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Characterization, Mechanisms and Applications in the Chemistry of Cyanine Dyes: A Review

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Abstract

In this paper review, some of the important characterizations and mechanisms in the chemistry of cyanine dyes were explained. This include topics like absorption spectral behaviour, general characterization of cyanine dyes, photosensitisation effects of cyanine dyes in silver halide emulsion, photosensitisation-structure correlation of cyanine dyes, colour spectrophotometric measurements of cyanine dyes, fluorescence spectra of cyanine dyes, IR and ¹H NMR spectra of cyanine dyes, general view in the visible spectra of cyanine dyes, stability of cyanine dyes, cyanine dyes in photodynamic therapy, synthesis mechanisms of monomethine cyanine dyes and synthesis mechanisms of trimethine cyanine dyes. In addition, in the introduction section of this review paper some light is shed on important uses and applications of cyanine dyes. Reviewing some of the important characterizations and synthesis mechanisms in the chemistry of cyanine dyes is interesting and can be considered as a novel or patent idea to which little attention has been paid in the chemistry literature.

Keywords: cyanine dyes, characterization of cyanine dyes, applications of cyanine dyes, absorption spectra of cyanine dyes, emission spectra of cyanine dyes, stability of cyanine dyes, synthesis mechanisms of cyanine dyes.

1. Introduction

Cyanine dyes (Fasiulla et al., 2008; Deligeorgiev et al., 1998; Champagne et al., 2006; Rongqi, 2006; Kovalska et al., 2010; Kabatc, Paczkowski, 2010; Yakubovskiy et al., 2010; Klochko et al., 2010; Yashchuk et al., 2007; Boto et al., 2008; Gadjev et al., 1999; Keisar et al., 2014; Yi et al., 2014; Owens et al., 2014) occupy an important and vital position in the chemistry of dyes and pigments because of their multiple uses and applications in various fields of science, technology, engineering, pharmacology and medicine. These may include but not limited to determination of carbon-carbon bond length, in textile industry, as corrosion inhibitors, as electrophotographic photoreceptors, in printing inks, as synthetic drugs, as inhibitors for cell growth and division in many biological process, as cosmetic ingredients, as reagents in biomedicine, as indicator for solvent polarity, as suitable model systems to understand and study the colour of organic compounds, as photorefractive materials, dyes for polymers, in laser printers, in histological staining, as intercalating agents and as hormonal effects on plant growth. Numerous publications

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in the synthesis, characterisation and applications of cyanine dyes in the present time (Parvathy et al., 2015; Ferreira et al., 2015; Moreira et al., 2015; Upadhyayula et al., 2015; Arjona et al., 2016; Soriano et al., 2016; Shindy et al., 2016; Zielinska et al., 2010; Zanotti et al., 2011; Shindy et al., 2016a; Lynch et al., 2013; Zhao et al., 2013; Park et al., 2013) reflect the positive future and importance of these dyes in modern science and advanced technologies.

Because cyanine dyes have multidisciplinary uses and applications in various fields of science, technology, engineering, pharmacology and medicine, this paper review might be very interesting for the large heterogenous community groups of chemists, biologists, physicists, biotechnologists, pharmacologists and medical scientists. This paper review will also be informative, useful, and an excellent key reference work for chemists and researchers who are keen to have the fundamental understanding, principles and knowledge of cyanine dyes. Also, this paper review can be used and will be most valuable for students, particularly for the post graduate students in the field of heterocyclic and cyanine dyes chemistry. This paper review is recommended to everyone interested in the subject, to chemistry libraries and also for the personal bookshelves of every organic heterocyclic and cyanine dyes chemist.

2. Some characterization of cyanine dyes

2.1. Absorption spectral behavior (Mojzych, Henary, 2008; Shindy et al., 2000; Shindy et al., 2001; Shindy et al., 2002; Shindy et al., 2002a; Shindy, 1999; Shindy et al., 2006):

Absorption spectra bands in the visible region of the spectrum correspond to transitions of electrons from ground state of a molecule to an excited state. Many substances do not absorb light in the visible range of the spectrum. Such substances are not coloured compounds. Compounds that absorb light in the visible region of the spectrum are coloured compounds, and generally have some weakly bound or delocalized electrons. Cyanine dyes are one of these coloured compounds which have delocalized electrons. Cyanine dyes belong to the category of complex organic compounds which have very intense absorption spectra bands in the visible region of the spectrum. This strong absorption of light at particular wavelengths makes solutions of these molecules brightly coloured. A solution of a dye shows the colour of the light that is not absorbed. The strong absorption leads to many applications of these dyes in technology. For example, these dyes are used to colour plastics, fabrics, and hair. They can also be used to filter and produce coloured light and as laser medium in medical applications. The polymethine cyanine dyes generally show absorption bands in the visible region of the spectra, and each extension for the methine units causes a bathochromic shifts for the absorption bands. Depending on the structure absorption of the pentamethine, cyanine dyes can reach a near-infrared region (>700 nm) and heptamethine cyanine dyes may show absorption bands beyond 1000 nm.

2.2. General characterization of cyanine dyes (Mojzych, Henary, 2008; Shindy et al., 2000; Shindy et al., 2001; Shindy et al., 2002; Shindy et al., 2002a; Shindy, 1999; Shindy et al., 2006; Dioxn et al., 2005):

Cyanine dyes are highly coloured compounds, partially soluble in non polar organic solvents and easily soluble in polar organic solvents giving coloured solutions, accompanied in many cases by pale to intense fluorescence. The intensity and colour of the fluorescence depends upon the type of dye and solvent used. The dyes are soluble in concentrated H₂SO₄ liberating iodine vapour on warming. They are also pH-sensitive dyes, and hence their ethanolic solutions give changeable colours in acid and base media being yellow or colourless on acidification and getting back (restore) their permanent intense colour on basification.

In addition, the solutions of cyanine dyes in solvents having different polarities exhibits either general solvent effects (increasing wavelength and/or bathochromic shift with increasing solvent polarity) and/or specific solvent effects (decreasing wavelength and/or hypsochromic shift with increasing solvent polarity). The specific solvent effects of cyanine dyes is illustrated due to hydrogen bond and/or molecular complex formation between the molecules of solvents and cyanine dyes molecules.

Besides, the solutions of cyanine dyes in aqueous universal buffer solutions having varies pH media gives either positive halochromism (increasing wavelength and/or bathochromic shift with changing pH of the buffer solution) and/or negative halochromism (decreasing wavelength and/or hypsochromic shift with changing the pH of the buffer solution). The negative halochromism of

cyanine dyes is explained due to protonation for the lone pair electrons which represents the source of the electronic charge transfer pathways inside the cyanine dye molecule via acidic H proton.

Furthermore, cyanine dyes have unusual optical properties, and high fluorescent quantum yield of their aggregates, strongly absorbing in the visible region, highly fluorescent in monomers and aggregates both in solution and organized media. The two types of aggregates that are known for cyanine dyes are H-aggregate recognised by their blue shifted broad absorption band and J-aggregate that exhibits a sharp red shifted absorbance with respect to the monomer absorption. The ease of formation of aggregates in conjunction with their potential applications in optical devices, photosensitises, and fluorescent probes for bio-membrane fluidity made cyanine dyes particularly interesting.

2.3. Photosensitization effect of cyanine dyes in silver halide emulsion (Mishra et al., 2000; Finar, 1990: 893-894):

Cyanine dyes (mainly refers to spectrum sensitisation added dyes) are used as an essential photography organic matter of new variety photosensitive material because of their unrivalled ability to impart light sensitivity to silver halide emulsions in a region of the spectrum to which the silver halide is normally not sensitive. Hence, by using cyanine dyes it is possible to make photographic emulsions sensitive to all parts of the visible spectrum, which are then termed as panchromatic. For instances, photographic plates of silver chloride emulsions are sensitive from 350 to 450 nm and those of silver bromide emulsions, from 350 to 530 nm. By using cyanine, the photographic plates of silver bromide emulsions sensitised from the region 350-530 nm to the green region 350-600 nm. Pinacyanol cyanine dye sensitised the emulsion to the red region 350-710 nm and kryptocyanine cyanine dye sensitised it to the infra-red radiation. Therefore, the synthesis and application research of cyanine dyes is very important for the domestic and international foreign film factory.

2.4. Photosensitization-structure correlation (Shindy et al., 2002; Shindy et al., 2006a; El-Aal et al., 1997):

Photosensitisation-structure correlation properties of cyanine dyes were usually determined by studying their electronic visible absorption spectra in 95 % ethanol solution. The dyes are thought to be better photosensitisation when they absorb light at longer wavelength (bathochromic and/or red shifted dyes) and consequently, photosensitisation of the dyes decrease in the dyes which absorb light at shorter wavelength (hypsochromic and/or blue shifted dyes).

The photosensitisation of the cyanine dyes is very markedly dependent on the structure and nature of the dyes. Generally, photosensitisation of the dyes increases (decreases) by increasing (decreasing) conjugation in the dye molecule. Also, the photosensitisation of the dyes increases (decreases) by decreasing (increasing) the electronegativity of the hetero atoms present in the heterocyclic system of the dye. Electron donating groups increase the photosensitisation of the dyes while electron accepting groups decrease the photosensitisation. Increasing number of methine groups give better photosensitisers dyes, and dyes which have two conjugated charge transfer pathways inside the dye molecule are better photosensitisers than those which have one conjugated charge transfer pathway. Also, higher planarity dyes are better photosensitisers than their contrast lower planarity dyes.

2.5. Colour spectrophotometric measurements of cyanine dyes (Finar, 1990: 869; Shindy et al., 2012):

Colour spectrophotometric measurements for the cyanine dyes can be made by measuring their electronic visible absorption spectra in 95 % ethanol solution. The dyes are thought to be darker in colour when they absorb light at longer wavelength (bathochromic shifted or red shifted dyes), and consequently the lightening of the dye colour increase when they absorb light at shorter wavelength (hypsoochromic shifted and/or blue shifted dyes). So, we may say that the colour of one dye is darker than the other one if the wavelength of the maximum absorption spectrum of the former is longer than that of the latter one. Inversely, we may say that the colour of one dye is lighter than that of the other one if the wavelength of the maximum absorption spectrum of the former is shorter than that of the latter one.

In addition, colour spectrophotometric measurements for the cyanine dyes can be investigated by measuring their electronic visible absorption spectra in pure solvents having different polarities. The dyes tend to give darker colours and longer wavelength bands (bathochromic shifted or red shifted bands) in the solvents which have higher polarity or dielectric constants. So, we can say that, this solvent is more polar than the other one when the wavelength of the maximum absorption spectra bands of the dye in the former solvent is longer than that of the latter one. Inversely, the dyes tend to give lighter colours and/or shorter wavelength bands (hypsochromic shifted or blue shifted bands) in the solvents which have lower polarity and/or dielectric constants. So, we can say that, this solvent is less polar than the other one when the wavelength of the maximum absorption spectra bands of the dye in the former solvent is shorter than that of the latter one. Therefore, cyanine dyes have extensive uses as indicator for solvent polarity. Deviation from this rule occurs when there are specific solvent interactions between the dye and the solvent like hydrogen bonding and/or molecular complex formation.

Besides, colour spectrophotometric measurements for the cyanine dyes can be examined by measuring their electronic visible absorption spectra in aqueous universal buffer solutions. The dyes tend to give darker colours and/or longer wavelength bands (bathochromic shifted or red shifted bands) in the buffer solutions having higher pH media or basic media. So, we can say that this buffer solution is more basic than the other one when the wavelength of the maximum absorption spectra bands of the dye in the former buffer is longer than that of the latter one. Inversely, the dyes tend to give lighter colours and/or shorter wavelength bands (hypsochromic shifted or blue shifted bands) in the buffer solutions having lower pH media or acidic media. So, we can say that this buffer solution is more acidic than the other one when the wavelength of the maximum absorption spectra bands of the dye in the former buffer is shorter than that of the latter one. Therefore cyanine dyes can be used as indicator for the pH of the buffer solutions or as indicators in acid-base titrations in analytical chemistry.

2.6. Fluorescence spectra of cyanine dyes (Iakowicz, 1983: 2-3, 5-6):

Fluorescence spectral data are generally presented as emission spectra. A fluorescence emission spectrum is a plot of the fluorescence intensity versus wavelength (in nanometers) or wave numbers (in cm^{-1}). Emission spectra vary widely and are dependent upon the chemical structure of the cyanine fluorophore and the solvent in which it is dissolved. Generally, the fluorescence emission spectrum appears to be a mirror image of the absorption spectrum.

The emission from cyanine fluorophore generally occurs at wavelengths which are longer than those of light absorption. The loss of energy between absorption and reemission of light is called Stokes' shift. Stokes' shift is a result of several dynamic processes. These processes include energy losses due to dissipation of vibrational energy, redistribution of electrons in the surrounding solvent molecules induced by the altered (generally increased) dipole moment of the excited cyanine fluorophore, reorientation of the solvent molecules around the excited state dipole, and specific interactions between the fluorophore and the solvent or solutes. Specific interactions include hydrogen bonding and formation of charge transfer complexes.

The Stokes' shift of many cyanine dyes are in between 10-40 nm. A large Stokes' shifts between the excitation spectrum wavelength and emission spectrum wavelength of a dye can lead to greater sensitivity and higher resolution at physiological concentrations.

2.7. IR and ^1H NMR spectra of cyanine dyes (Moreda, Forrester, 1997):

The IR and ^1H NMR spectra of cyanine dyes are often distinguished by the appearance of IR bands and ^1H NMR signals characteristic for: N-Me, N-MeCH₂, CH=N, -CH=CH-, -CH=CH-conjugated.

In many cases the ^1H NMR spectra of cyanine dyes gives broad, multiple and poor resolved peaks. This may be attributed to the following reasons:

- i) Cyanine dyes are complex organic compounds.
- ii) Cyanine dyes are electronic charge transfer compounds. So, the signals of the ^1H NMR spectra will be complicated with these electronic charge transfer leading to broad and multiple signals.
- iii) The molecular motion of the polymethine chain inside the dyes molecules (due to the mesomeric structures of the cyanine dyes) leads to poor resolved peaks.

2.8. General view in the visible spectra of cyanine dyes (Shindy et al., 2015; Shindy et al., 2015a; Shindy et al., 2015b; Shindy et al., 2016b; Winstead, Willams, 2011):

As a general view, the electronic visible absorption spectra of cyanine dyes reveals wavelength bands in the following approximately visible range values:

- i) 400-500 nm for the monomethine cyanine dyes (simple cyanine dyes).
- ii) 500-600 nm for the trimethine cyanine dyes (carbocyanine dyes).
- iii) 600-700 nm for the pentamethine cyanine dyes (dicarbocyanine dyes).
- iv) 700-980 nm for the heptamethine cyanine dyes (tricarbo-cyanine dyes).

The minimum and maximum wavelength values of these bands may go up and down approximately by 20-50 nm according to the types of the substituents and nature of the heterocyclic nucleus in the cyanine dyes structure.

2.9. Stability of cyanine dyes (Yao et al., 2015; Shindy, 2012; Shindy, 2015; Shindy et al., 2014; Kim, 2006):

When making fluorescent tags, higher stability cyanine dyes is required, but there are lack and/or poor stability problems for cyanine dyes on light, heat, and/or oxygen. The main factors of light oxidation and fade of dye are redox active substances such as singlet oxygen, oxygen compounds, and peroxides. Lack stability of cyanine dyes against the mentioned conditions have a large influence on the application of cyanine dyes in various aspects. For example, cyanine dyes have a wide uses and application in CD-R and DVD-R industry as disc media, and the standard characteristics of CD-R were established on cyanine-based optical recording disk, but these disks have lack chemical stability. So, they are unsuitable for archival CD and DVD use, as they can fade and become unreadable in few years. In addition, most cyanine dyes are valueless as fabric dyes because their fugitive and/or lack stability to light. For these reasons, finding out the effective methods and ways to increase the stability of cyanine dyes have very important meaning. The concentration of dyes, heterocyclic mother nucleus, oxygen in atmosphere, single and/or double cyanines and stabilizers will effect on the stability of the cyanine dye.

Double-cyanine dyes are better light stability than mono-cyanine dyes (single cyanine dyes). This is probably because in double-cyanine dyes there are two single cyanine dyes can be the base of each other, that is the introduction of the substituent with high space steric, hindering the attack of singlet oxygen or ultra-oxygen anion and improving the oxidation resistance and light stability of the dye. In addition, stabilized cyanine dyes are higher stability than the non-stabilized cyanine dyes. Therefore, recent cyanine disks contain stabilizers that slow down the deterioration significantly. As general, now days the stability of many cyanine dyes have been improved by introducing some metals like Ni (Nickel), Cu (Copper) and/or Co (Cobalt) to their structures. The cyanine dyes obtained in these cases called metal stabilized cyanine dyes.

3. Cyanine dyes in photodynamic therapy (PDT) (Shindy et al., 2012; Yao et al., 2015; Shindy et al., 2016c)

Photodynamic therapy is a new method for treatment of cancer. Due to its excellent properties, cyanine dyes are used in light power treatment. Photodynamic therapy has many advantages compared with surgery chemotherapy and radiotherapy treatment in treating cancer. First of all, it can have special light sensitive materials accumulate in tumor selectively, which will not damage the body normal tissues cells. Secondly, only local anesthetic is needed which saves a lot of medical bills. Finally, the side effect is small, which does not cause other damage in the body. Because of its light selectivity and specificity, photodynamic therapy only damage tumor tissue without harming the body normal cells.

Particularly, merocyanine dyes can distinguish some certain cells and selectively enter into cancer cells, then kill it as photosensitizers directly using for photodynamic therapy (PDT) or as radiation sensitizers for the treatment of solid tumors, where the affinity between cyanine dyes and tumor cells is much higher than that between cyanine dyes and normal cells. Merocyanine dyes are also used as antitumor drugs and combining PDT with drug therapy has become a tendency and will certainly promote the treatment of tumors.

4. Synthesis mechanisms of some cyanine dyes (Shindy, 1999; Finar, 1990; Hamer, 1964; Shindy, 2007; Koraiem et al., 1989; Shindy et al., 2006a; Shindy, Koraiem, 2008; Koraiem et al., 1990; Shindy, 2007a)

4.1. Mechanism of monomethine cyanine dyes:

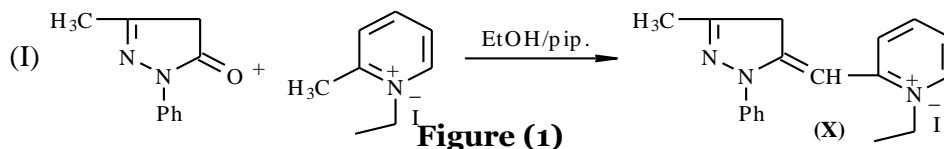


Figure (1)

The formation of the dye (X) is suggested to proceed as follows:

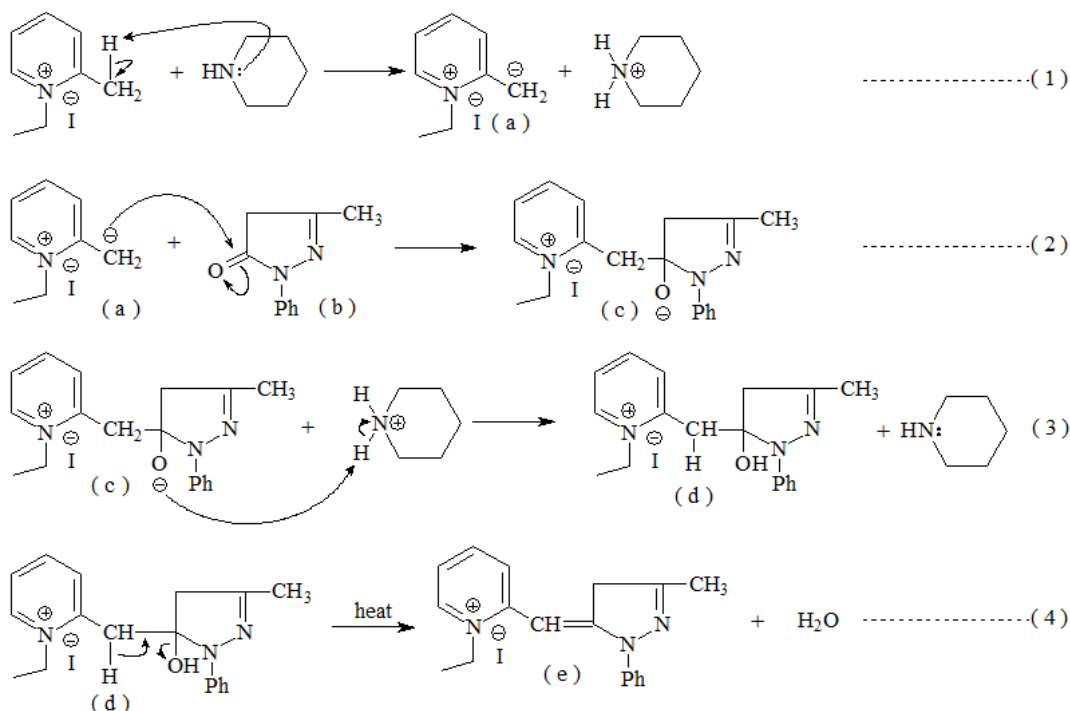


Figure (2)

The first step in this suggested mechanism is attacking of basic catalyst piperidine to the active methyl group of the quaternary salt to form the carbanion ion (a) (first step). The carbanion ion (a) attacks the positive centre of the compound (b) to obtain the intermediate compound (c) (second step). The intermediate compound (c) directly abstracts the proton H^+ from piperidine- H^+ to form compound (d) as intermediate compound (third step). The latter intermediate compound (d) under heat refluxing conditions gave the compound (E) (fourth step), **Figure (2)**.

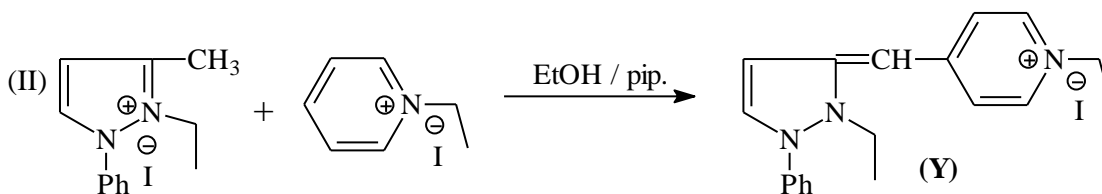
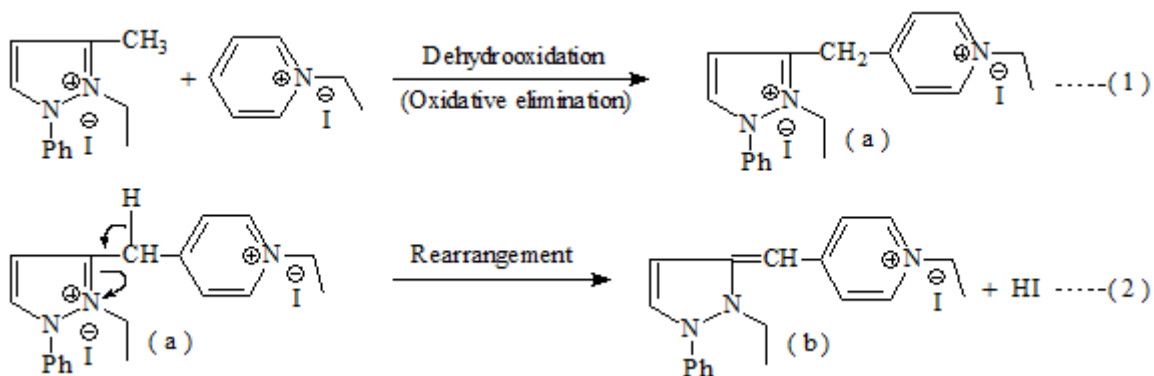


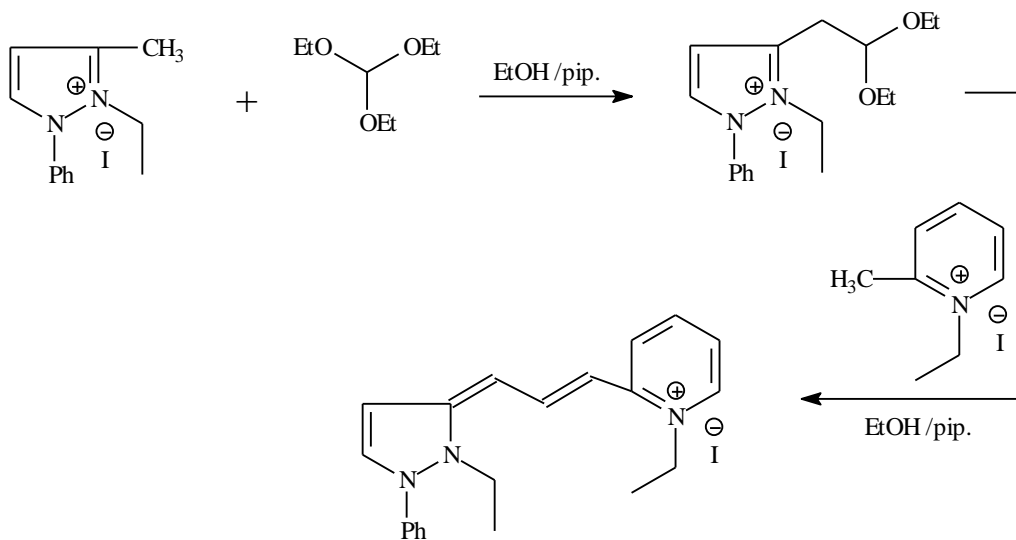
Figure (3)

The formation of the dye (Y) is suggested to proceed as follows:

**Figure (4)**

The first step in this mechanism involves dehydrooxidation (oxidative elimination) of the active CH₃ hydrogen atom of the pyrazolone iodide salt and the active 4-H of pyridinium iodide salt to form the intermediate compound (a). The second step involves rearrangement process of compound (a) by losing HI molecule to give the stable monomethine (b), **Figure (4)**.

4.2. Mechanism of trimethine cyanine dyes:

**Figure (5)**

The suggested mechanism for this reaction is as follows:

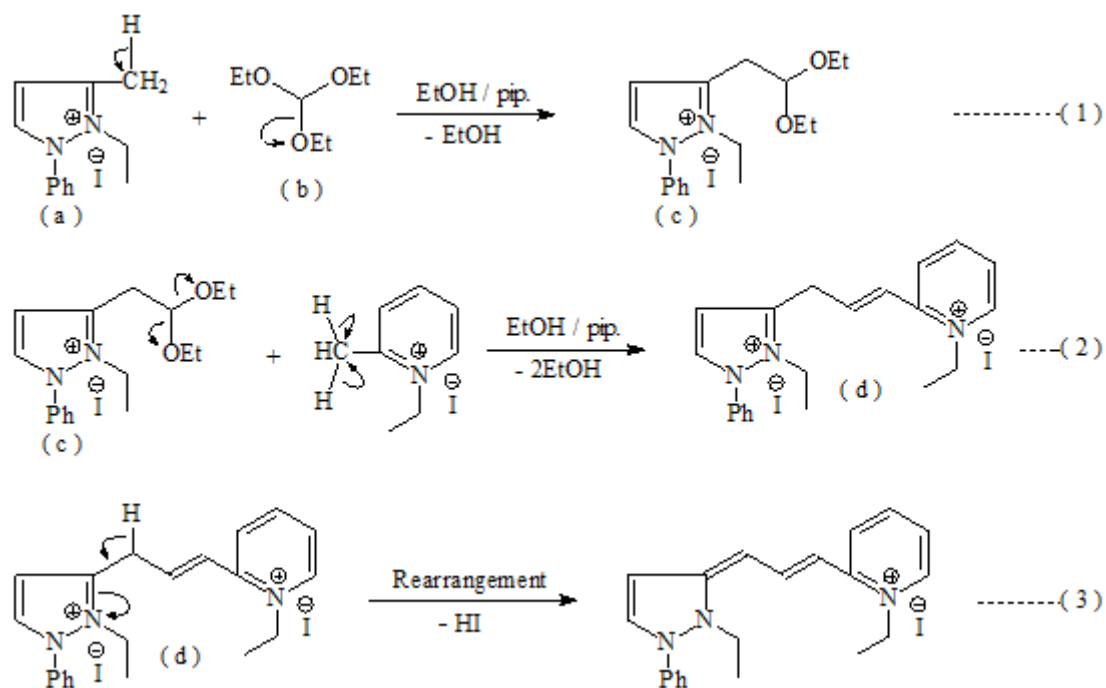


Figure (6)

The reaction proceeded via interaction of compound (a) with compound (b) losing of EtOH molecule to give compound (c), (first step). Compound (c) undergoes condensation reaction with α -picoline quaternary salt losing 2EtOH molecule to give the unstable compound (d), (second step). The unstable compound (d) undergoes rearrangement process losing HI molecule to give the trimethine compound (E), (third step), **Figure (6)**.

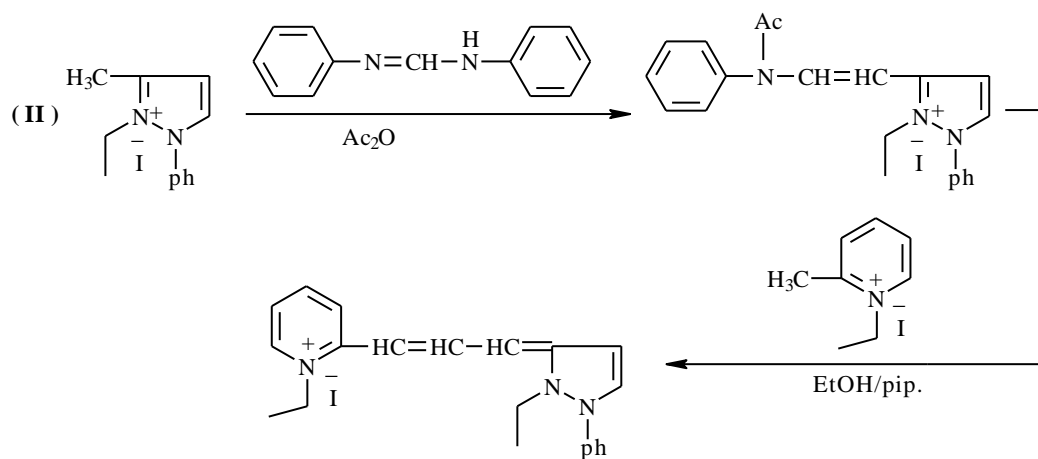


Figure (7)

The mechanism of this reaction is suggested to proceed as shown by the equations 1-7, **Figure (8)**:

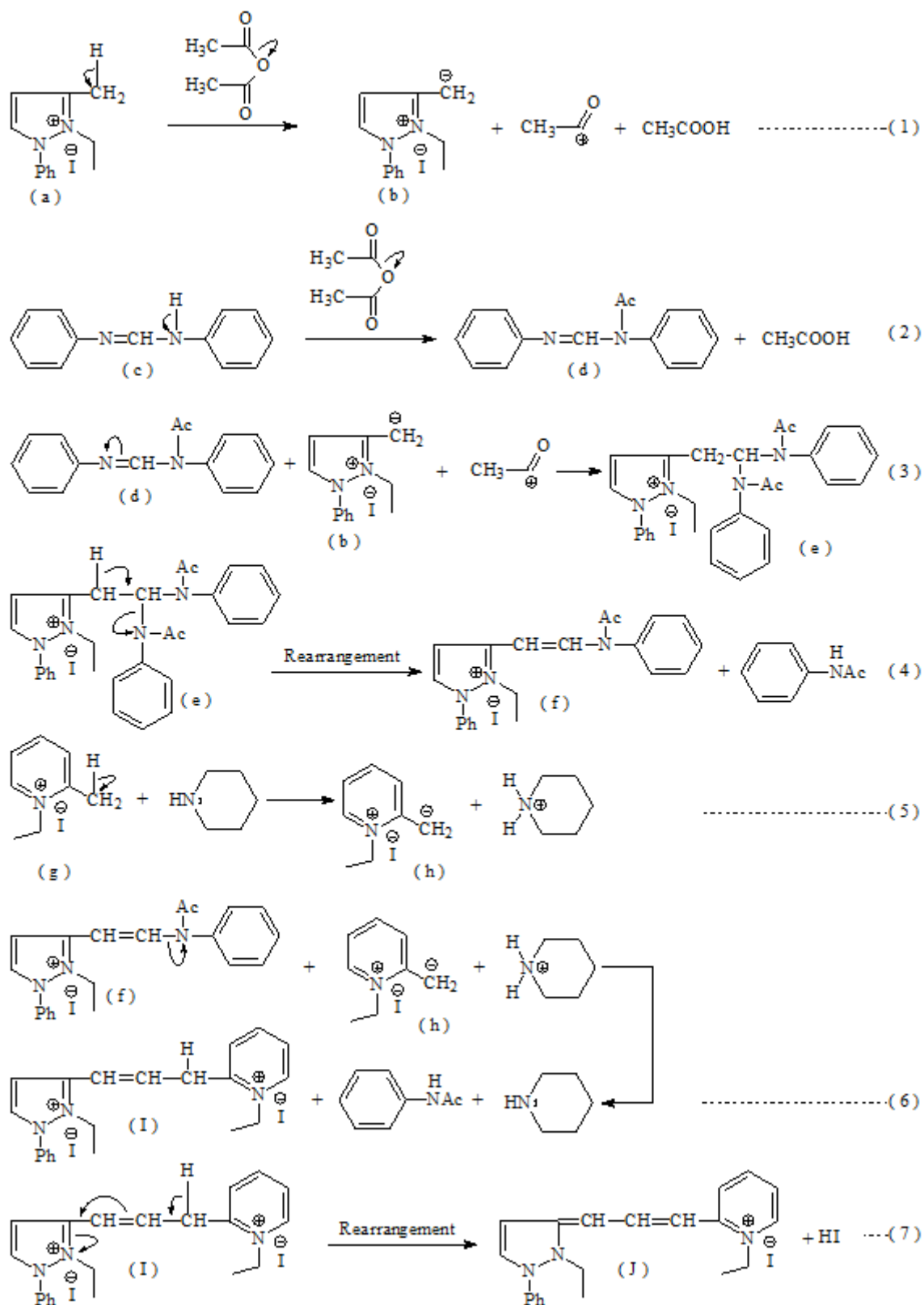


Figure (8)

5. Conclusion

The developments of cyanine dyes synthesis and their applications in photographic and non-photographic multidisciplinary areas are growing continuously and rapidly. Of course, this will make the present and the future of cyanine dyes chemistry effective, fruitful and very bright.

6. Current future developments

The current and the future research developments aim to provide novel synthetic methods for the preparation of different classes of highly antimicrobial active, Anti-tumour, p-H sensitive, highly photographic sensitizers, non toxic, high stability, light fastness, near IR (Infrared), fluorescent, anti corrosion, strong labelled DNA and extra conjugated cyanine dyes. Such as oxadiazine cyanine dyes, thiazole cyanine dyes, metal stabilized cyanine dyes, pentamethine cyanine dyes, heptamethine cyanine dyes, nonamethine cyanine dyes, undecamethine cyanine dyes and tridecamethine cyanine dyes.

7. Conflict of interest

There is no conflict of interest.

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References

- Arjona et al., 2016 – Arjona, A., Stolte, M., Wilerthner, F. (2016). Conformational switching of π -conjugated junctions from merocyanine to cyanine states by solvent polarity. *Angewandte Chemie*, 55 (7), 2470-2473.
- Boto et al., 2008 – Boto, R.E.F., Santos, P.F., Reis L.V., Almeida P. (2008). Synthesis and characterization of new mono- and dicarboxyalkyl selenocarbocyanines. *Dyes and Pigments*, 76, 165-172.
- Champagne et al., 2006 – Champagne, B., Guillaume, M., Zutterman, F. (2006). TDDFT Investigations of the optical properties of cyanine dyes. *Chemical physics letters*, 425 (1-3), 105-109.
- Deligeorgiev et al., 1998 – Deligeorgiev, T. G., Daphinka, D. A., Kim, Z., S. H. and Sabnis R.W. (1998). Preparation of monomethine cyanine dyes for nucleic acid detection. *Dyes and Pigments*, 37(3), 205-211.
- Dioxn et al., 2005 – Dioxn, A., Duncan, C. and Samha, H. (2005). Self assembly of cyanine dye on clay nanoparticles. *American journal of undergraduate research*, 3 (4), 29-33.
- El-Aal et al., 1997 – El-Aal, R. M., Shindy, H. A., and Koraiem, A. I. M. (1997). Synthesis and Electronic Absorption Spectra of Some New Penta- and Dimethine Cyanine Dyes. *Heteroatom Chemistry*, 8 (3), 259-266.
- Fasiulla et al., 2008 – Fasiulla, M.H., Khan, M., Harish M.N.K, Keshavayya, J., Reddy, K.R. (2008). Synthesis spectral, magnetic and antifungal studies on symmetrically substituted metal (II) octain inophthalocyanine pigments. *Dyes and Pigments*, 76, 557-563.
- Ferreira et al., 2015 – Ferreira, D.P., Conceicao, D.S., Prostota, Y., Santos, P.F., Ferreira, L.F.V. (2015). Fluorescence "rhodamine-like" hemicyanines derived from the 6-(N,N-diethylamino)-1,2,3,4-tetrahydroxanthylum system. *Dyes and Pigments*, 112, 73-80.
- Finar, 1990 – Finar, I. L. (1990). Organic Chemistry, Vol. 1, *The fundamental principles*, sixth edition, 893-894.
- Gadjev et al., 1999 – Gadjev, N. I., Deligeorgiev, T. G., Kim, S. H. (1999). Preparation of monomethine cyanine dyes as noncovalent labels for nucleic acids, *Dyes and Pigments*, 40, 181-186.
- Hamer, 1964 – Hamer, F.M. (1964). The cyanine dyes and related compounds, *New York, interscience publishers Inc.*, 198.
- lakowicz, 1983 – lakowicz, J. R. (1983). Principles of fluorescence spectroscopy, plenum press, *New York and London*, 2-3, 5-6.

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

Keisar et al., 2014 – Keisar, O. R., Finfer, E. K., Ferber, S., Finaro, R., Shabat, D. (2014). Synthesis and use of QCY7-derived modular probes for the detection and imaging of biologically relevant analytes. *Nature Protocols*, 9 (1), 27–36.

Kim, 2006 – Kim, S. (2006). *Functional dyes*, Elsevier B. V. 47–84.

Klochko et al., 2010 – Klochko, O. P., Fedyunyayeva, I. A., Khabuseva, S. U., Semenova, O. M., Terpetschnig, E. A., Patsenker, L. D. (2010). Benzodipyrrolium–based biscyanine dyes: synthesis, molecular structure and spectroscopic characterization. *Dyes and Pigments*, 85, 7–15.

Koraïem et al., 1989 – Koraïem, A. I. M., El-Maghraby, M. A, Khalafallah, A. K. and Shindy H. A. (1989). Studies on the Synthesis and Solvatochromic Behaviour of Mono- and Tri-Methine Cyanines: Methine Cyanine Dyes, Synthesis And Solvatochromism, *Dyes and Pigment*, 11, 47–63.

Koraïem et al., 1990 – Koraïem, A. I. M., Khalil, Z.H. and Abu El-Hamd, R. M. (1990). Synthesis and spectra of some asymmetric trimethine cyanine dyes. *Dyes and Pigments*, 13 (4), 289–299.

Kovalska et al., 2010 – Kovalska, V. B., Volkova, K. D., Manaev, A. V., Losytskyy M. Y., Okhrimenko, I. N., Traven, V. F., Yarmoluk, S. M. (2010). 2-Quinolone and Coumarin polymethines for the detection of proteins using fluorescence. *Dyes and Pigments*, 34, 159–164.

Lynch et al., 2013 – Lynch, D. E., Chowdhury, M. Z., Luu, N, Wane, E. S., Heptinstall, J., Cox, M. J. (2013). Water soluble bis (indolenine) squaraine salts for use as fluorescent protein – sensitive probes. *Dyes and Pigments*, 96, 116–124.

Mishra et al., 2000 – Mishra, A., Behera, R. K., Behera, P. K., Mishra, B. k. and Behera, G. B. (2000). Cyanines during the 1990s. *Chem. Review*, 100 (6), 1973–2011.

Mojzych, Henary, 2008 – Mojzych, M. and Henary, M. (2008). Synthesis of cyanine dyes. *Top Heterocycl Chem*, 14, 1–9.

Moreda, Forrester, 1997 – Moreda, W. and Forrester, A. R. (1997). Novel Heterocyclic dyes as DNA markers, part II, Structure and Biological activity. Department of chemistry, *University of Aberdeen, Meston Building, Meston Walk, Aberdeen AB9 2UE. UK*.

Moreira et al., 2015 – Moreira, B. G., You Y., Owczarzy R. (2015). Cy3 and Cy5 dyes attached to oligonucleotide terminus stabilize DNA duplexes: Predictive thermodynamic model. *Biophysical Chemistry*, 198, 36–44.

Owens et al., 2014 – Owens, E. A., Tawney, J.G. and Henary, M.M. (2014). 2-[(E)-2-[(3E)-2-Chloro-3-[(2E)-2-[1,1-dimethyl-3-(3-phenylpropyl)-1,3-dihydro-2H-benzo[e]indol-2-ylidene]-ethylidene]cyclohex-1-en-1-yl]ethyl]-1,1-dimethyl-3-(3-phenylpropyl)-1H-benzo[e]indolium Iodide. *Molbank*, 8, 1–8.

Park et al., 2013 – Park, J., Kim, D., Lee, K., Kim, Y. (2013). Reactive cyanine fluorescence dyes indicating pH perturbation of biomolecules. *Bull. Korean Chem. Soc.*, 34, 1, 1–4.

Parvathy et al., 2015 – Parvathy, S., Liji, P.T., Kalaiyarasi A. and Venkatraman, R.R. (2015). Synthesis and characterization of heterocyclic cyanine dyes. *Der Chemica Sinica*, 6(1), 42–45.

Rongqi, 2006 – Rongqi C. (2006). The development and application of green dye, *Printing and dyeing*, (6): 45.

Shindy, 1999 – Shindy, H. A. (1999). Synthesis and Visible Spectral Behaviour of Some New Photosensitizers: Monomethine, Dimethine, Trimethine, Styryl and Mixed Cyanine, *Dyes J. Chem. Research (S)*, 700–701., *J. Chm. Research, (M)*, 3001–3017.

Shindy, 2007 – Shindy, H.A. (2007). Synthesis, Characterization and Visible Spectral Behaviour of some Novel Methine, Styryl, and Aza-styryl Cyanine Dyes. *Dyes and Pigments*, 75 (2). 344–350.

Shindy, 2007a – Shindy, H. A. (2007). Synthesis, Absorption Characteristics and Solvatochromism of some Novel Heterocyclic Cyanine Dyes. *Coloration Technology*, 123 (5), 298–305.

Shindy, 2012 – Shindy, H.A. (2012). Basics, Mechanisms and Properties in the Chemistry of Cyanine Dyes: A Review Paper. *Mini-Reviews in Organic Chemistry*, 9 (4), 352–360.

Shindy, 2015 – Shindy, H. A. (2015). Synthesis of Different Classes of Benz (Naphth) / Five Membered Heterocyclic Cyanine Dyes: A Review. *Revue Roumaine de Chimie*, 60 (1), 5–13.

[Shindy et al., 2000](#) – Shindy, H. A., El-Aal, R. M., and Koraiem, A.I.M. (2000). Synthesis and Spectral Behaviour of Some New Uninuclear Pyrimidine 2[2(4)]-Mono (Tri)-Methine Cyanine Dyes. *Journal of the Chinese Chemical Society*, 47, 519-525.

[Shindy et al., 2001](#) – Shindy, H. A., Koraiem, A. I. M., Khalafallah A.K. and Soleiman, H.A. (2001). New Cyanine Dyes from 4,9-Dioxopiperidino[2,3-g]-1,2,3,4,6,7,8,9-Octahydroquinolinoquinone. *Indian Journal of Chemistry*, 40B, 426-429.

[Shindy et al., 2002](#) – Shindy, H. A. and Koraiem, A. I. M. (2002). Synthesis and Absorption-Structure Relationship of Some New Photosensitizers Cyanine Dyes. *Proc. Ind. Acad. Sci. (Chem. Sci.)*, 114 (2), 125-136.

[Shindy et al., 2002](#) – Shindy, H. A., El-Maghraby, M. A. and Eissa, F. M. (2002). Novel Cyanine Dyes: Synthesis, Characterization and Photosensitization-Structure Correlation. *Journal of the Chinese Chemical Society*, 49, 1061-1068.

[Shindy et al., 2002a](#) – Shindy, H. A., El-Maghraby, M. A. and Eissa, F. M. (2002). Novel quinone cyanine dyes: Synthesis and Spectral studies. *Dyes and Pigments*, 52, 79-87.

[Shindy et al., 2006](#) – Shindy, H. A., El-Maghraby, M. A. and Eissa, F. M. (2006). New Photosensitizers Cyanine Dyes: Synthesis and Properties. *Indian Journal of Chemistry*, 45B, 1197-1203.

[Shindy et al., 2006a](#) – Shindy, H. A., El-Maghraby, M. A. and Eissa, F. M. (2006). Synthesis, Photosensitization and Antimicrobial Activity of Certain Oxadiazine Cyanine Dyes. *Dyes and Pigments*, 70, 110-116.

[Shindy et al., 2006a](#) – Shindy, H.A., El-Maghraby, M. A and Eissa, F. M. (2006). Cyanine Dyes of New Heterocyclic Ring System: Synthesis and Structure-Spectra Studies. *Dyes and Pigments*, 68 (1), 11-18.

[Shindy et al., 2012](#) – Shindy, H. A., El-Maghraby, M. A. and Eissa, F. M. (2012). Synthesis and Colour Spectrophotometric Measurements of some Novel Merocyanine Dyes, *Dyes and Pigments*, 92 (3), 929-935.

[Shindy et al., 2014](#) – Shindy, H. A., El-Maghraby, M. A. and Eissa, F. M. (2014). Effects of Chemical structure, solvent and solution pH on the visible spectra of some new methine cyanine dyes. *European Journal of Chemistry*, 5 (3), 451-456.

[Shindy et al., 2015](#) – Shindy, H. A., Goma, M. M. and Harb, N. A. (2015). Synthesis, Spectral Behavior and Biological Activity of some Novel 1,3,4-Oxadiazine Cyanine Dyes. *European Journal of Chemistry*, 6 (2), 151-156.

[Shindy et al., 2015a](#) – Shindy, H. A., Khalafalla, A. K., Goma, M. M. and Eed A., H. (2015). Synthesis and photosensitization evaluation of some novel polyheterocyclic cyanine dyes. *European Reviews of Chemical Research*, 5 (3), 180-188.

[Shindy et al., 2015b](#) – Shindy, H. A., Goma, M. M. and Harb, N. A. (2015). Novel carbocyanine and dicarbocyanine dyes: synthesis, spectral characterization and biological activity. *Revue Roumaine de Chimie*, 60 (10), 965-974.

[Shindy et al., 2016](#) – Shindy, H. A., Khalafalla, A. K., Goma, M. M. and Eed A., H. (2016). Polyheterocyclic compound in the synthesis and spectral studies of some novel methine cyanine dyes. *Revue Roumaine de Chimie*, 61 (3), 139-145.

[Shindy et al., 2016a](#) – Shindy, H. A., Khalafalla, A. K., Goma, M. M. and Eed A., H. (2016). Novel hemicyanine and aza-hemicyanine dyes: synthesis, spectral investigation and antimicrobial evaluation. *European Journal of Molecular Biotechnology*, 13 (3), 94-103.

[Shindy et al., 2016b](#) – Shindy, H. A., Goma, M. M. and Harb, N. A. (2016). Novel carbocyanine and bis carbocyanine dyes: synthesis, visible spectra studies, solvatochromism and Halochromism. *Chemistry International*, 2 (4), 222-231.

[Shindy et al., 2016c](#) – Shindy, H. A., Khalafalla, A. K., Goma, M. M. and Eed A., H. (2016). Synthesis, photosensitization and antimicrobial activity evaluation of some novel Merocyanine dyes, *Chemistry International*, 2 (3), 114-120.

[Shindy, Koraiem, 2008](#) – Shindy, H. A. and Koraiem, A. I. M. (2008). Synthesis and Colour Spectroscopic Investigation of Some Hemicyanine Dyes. *Coloration Technology*, 124 (5), 290-294.

[Soriano et al., 2016](#) – Soriano, E., Holder, C., Levitz, A. and Henary, M. (2016). Benz [c,d] indolium-containing monomethine cyanine dyes: synthesis and photophysical properties. *Molecules*, 21 (1), 23-37.

[Upadhyayula et al., 2015](#) – *Upadhyayula S., Nunes, V., Espinosa, E. M., Larsen, J. M., Bao, D., Shi D., Mac, J. T., Anvari, B., and Vullev, V.* (2015). Photoinduced dynamics of a cyanine dye: parallel pathways of non-radiative deactivation involving multiple excited-state twisted transitions. *Chemical Science (Chem. Sci.)*, 6, 2237-2251.

[Winstead, Willams, 2011](#) – *Winstead, A. and Willams, R.* (2011). Application of microwave assisted organic synthesis to the development of near-IR cyanine dye probes, *Enviromentals and Biosensors*, Prof. V. Somerset (Ed.), 237-254.

[Yakubovskiy et al., 2010](#) – *Yakubovskiy, V. P., Shandura, M. P., Kovtum, Y. P.* (2010). Boradipyrromethene cyanines derived from conformationally restricted nuclei. *Dyes and Pigments*, 87, 17–21.

[Yao et al., 2015](#) – *Yao, X., Fang, R., Pang, H. and Liu, G.* (2015). Research on synthesis and properties of water-soluble symmetrical squarylium double-cyanine dyes. *The open materials science journal*, 9, 113-118.

[Yashchuk et al., 2007](#) – *Yashchuk, V. M., Gusak, V. V., Dmytruk, I. M., Prokopets, V. M., Kudrya, V.Yu., Losytsky, M.Y., Tokar, V. P., Gumenyuk, Ya. O., Yarmoluk, S. M., Kovalska, V. B., Kryvorotenko D. V.* (2007). *Molecular Crystals and Liquid Crystals*, V. 467, iss. 1, p. 325–338.

[Yi et al., 2014](#) – *Yi, X., Wang, F., Qin, W., Yang, X., Tuan, J.* (2014). Near-Infrared fluorescent probes in Cancer imaging and therapy: an emerging field. *International Journal of Nanomedicine*, 9, 1347–1365.

[Zanotti et al., 2011](#) – *Zanotti, K. J, Silva, G. L., Creeger, Y., Robertson, K. L., Waggoner, A. S., Berget, P. B. and Armitage, B. A.* (2011). Blue fluorescent dye-protein complexes based on fluorogenic cyanine dyes and single chain antibody fragments. *Organic Biomolecular Chemistry*, 9, 1012-1020.

[Zhao et al., 2013](#) – *Zhao, J., Lv, Y., Ren, H., Sun, W., Liu, Q., Fu, Y., Wang, L.* (2013). Synthesis, spectral properties of cyanine dyes β -cyclodextrin and their application as the supramolecular host with spectroscopic probe. *Dyes and Pigments*, 96, 180–188.

[Zielinska et al., 2010](#) – *Zielinska, J., Saczko, J., Kulbacka, M., Majkowski, K., Wilk, A.* (2010). New approach to hydrophobic cyanine-type photosensitizer delivery using polymeric oil-cored nanocarriers: Hemolytic activity, in vitro cytotoxicity and localization in cancer cells. *Journal of Pharmaceutical Sciences*, 39, 322-335.