pyridinium cyanine dye, *Journal of Molecular Structure*, **2009**, *920*, 332-341.

[3] Boto, R.E.F., Santos, P.F., Reis, L.V., Almeida, P. Synthesis and characterization of new mono- and dicarboxyalkylselenacarbocyanines, *Dyes and Pigments*, **2008**, *76*,165-172.

[4] Kabatc, J. and Paczkowski, J. Monomeric asymmetric two- and three- cationic monomethine cyanine dyes as novel photoinitiators for free-radical polymerization, *Dyes and Pigments*, **2010**, *86*, 133-142.

[5] Deligeorgiev, T. G., Zaneva, D. A., Kim S. H. and Sabnis R. W. Preparation of monomethine cyanine dyes for nucleic acid detection, *Dyes and Pigments*, **1998**, *37*, 205-211.

[6] Yakubovskyi, V. P., Shandura, M. P., Kovtum Y. P. Boradipyrromethene-cyanines derived from conformationally restricted nuclei, *Dyes and Pigments*, **2010**, *87*, 17-21.

[7] Klochko, O. P., Fedyunyayeva, I. A., Khabuseva, S. U., Semenova, O. M., Terpetschnig, E. A., Patsenker, L. D. Benzodipyrrolenine-based biscyanine dyes: Synthesis, molecular structure and spectroscopic characterization, *Dyes and Pigments*, **2010**, *85*, 7-15.

[8] Poronikb, Ye. M., Kovtunb, Yu. P., Vasyluka, S. V., Viniychukb, O. O., Yashchuka V. M. and Kachkovskyb, O. D. Braking of symmetrical charge distribution in xanthylocyanine chromophores detecting by their absorption spectra, *Journal of Molecular Structure*, **2011**, *990*, 6-13.

[9] Pronkin, P. G. and Tatikolov, A. S. Study of electronic excitation energy transfer between cyanine dye molecules noncovalently bound to DNA, *High Energy Chemistry*, **2011**, *45*, 140-146.

[10] Ornelas C., Lodescar, R., Durandin A., Canary J. W., Pennell, R., Liebes L. F., Weck,M. Combining aminocyanine dyes with polyamide dendrons: A promising strategy for imaging in the near-infrared region, *Chemistry-A European Journal*, **2011**, *17*, 3619-3629

[11] Hamer, F.M. *The cyanine dyes and related compounds*, New York, interscience publishers Inc., **1964**, pp. 198.

[12] Rongqi, C., The development and application of green dye, *printing and dyeing*, **2006,** (6): 45.

[13] Matsuoka, M. (Ed.), *Infrared Absorbing dyes*, Plenum Press, New York, **1990**, pp. 220.

[14] Tyutyulkov, N., Fabian, J., Mehlhorn, A., Dietz, F. and Tdjer, A., *Polymethine Dyes, Structure and Properties* (Sofia: St. Kliment Ohridski University Press. **1991**).

[15] Abu El-Hamd R.M. Electronic spectra of some new synthesized methine cyanine dyes, *Asw. Sc. Tech. Bull*., **1995**, *16*, 2-26.

[16] Koraiem, A.I.M. and Shindy, H.A. Orientation in the synthesis and absorption spetra of 1H-pyrazolo[4,5-d][1,3]oxazole methine cyanine dyes, *Chemical Paper*,**1998**, *52*, 762-770.

[17] Shindy, H.A. Synthesis and visible spectral behaviour of some new photosensitizers: Monomethine, dimethine, trimethine, styryl and mixed cyanine dyes., *J. Chem. Research*, **1999**, *(S)*, 700-701,*(M)*, 3001-3017.

[18] Koraiem, A.I.M.; El-Maghraby, M.A.; Abu El-Hamd, R.M. Synthesis and electronic spectra of some mono-, di- and tri- cationic di- and tetramethine cyanine dyes., *Dyes and Pigments*, **1990**, *14*, 59-72.

[19] Koraiem, A.I.M. Apocyanine dyes from 4,5-dioxo-3-methyl-1-phenyl-pyrazoline, *J. Prakt. Chem.*, **1984**, *326*, 811–816.

[20] Shindy, H.A.; El-Maghraby, M.A.; Essia, F.M. Novel quinone cyanine dyes: Synthesis and spectral studies, *Dyes and Pigments*, **2002**, *52*, 79-87.

[21] Shindy, H.A.; El-Maghraby, M.A.; Essia, F.M.Novel cyanine dyes: Synthesis, characterization and photosensitization-structure correlation, *Journal of the Chinese Chemical Society***, 2002**, *49*, 1061-1068.

[22] Shindy, H.A.; El-Maghraby, M.A.; Essia, F.M. New photosensitizer cyanine dyes: Synthesis and properties, *Indian Journal of Chemistry*, **2006**, *45B*, 1197-1203.

[23] Abd El-Aal, R. M. Thiazoline and thiazoloxazole in the synthesis of novel meso-substituted mono-, tri- and hepta- methine cyanine dyes, *Dyes and Pigments*, **2004**, *61*, 251-261.

[24] Shindy, H.A. Synthesis, characterization and visible spectral behaviour of some novel methane, styryl and aza-styryl cyanine dyes, *Dyes and Pigments*, **2007**, *75*, 344-350.

[25] Shindy, H. A and Koraiem, A. I. M. Synthsis and absorption-structure relationship of some new photosensitizers cyanine dyes, Proc. *Indian Academy of Sciences (Chemical Sciences)*, **2002**, *114*, 125-136.

Received: July 29, 2011 Revised: October 22, 2011 Accepted: October 25, 2011