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New role for photoexcited organic dye, Na_2 eosin Y *via* the direct hydrogen atom transfer (HAT) process in photochemical visible-light-induced synthesis of spiroacenaphthylenes and 1*H*-pyrazolo[1,2-*b*] phthalazine-5,10-diones under air atmosphere

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ABSTRACT

A green multi-component tandem strategy for metal-free synthesizing spiroacenaphthylenes and 1*H*-pyrazolo [1,2-*b*]phthalazine-5,10-diones *by* Knoevenagel-Michael cyclocondensation is reported via organic dye Na_2 eosin Y-derived photoexcited states functions as a direct hydrogen atom transfer (HAT) catalyst via visible light-mediated in aqueous ethyl lactate at ambient temperature under air atmosphere. This study paves the new role for further use of a metal-free organic dye with commercial availability and inexpensiveness, Na_2 eosin Y in photochemical synthesis with use of the lowest amount of catalyst, energy-effectiveness, excellent yields, operational simplicity, time-saving aspects of the reaction and high atom economy, thus meeting some features of sustainable and green chemistry. Notably, this cyclization is also runnable on gram scale, which highlights the potentiality of using this reaction in industrial uses.

1. Introduction

Eosin Y is a metal-free organic dye with easy availability that has gained a wide application in recent years, having economic and ecological superiority for substituting transition-metal-based photocatalysts [1].

In eosin Y-catalyzed photoredox reactions, successfully oxidized/reduced target substrates by its incited mode is normally dependent up on if the potential oxidability or reducibility of the substrates lies in the scope of that of eosin Y (Scheme 1) [1a].

The range of eosin Y-catalyzed photochemical reactions has been restricted by the mentioned electrochemical requisites. Being highly different from other organic dyes, eosin Y has unique xanthene and phenol moieties, and also prominent acid–base features, which may result in four differing constructs. There are ample documentations that the anionic types of eosin Y exhibit photocatalytic property in most of previous reports on photoreactions while the neutral types assumedly have typical inactivity and are ignorable in potentially applied synthesis processes [2]. In recent years, a team of Wang [3] and Wu [4] has been encouraged by the structural attributes of eosin Y, making an innovation in the discovery of novel activating states of photoexcited eosin Y. The group discovered that neutral eosin Y-originated incited modes could function as photoacids and direct hydrogen atom transfer (HAT) catalysts for activating glycals and native C–H bonds in respective order (Scheme 2) [1a].

Hydrogen atom transfer (HAT) is a basic stage possibly responsible for multiple processes chemically, environmentally, and biologically. In particular, benzophenone- and quinone-mediated direct HAT catalysis has been launched as an instrument that enables activating C–H bond under light radiation in recent years [5,6]. Recently, Direct HAT catalysis mediated by benzophenone and quinone has been discovered as an effective technique for activating C–H bond by irradiation [5,6]. Due to eosin Y and quinones [5] being similar, Wu and colleagues hypothesized that when exposed to visible spectrum, eosin Y under excitation may operate as a direct HAT catalyst, activating a C–H bond and generating radical species for additional functions [4]. Due to its captodative and steric properties, the radical species derived from eosin Y is unlikely to undergo the kinds of side reactions seen in HAT catalysis with diaryl ketones, allowing for a reverse transfer of hydrogen atom. Based on this mechanics, Wu and colleagues discovered that when exposed to visible spectrum, eosin Y in neutral form can effectively trigger numerous C(sp^3)-H and C(sp^2)-H bonds to start generating the corresponding radicals of carbon, allowing radical introduction to multiple alkenes with electron deficiency. This approach has a wide substrate purview and a

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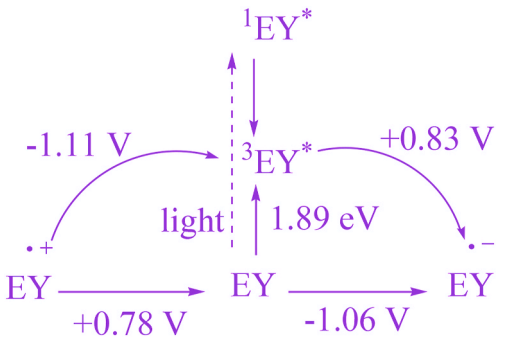


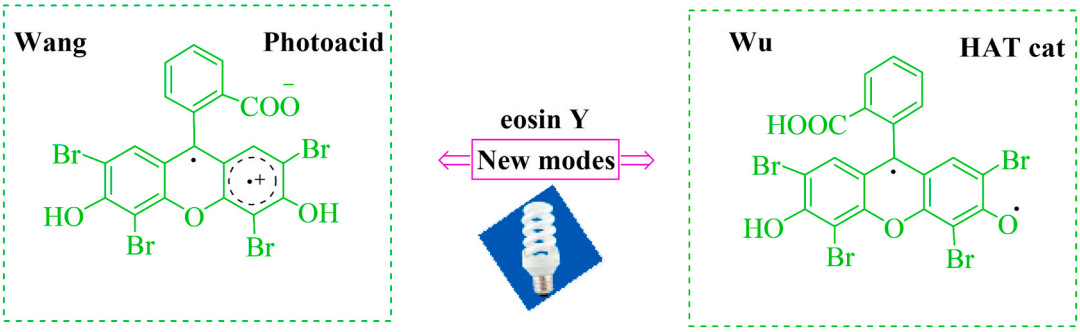
Scheme 1. Oxidative and reductive quenching cycles of Eosin Y with their corresponding potentialities [1a].

high group tolerance. The required C–H alkylation compounds were produced in high yields and with high site selection. With good site selection, a number of C(sp^3)-H and C(sp^2)-H bonds of ethers, thioethers, alcohols, aldehydes, and cyclohexanes were radical alkylated (e.g., 10 c). This method may also be used toward a variety of tri- and tetrasubstituted olefins with different features. This HAT catalysis approach, in particular, overcomes the substrate constraints of classic SET-based redox reactions [1a].

Also, visible light irradiation has been a reliable approach for green chemists because of its plentiful reserves of the energy, low cost and its renewable source of energy in the eco-friendly synthesis of organic compounds [7,8]. In general, light emitting diodes and compact fluorescent lights are employed as the sources of visible light for various transformations.

Spiropyrans, pyrazolophthalazines and their analogues have attracted attention to them because of their biological activities such as anticancer [9], fungicidal [10], anti HIV [11], antimalarial [12], antitubercular [13], in addition these spirocycles are MDM2 inhibitor [14] and progesterone receptor modulator [15], anti-inflammatory [16], anti microbiological [17], vasorelaxant [18], cardiotonic [19] and anticonvulsant [20]. Some of them are shown with biological characteristics in Fig. 1.

Numerous approaches for synthesizing spiroacenaphthylenes and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones using MCRs have been reported opposite different catalysts such as Et_3N [21], [BDDMA]Cl [22], DABCO [23], DBU [24], Fe_2O_3 [25], $NiFe_2O_4$@SiO_2@Melamine [26], Isinglass [27], SBA-Pr-SO_3H [28], $InCl_3$ [29], $NiCl_2{\cdot}6H_2O$ [30], [Bmim]OH [31], Ultrasound-assisted [32], *P*-TSA [33], STA [34], CuI



Scheme 2. Exploration of photoexcited eosin Y as a photoacid or HAT catalyst [1a].

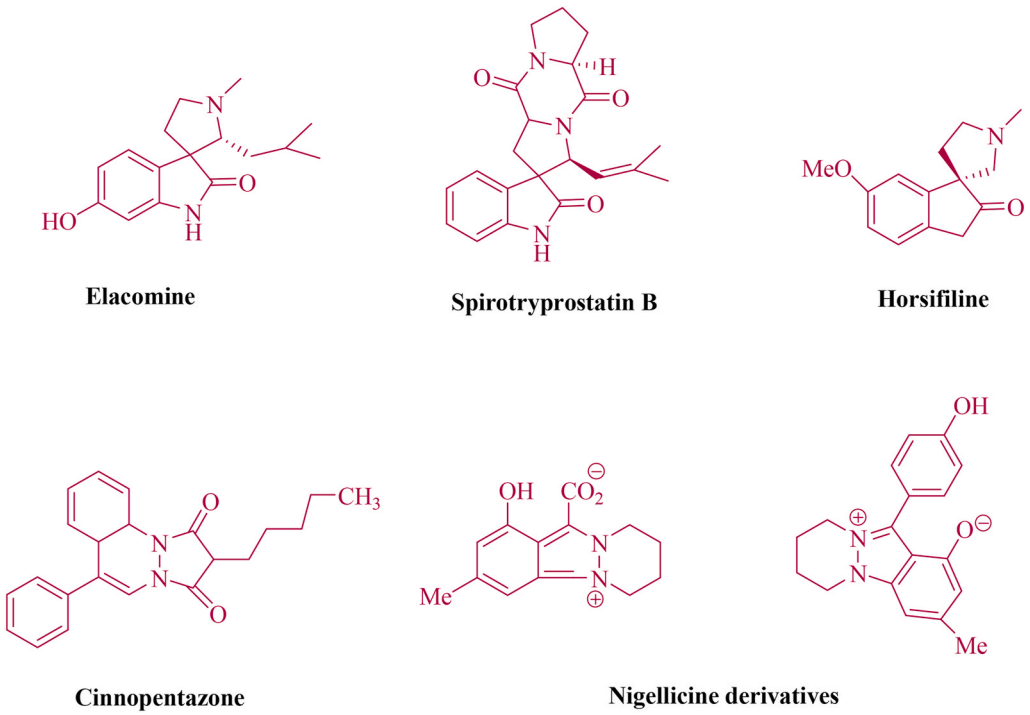
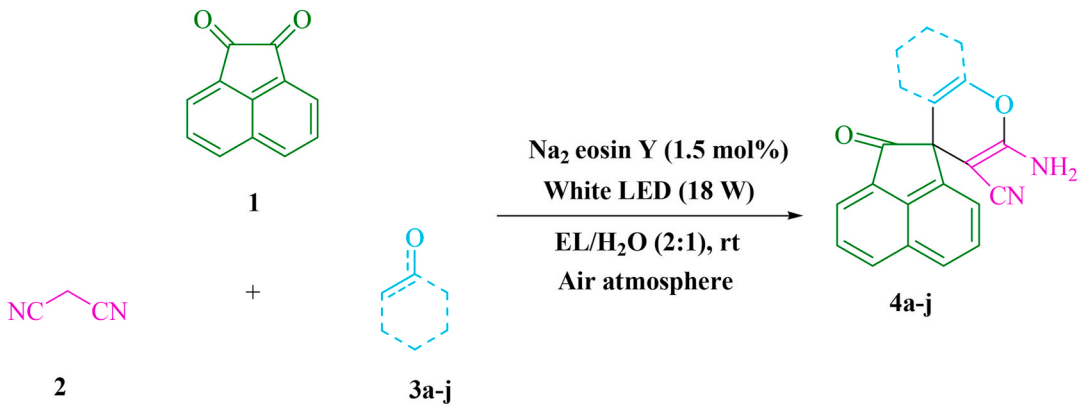
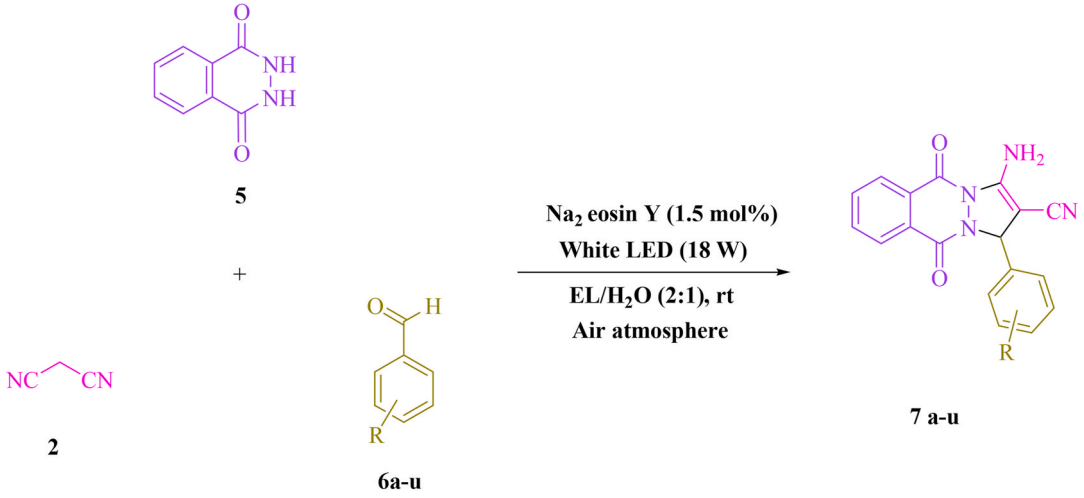


Fig. 1. Some alkaloids containing biologically active compounds and heterocyclic spirooxindoles unit with two ring junction nitrogen atoms.



Scheme 3. Synthesis of spiroacenaphthylenes.



Scheme 4. Synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones.

nanoparticles [35], PTSA/[Bmim]Br [36], TBBAD [37], $Cu(OAc)_2.H_2O$ [38], K_2CO_3 [39], *β*-Cyclodextrin [40], $[Bu_3NH][HSO_4]$ [41], CuO nanoparticles [42], NZF@HAP-Cs [43], theophylline [44], carboxymethyl cellulose [45], STA-Amine-Si-Magnetite [46] and Nano-ZnO [47]. These procedures resulted in numerous cases. Though, some of synthetic policies contain also restrictions regarding the metal catalyst, harsh reaction circumstances, expensive reagents, monotonous workup process, unacceptable yield, long reaction time, environmental hazard, and using the homogeneous catalyst that are problematically detached from the mixture of reaction.

Given the above considerations and our interest in developing spiroacenaphthylenes and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones production, the study of photocatalyst under green circumstances for the proper synthesis of these heterocyclic compounds has been an important goal. This study paves the new role for further use of a metal-free organic dye with commercial availability and inexpensiveness, Na_2 eosin Y in above photochemical synthesis. Evidence indicates that Na_2 eosin Y-derived photoexcited states functions as a direct hydrogen atom transfer (HAT) catalyst to synthesize spiroacenaphthylenes and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones photochemically via Knoevenagel-Michael cyclocondensation via visible light-mediated in aqueous ethyl lactate at ambient temperature under air atmosphere. This reaction is a fruitful one-pot approach under highly effective, mild and facile reaction conditions.

2. Experimental

2.1. General

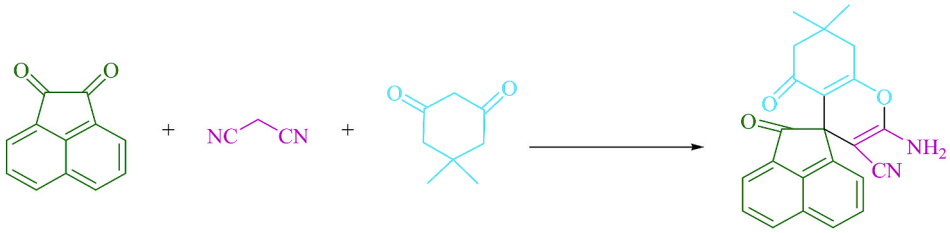
Using a 9100 electro-thermal device, the melting points of all compounds were found. In addition, the nuclear magnetic resonance recording, the spectrum (1HNMR and 13CNMR) was performed on a Bruker (DRX-400), Bruker (DRX-300) and Bruker (DRX-100) instruments using DMSO-d_6 as solvent. Mass spectra were recorded using an Agilent Technology (HP) spectrometer operating at an ionization potential of 70 eV. We bought the entire reagents from the chemical companies called Fluka, Merck, and Acros and used without additional treatment.

2.1.1. Overall process of preparing (4a-j)

To a mixture of malononitrile (**2**, 1.0 mmol), acenaphthequinone (**1**, 1.0 mmol) and various reagents including *α*-methylencarbonyl compounds/enols (**3a-j**, 1.0 mmol) in a EL[1]/H_2O (2:1) (3 mL), was added Na_2 eosin Y (1.5 mol%), under white light emitting diode (LED) (18 W) irradiation (Scheme 3). The mixture was stirred for 4 h at ambient temperature. The reaction progress was monitored by TLC utilizing *n*-hexane/EtOAc (3:1) as an eluent. After completing the reaction, the achieved solid was filtered, rinsed with water and the crude solid was recrystallized from ethanol to provide the pure material without

[1] Ethyl lactate.

Table 1
Optimization table of photocatalyst for the synthesis of **4a**.



Entry	Photocatalyst	Solvent (3 mL)	Time (h)	Isolated Yields (%)
1		EL/H_2O (2:1)	5	46
2	Na_2 eosin Y (0.5 mol%)	EL/H_2O (2:1)	4	77
3	Na_2 eosin Y (1.0 mol%)	EL/H_2O (2:1)	4	84
4	Na2 eosin Y (1.5 mol%)	EL/H2O (2:1)	4	93
5	Na_2 eosin Y (2 mol%)	EL/H_2O (2:1)	4	93
6	Riboflavin (1.5 mol%)	EL/H_2O (2:1)	4	64
7	Fluorescein (1.5 mol%)	EL/H_2O (2:1)	4	69
8	Phenanthrenequinone (1.5 mol%)	EL/H_2O (2:1)	4	56
9	9*H*-Xanthen-9-one (1.5 mol%)	EL/H_2O (2:1)	4	58
10	Rose bengal (1.5 mol%)	EL/H_2O (2:1)	4	67
11	Xanthene (1.5 mol%)	EL/H_2O (2:1)	4	49
12	Erythrosin B (1.5 mol%)	EL/H_2O (2:1)	4	48
13	Acenaphthenequinone (1.5 mol%)	EL/H_2O (2:1)	4	52
14	Alizarin (1.5 mol%)	EL/H_2O (2:1)	4	59
15	Rhodamine B (1.5 mol%)	EL/H_2O (2:1)	4	72

[a]Reaction condition: acenaphthequinone (1 mmol), malononitrile (1 mmol) and dimedone (1 mmol) in EL/H_2O (2:1) (3 mL), white LED (18 W), and various photocatalysts at rt.
[b] Isolated yield.

requiring more purification.

2.1.2. Overall process of preparing (7a-u)

To a mixture of phthalhydrazide (**5**, 1.0 mmol), malononitrile (**2**, 1.0 mmol) and aromatic aldehydes (**6a-u**, 1.0 mmol) in a EL/H_2O (2:1) (3 mL), was added Na_2 eosin Y (1.5 mol%), under white light emitting diode (LED) (18 W) irradiation (Scheme 4). The mixture was stirred for 3 h at ambient temperature. The reaction progress was monitored by TLC utilizing *n*-hexane/EtOAc (3:1) as an eluent. After completing the reaction, the achieved solid was filtered, rinsed with water and the crude solid was recrystallized from ethanol to provide the pure material without requiring more purification.

The products were classified after the comparison of spectroscopic information (1HNMR, 13CNMR, mass). Support for this manuscript can be found in the following:

2.1.3. 2-Amino-7,7-dimethyl-2,5-dioxo-5,6,7,8-tetrahydro-2H-spiro [acenaphthylene-1,4-chromene]-3-carbonitrile (4a)

Yield: 93%; M.p. 262–264 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 1.02 (3H, s, CH_3), 1.04 (3H, s, CH_3), 2.04–2.13 (1H, m, CH_2), 2.50–2.51 (1H, m, CH_2), 2.63 (2H, s, CH_2), 7.32 (2H, s, NH_2), 7.37–7.85 (6H, m, ArH).

2.1.4. 2-Amino-2,5-dioxo-2H,5H-spiro[acenaphthylene-1,4-pyrano[3,2-c] chromene]-3-carbonitrile (4f)

Yield: 89%; M.p. >300 °C; ^{1}HNMR (300 MHz, DMSO-d_6): 7.41 (2H, s, NH_2), 7.68–8.37 (10H, m, ArH).

2.1.5. 3-Amino-1-(phenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b] phthalazine-2-carbonitrile (7a)

Yield: 96%; M.p. 272–274 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.14 (1H, s, $H_{benzylic}$), 7.33–7.48 (5H, m, H_{Ar}), 7.97–8.29 (6H, m, NH_2 and H_{Ar}).

2.1.6. 3-Amino-1-(2-nitrophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo [1,2-b]phthalazine-2-carbonitrile (7b)

Yield: 91%; M.p. 263–265 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.62 (1H, s, CHAr), 7.61 (1H, t, J = 9.6 Hz, ArH), 7.73 (1H, t, J = 9.6 Hz, ArH), 7.85–7.91 (2H, m, ArH), 7.97–8.30 (6H, m, NH_2 and ArH).

2.1.7. 3-Amino-1-(4-methylphenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo [1,2-b]phthalazine-2-carbonitrile (7c)

Yield: 94%; M.p. 254–256 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 2.30 (3H, s, CH_3), 6.10 (1H, s, CHAr), 7.18 (2H, d, J = 8.0 Hz, ArH), 7.34 (2H, d, J = 8.0 Hz, ArH), 7.97–8.28 (6H, m, NH_2 and ArH).

2.1.8. 3-Amino-1-(4-fluorophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo [1,2-b]phthalazine-2-carbonitrile (7e)

Yield: 97%; M.p. 265–267 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.17 (1H, s, CHAr), 7.20 (2H, t, J = 8.8 Hz, ArH), 7.53–7.57 (2H, m, ArH), 7.96–8.26 (6H, m, NH_2 and ArH).

2.1.9. 3-Amino-1-(3-nitrophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo [1,2-b]phthalazine-2-carbonitrile (7g)

Yield: 96%; M.p. 268–270 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.31 (1H, s, CHAr), 6.94–7.05 (4H, m, ArH), 7.83–8.30 (6H, m, NH_2 and ArH).

2.1.10. 3-Amino-1-(2-chlorophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (7h)

Yield: 86%; M.p. 255–257 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.47 (1H, s, $H_{benzylic}$), 7.39–7.65 (4H, m, H_{Ar}), 7.91–8.31 (6H, m, NH_2 and H_{Ar}).

2.1.11. 3-Amino-1-(4-nitrophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo [1,2-b]phthalazine-2-carbonitrile (7 m)

Yield: 94%; M.p. 226–228 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.08 (1H, s, CHAr), 7.13–7.27 (4H, m, ArH), 7.97–8.29 (6H, m, NH_2 and ArH).

2.1.12. 3-Amino-1-(3,4,5-trimethoxyphenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (7n)

Yield: 85%; M.p. 251–253 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 3.66 (3H, s, OCH_3), 3.76 (6H, s, 2 × OCH_3), 6.07 (1H, s, $H_{benzylic}$), 6.78 (2H, s, H_{Ar}), 7.89–8.29 (6H, m, NH_2 and H_{Ar}).

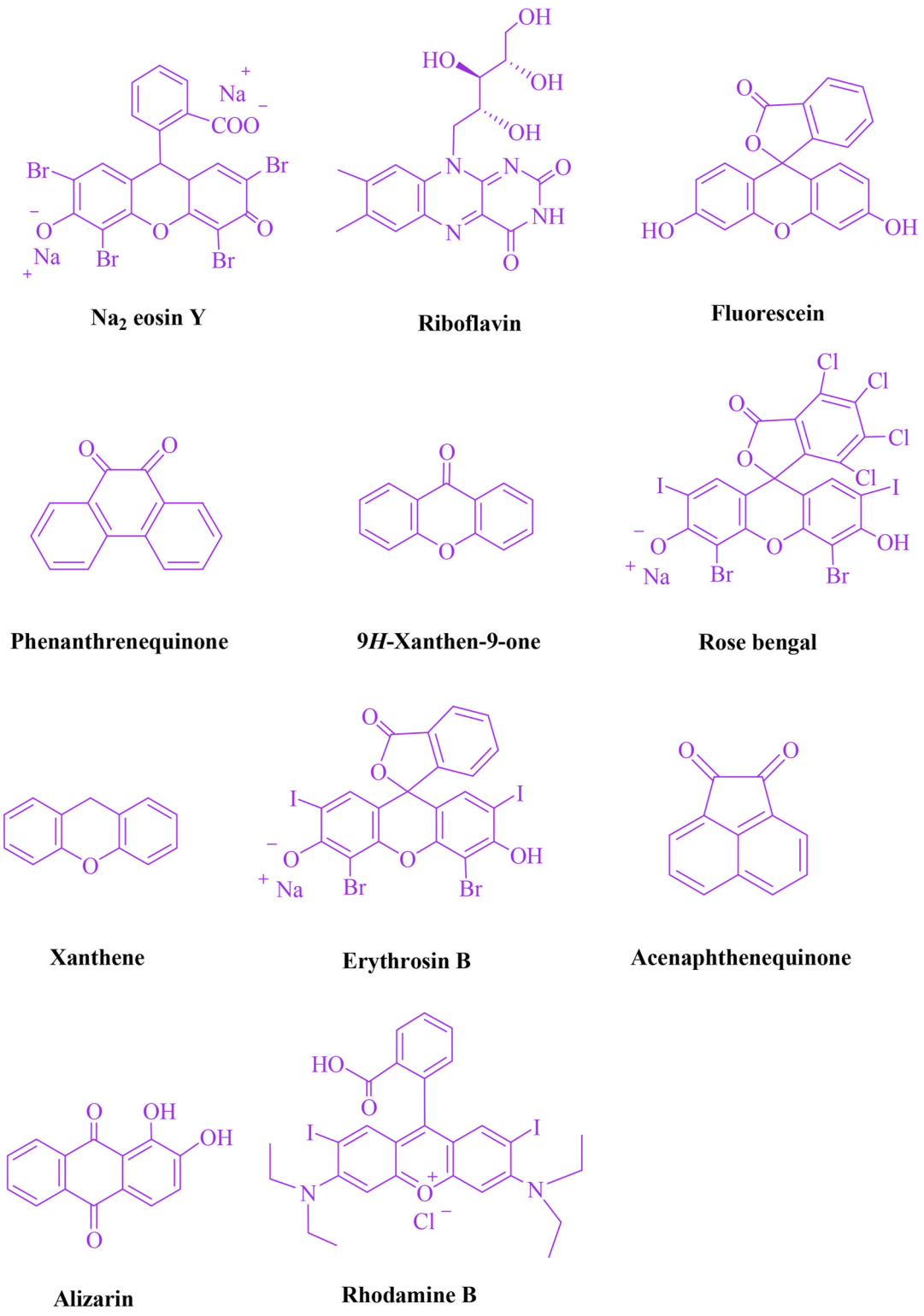


Fig. 2. Photocatalysts tested in this study.

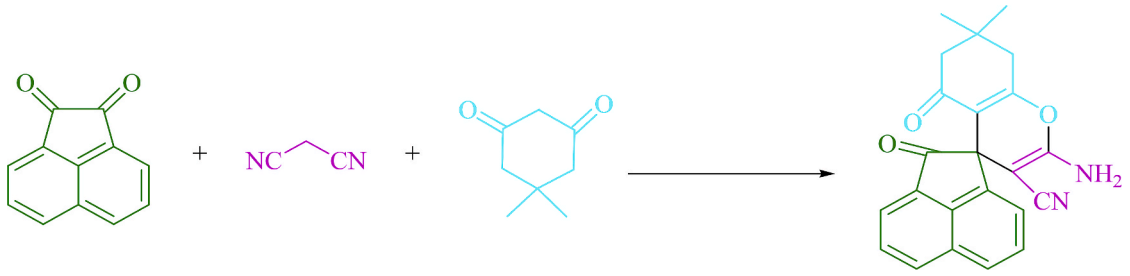
^{13}CNMR (100 MHz, DMSO-d_6): 56.5, 60.3, 61.7, 63.8, 104.6, 116.1, 127.1, 127.7, 129.2, 129.4, 134.1, 134.6, 135.0, 137.7, 151.0, 152.8, 153.9, 157.2.

MS (EI) m/z (%): 406 (M^+, 22), 389 (25), 366 (9), 275 (9), 239 (100), 162 (12), 145 (9), 130 (20), 104 (51), 76 (46), 43 (28).

2.1.13. 3-Amino-1-(4-chlorophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (7°)

Yield: 90%; M.p. 271–273 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 6.15 (1H, s, $H_{benzylic}$), 7.43 (2H, d, $J = 11.2$ Hz, H_{Ar}), 7.54 (2H, d, $J = 11.2$ Hz, H_{Ar}), 7.88–8.28 (6H, m, NH_2 and H_{Ar}).

Table 2
Optimization table of solvent and visible-light for the synthesis of **4a**.



Entry	Light Source	Solvent (3 mL)	Time (h)	Isolated Yields (%)
1	White light (18 W)	EtOAc	4	71
2	White light (18 W)	EtOH	4	76
3	White light (18 W)	EL	4	79
4	White light (18 W)	MeOH	4	68
5	White light (18 W)	H_2O	4	73
6	White light (18 W)		4.5	67
7	White light (18 W)	H_2O/EtOH (1:1)	4	81
8	White light (18 W)	H_2O/EtOH (1:2)	4	76
9	White light (18 W)	H_2O/EtOH (2:1)	4	85
10	White light (18 W)	EL/H_2O (1:1)	4	87
11	White light (18 W)	EL/H_2O (1:2)	4	83
12	**White light (18 W)**	**EL/H_2O (2:1)**	**4**	**93**
13	White light (18 W)	Toluene	5.5	30
14	White light (18 W)	$CHCl_3$	6	21
15	White light (18 W)	THF	5	36
16	White light (18 W)	CH_2Cl_2	6	17
17	White light (18 W)	DMSO	5	23
18	White light (18 W)	DMF	5	29
19	White light (18 W)	CH_3CN	5.5	19
20	Green light (18 W)	EL/H_2O (2:1)	4	91
21	Blue light (18 W)	EL/H_2O (2:1)	4	87
22		EL/H_2O (2:1)	6	<5
23	White light (10 W)	EL/H_2O (2:1)	4	82
24	White light (12 W)	EL/H_2O (2:1)	4	88
25	White light (20 W)	EL/H_2O (2:1)	4	93

[a]Reaction condition: acenaphthequinone (1 mmol), malononitrile (1 mmol) and dimedone (1 mmol), Na_2 eosin Y (1.5 mol%) at rt.
[b] Isolated yield.

2.1.14. 3-Amino-1-(3-methylphenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (7s)

Yield: 92%; M.p. 249–251 °C; ^{1}HNMR (400 MHz, DMSO-d_6): 2.30 (3H, s, CH_3), 6.08 (1H, s, $H_{benzylic}$), 7.14–7.26 (4H, m, H_{Ar}), 7.97–8.29 (6H, m, NH_2 and H_{Ar}).

2.1.15. 3-Amino-1-(3-chlorophenyl)-5,10-dihydro-5,10-dioxo-1H-pyrazolo[1,2-b]phthalazine-2-carbonitrile (7u)

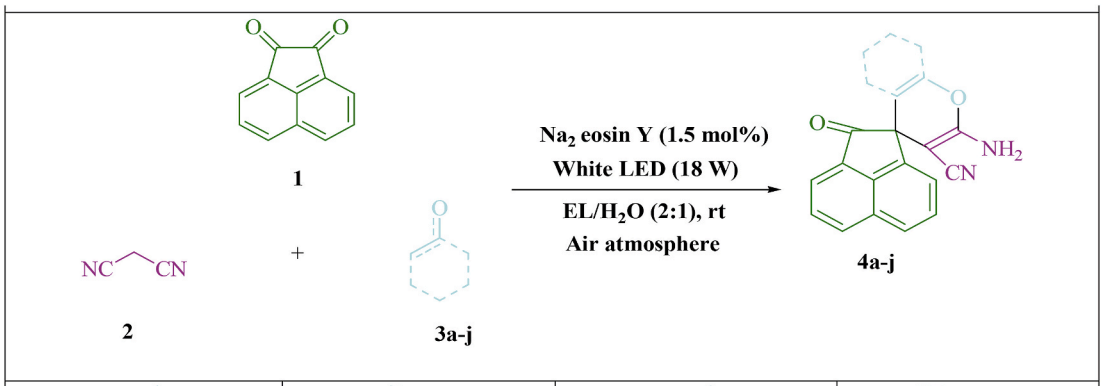
Yield: 84%; M.p. 267–269 °C; ^{1}HNMR (300 MHz, DMSO-d_6): 6.15 (1H, s, CHAr), 7.39–7.41 (2H, m, ArH), 7.44–7.48 (1H, m, ArH), 7.65 (1H, s, ArH), 7.88–8.29 (6H, m, NH_2 and ArH).

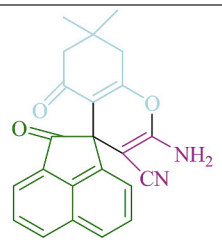
3. Results and discussion

Initially, the reaction between malononitrile (1.0 mmol), acenaphthequinone (1.0 mmol) and dimedone (1 mmol) for the preparation of **4a** was studied in EL/H_2O (2:1) (3 mL) promoted by light emitting diode (LED) irradiation at ambient temperature. Table 1 illustrates the results. Without the presence of photocatalyst, a 46% of **4a** was seen at rt for 5 h in 3 mL EL/H_2O (2:1). This reaction was promoted by examining a variety of organic photocatalysts including Na_2 eosin Y, riboflavin, fluorescein, phenanthrenequinone, 9*H*-xanthen-9-one, rose Bengal, Xanthene, erythrosin B, acenaphthenequinone, Alizarin and rhodamine B (Fig. 2) in similar settings. Satisfactorily, the progress of this reaction and obtaining the matching product **4a** were observed in 46–93% yields (Table 1). According to our findings, Na_2 eosin Y was of superior functioning for this reaction. The yield was increased to 93% by using 1.5 mol% Na_2 eosin Y (Table 1, entry 4). Also, low yield of products were detected in toluene, $CHCl_3$, THF, CH_2Cl_2, DMSO, DMF and CH_3CN (Table 2). While the reaction proceeded sluggishly in EtOAc, EtOH, EL, MeOH, H_2O, solvent-free, H_2O/EtOH and EL/H_2O the yield and reaction rate increased (Table 2). In EL/H_2O (2:1), the reaction proceeded very well, and 93% yield was obtained under identical conditions (Table 2, entry 12). The yield was screened by various light sources, revealing that it rose somewhat by white light (Table 2, entry 12). An experimental control revealed that a miniscule of the product was detectable without the use of light source (Table 2, entry 22). The observation sindicate the essentiality of Na_2 eosin Y and visible light to successfully form the product 4a. Also, the optimized settings were determined by varying the intensities of white LED (10 W, 12 W, 18 W and 20 W) irradiation. Based on Table 2, the best outcomes were found in the presence of white LED (18 W) irradiation (Table 2, entry 12). As observed in Table 3 and Scheme 3 it was indicated that this technique can work with various substrates.

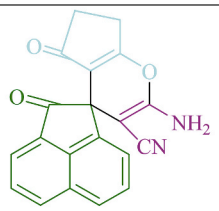
Also in continuation, the reaction between phthalhydrazide (1 mmol), benzaldehyde (1 mmol) and malononitrile (1 mmol) for the preparation of **7a** was studied in EL/H_2O (2:1) (3 mL) promoted by light emitting diode (LED) irradiation at ambient temperature. Table 4 illustrates the results. Without the presence of photocatalyst, a 51% of **7a** was seen at rt for 4.5 h in 3 mL EL/H_2O (2:1). This reaction was promoted by examining a variety of organic photocatalysts including Na_2 eosin Y, riboflavin, fluorescein, phenanthrenequinone, 9*H*-xanthen-9-one, rose Bengal, Xanthene, erythrosin B, acenaphthenequinone, Alizarin and rhodamine B (Fig. 2) in similar settings. Satisfactorily, the progress of this reaction and obtaining the matching product **7a** were observed in 51–96% yields (Table 4). According to our findings, Na_2

Table 3
Photoexcited organic dye Na_2 eosin Y as photocatalyst for synthesis of spiroacenaphthylenes.

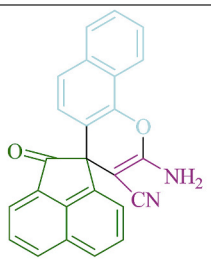




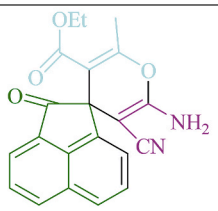
4a (4 h, 93%)
Mp. 262-264 °C
Lit. 263-265 °C [27]



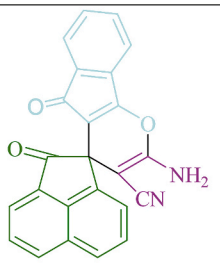
4b (3.5 h, 95%)
Mp. 300-302 °C
Lit.. 302-303 °C [27]



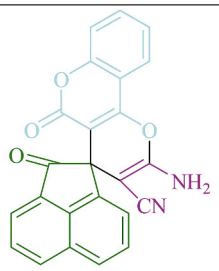
4c (4.5 h, 88%)
Mp. Mp>300 °C
Lit. Mp>300 °C [21]



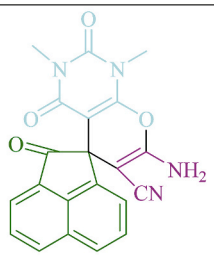
4d (4 h, 91%)
Mp. Mp>300 °C
Lit. Mp>300 °C [21]



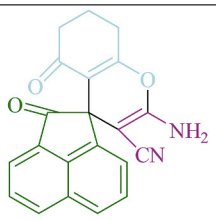
4e (5 h, 86%)
Mp. Mp>300 °C
Lit. Mp>300 °C [21]



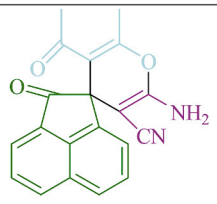
4f (5 h, 89%)
Mp. Mp>300 °C
Lit.. Mp>300 °C [22]



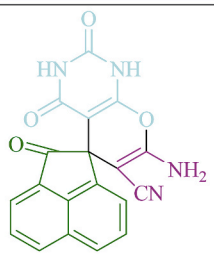
4g (5 h, 93%)
Mp. 278-280 °C
Lit. 276-278 °C [26]



4h (3.5 h, 92%)
Mp. 243-245 °C
Lit. 242-244 °C [22]



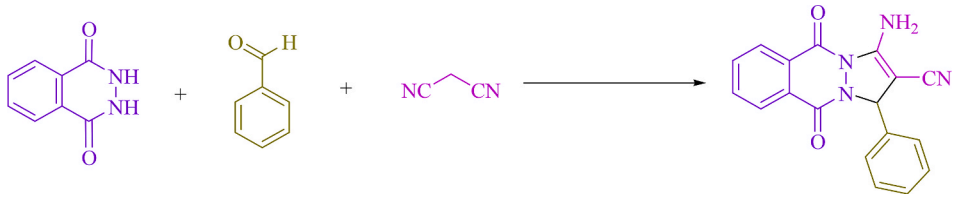
4i (3 h, 95%)
Mp. Mp>300 °C
Lit. Mp>300 °C [21]



4j (4.5 h, 91%)
Mp. 282-284 °C
Lit. 283-285 °C [26]

eosin Y was of superior functioning for this reaction. The yield was increased to 96% by using 1.5 mol% Na_2 eosin Y (Table 4, entry 4). Also, low yield of products were detected in toluene, $CHCl_3$, THF, CH_2Cl_2, DMSO, DMF and CH_3CN (Table 5). While the reaction proceeded sluggishly in EtOAc, EtOH, EL, MeOH, H_2O, solvent-free, H_2O/EtOH and EL/H_2O the yield and reaction rate increased (Table 5). In EL/H_2O (2:1), the reaction proceeded very well, and 96% yield was obtained under identical conditions (Table 5, entry 12). The yield was screened by various light sources, revealing that it rose somewhat by white light (Table 5, entry 12). An experimental control revealed that a miniscule of the

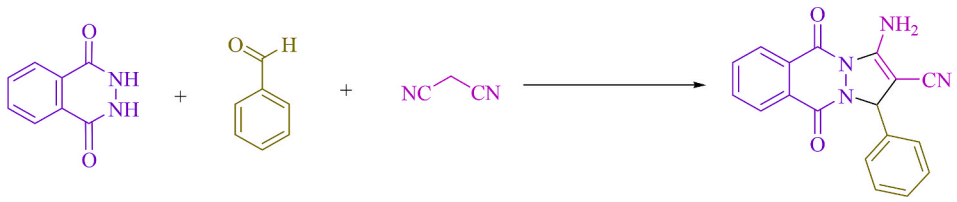
Table 4
Optimization table of photocatalyst for the synthesis of **7a**.



Entry	Photocatalyst	Solvent (3 mL)	Time (h)	Isolated Yields (%)
1		EL/H_2O (2:1)	4.5	51
2	Na_2 eosin Y (0.5 mol%)	EL/H_2O (2:1)	3	82
3	Na_2 eosin Y (1.0 mol%)	EL/H_2O (2:1)	3	91
4	**Na_2 eosin Y (1.5 mol%)**	**EL/H_2O (2:1)**	**3**	**96**
5	Na_2 eosin Y (2 mol%)	EL/H_2O (2:1)	3	96
6	Riboflavin (1.5 mol%)	EL/H_2O (2:1)	3	70
7	Fluorescein (1.5 mol%)	EL/H_2O (2:1)	3	74
8	Phenanthrenequinone (1.5 mol%)	EL/H_2O (2:1)	3	59
9	9*H*-Xanthen-9-one (1.5 mol%)	EL/H_2O (2:1)	3	54
10	Rose bengal (1.5 mol%)	EL/H_2O (2:1)	3	58
11	Xanthene (1.5 mol%)	EL/H_2O (2:1)	3	55
12	Erythrosin B (1.5 mol%)	EL/H_2O (2:1)	3	61
13	Acenaphthenequinone (1.5 mol%)	EL/H_2O (2:1)	3	63
14	Alizarin (1.5 mol%)	EL/H_2O (2:1)	3	68
15	Rhodamine B (1.5 mol%)	EL/H_2O (2:1)	3	76

[a]Reaction condition: phthalhydrazide (1 mmol), benzaldehyde (1 mmol) and malononitrile (1 mmol) in EL/H_2O (2:1) (3 mL), white LED (18 W), and various photocatalysts at rt.
[b] Isolated yield.

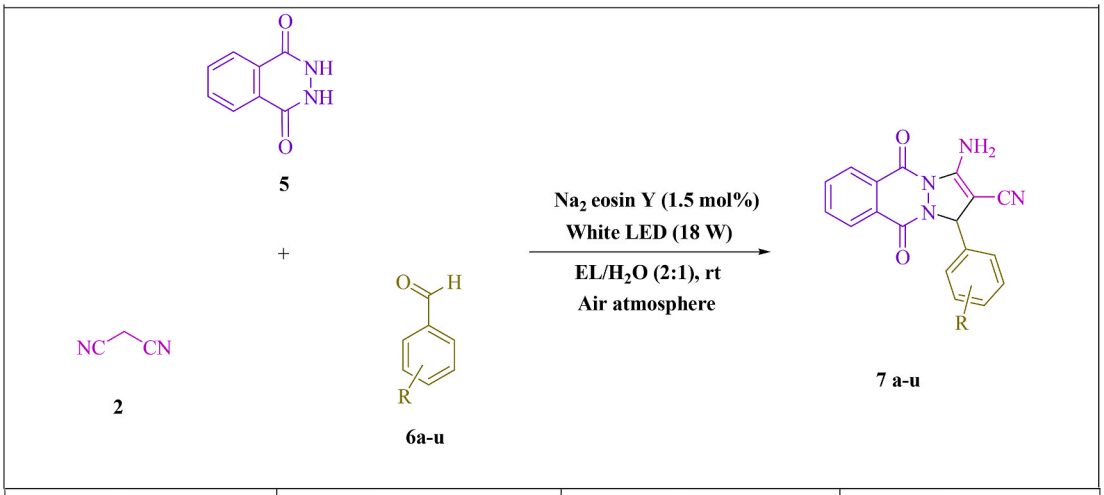
Table 5
Optimization table of solvent and visible-light for the synthesis of **7a**.

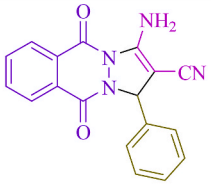
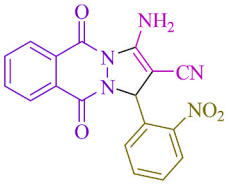
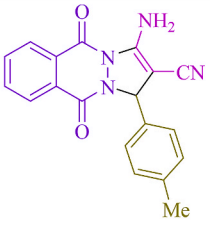
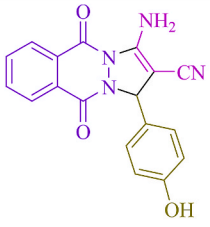
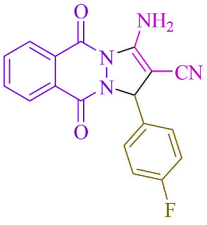
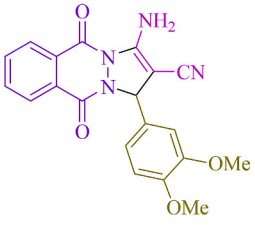
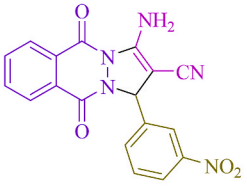
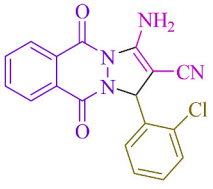
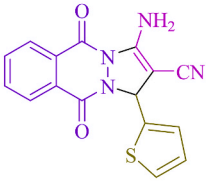
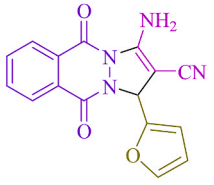
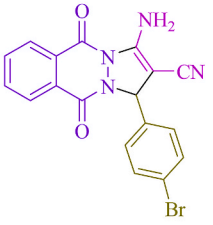
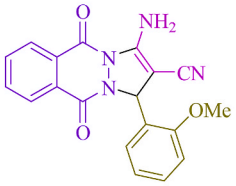


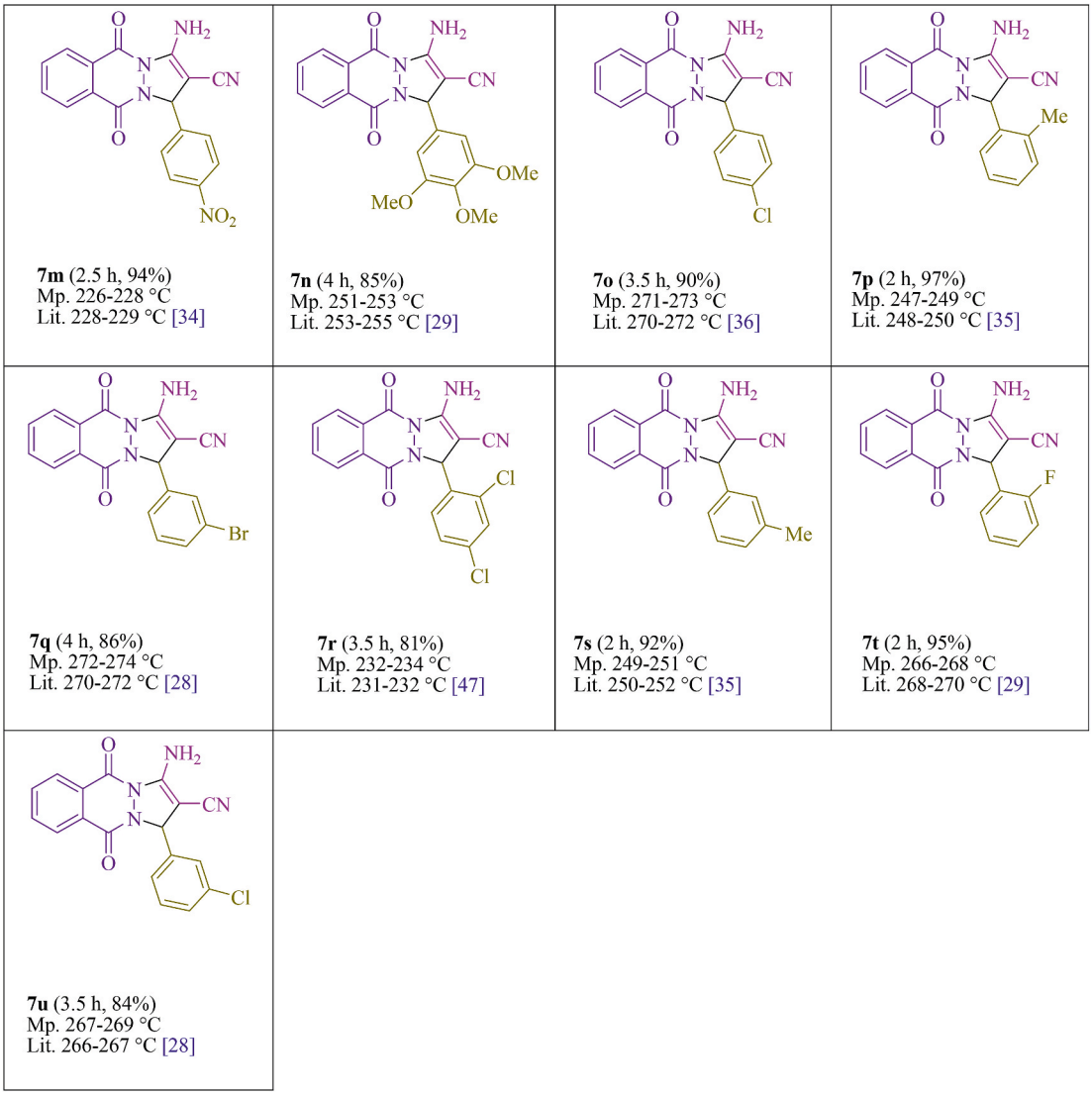
Entry	Light Source	Solvent (3 mL)	Time (h)	Isolated Yields (%)
1	White light (18 W)	EtOAc	3	75
2	White light (18 W)	EtOH	3	81
3	White light (18 W)	EL	3	84
4	White light (18 W)	MeOH	3	74
5	White light (18 W)	H_2O	3	76
6	White light (18 W)		3	62
7	White light (18 W)	H_2O/EtOH (1:1)	3	85
8	White light (18 W)	H_2O/EtOH (1:2)	3	81
9	White light (18 W)	H_2O/EtOH (2:1)	3	88
10	White light (18 W)	EL/H_2O (1:1)	3	90
11	White light (18 W)	EL/H_2O (1:2)	3	85
12	**White light (18 W)**	**EL/H_2O (2:1)**	**3**	**96**
13	White light (18 W)	Toluene	4	27
14	White light (18 W)	$CHCl_3$	4.5	18
15	White light (18 W)	THF	3.5	29
16	White light (18 W)	CH_2Cl_2	4.5	12
17	White light (18 W)	DMSO	4	32
18	White light (18 W)	DMF	3.5	35
19	White light (18 W)	CH_3CN	4	25
20	Green light (18 W)	EL/H_2O (2:1)	3	93
21	Blue light (18 W)	EL/H_2O (2:1)	3	89
22		EL/H_2O (2:1)	4.5	<5
23	White light (10 W)	EL/H_2O (2:1)	3	84
24	White light (12 W)	EL/H_2O (2:1)	3	91
25	White light (20 W)	EL/H_2O (2:1)	3	96

[a]Reaction condition: phthalhydrazide (1 mmol), benzaldehyde (1 mmol) and malononitrile (1 mmol), Na_2 eosin Y (1.5 mol%) at rt.
[b] Isolated yield.

Table 6
Photoexcited organic dye Na_2 eosin Y as photocatalyst for synthesis of 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones.



 **7a** (3 h, 96%) Mp. 272-274 °C Lit. 270-272 °C [35]	 **7b** (2 h, 91%) Mp. 263-265 °C Lit. 265-266 °C [28]	 **7c** (3 h, 94%) Mp. 254-256 °C Lit. 253-255 °C [35]	 **7d** (4 h, 87%) Mp. 271-273 °C Lit. 270-272 °C [29]
 **7e** (2 h, 97%) Mp. 265-267 °C Lit. 263-265 °C [28]	 **7f** (4 h, 89%) Mp. 234-236 °C Lit. 233-237°C [34]	 **7g** (2.5 h, 96%) Mp. 268-270 °C Lit. 269-271 °C [36]	 **7h** (3 h, 86%) Mp. 255-257 °C Lit. 257-259 °C [34]
 **7i** (2.5 h, 92%) Mp. 244-246 °C Lit. 246-248 °C [40]	 **7j** (2.5 h, 95%) Mp. 286-288 °C Lit. 285-287 °C [41]	 **7k** (4 h, 88%) Mp. 267-269 °C Lit. 265-267 °C [28]	 **7l** (3 h, 94%) Mp. 154-156 °C Lit. 153-155 °C [43]



7m (2.5 h, 94%)
Mp. 226-228 °C
Lit. 228-229 °C [34]

7n (4 h, 85%)
Mp. 251-253 °C
Lit. 253-255 °C [29]

7o (3.5 h, 90%)
Mp. 271-273 °C
Lit. 270-272 °C [36]

7p (2 h, 97%)
Mp. 247-249 °C
Lit. 248-250 °C [35]

7q (4 h, 86%)
Mp. 272-274 °C
Lit. 270-272 °C [28]

7r (3.5 h, 81%)
Mp. 232-234 °C
Lit. 231-232 °C [47]

7s (2 h, 92%)
Mp. 249-251 °C
Lit. 250-252 °C [35]

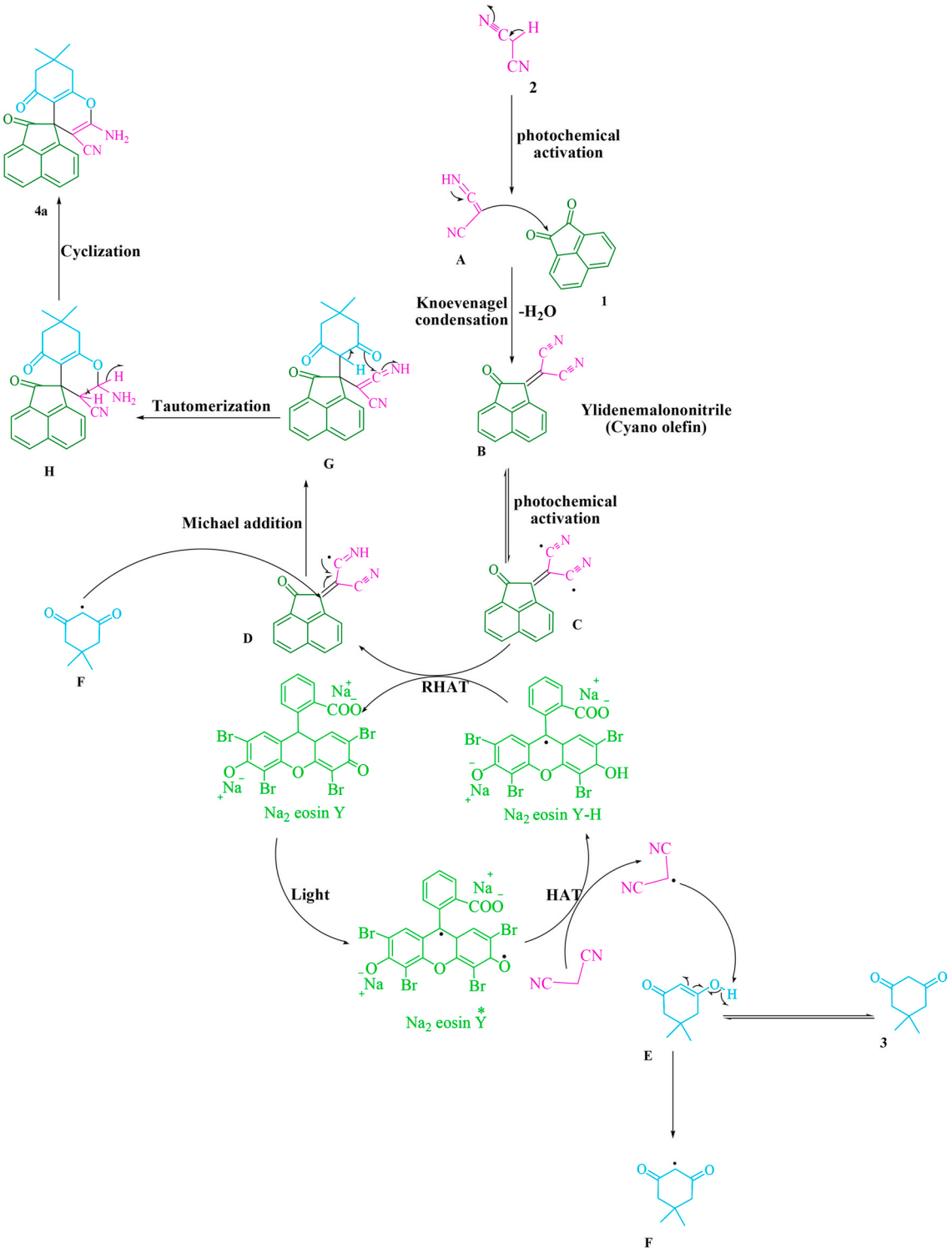
7t (2 h, 95%)
Mp. 266-268 °C
Lit. 268-270 °C [29]

7u (3.5 h, 84%)
Mp. 267-269 °C
Lit. 266-267 °C [28]

product was detectable without the use of light source (Table 5, entry 22). The observation sindicate the essentiality of Na_2 eosin Y and visible light to successfully form the product 7a. Also, the optimized settings were determined by varying the intensities of white LED (10 W, 12 W, 18 W and 20 W) irradiation. Based on Table 5, the best outcomes were found in the presence of white LED (18 W) irradiation (Table 5, entry 12). As observed in Table 6 and Scheme 4 it was indicated that this technique can work with various substrates.

Scheme 5 shows the suggested mechanism for synthesizing spiroacenaphthylenes. With the use of visible light, malononitrile (**2**) is subjected totautomerisation to give (**A**). Afterwards, (**A**) and acenaphthequinone (**1**) react to form arylidenemalononitrile (**B**), undergoing an activation photochemically for the formation of a radical intermediate (**C**), in which visible light can partially affect with exerting extra energy to accelerate the reaction. As reported in previous studies [1a,1d,4], eosin Y-originated photoexcited modes can function as direct hydrogen atom transfer (HAT) catalysts for activating C–H bonds. The malononitrile radical is formed by the promotion of visible light triggered Na_2 eosin Y* via a HAT procedure. Ground-state Na_2 eosin Y and the intermediate **D** are regenerated by occurring reverse hydrogen atom transfer (RHAT) process between eosin Na_2 Y–H and radical adduct **C**. Then, malononitrile radical extracts a hydrogen atom from (**E**) to produce intermediate (**F**). Subsequently, intermediate (**D**) and (**F**) coalesce to generate (**G**) as Michael acceptor, additionally undergoing tautomerisation and intramolecular cyclization for the product formation (**4**).

Scheme 6 shows the suggested mechanism for synthesizing **7a-u**. With the use of visible light, malononitrile (**2**) is subjected totautomerisation to give (**I**). Afterwards, (**I**) and aldehyde derivatives (**6**) react to form arylidenemalononitrile (**J**), undergoing an activation photochemically for the formation of a radical intermediate (**K**), in which visible light can partially affect with exerting extra energy to accelerate the reaction. As reported in previous studies [1a,1d,4], eosin Y-originated photoexcited modes can function as direct hydrogen atom transfer (HAT) catalysts for activating C–H bonds. The malononitrile radical is formed by the promotion of visible light triggered Na_2 eosin Y* via a HAT procedure. Ground-state Na_2 eosin Y and the intermediate **L** are regenerated by occurring reverse hydrogen atom transfer (RHAT) process between eosin Na_2 Y–H and radical adduct **K**. Subsequently, intermediate (**L**) and (**5**) coalesce to generate (**M**) as Michael acceptor, additionally undergoing tautomerisation and intramolecular cyclization for the product formation (**7**).



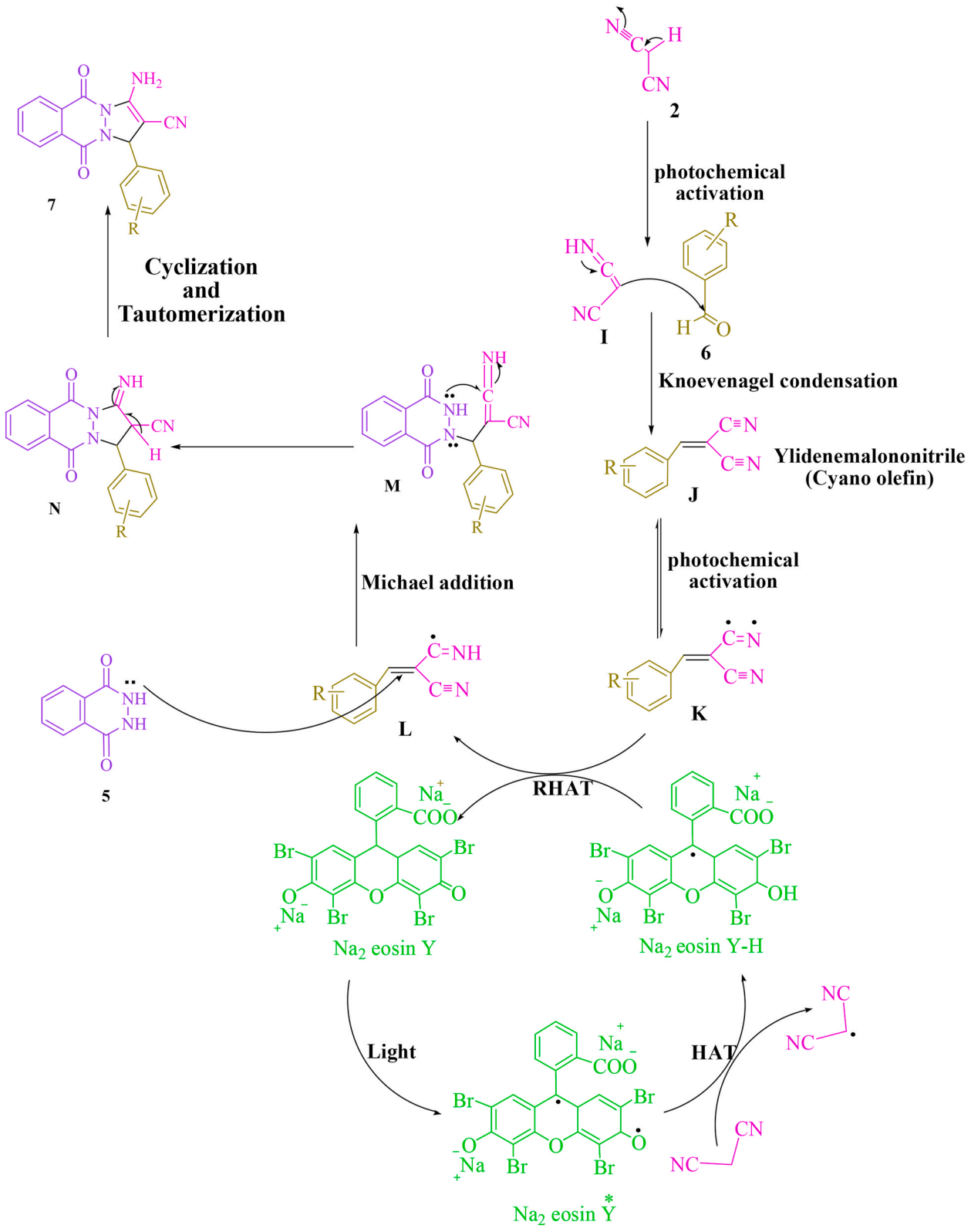
Scheme 5. Recommended mechanistic path for synthesizing spiroacenaphthylenes.

4. Study on the mechanism of photocatalytic reactions with eosin Y

Most importantly, Eosin Y is employed as a photoredox catalyst in the synthetic process of organics. In recent years, Rossi [48], Mahmood [49], Majek [2b], Eid [50] and et al. have studied the use of Eosin Y in photoredox reactions and the effect of UV light, PH and also the effect of temperature on the rate of reactions.

5. Effect of the light source on the eosin Y-mediated photocatalysis

Catalytically, the features of Eosin Y depend upon its reduction/oxidation potentiality [48]: the oxidation and reduction potentials vary from −1.06 V to1.10 V and +0.78 V to+0.83 V, respectively (Scheme 1). Its absorption is maximized at 539 nm, with a molar extinction coefficient of $\varepsilon = 60803\ M^{-1}\ cm^{-1}$ (Fig. 3a and b). Accordingly, light-emitting diodes (LEDs) are typically utilized conveniently as lighting sources for



Scheme 6. Recommended mechanistic path for synthesizing 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-dione derivatives.

activating Eosin Y (maximal emission about 530 nm). Once excited by light, Eosin Y experiences a fast intersystem transition from the ground state to the lowermost energy triplet state. It cannot directly undergo the singlet–triplet transition, but Eosin Y electrons are excited by light to a greater excited singlet state from where they undergo quick relaxation to the lowermost excited singlet state. This is where only excited electrons experience an intersystem transition to the high reactive triplet state, with a lifespan of 24 ms [48].

The interaction of pH and UV light on the rate of radical production has also been investigated. The initial rate is also enhanced by EY concentrations at low pH, but the initial rate shows a significant enhancement by UV light. There as on for this is because extra radicals form

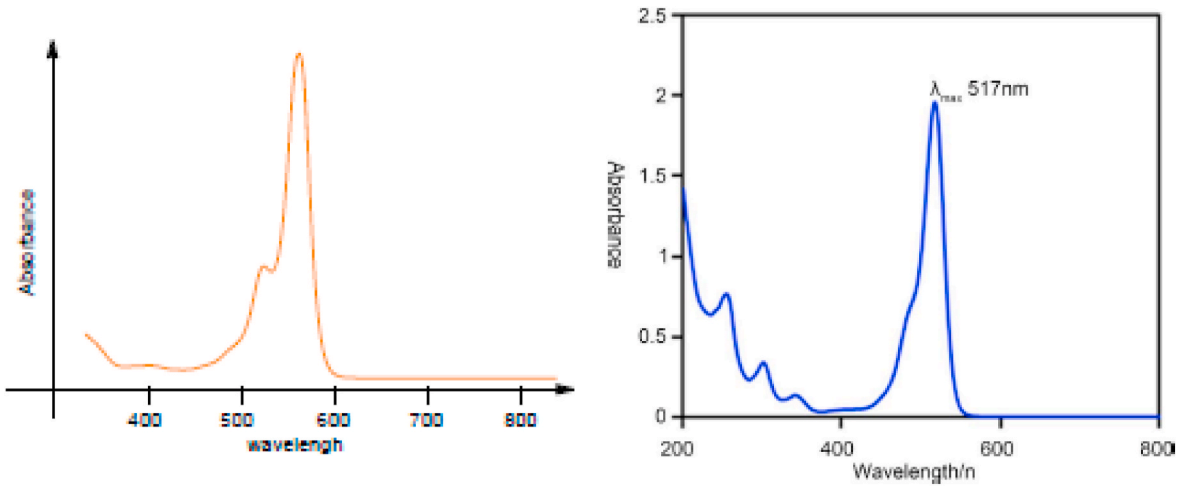


Fig. 3. a. Eosin Y absorption spectrum in EtOH solution [48].
b. The Spectrum of Eosin Y in aqueous solution [49].

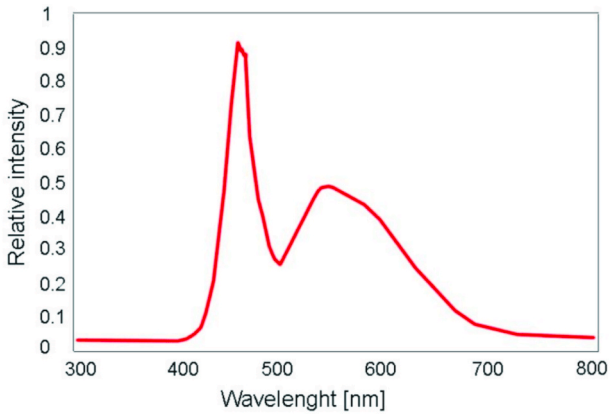


Fig. 4. Emission spectrum of a commercial white light LED [51].

when the dye molecules are excited by UV light [50].

The source of irradiation is another reaction factor that has not been clearly and consistently documented in previous research [2b]. Our research team is among the researchers who have employed commercially available narrow-band LEDs with a maximal intensity at 535 nm. Irradiation of other reactions was done by broad-band compact fluorescent lamps (CFLs). To determine quantum yields, it is necessary to utilize narrowband lighting sources because the optical density of the samples varies with the wavelength. In this study, therefore, the influence of various irradiations was investigated throughout the photocatalytic reaction. Despite the undetermined types of CFLs in previous research, analogous spectral arrays are covered by most of commercially-available CFLs in which the UV edge individually is significantly <400 nm and with considerable radiation power in the area of 400–500 nm. Similarly, a wavelength range is observed in the spectra of commercially available LEDs [2b] (Fig. 4 [51]).

6. Effect of PH on the eosin Y-mediated photocatalysis

Once Eosin Y is in a solution, it is in equilibrium with four varying types as it contains two rather acidic protons (pKa 2.0 and 3.8 in water, Scheme 7), all of which depend on the pH. At pH < 2, the protonated spirocyclic type EY1 equilibrates with the neutral type EY2. At 2 < pH > 3.8, however, the mono anionic type EY3 equilibrates with the dianionic type EY4, becoming dominant at pH > 3.8. Only EY3 and EY4 have catalytic activity, but this function as resulted in uncertainties in bulk of literature concerning the quality of the dye responsible for the

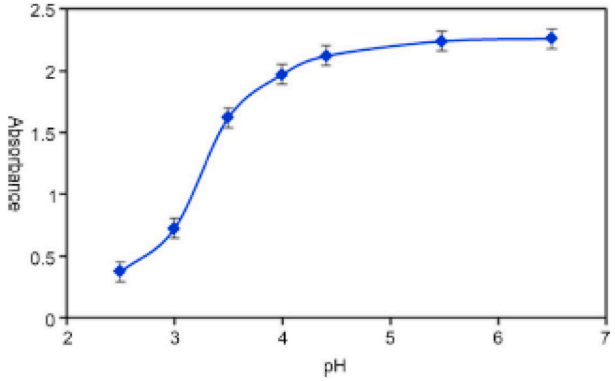
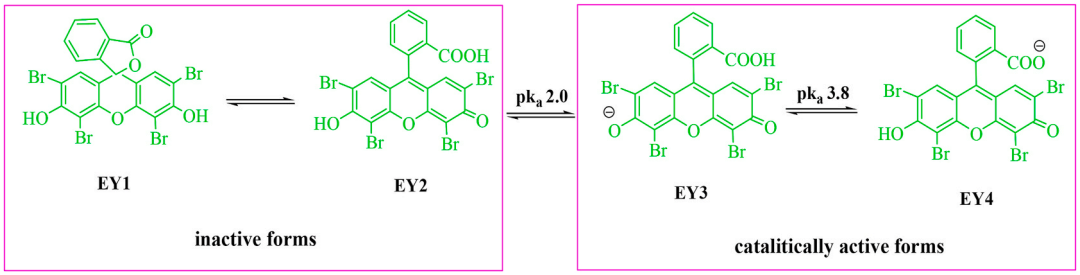


Fig. 5. Effect of pH on the absorbance, at λ_{max} = 517 nm, of Eosin Y solution [49].



Scheme 7. Acid–base equilibria of Eosin Y in water [48].

transmutation. To assure that the dianionic type EY4 is present, Eosin Y sodium salt is utilized as a photocatalyst, though it is necessary to take account of the reaction situations of chemical transmutation in the experiment [48].

Eid [50] investigated the impact of pH on the absorbance values of the binary complexes in the pH ranging from 2.6 to 4.5; adjusting to a pH of 5 leads to negative absorbance values.

A pH of 3.5 resulted in the optimal absorbance values. Two ml of 0.4 M acetate buffer could sufficiently optimize the pH level. When the drug-dye solution is mixed at neutral pH, it is necessary to add the buffer solution for the uppermost color intensity and maximal accuracy.

Similarly, Mahmood [49] examined the impact of pH on absorbance. The absorbance of EY (Fig. 5) rises with raising the pH of its solution, and its reduction is minimal in the pH level of about 4, above which it rises with pH. In contrast, radicals undergo destruction at minimum pH values.

7. Effect of temperature on the eosin Y-mediated photocatalysis

The effect of temperature on the absorbance value of binary complexes was researched by Eid [50]. The color intensity was finally maximal at ambient temperature, and an increase in the temperature led to forming a deposit possibly because of coagulating the created complex. Consequently, room temperature is ideal for Eosin Y catalytic reactions.

8. Conclusion

Current survey revealed that organic dye Na_2 eosin Y-derived photoexcited states functions as a direct hydrogen atom transfer (HAT) catalyst can be employed for photochemically metal-free synthesizing spiroacenaphthylenes and 1*H*-pyrazolo[1,2-*b*]phthalazine-5,10-diones via three-condensation domino reaction of tandem Knoevenagel-Michael cyclocondensation via visible light-mediated in aqueous ethyl lactate at ambient temperature under air atmosphere. The use of the lowest amount of catalyst, utilizing great yields, efficient sides of the reaction, direct work-up with no column chromatographic separation, secure reaction circumstances, appropriate and expedient procedure and avoiding the hazardous catalysts or solvents are the most conspicuous pros of this green protocol. These characteristics have caused this procedure to be highly beneficial in facing the environmental worries and industrial needs.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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