

Sustainable and Advanced LED-Implanted Microfluidic Photoreactor with Coupled Optical Fiber Enabling Efficient Photocatalytic Synthesis Beside Online Reaction Progress Monitoring

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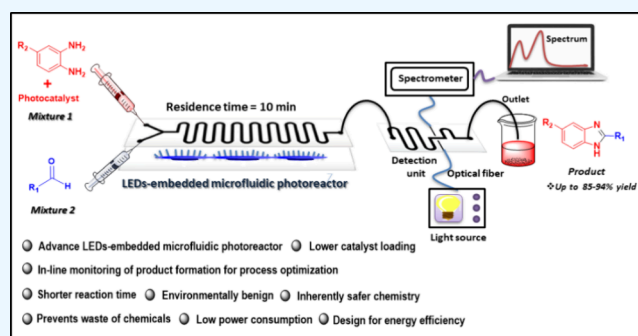
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ABSTRACT: The conventional methods for the photoinduced synthesis of benzimidazoles may need further improvement regarding a safer and energy-efficient synthesis platform with in-process monitoring for maximum yield within a much reduced reaction time. This work describes the use of a novel optofluidic Lab-on-a-Chip technology for safer, energy-efficient, and expedited synthesis of benzimidazole derivatives in excellent yields along with real-time quantitative measurement during product formation. This innovative method involves synthesis within LED-embedded microfluidic reactors, allowing for rapid synthesis of benzimidazole derivatives via photoinduced condensation cyclization reactions of aryl aldehydes and *o*-phenylenediamines using a Rose Bengal/fluorescein photocatalyst. It results in good to excellent yields (85–94%) in a notably shorter period of time (10 min) as compared to that for the batch protocol reaction (2–3 h). The incorporation of a reaction-monitoring microfluidic device precisely connected to the microfluidic reactor (microreactor) unit successfully avoids interference from light sources, ensuring consistent UV–vis spectroscopic observations of the produced benzimidazole derivatives. This LED-embedded microfluidic device's capability of photoinduced synthesis, along with real-time spectroscopic analysis, represents a promising breakthrough in organic synthesis. The proposed approach minimizes the potential for accidents, prevents waste of chemicals, maximizes atom economy, and designs an energy-efficient synthesis route, along with real-time in-process monitoring.



1. INTRODUCTION

Benzimidazole and its derivatives are indispensable scaffolds in a variety of agrochemicals and naturally occurring compounds.^{1,2} It shows an extensive range of biological and therapeutic properties, including antihypertensive,³ anticancer,⁴ antiviral,⁵ and antifungal⁶ activity. Benzimidazole core scaffolds have been also employed as conjugated and functional group polymers,⁷ NHC (*N*-heterocyclic carbene) precursors,⁸ and convenient precursors to ionic liquids,⁹ with prospective uses in photophysical domains, such as organic light-emitting diode (OLED) technology¹⁰ acting as ligands in metal-mediated reactions.¹¹ As a result, the synthesis of benzimidazoles and their derivatives has been particularly appealing because of their broad application potential. Condensation and intramolecular cyclization of aryl aldehydes and *o*-phenylenediamines have long been essential approaches for the synthesis of substituted benzimidazoles. These reactions have mostly been performed by employing metal catalysts,^{12–15} Brønsted acids,^{16–18} various heterogeneous acidic catalysts,^{19–21} and ionic liquids.^{22–24} Despite their effectiveness, most of these methods suffer from some

disadvantages such as harsh reaction conditions, including strong acids, high catalyst loadings, expensive or toxic catalysts or reagents, and low reaction efficiency even at prolonged reaction times. Therefore, it is desirable to discover highly efficient and environmentally friendly synthetic routes through a sustainable strategy to access such heterocyclic compounds.

On the other hand, visible-light photoredox catalysis under benign reaction conditions and low catalyst loadings has emerged as a fascinating and powerful platform to promote several synthetic organic transformations via a unique single electron transfer (SET) process in a clean, inexpensive, and renewable manner.²⁵ In particular, the dehydration–cyclization reaction between aryl aldehydes and *o*-phenylenediamines

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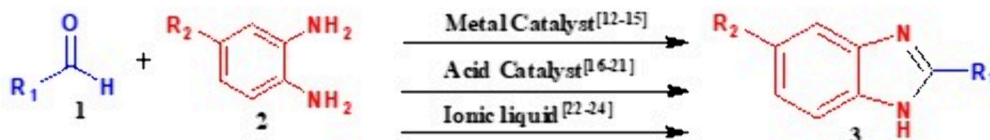
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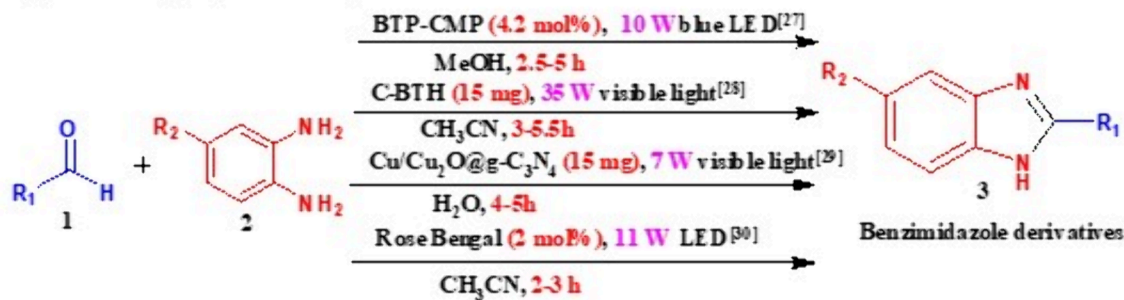
Scheme 1. Comparative Synthesis of Benzimidazoles in the Previous Reported Works and This Work

Previous work

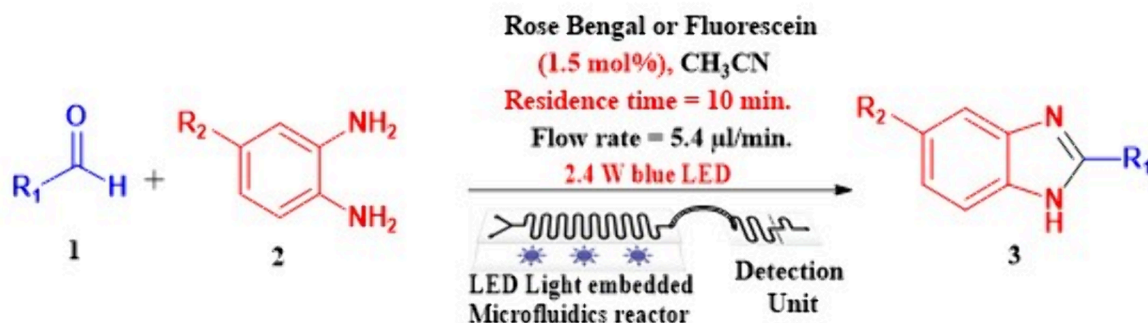
(a) Classical method for the synthesis of benzimidazoles in batch condition



(b) Visible light promoted synthesis of benzimidazoles in batch condition



- Longer reaction time
- High catalyst loading
- High power light source
- Large amount of waste
- Low reaction efficiency
- Harsh reaction condition

This work:

- Advance LEDs-embedded microfluidic photoreactor
- Lower catalyst loading
- Shorter reaction time
- In-line monitoring of product formation for process optimization
- Prevents waste of chemicals
- Inherently safer chemistry
- Environmentally benign
- Low power consumption
- Design for energy efficiency

induced by visible light photoredox catalysis has extensively used as a versatile tool to synthesize benzimidazole derivatives. Several innovative endeavors have demonstrated the enormous potential of photoredox catalysis with visible light for the synthesis of benzimidazoles using aryl aldehydes and *o*-phenylenediamines. For example, Samanta et al.²⁶ reported the use of 3,6-di(pyridin-2-yl)-1,2,4,5-tetrazine (pytz), An et al.²⁷ illustrated the use of thiophene-embedded conjugated microporous polymers (BTP-CMP) as photocatalysts for benzimidazole synthesis, Jakhade et al.²⁸ introduced an

efficient CTAB-Coated Bi₂WO₆ photocatalyst, and Singh et al.²⁹ utilized a unique Cu/Cu₂O@g-C₃N₄ photocatalyst and for the synthesis of benzimidazoles. Additionally, Kovvuri et al.³⁰ and Li et al.³¹ used Rose Bengal and fluorescein as photocatalysts to show visible-light-induced condensation cyclization reactions to synthesize substituted benzimidazoles. Notably, all of these reactions are performed in batch systems.

Recently, the application of microfluidic reactors has been a very capable approach in organic chemistry,³² and one of the research domains in which microfluidics has revealed higher

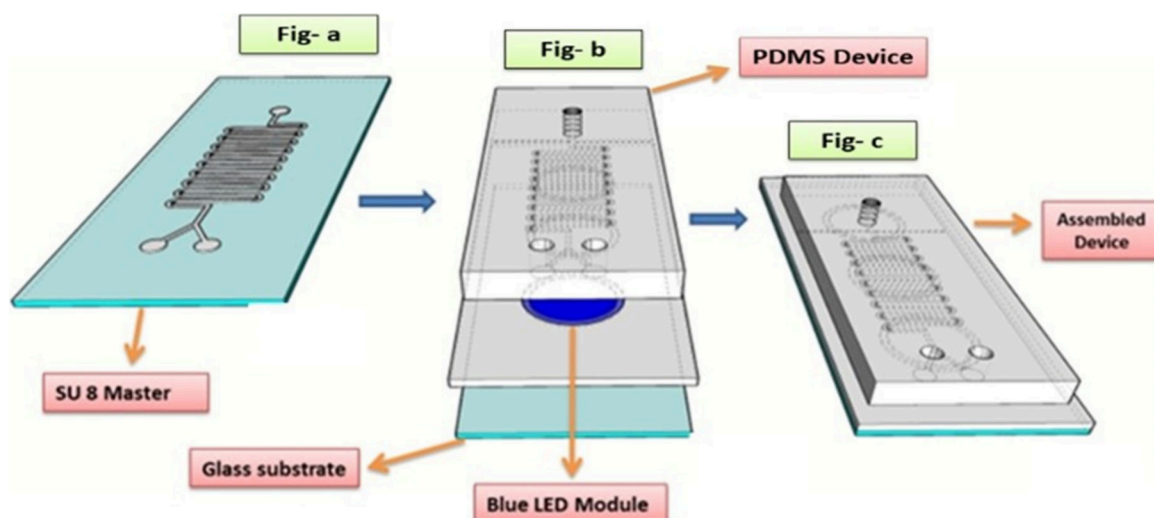


Figure 1. Schematic diagram for fabrication of the device: (a) Fabricated SU-8 master. (b) Alignment of all the components, including the PDMS, microfluidic reactor, LED source, and glass substrate. (c) Final assembly of all the microfluidic reactor device.

potential is photochemistry with visible light.³³ Moreover, it is well documented that photochemical transformation in a microreactor with a high surface-to-volume ratio would improve the energy transfer efficiency between the light source and reaction mixture with lower catalyst loadings due to the inherently outstanding mass transfer and small illumination path over the conventional batch reactor.³⁴ There are numerous benefits when directing conversions in microfluidic reactors in comparison to batch reactions. Specifically, these include added foreseeable reaction scale-up, reduced safety threats, enhanced reproducibility, boosted yields, shorter reaction times, and lower catalyst loadings.

In batch reactors, only substrate molecules adjacent to the exterior of the solution engross optical power when they are available in elevated concentrations and have high molar absorption coefficients. Additional limitations are that major products, which have extended residence time in batch reactors, can also engross light and be converted into secondary products. However, in the microfluidic reactor, light is absorbed throughout the whole reaction mixture in a microfluidic system, even when the substrate exists in a small concentration and has a minor molar absorption coefficient. Furthermore, the primary product is prohibited from amassing owing to its quicker residence time in the illuminated section.

Having all of these advantages in mind, herein, we report a visible-light-promoted photoredox catalysis in novel LED-embedded microfluidic photoreactors for the synthesis of substituted benzimidazoles using aryl aldehydes and *o*-phenylenediamines with a green and readily accessible Rose Bengal/fluorescein photocatalyst. In this innovative design, LEDs are embedded at the bottom of the microchannel of microfluidic photoreactor, which leads to an efficient visible-light-promoted photoredox catalysis.

Furthermore, we have integrated the optoelectronic components with the microchannel via the optical fiber to precisely monitor and measure the UV–vis absorbance characteristics of the reaction mixture in the microfluidic reactor to define the completion of the reaction.

The optical fiber-coupled microfluidics empowers real-time monitoring, detailed control, and multiplexed measurements, which enhance organic synthesis by minimizing waste and improving safety. These fibers act as channels for light,

allowing for the efficient delivery and collection of photons within the microfluidic reactor. This innovative system employs optoelectronic mechanisms and microfluidic channels to produce a precise environment for chemical reactions on a minuscule scale.

Overall, the execution of an optical-fiber-coupled LED-embedded microfluidic reactor in organic synthesis and consecutive UV–vis absorbance measurement represent substantial advancements in the field of organic synthesis and analysis. This technology holds promise for streamlining the process of synthesizing complex molecules with high precision and efficiency.

LED-embedded microfluidic reactors offer several key advantages, including better control over light delivery, which can lead to more consistent and efficient reaction processes. These reactors ensure direct and proximate illumination of reaction sites by embedding LEDs within the microfluidic devices. The principle of the *inverse square law* states that the light intensity decreases with the square of the distance from the source. The closer proximity of the LEDs to the reaction area increases the likelihood of photons being absorbed by the reactants, thus boosting the efficiency of photon-induced processes, such as photochemical reactions. This design reduces the distance that light travels, enhancing the optical intensity and the quantum yield. This design also contributes to a more compact and integrated setup, which is particularly beneficial for portable or miniaturized systems where space is limited.

Scheme 1 represents the comparative synthesis of benzimidazoles in previously reported works and in this work.

2. DESIGN AND FABRICATION

The proposed microfluidic device was made using a PDMS polymer via a customized microfabrication technique. The lengths of the microchannels in the fabricated microreactor unit and the reaction monitoring unit device were taken as 56 and 4 cm, respectively. The width and height of both the microreactor unit and reaction monitoring units were taken as 600 and 150 μm , respectively. Furthermore, as the blue LEDs were intended to align beneath the proposed microreactor channel, they were positioned and cast using the PDMS

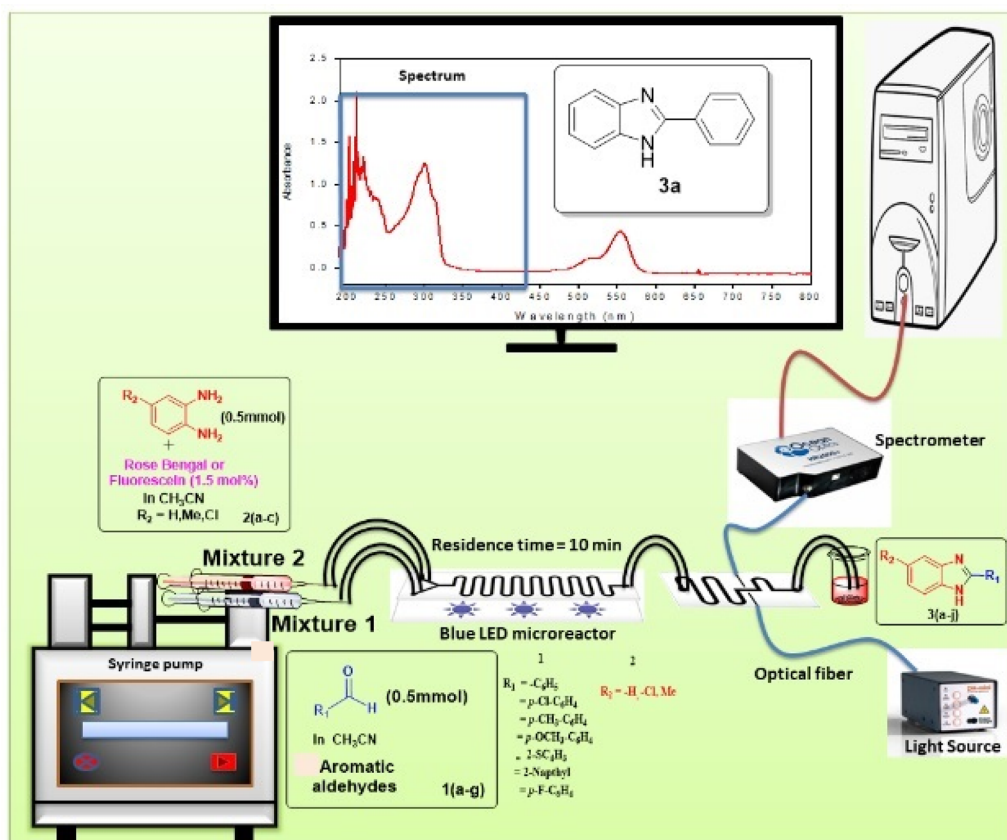


Figure 2. Schematic of the experimental setup for microfluidics synthesis of 2-aryl benzimidazoles with photocatalyst via condensation–cyclization of aryl aldehydes and *o*-phenylenediamines in visible light, as well as the monitoring of product formation.

polymer in such a way that this microfluidic device sits on top of it (figure 1). This procedure necessitates the creation of a SU-8 master mold via a general photolithographic process,^{35–37} which serves as a master mold for developing desired copies of the microfluidic channels via soft lithography using the PDMS elastomer. The initial steps, as usual, include substrate selection, SU-8 spin coating, pre-exposure bake, SU-8 UV exposure, post-exposure bake, SU-8 development, and rinse drying, which is similar to our previously reported studies^{35–40} (mentioned in the Supporting Information). Furthermore, as reported in our previously reported study,⁴¹ subsequent to the fabrication of the SU-8 master, the PDMS device was fabricated using the soft lithography technique. Furthermore, appropriate inlets and outlet ports were punched within the fabricated polymer microfluidic channel device. The blue LED module was securely mounted over the glass slide before being cast with the PDMS layers, thereby establishing a leveled surface for subsequent attachment of the microfluidic device.

To achieve an even platform, the top/front face of the blue LED module was cast with a 10:1 mixture of PDMS prepolymer and its curing agent and then cured at 70 °C in order to obtain a uniform surface for further microfluidic device placement and bonding. Following that, the PDMS-casted top face of blue LED module was then bonded using the corona-discharge treatment to the fabricated microfluidic channel device in such a way that the microfluidic device perfectly aligned on the top of the blue LED module as indicated in Figure 1c. The details regarding the corona discharge treatment have been included in the Supporting

Information in section 5 on page S9. Using this novel approach, the miniature blue LEDs embedded at several segments of the microchannel (Figure 1b) allowed for appropriate coupling of irradiation within the microchannel for proper light-sensitized reaction. After the assembly of the complete device, the optical microfluidic device is ready to be tested, as shown in Figure 1c. The schematic diagram for the fabrication steps of the aforementioned novel device is shown in Figure 1a–c.

3. EXPERIMENTAL SET-UP

Aromatic aldehyde 1 (0.5 mmol) in 2 mL of CH₃CN and *o*-phenylenediamine 2 (0.5 mmol) with Rose Bengal/fluorescein (1.5 mol %) photocatalysts in 2 mL of CH₃CN were taken in different syringe pumps connected to the respective two inlets of the microfluidic reactor. Further, both substrates were pumped, simultaneously, through the microfluidic reactor irradiated with the three embedded 2.4 W blue LEDs, and a residence time of 10 min was maintained by adjusting the flow rate via a peristaltic pump.

Furthermore, the product of the reaction, i.e., 2-aryl benzimidazole 3, coming out of the microfluidic reactor was analyzed via passing through the reaction monitoring microfluidic device. In this microfluidic device, the microchannel was optically coupled with a light source (Ocean Optics) and a fiber optic spectrometer (USB-4000, Ocean Optics) via respective optical fibers.

Figure 2 presents the schematic of the experimental setup for the microfluidic synthesis of 2-aryl benzimidazoles via condensation–cyclization of aryl aldehydes and *o*-phenylenedi-

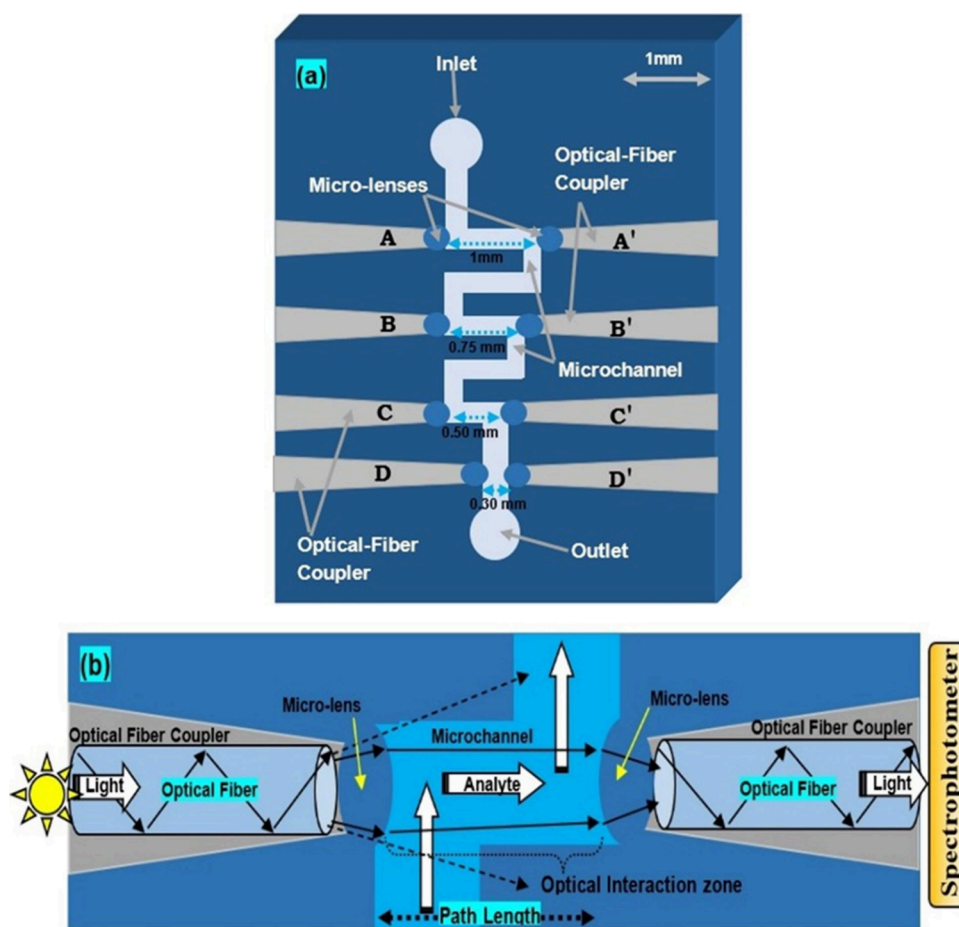


Figure 3. (a) Schematic design of the novel reaction progress monitoring microfluidics device containing a “microlens coupled microchannel”, along with optical fiber coupler structures. The A–A′, B–B′, C–C′, and D–D′ parts of the figure denote the position of the optical source and sensor, with optical fiber coupler structures at optical path distances of 1, 0.75, 0.5, and 0.30 mm, respectively. (b) Enlarged view of the schematic diagram of the interaction zone of the reaction mixture in the microlens-coupled “z-shaped microchannel”, with optical energy received from the light source and conducted to a spectrometer via individual optical fibers.

amines using a photocatalyst in visible light along with the monitoring of product formation.

The schematic design of the novel reaction-progress-monitoring microfluidic device containing a “microlens-coupled microchannel”, along with optical fiber coupler structures, is depicted in Figure 3a. The A–A′, B–B′, C–C′, and D–D′ parts of the figure denote the position of the optical source and sensor, with optical fiber coupler structures at optical path distances of 1, 0.75, 0.5, and 0.30 mm, respectively. Figure 3b presents the enlarged view of the schematic diagram of the interaction zone of the reaction mixture in a microlens-coupled “z-shaped microchannel”, with optical energy received from a light source and conducted to spectrometer via individual optical fibers. The overall experimental setup is very similar to our earlier reported studies.^{35–40} The purpose of setting parts A–A′, B–B′, C–C′, and D–D′ to 1, 0.75, 0.5, and 0.3 mm in the monitoring microfluidic device has been mentioned in the Supporting Information, subsection 6. Figure 4 shows the actual image of a fully assembled experimental setup for the synthesis of benzimidazole derivatives in a microfluidic photoreactor with a monitoring unit.

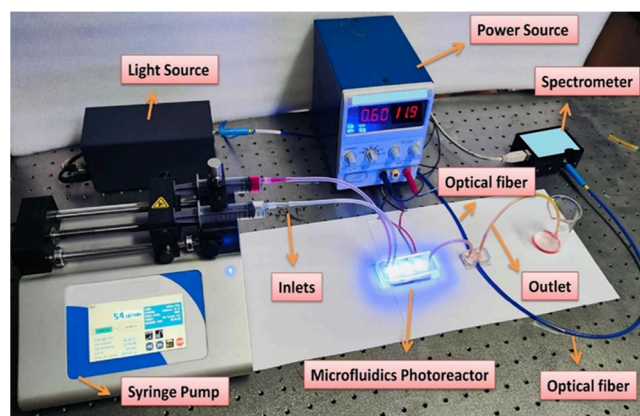
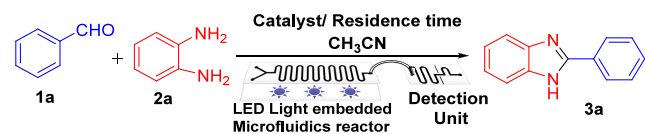


Figure 4. Fully assembled setup for the synthesis and monitoring of benzimidazole derivatives.

4. RESULTS AND DISCUSSION

We turned our attention toward the applications of LED-embedded PDMS-polymer microfluidic reactors for the visible-light-promoted photocatalytic synthesis of benzimidazoles. Here, the reaction conditions have been optimized in terms of the wavelength of the light source, the residence time, and the quantity of photoredox catalyst (Table 1).

Table 1. Optimization of Reaction Conditions in the Microfluidic Reactor under Photocatalytic Conditions^a

entry	Catalysts (mol %)	Light Source	residence time (min)	yield (%) ^b
1	Rose Bengal (2 mol %)	white	18	72
2	Rose Bengal (2 mol %)	red	18	62
3	Rose Bengal (2 mol %)	green	18	68
4 ^c	Rose Bengal (2 mol %)	blue	18	92
5 ^d	Rose Bengal (2 mol %)	blue	10	92
6	Rose Bengal (1.5 mol %)	blue	10	91
7	Rose Bengal (1 mol %)	blue	10	72
8	fluorescein (2 mol %)	blue	10	93
9	fluorescein (1.5 mol %)	blue	10	92
10	fluorescein (1 mol %)	blue	10	80
11 ^e		blue	30	Trace
12 ^f	Rose Bengal/fluorescein (1.5 mol %)	no light (with heat)	30	Trace

^aReactions conditions: a mixture of benzaldehyde **1a** (0.5 mmol, 1 equiv) with 2 mL of CH₃CN and *o*-phenylenediamine **2a** (0.5 mmol, 1 equiv) with Rose Bengal/fluorescein (1.5 mol %) in 2 mL of CH₃CN was pumped through microfluidics device irradiated with 2.4 W blue led light. ^bIsolated yields after column chromatography. ^cReaction performed at 3 μL/min flow rate. ^dReaction performed at 5.4 μL/min flow rate. ^eIn the absence of any catalyst. ^fIn the absence of any light source, reaction was conducted at 80 °C on hot plate within the microreactor.

For the optimization studies, we started our experiment in a microfluidic reactor utilizing benzaldehyde **1a** (0.5 mmol) and *o*-phenylenediamine **2a** (0.5 mmol) as the model substrates with Rose Bengal (2 mol %) as the photocatalyst in CH₃CN solvent, which was irradiated by white, red, green, or blue LEDs light for residence time of 18 min. Here, the reaction occurs with relatively lower yields of **3a**, i.e., 72% with the white LEDs (Table 1, entry 1), 62% with the red LEDs (Table 1, entry 2), and 68% with the green LEDs (Table 1, entry 3), and much higher yield (i.e., 92% yield) with the blue LEDs (Table 1, entry 4). The aforementioned investigation (Table 1, entries 1–4) indicated that the employment of blue LEDs light resulted in much higher yields. Further, to derive an optimum minimum residence time for the augmented yield of the desired product **3a**, we repeated the above-mentioned experiments with the blue LEDs at a lower residence time of 10 min, which resulted in a similar higher yield, i.e., 92% (Table 1, entry 5). Further, the reduction in residence time resulted in a decrease in yield.

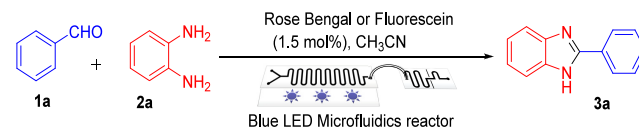
Additionally, the optimum loading quantity of two different catalysts (i.e., Rose Bengal and fluorescein) was quantified in subsequent experiments (Table 1, entries 5–10). The investigations show that optimum 1.5 mol % photocatalyst loading provides larger yields of product **3a** for both photocatalysts, i.e., 91% for Rose Bengal (Table 1, entry 6) and 92% for fluorescein (Table 1, entry 9) at a lower residence time (i.e., 10 min). Moreover, reducing the amount of photocatalyst (i.e., 1 mol %) adversely affected the yields of product **3a** (Table 1, entries 7 and 10 at residence time of 10 min). On the other hand, a larger photocatalyst amount (i.e., 2 mol %) at 10 min residence time did not result in a noticeable increase in the yield (Table 1, entries 5 and 8). With this, it can

be concluded that the 1.5 mol % optimum amount of the Rose Bengal or fluorescein photocatalyst in CH₃CN is more productive regarding both chemical yields and catalytic efficiency. The overall reasons for the observed lower catalyst loading have been explained in the Supporting Information in section 11.

We conducted distinct control experiments on the effectiveness of photocatalysts and the impact of visible light irradiation toward the advancement of the reaction (Table 1, entries 11 and 12). All of these investigations illustrate the significance of the sufficient amount of photocatalysts and visible light irradiation for the synthesis of benzimidazoles in the microfluidic reactors. To ensure the absence of a heating effect of the illuminating LEDs on the conducted reaction, the experiment was performed at 80 °C for 30 min on a hot-plate within the microreactor in the absence of any light source, which resulted in the formation of a trace amount of product (Table 1, entry 12). This ensures the insignificance of the heating effect of illuminating LEDs on the conducted reaction.

In conclusion, optimization studies indicated that 1.5 mol % photocatalyst (i.e., Rose Bengal or fluorescein) in CH₃CN (as a solvent) irradiated with blue LEDs at 10 min residence time in microreactor provides the best conditions for our aforesaid reaction.

Two different solutions, i.e., benzaldehyde **1a** in CH₃CN and *o*-phenylenediamine **2a** with Rose Bengal/fluorescein in CH₃CN, were respectively taken in two separate syringe pumps. Further, various similar flow rates (Table 2) ranging

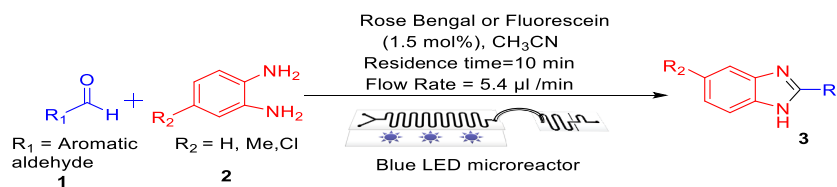
Table 2. Effect of Residence Time^a in PDMS microreactor on photocatalytic synthesis of benzimidazole derivatives with Rose Bengal/Fluorescein^b

S.N.	flow rate (μL/min)	residence time (min)	yields (%) ^c with Rose Bengal	yields (%) ^c with fluorescein
1	27.0	2	18	23
2	13.5	4	43	46
3	9.0	6	64	70
4	6.7	8	79	81
5	5.4	10	91	92
6	4.5	12	91	92

^aNamely, the flow rate of reactants. ^bReaction conditions: a mixture of benzaldehyde **1a** (0.5 mmol) in 2 mL of CH₃CN and *o*-phenylenediamine **2a** (0.5 mmol) with Rose Bengal/fluorescein (1.5 mol %) in 2 mL of CH₃CN was pumped through microfluidics device irradiated with three 2.4 W blue LEDs embedded in microfluidic reactors, ^cIsolated yields of chromatographically pure products with Rose Bengal and fluorescein photocatalysts. Dimensions of microfluidic reactor: length 60 cm, width 600 μm, and height 150 μm.

from 27.0 to 4.5 μL/min for both the reactants were employed via the respective syringe pumps to analyze the effect of different residence times of the reaction mixture inside the PDMS microfluidic reactor on the yield of the product. While the equivalent flow rates of both reactants were reduced from 27.0 to 4.5 μL/min (Table 2, entries 1–6), the yield of 2-phenylbenzimidazole **3a** increased from 18% to 91% with the Rose Bengal catalyst and 23% to 92% with the fluorescein catalyst, attaining a peak yield at 5.4 μL/min only with 10 min

Table 3. Substrate Scope in Microfluidics Reactors



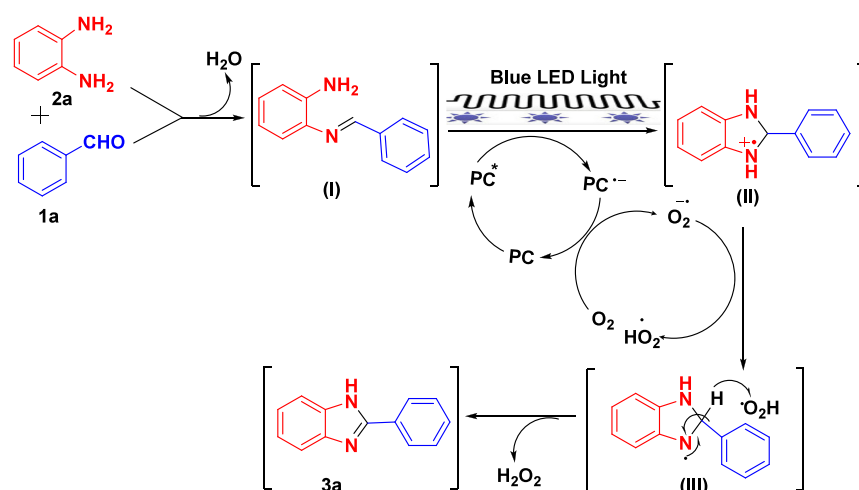
Entry	Aromatic Aldehyde (Substrate 1)	O-Phenylenediamines (Substrate 2)	2-Aryl benzimidazole 3	Rose Bengal	Fluorescein	melting point(°C)/color
				Yields (%) ^b	Yields (%) ^c	
1.				91	92	291-292/white
2.				92	94	293-294/ light brown
3.				90	91	273-274/white
4.				90	92	225-227/white
5.				85	88	>320/ light brown
6.				86	89	210-212/white
7.				89	90	231-232/ off-white
8.				89	91	175-176/ buff color solid
9.				87	90	162-164/ light brown
10.				88	90	181-183/white

^aReactions conditions: aryl aldehydes **1** (0.5 mmol) with 2 mL of CH₃CN and *o*-phenylenediamines **2** (0.5 mmol) with Rose Bengal/fluorescein (1.5 mol %) in 2 mL of CH₃CN were pumped through the microfluidic device irradiated with three 2.4 W blue LED light, and a residence time of 10 min was applied. ^{b,c}Isolated yields after column chromatography.

residence time (Table 2, entry 5). Surprisingly, excellent yield of the product **3a** inside the microreactor was observed with only 10 min residence time (Table 2, entry 5), which is

significantly lower compared to the 2–3 h reaction time for batch reactors.^{30,31} This can be explained by the augmented illumination uniformity and shorter path length of the light

Scheme 2. Plausible Reaction Mechanism for the Synthesis of 2-Phenyl Benzimidazoles under Microfluidic Conditions in the Presence of Photocatalyst



source for LEDs coupled inside the microreactor, signifying the greater optical power present in the introduced reaction mixture. In our experiments, facts related to the power of the LEDs and optical intensity are mentioned in the Supporting Information, section 12. The relationship between flow rate, residence time, and yield has been presented in the Supporting Information in section 9.

In general, the reaction inside the microreactor provided the highest yield at an optimum flow rate of 5.4 $\mu\text{L}/\text{min}$, and nearly no changes were observed when the flow rate was decreased 4.5 $\mu\text{L}/\text{min}$ (Table 2, entries 6). The Reynold's number for the optimum flow rate of 5.4 $\mu\text{L}/\text{min}$ is presented in the Supporting Information in section 10.

4.1. Substrate Scope in Microfluidics Reactors. With the optimized conditions in hand, we turned our consideration to determining the substrate scope for the photocatalytic condensation–cyclization reaction of aryl aldehydes (**1**) with *o*-phenylenediamines (**2**) in the microfluidic reactor as shown in Table 3. A variety of aryl aldehydes reacted smoothly with unsubstituted or chloro/methyl-substituted *o*-phenylenediamines in the PDMS microfluidic reactor under the flow conditions to yield the desired substituted benzimidazoles efficiently (85–94% yields) in only 10 min with both Rose bengal and fluorescein catalysts.

As presented in Table 3, aromatic aldehydes carrying electron-donating or electron-withdrawing substituents yielded the desired benzimidazoles in excellent yields with both catalysts in a microfluidic reactor. The microfluidic system was also effective for heteroaryl aldehydes and the sterically hindered 2-naphthaldehyde, providing decent yields (85–89%, Table 3, entries 5 and 6). The reactivity of the rose bengal photocatalyst in comparison with that of the fluorescein photocatalyst is slightly lower, but the selectivity remained unchanged (Table 3). When compared to traditional batch systems, the current smooth procedure of the microfluidic system was good in terms of reaction time, i.e., only 10 min in the microfluidic system compared to the batch systems (2–3 h),^{30,31} and further improvement of yields as a result of superior mixing. These developments will accelerate the synthesis of these bioactive benzimidazoles derivatives.

A plausible mechanism for the synthesis of 2-aryl benzimidazoles with the condensation of aryl aldehyde and

o-phenylenediamine under microfluidic conditions in the presence photocatalyst (i.e., fluorescein/Rose Bengal) is depicted in Scheme 2. First, the imine intermediate (I) is formed by condensation of benzaldehyde **1a** and *o*-phenylenediamine **2a** (as shown in Figure 3). Under visible light irradiation, PC*, the excited state of the photocatalyst (PC), can abstract an electron from the imine via a single electron transfer (SET) process.⁴² The oxidation of the photocatalyst radical anion (PC•⁻) back to the ground-state PC completes the photoredox cycle through O₂, diffusing via PDMS microchannel walls.⁴³ The desired product **3a** is obtained by the imine radical cation (II) donating one hydrogen atom to the dioxygen radical anion, resulting in the formation of III and hydrogen abstraction by a hydroperoxy radical (HO₂•).

4.2. Typical Procedure for the Synthesis of 2-Aryl Benzimidazoles in a PDMS Photocatalytic Microfluidic Reactor. Aryl aldehyde **1** (0.5 mmol) in 2 mL of CH₃CN solution was filled in the first syringe pump, and *o*-phenylenediamines **2** (0.5 mmol) with Rose Bengal/fluorescein (1.5 mol %) in 2 mL of CH₃CN solution was filled in another syringe pump. Further, these solutions were pumped into the respective inlets of photocatalytic microfluidic devices. The reaction mixture introduced into the microreactor was further irradiated with three embedded 2.4 W blue LEDs. The flow rate of both aforementioned solutions was adjusted in such a way that the 10 min residence time of the reaction mixture was maintained. Within the 10 min residence time, complete consumption of starting materials was observed through optical fiber and TLC. After completion of the reaction, the solvent was evaporated under a vacuum and the residue was purified by column chromatography by using hexane/ethyl acetate as the eluent to afford the final product.

5. CONCLUSION

Under the specified continuous-flow photocatalytic microfluidic conditions, environmentally friendly and sustainable green chemistry was successfully implemented. In comparison to the traditional batch conditions, the suggested LED-embedded PDMS microreactor demonstrated improved synthesis yields (i.e., 85–94%) with minimal photocatalyst loading (1.5 mol %) and much lower reaction time (i.e., only 10 min).

The efficiency of this proposed blue-light LED-embedded microreactor is evidenced via the synthesis of structurally diverse 2-aryl benzimidazoles through visible light photoredox-catalyzed condensation cyclization reactions of aryl aldehydes **1** with *o*-phenylenediamines **2** in the presence of a Rose Bengal/fluorescein photocatalyst.

There are restrictions on the amount of visible light that can enter the reaction mixture during a photocatalytic reaction in a traditional batch reaction procedure. As a result, light may not reach a deeper level of the reaction volume during a reaction, which could lead to incomplete reactions. An innovative microfluidic reactor with integrated LEDs was created in response to this problem. Since the reaction utilizing the LEDs integrated within the microfluidic reactor used around ten times less optical power than the previously mentioned conventional batch reaction procedure, it was determined to be more effective. This is because the embedded LEDs in our microfluidic reactor were around ten times closer to the flowing reaction mixture. Noteworthy, to our best knowledge, this is the first report in organic synthesis that details the fabrication of microfluidic reactors with embedded LED lights. Embedding light sources beneath microfluidic reactors offers numerous advantages for enhancing the energy efficiency and improving the performance of photochemical reactions. It enables precise control over illumination, reduces light loss, and facilitates efficient photon absorption, contributing to sustainable and cost-effective operation.

Furthermore, it also includes innovative reaction progress monitoring with the help of the optical fiber coupled microdevice. To avoid the interference of light with the reaction unit, an additional novel reaction progress monitoring microfluidic device was fabricated and equipped with an optical fiber port that was attached to the microfluidic photoreactor unit for reaction progress monitoring. Through advanced photonics, the microdevice can precisely monitor and measure the UV–vis absorbance characteristics of the reaction mixture, which serve as crucial indicators of the reaction progress. The use of optical fibers enhances the sensitivity and accuracy of UV–vis absorbance measurements, enabling real-time monitoring of chemical transformations within the microfluidic reactor. The data obtained from this integrated system not only provide valuable insights into the kinetics of organic reactions but also enable rapid optimization of reaction conditions.

The PDMS-based LEDs-implanted microfluidic photoreactor has shown success; however, it has a few limitations, such as complexity, degradation of LEDs and microfluidic channels with time, commercial unavailability of LEDs with some specific intensities or wavelengths, and the need for a consistent power source. However, many of these limitations are being addressed by existing researchers with the current advancement of microtechnology.

Overall, in this procedure, the process safety is enhanced by the containment of potentially unsafe constituents due to reaction within a closed microfluidic photoreactor. The proposed approach prevents waste of chemicals and designs an energy-efficient synthesis route, along with online in-process monitoring. This LEDs-embedded microfluidic device's capability for photoinduced synthesis along with real-time spectroscopic analysis represents a promising breakthrough that may be used for the synthesis of various privileged scaffolds.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.4c04836>.

General experimental details and spectral data of all compounds (UV–vis, ¹H NMR, ¹³C NMR) (PDF)

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Notes

The authors declare no competing financial interest.

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