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Original Scientific Article

Eosin Y Catalyzed Visible-light-promoted One –Pot Facile Synthesis of 1,3,4- Thiadiazole

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Abstract. A novel one-pot visible light irradiated synthesis of 1,3,4-thiadiazole from aldehydes and thioacyl hydrazides have been reported in presence of eosin Y as an organophotoredox catalyst at room temperature under aerobic condition. This synthesis includes application of air and visible light as inexpensive, readily available, non-toxic and sustainable regents, which fulfils the basic principle of green chemistry.

Keywords: Eosin Y, visible-light, organophotoredox, green chemistry, aerobic condition

INTRODUCTION

Sunlight is a unique and renewable natural source.[1] The development of methods to efficiently harness the solar radiation energy has emerged as one of the central scientific challenges of the twenty first century.[2–3] Therefore, some pioneering researchers have dedicated to converting solar energy into chemical energy for chemical transformations.[4–5] Recently, a surge of interest from the synthetic community has brought photoredox manifolds to the forefront of catalysis. In this sequence visible light photoredox catalysis has recently received much attention in organic synthesis owing to ready availability, sustainability, non-toxicity and ease of handling of visible light.[6–11] In their revolutionary work in this area, MacMillan,[12] Yoon[13] and Stephenson[14–15] have used Ruthenium and Iridium complexes as the photoredox catalyst, which has inspired the development of several powerful methods for various chemical transformations useful in organic synthesis.[16]

However, these transition metal based photocatalysts disadvantageously exhibit high cost, low sustainability and potential toxicity. Recently, a superior alternative to transition metal photoredox catalysts, especially metal-free organic dyes such as eosin Y, fluorescein, Rose Bengal, nile red, perylene and rhodamine B have been used as economically and ecologically superior surrogates for Ru(II) and Ir(II) complexes in visible-light promoted organic transformations involving SET[17–20] (single electron transfer). These organic dyes have got much more attention with the last few years also due to easy handling, eco-friendly and have great potential for applications in visible-light-mediated organic synthesis,[21–24] which fulfils the basic principle of green chemistry.

The five-membered heterocyclic compounds have a great application and importance in heterocyclic chemistry. Among them thiadiazole is a versatile moiety that exhibits a wide variety of biological activities. Thiadiazole moiety acts as “hydrogen binding domain” and “two-electron donor system”. It also acts as a constrained pharmacophore. Many drugs containing thiadiazole nucleus are available in the market such as acetazolamide, methazolamide, sulfamethazole, etc. 1,3,4-thiadiazoles are associated with diverse pharmacological activities such as analgesic,[25] antidepressant, anxiolytic,[26] anticonvulsant,[27–28] anti-inflammatory,[29] antimicrobial,[30] anti-tubercular,[31] antitumor,[32] and anti-viral activities.[33]

The synthesis of 1,3,4-thiadiazole have not been reported by photooxidation reaction so far. Meanwhile the aerobic oxygen has received a great importance in research during present time.[34–35] In general, organosulfur/nitrogen compounds have been frequently used as precursors in radical reactions because they form radicals very readily.[36–38] Encouraged by organocatalytic visible-light-mediated aerobic oxidative transformations[39–40] and in continuation of our work on develop-

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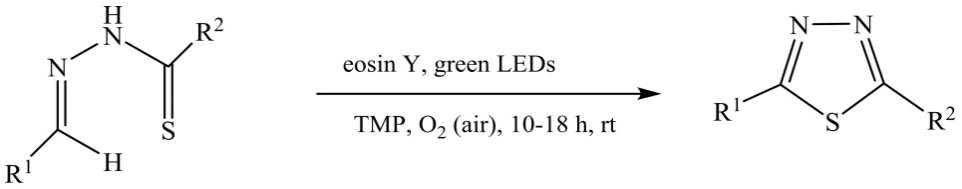


Scheme 1. Eosin Y catalysed visible light promoted synthesis of 1,3,4-thiadiazole.

ment of novel environmentally benign synthesis[41–44] herein we report a simple, visible light irradiated, efficient and green protocol for the synthesis of 1,3,4-thiadiazoles, using eosin Y as photocatalyst with excellent yield as depicted in Scheme 1.

EXPERIMENTAL

Melting points were determined by open glass capillary method and are uncorrected. All chemicals used were reagent grade and were used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX (400 MHz and 75 MHz) FT spectrometer in DMSO using TMS as an internal reference (chemical shift in δ, ppm). Mass spectra were recorded on JEOL SX-303 (FAB) mass spectrophotometer at 70ev. Elemental analyses were carried out using a Coleman automatic C,H,N analyser.

General Procedure for the Synthesis of 2,5-disubstituted 1,3,4-thiadiazole 4(a−n):

A solution of an aldehyde **1(a−n)** (1.0 mmol) and an thioacylhydrazide **2(a−n)** (1.0 mmol) in MeCN (3 mL) was heated at 65 °C for 2−6 h to form the corresponding thioacylhydrazone (as monitored by TLC). Then, eosin Y (2.0 mol%) and TMP (2.0 equiv.) were added and the mixture was irradiated with green LEDs (2.4 W, 120 lm) with stirring under an air atmosphere at rt for 10−18 h. After completion of the reaction (monitored by TLC), water (5 mL) was added and the mixture was extracted with EtOAc (3 × 5 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting product was purified by silica gel column chromatography using a gradient mixture of hexane/ethyl acetate as eluent to afford an analytically pure sample of **4(a−n)**. All the products are known compounds and were characterized by the comparison of their spectral data with those reported in the literature. In the ^{1}H NMR spectra, signal of respective protons of newly synthesized compounds **4(a−n)** showed the peaks for -CH_3, -OCH_3 and aromatic protons.

***4a**. 2-(4-chlorophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 180 ºC, *m*/*z*: 272.02; Mol. Wt: 272.75; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 5H, ArH), 7.65−7.74 (d, 2H, *J* = 8.1 Hz, 2′, 6′-ArH), 8.02−8.15 (d, 2H, *J* = 8.4 Hz, 3′, 5′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 128.7, 128.9, 129.2, 129.3, 130.9, 131.6, 133.5, 134.3, 174.1; Anal. Calcd for $C_{14}H_9ClN_2S$: C, 61.65; H, 3.33; N, 10.27. Found: C, 61.42; H, 3.31; N, 10.25.

***4b**. 2-(3-chlorophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 187 ºC, *m*/*z*: 272.02; Mol. Wt: 272.75; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 5H, ArH), 7.65−7.74 (dd, 1H, *J* = 8.1 Hz, *J* = 8.9 Hz, 5′-ArH), 7.80−7.85 (d, 1H, *J* = 8.1 Hz, 4′-ArH), 7.91−8.00 (d, 1H, *J* = 8.3 Hz, 6′-ArH), 8.04−8.13 (s, 1H, 2′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 127.4, 128.7, 128.8, 129.0, 129.2, 130.9, 133.5, 134.8, 134.9, 174.1; Anal. Calcd for $C_{14}H_9ClN_2S$: C, 61.65; H, 3.33; N, 10.27. Found: C, 61.42; H, 3.31; N, 10.25.

***4c**. 2-(2-chlorophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 195 ºC, *m*/*z*: 272.02; Mol. Wt: 272.75; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 7H, ArH, 4′, 5′- ArH), 7.65−7.70 (d, 1H, *J* = 8.1 Hz, 3′-ArH), 7.73−7.78 (d, 1H, *J* = 8.1 Hz, 6′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 127.3, 128.7, 128.9, 129.2, 129.3, 130.1, 130.9, 132.2, 133.5, 136.9, 174.1; Anal. Calcd for $C_{14}H_9ClN_2S$: C, 61.65; H, 3.33; N, 10.27. Found: C, 61.42; H, 3.31; N, 10.25.

***4d.** 2-(4-methoxyphenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 215 ºC, *m*/*z*: 268.07; Mol. Wt: 268.33; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 3.83 (s, 3H, -OCH_3), 7.41−7.50 (m, 5H, ArH), 7.58−7.69 (d, 2H, *J* = 8.1 Hz, 3′, 5′-ArH), 8.05−8.13 (d, 2H, *J* = 8.4 Hz, 2′, 6′- ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 55.8, 114.8, 125.8, 128.5, 128.7, 129.2, 130.9, 133.5, 160.6, 174.1; Anal. Calcd for $C_{15}H_{12}N_2$ OS: C, 67.14; H, 4.51; N, 10.44. Found: C, 67.12; H, 4.50; N, 10.40.

***4e**. 2,5-diphenyl-1,3,4-thiadiazole*
m.p. 140 ºC, *m*/*z*: 238.06; Mol. Wt: 238.31; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−8.03 (m, 10H, ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 128.7, 129.2, 130.9, 133.5, 174.1; Anal. Calcd for $C_{14}H_{10}N_2$ S: C, 70.56; H, 4.23; N, 11.76. Found: C, 67.12; H, 4.50; N, 10.40.

***4f.** 2-(4-bromophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 250 ºC, *m*/*z*: 317.96; Mol. Wt: 317.20; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 5H, ArH),

7.63−7.84 (d, 2H, *J* = 8.2 Hz, 2′, 6′-ArH), 8.00−8.13 (d, 2H, *J* = 8.5 Hz, 3′, 5′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 123.1, 128.7, 129.2, 129.7, 130.9, 132.1, 132.5, 133.5, 174.1; Anal. Calcd for $C_{14}H_9BrN_2S$: C, 53.01; H, 2.86; N, 8.83. Found: C, 52.99; H, 2.84; N, 8.81.

4g. *2-(3-bromophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 258 ºC, *m*/*z*: 317.96; Mol. Wt: 317.20; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 5H, ArH), 7.67−7.78 (d, 1H, *J* = 8.2 Hz, *J* = 8.7 Hz, 5′-ArH), 7.81−7.89 (d, 1H, *J* = 8.3 Hz, 4′-ArH), 7.90−8.02 (d, 1H, *J* = 8.1 Hz, 6′-ArH), 8.04−8.14 (s, 1H, 2′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 122.2, 128.1, 128.7, 129.2, 129.9, 130.9, 131.4, 133.1, 133.5, 135.7, 174.1; Anal. Calcd for $C_{14}H_9BrN_2S$: C, 53.01; H, 2.86; N, 8.83. Found: C, 52.99; H, 2.84; N, 8.81.

4h. *2-(4-nitrophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 230 ºC, *m*/*z*: 283.04; Mol. Wt: 283.31; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 5H, ArH), 7.70−7.94 (d, 2H, *J* = 8.1 Hz, 2′, 6′-ArH), 8.01−8.18 (d, 2H, *J* = 8.3 Hz, 3′, 5′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 124.4, 128.4, 128.7, 129.2, 130.9, 133.5, 139.6, 147.9, 174.1; Anal. Calcd for $C_{14}H_9N_3O_2S$: C, 59.35; H, 3.20; N, 14.83. Found: C, 59.31; H, 3.18; N, 14.81.

4i. *2-(3-nitrophenyl)-5-phenyl-1,3,4-thiadiazole*
m.p. 242 ºC, *m*/*z*: 283.04; Mol. Wt: 283.31; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 7.41−7.60 (m, 5H, ArH), 7.69−7.79 (d, 1H, *J* = 8.1 Hz, *J* = 8.7 Hz, 5′- ArH), 7.82−7.88 (d, 1H, *J* = 8.2 Hz, 4′- ArH), 7.90−8.03 (d, 1H, *J* = 8.2 Hz, 6′-ArH), 8.04−8.16 (s, 1H, 2′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 122.8, 123.9, 128.7, 129.2, 130.1, 130.9, 133.5, 134.4, 148.4, 174.1; Anal. Calcd for $C_{14}H_9N_3O_2S$: C, 59.35; H, 3.20; N, 14.83. Found: C, 59.31; H, 3.18; N, 14.81.

4j. *2-phenyl-5-(p-tolyl)-1,3,4-thiadiazole*
m.p. 155 ºC, *m*/*z*: 252.07; Mol. Wt: 252.33; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 2.34 (s, 3H, -CH_3), 7.41−7.60 (m, 5H, ArH), 7.69−7.80 (d, 2H, *J* = 7.9 Hz, 3′,5′-ArH), 7.90−7.98 (d, 2H, *J* = 8.1 Hz, 2′,6′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 21.3, 127.4, 128.7, 129.2, 129.5, 130.5, 130.9, 131.7, 133.5, 174.1; Anal. Calcd for $C_{15}H_{12}N_2S$: C, 71.40; H, 4.79; N, 11.10. Found: C, 71.38; H, 4.77; N, 11.08.

4k. *2-(4-chlorophenyl)-5-(p-tolyl)-1,3,4-thiadiazole*
m.p. 160 ºC, *m*/*z*: 286.03; Mol. Wt: 286.78; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 2.34 (s, 3H, -CH_3), 7.29−7.38 (d, 2H, *J* = 7.8 Hz, 3′′, 5′′-ArH), 7.46−7.55 (d, 2H, *J* = 8.2 Hz, 3′, 5′-ArH), 7.65−7.74 (d, 2H, *J* = 7.8 Hz, 2′′, 6′′-ArH), 8.02−8.15 (d, 2H, *J* = 8.2 Hz, 2′, 6′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 21.3, 127.4, 128.9, 129.3, 129.5, 130.5, 131.6, 131.7, 134.3, 174.1; Anal. Calcd for $C_{15}H_{11}ClN_2S$: C, 62.82; H, 3.87; N, 9.77. Found: C, 62.80; H, 3.85; N, 9.75.

4l. *2-(3-chlorophenyl)-5-(p-tolyl)-1,3,4-thiadiazole*
m.p. 162 ºC, *m*/*z*: 286.03; Mol. Wt: 286.78; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 2.34 (s, 3H, -CH_3), 7.29−7.38 (d, 2H, *J* = 7.8 Hz, 3′′, 5′′-ArH), 7.65−7.74 (d, 2H, *J* = 7.8 Hz, 2′′, 6′′-ArH), 7.77−7.84 (dd, 1H, *J* = 8.1 Hz, *J* = 8.9 Hz, 5′-ArH), 7.86−7.89 (d, 1H, *J* = 8.1 Hz, 4′-ArH), 7.91−8.00 (d, 1H, *J* = 8.3 Hz, 6′-ArH), 8.04−8.13 (s, 1H, 2′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 21.3, 127.4, 128.8, 129.0, 129.5, 130.5, 131.7, 134.8, 134.9, 174.1; Anal. Calcd for $C_{15}H_{11}ClN_2S$: C, 62.82; H, 3.87; N, 9.77. Found: C, 62.80; H, 3.85; N, 9.75.

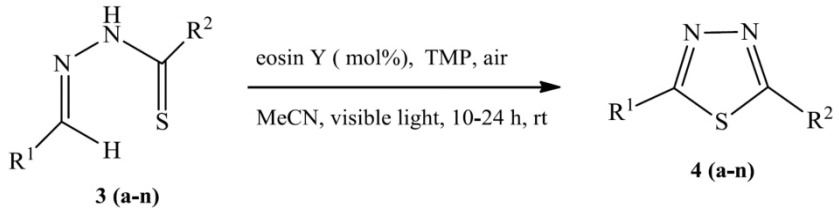
4m. *2-(2-chlorophenyl)-5-(p-tolyl)-1,3,4-thiadiazole*
m.p. 168 ºC, *m*/*z*: 286.03; Mol. Wt: 286.78; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 2.34 (s, 3H, -CH_3), 7.29−7.38 (d, 2H, *J* = 7.8 Hz, 3′′, 5′′-ArH), 7.41−7.60 (m, 7H, ArH, 4′, 5′-ArH), 7.65−7.74 (d, 2H, *J* = 7.8 Hz, 2′′, 6′′-ArH), 7.75−7.84 (d, 1H, *J* = 8.2 Hz, 3′-ArH), 7.86−7.98 (d, 1H, *J* = 8.2 Hz, 6′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 21.3, 127.3, 127.4, 128.9, 129.3, 129.5, 130.1, 130.5, 131.7, 132.2, 136.9, 174.1; Anal. Calcd for $C_{15}H_{11}ClN_2S$: C, 62.82; H, 3.87; N, 9.77. Found: C, 62.80; H, 3.85; N, 9.75.

4n. *2-(4-methoxyphenyl)-5-(p-tolyl)-1,3,4-thiadiazole*
m.p. 220 ºC, *m*/*z*: 282.08; Mol. Wt: 282.36; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*/ppm: 2.34 (s, 3H, -CH_3), 3.83 (s, 3H, -OCH_3), 7.29−7.38 (d, 2H, *J* = 7.8 Hz, 3′′, 5′′-ArH), 7.58−7.69 (d, 2H, *J* = 8.1 Hz, 3′, 5′-ArH), 7.65−7.74 (d, 2H, *J* = 7.8 Hz, 2′′, 6′′-ArH), 8.05−8.13 (d, 2H, *J* = 8.4 Hz, 2′, 6′-ArH), ^{13}C NMR (75 MHz, DMSO-d_6) *δ*/ppm: 21.3, 55.8, 114.8, 125.8, 127.4, 128.5, 129.5, 130.5, 131.7, 160.6, 174.1; Anal. Calcd for $C_{16}H_{14}N_2$ OS: C, 68.06; H, 5.00; N, 9.92. Found: C, 68.03; H, 4.98; N, 9.89.

RESULTS AND DISCUSSION

In order to work out the envisaged protocol, a key reaction was conducted with thioacylhydrazone **3(a−n)** in MeCN containing 2 mol% of eosin Y under an air atmosphere (without air bubbling) by irradiation with visible light (green light-emitting diodes (LEDs), λ max= 535 nm) at rt. The reaction delivered the desired 2,5-disubtituted 1,3,4-thiadiazole **4(a−n)** in 12 % isolated yield after 24h (Table 1, entry 1). Following this experiment, a series of control experiments were performed, which indicates that an organic base is essential to give the desired product with high yield (97 %) (Table 1, entry 2) and TMP was found to be the best base (Table 2, entry 2 versus 6, 7, 9). There was no product formation or it was formed in traces in the absence (−) of any one of the reagents/catalyst (Table 1, entries

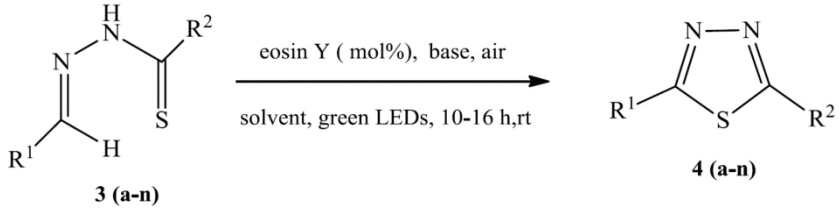
Table 1. Screening and control experiments[a]



Entry	Visible Light	Eosin Y	Air	Time / h	Yield / %[b]
1	+	+	+	24	12[c]
2	+	+	+	10	97
3	−	+	+	24	n.r.[d]
4	+	−	+	24	n.r.
5	+	+	−	24	n.r.
6	+	+	+	10	45[e]
7	+	+	N_2	24	trace
8	+	+	O_2	10	97
9	+	+	+	10	97[f]
10	+	+	+	10	60[g]
11	+	+	+	10	42[h]

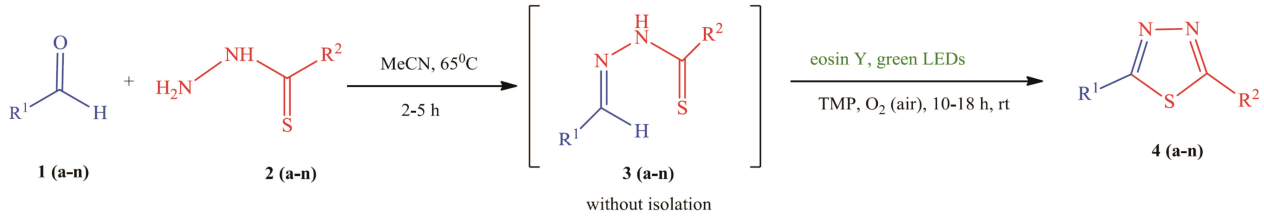
[a]Reaction conditions: thioacylhydrazone (1.0 mmol), eosin Y (2.0 mol%), TMP (2.0 equiv.), MeCN (3.0 mL), green LEDs 2.4W, 120 lm irradiation under an air atmosphere at rt.
[b]Isolated yield of the product (4a−n). n.r. = no reaction.
[c]The reaction was conducted without TMP base in MeCN.
[d]The reaction was carried out in the dark.
[e]The reaction was carried out using 20 W CFL (compact fluorescent lamp).
[f]The reaction was carried out with 3.0 equiv. of TMP.
[g]The reaction was carried out 1.0 equiv. of TMP.
[h]The reaction was carried out with 1.0 mol% of eosin Y.

Table 2. Optimization of reaction conditions[a]



Entry	Eosin Y / mol %	Base	Solvent[c]	Time / h	Yield / %[b]
1	3	TMP	MeCN	10	97
2	2	TMP	MeCN	10	97
3	1	TMP	MeCN	10	42
4	2	TMP	MeOH	16	72
5	2	TMP	EtOH	16	62
6	2	DBU	MeCN	16	52
7	2	DABCO	MeCN	16	55
8	2	TMP	DMSO	10	82
9	2	Et_3N	MeCN	16	65

[a]Reaction conditions: thioacylhydrazone (1.0 mmol), eosin Y (2.0 mol%), TMP (2.0 equiv.), MeCN (3.0 mL), green LEDs 2.4W, 120 lm irradiation under an air atmosphere at rt.
[b]Isolated yield of the product (4a−n).



Scheme 2. One-pot facile synthesis of 1,3,4-thiadizole directly from aldehyde and thioacylhydrazide.

3−5). The reaction did not proceed satisfactorily when a household 20 W fluorescent lamp was used instead of green LEDs (Table 1, entries 6 versus 2). Notably, the same result was obtained on using O_2 (balloon) instead of an air atmosphere (Table 1, entry 8 versus 2), whereas in the absence of any gas or under a nitrogen atmo-sphere no product formation was detected (Table 1, entry 5, 7). These results establish that visible light, base, photocatalyst and air all are essential (+) for the reaction and support the photocatalytic model of the reaction. Thiadiaazole exhibit various biological activities and has greater synthetic utility in medicinal chemistry. The use of novel one-pot visible light irradiated synthesis using eosin Y as an organophotoredox catalyst fullfill the basic need of green chemistry.

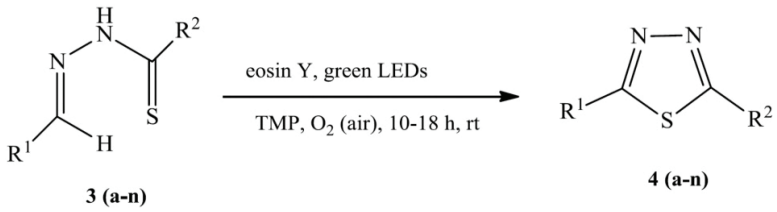
Next, the reaction conditions were optimized with respect to solvents and the catalyst used in the reaction. In all the tested solvents (MeCN, DMSO, MeOH and EtOH) the yield of 4a−n was >55 % (Table 2), which indicates that the reaction is not very sensitive to reaction media. MeCN was the best solvent in terms of the reaction time and yield (Table 2, entry 1), hence it was used throughout the synthesis. When the amount of the catalyst was decreased from 2 mol% to 1 mol%, the yield of **4(a−n)** considerably reduced (Table 2, entry 3), but the use of 3 mol% of the catalyst did not affect the yield (Table 2, entry 1).

Under the established reaction conditions in hand, the reaction was tried in a one-pot procedure starting directly from an aldehyde **1(a−n)** and an thioacylhydrazide **2(a−n)** to give the desired product **4(a−n)** as depicted in Scheme 2.

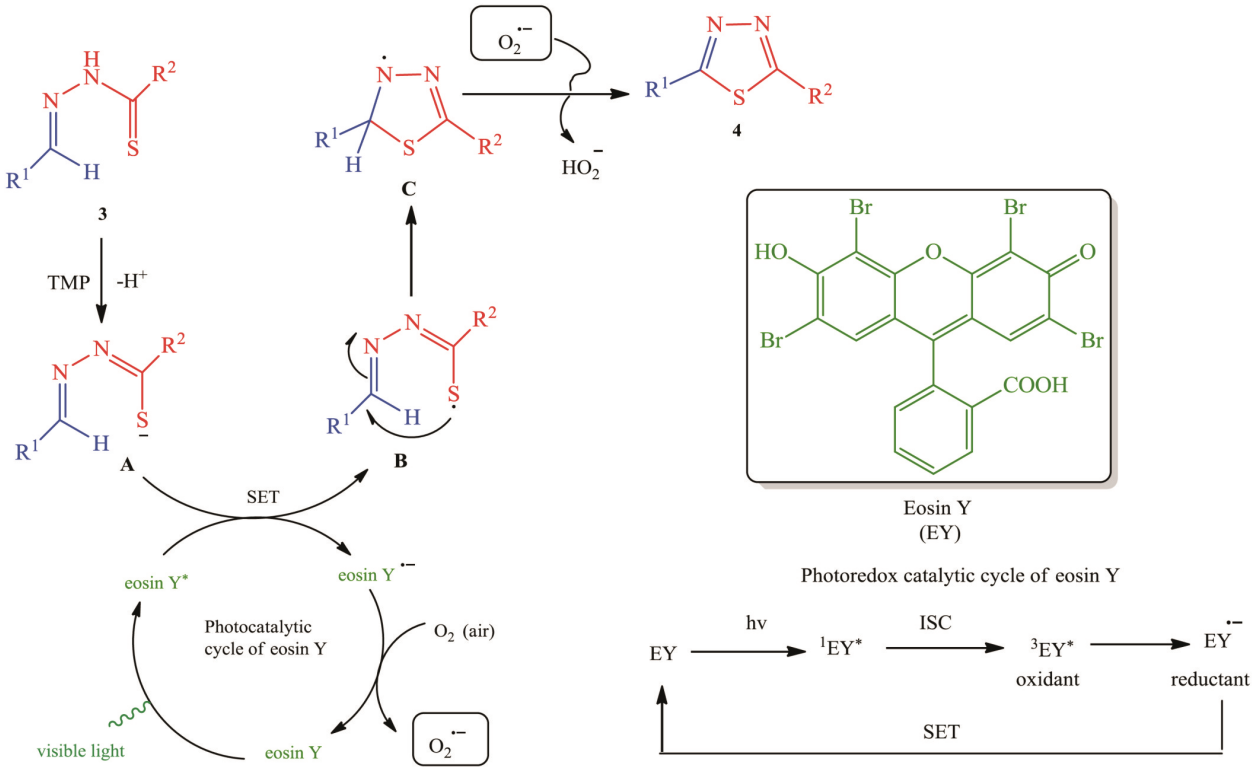
To our delight, it worked well and a number of symmetrical and unsymmetrical 2, 5-disubstituted 1,3,4-thiadiazoles were successfully synthesized starting directly from various aldehydes **1(a−n)** and thioacylhydrazides **2(a−n)** (Tables 3).

This clearly shows that the reaction is very mild and applicable to aryl and alkyl, tolerates considerable functional group variations like MeO, Br, Cl and NO_2 in

Table 3. Eosin Y catalysed synthesis of 1,3,4-thiadizole



Entry	R^1	R^2	Product	Time / h	Yield / %
1	4-Cl.C_6H_4	C_6H_5	4a	14	82
2	3-Cl.C_6H_4	C_6H_5	4b	14	85
3	2-Cl.C_6H_4	C_6H_5	4c	13	87
4	4-OCH_3.C_6H_4	C_6H_5	4d	10	96
5	C_6H_5	C_6H_5	4e	10	92
6	4-Br.C_6H_4	C_6H_5	4f	14	85
7	3-Br.C_6H_4	C_6H_5	4g	14	86
8	4-O_2N.C_6H_4	C_6H_5	4h	18	78
9	3-O_2N.C_6H_4	C_6H_5	4i	18	84
10	4-CH_3.C_6H_4	C_6H_5	4j	10	96
11	4-Cl.C_6H_4	4-CH_3.C_6H_4	4k	12	83
12	3-Cl.C_6H_4	4-CH_3.C_6H_4	4l	12	86
13	2-Cl.C_6H_4	4-CH_3.C_6H_4	4m	11	89
14	4-OCH_3.C_6H_4	4-CH_3.C_6H_4	4n	10	97



Scheme 3. Proposed mechanism for the visible light irradiated synthesis of 1,3,4-thiadiazole using eosin Y as photocatalyst.

the substrate, which results the desired product **4(a–n)** in good to excellent yields (78–97 %). However, aldehydes **1(a–n)** and thioacylhydrazides **2(a–n)** with an electron-donating group on the aromatic ring appear to react faster and afford marginally higher yields in comparison to those bearing an electron withdrawing group.

On the basis of the above observations and the literature precedents, a plausible mechanism involving photoredox catalysis for the oxidative cyclization of acylhydrazones is depicted in Scheme 3. On absorption of visible light, the organophotoredox catalyst eosin Y (EY) is excited to its singlet state ^{1}EY* which through inter system crossing (ISC) comes to its more stable triplet state ^{3}EY* and undergoes a single electron transfer (SET). ^{3}EY* may undergo both reductive and oxidative quenching.[45–49] A SET from A to ^{3}EY* generates thioacyl radical B, which undergoes intramolecular cyclization (5-*endo-trig*) to form C followed by attack of $O_2^{\bullet-}$ to give the product **4**, successively. The formation of superoxide radical anion ($O_2^{\bullet-}$) during the reaction was confirmed by the detection of the resulting H_2O_2 using KI/starch indicator.[50]

CONCLUSION

In conclusion, we have developed a novel organocatalysed method for the synthesis of 1,3,4-thiadiazoles directly from aldehydes and thioacylhydrazides in a one-pot procedure by using inexpensive eosin Y as a powerful organophotoredox catalyst at rt. The reaction involves visible light, a base and O_2 (air) as a valuable reagents. This synthetic pathway includes a superior visible light promoted and Eosin Y organophotoredox catalysed methodology, which is superior in comparison to all other alternative synthetic methods for 1,3,4-thiadiazoles. This synthesis widens the scope of substrates for visible light photoredox reactions. The present methodology also offers many advantages of green chemistry such as high atom economy, reduced reaction time, one-pot consolidated procedure and high efficiency.

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REFERENCES

1. N. S. Lewis, *Science* **315** (2007) 798–801.
2. O. Morton, *Nature* **443** (2006) 19–22.
3. D. G. Nocera, *Daedalus* **135** (2006) 112–115.
4. D. Mandler and I. Willner, *J. Am. Chem. Soc.* **106** (1984) 5352–5353.
5. O. Ishitani, S. Yanagida, S. Takamuku, and C. Pac, *J. Org. Chem.* **52** (1987) 2790–2796.
6. D. A. Nicewicz and T. M. Nguen, *ACS Catal.* **4** (2014) 355.
7. J. Xiea, H. Jina, P. Xua, and C. Zhu, *Tetrahedron Lett.* **55** (2014) 36.
8. X. Lang, X. Chen, and J. Zhao, *Chem. Soc. Rev.* **43** (2014) 473.

9. J. Hu, J. Wang, T. H. Nguyen, and Zheng, *Beilstein J. Org. Chem*. **9** (2013) 1977.
10. D. Rovelli, M. Fagnoni, and A. Albini, *Chem. Soc. Rev*. **42** (2013) 97.
11. T. P. Yoon, M. A. Ischay, and J. N. Du, *Nat. Chem*. **2** (2010) 527.
12. D. A. Nicewicz and D. W. C. MacMillan, *Science* **322** (2008) 77.
13. M. A. Ischay, M. E. Anzovino, J. Du, and T. P. Yoon, *J. Am. Chem. Soc*. **130** (2008) 12886.
14. J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev*. **40** (2011) 102.
15. J. M. R. Narayanam, J. W. Tucker, and C. R. J. Stephenson, *J. Am. Chem. Soc*. **131** (2009) 8756.
16. J. W. Tucker and C. R. J. Stephenson, *J. Org. Chem*. **77** (2012) 1617.
17. X.-J. Yang, B. Chen, L.-Q. Zheng, L.-Z. Wu, and C.-H. Tung, *Green Chem*. **16** (2014) 1082.
18. Y. C. Teo, Y. Pan and C. H. Tan, *ChemCatChem*. **5** (2013) 235.
19. K. Fidaly, C. Ceballos, A. Falguières, M. S.-I. Veitia, A. Guy, and C. Ferroud, *Green. Chem*. **14** (2012) 1293.
20. D.-T. Yang, Q.-Y. Meng, J.-J. Zhong, M. Xiang, Q. Liu, and L.-Z. Wu, *Eur. J. Org. Chem*. (2013) 7528.
21. Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Davis, K. A. Jørgensen and W.-J. Xiao, *Angew. Chem. Int. Ed*. **51** (2012) 784.
22. D. P. Hari and B. König, *Org. Lett*. **13** (2011) 3852.
23. M. Neumann, S. Füldner, B. König, and K. Zeitler, *Angew. Chem. Int. Ed*. **50** (2011) 951.
24. V. Rey, S. Soria-Catro, J. E. Argüello, and A. B. Peñéñory, *Tetrahedron Lett*. **50** (2009) 4720.
25. S. Schenone, C. Brullo, O. Bruno, F. Bondavalli, A. Ranise, W. Filippelli, B. Rinaldi, A. Capuano, and G. Falcone, *Bioorg. Med. Chem*. **14** (2006) 1698.
26. F. Clerici and D. Pocar, *J. Med. Chem*. **44** (2001) 931.
27. M. R. Stillings, A. P. Wellbournt, and D. S. Walter, *J. Med. Chem*. **29** (1986) 2280.
28. C. B. Chapleo, M. Myers, P. L. Myers, J. F. Saville, A. C. B. Smith, M. R. Stillings, I. F.Tulloch, D. S. Walter, and A. P. Welbourn, *J. Med. Chem*. **29** (1986) 2273.
29. M. D. Mullicon, M. W. Willson, D. T. Conor, C. R. Kostlan, and D. J. Schrier, *J. Med. Chem*. **36** (1993) 1090.
30. S. Servi, M. Genc, S. Gur, and M. Koca, *Eur. J. Med. Chem*. **40** (2005) 687.
31. A. Foroumadia, S. Enamic, A. Hassanzadehb, M. Rajaeeb, K. Sokhanverb, M. Hasan, and A. Shafieea, *Bioorg. Med. Chem. Lett*. **15** (2005) 4488.
32. E. E. Oruc, S. Rollas, F. Kandemirli, N. Shvets, and A. S. Dimoglo, *Bioorg. Med. Chem. Lett*. **12** (2004) 5651.
33. J. Matysiak, *Chem. Pharm. Bull*. **54** (2006) 988.
34. E. Roduner, W. Kaim, B. Sarkar, V. B. Urlacher, J. Pleiss, R. Glser, W.-D. Einicke, G. A. Sprenger, U. Beifuß, E. Klemm, C. Liebner, H. Hieronymus, S.-F. Hsu, B. Plietker, and S. Laschat, *ChemCatchem* **5** (2013) 82.
35. Z. Shi, C. Zhang, C. Tang, and N. Jiao, *Chem. Soc. Rev*. **41** (2012) 3381.
36. D. P. Hari, T. Hering, and B. König, *Org. Lett*. **14** (2012) 5334.
37. S. Samanta, S. Das, and P. Biswas, *J. Org. Chem*. **78** (2013) 11184.
38. G. Crank and A. J. Mursydi, *PhotoChem. Photobio*. **53** (1990) 30.
39. Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Davis, K. A. Jørgensen, and W.-J. Xiao, *Angew. Chem. Int. Ed*. **51** (2012) 784.
40. J. Zhang, L. Wang, Q. Liu, Z. Yang, and Y. Huang, *Chem. Commun*. **49** (2013) 11662.
41. I. R. Siddiqui, P. K. Singh, V. Srivastava, and J. Singh, *Indian J. Chem.* **46B** (2007) 1716−1720.
42. V. Srivastava, P. K. Singh, and P. P. Singh, *Croat. Chem. Acta* **87(2)** (2014) 91.
43. V. Srivastava, P. K. Singh, and P. P. Singh, *Chemistry of Heterocyclic Compounds* **50(4)** (2014) 573.
44. P. K. Singh and I. R. Siddiqui, *Indian J. Chem*. **48B** (2009) 1013.
45. D. C. Neckers and O. M. Valdes-Aguilera, *Adv. Photochem*. **18** (1993) 315.
46. M. V. Encinas, A. M. Rufs, S. G. Bertolotti, and C. M. Previtali, *Polymer* **50** (2009) 2762.
47. T. Lizarides, T. McCormick, P. Du, G. Luo, B. Lindley, and R. Eisenberg, *J. Am. Chem. Soc.* **131** (2009) 9192.
48. S. H. Lee, D. H. Nam, and C. B. Park, *Adv. Synth. Catal.* **351** (2009) 2589.
49. T. Xiao, X. Dong, Y. Tang, and L. Zhou, *Adv. Synth. Catal.* **354** (2012) 3195.
50. G. K. Fekarurhobo, S. S. Angaye, and F. G. Obomann, *J. Emerg. Trends Engg. Appl. Sci. (JETEAS)*, **4** (2013) 394.