JOC The Journal of Organic Chemistry

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"Metal-Free" Nanoassemblies of AIEE-ICT-Active Pyrazine Derivative: Efficient Photoredox System for the Synthesis of Benzimidazoles

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Cite This: https://dx.doi.org/10.1021/acs.joc.0c01965 Read Online

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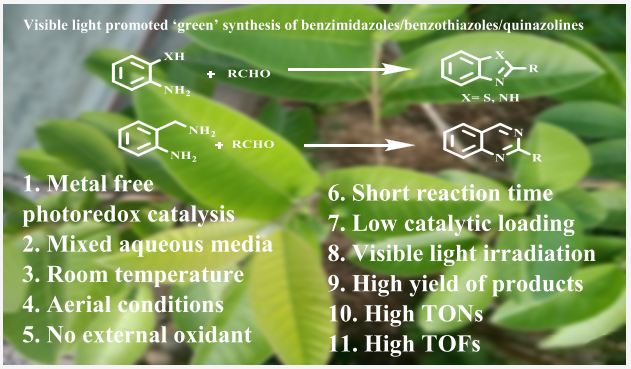
ABSTRACT: Supramolecular nanoassemblies of an AIEE-ICT-active pyrazine derivative (TETPY) having strong absorption in the visible region and excellent transportability have been utilized as an efficient photoredox catalytic system for the synthesis of a variety of benzimidazoles having electron-withdrawing/electron-releasing/aliphatic groups under "metal-free" conditions. The reaction protocol involves the successful harvesting of visible light by TETPY assemblies to catalyze the coupling of *o*-phenylenediamine/substituted diamines and substituted aromatic/heterocyclic/aliphatic aldehydes under aerial conditions using mixed aqueous media as the reaction solvent. TETPY assemblies could activate aerial oxygen to generate superoxide for completing the vital proton abstraction step without the need for any external metal/base/oxidant. Moreover, all the products are purified by recrystallization from organic solvents. The TETPY assemblies also exhibited high efficiency in catalyzing the synthesis of 2-substituted benzothiazoles and quinazolines in excellent yields.



INTRODUCTION

Benzimidazoles are well-known structural motifs for the preparation of building blocks having widespread applications in material, medicinal, and supramolecular chemistry.[1−3] The enormous utilization of benzimidazoles in diverse fields provides sufficient impetus to develop facile synthetic protocols to meet the demand−supply balance. Among different synthetic approaches explored, transition-metal-catalyzed condensation of readily available *o*-phenylenediamine and aldehydes/alcohols is a convenient route to attaining these derivatives.[4,5] Over the past few years, to widen the substrate scope, to restrict the formation of side products, and to improve the yield of the target compounds, a variety of methodologies such as ionic liquid-promoted benzimidazole synthesis,[6] utilization of additional oxidants,[7] molecular iodine-assisted synthesis of benzimidazoles under alkaline conditions,[8] cobalt-catalyzed synthesis of benzimidazoles through dehydrogenative coupling of aromatic diamines and alcohols,[9] and reduced graphene oxide-catalyzed synthesis of benzimidazoles[10] have been developed. Besides these methodologies, several other catalytic systems have been developed for the synthesis of benzimidazoles.[11−23] Although these reported methodologies are efficient with respect to substrate scope and yields, these are not impressive in terms of cost and environmental safety aspects due to the requirement of bases in stoichiometric amounts, organic solvents (dioxane, THF, toluene, and ethyl acetate) as reaction media, inert atmospheric conditions, requirement of additional ligands, and prolonged heating of the reaction mixture at high temperature. To get rid of the problems associated with thermal heating, a variety of metal-based[11,24,25] and organic dye-based[26,27] photoredox catalytic systems and catalyst-free systems[28,29] have been developed; unfortunately, most of these reported systems could not overcome the limitations such as requirement of organic solvents as reaction media, demand of high catalytic loading, longer reaction time, high energy source of radiation, and tedious purification methods. Furthermore, structural modifications of organic dyes to enhance their efficiency as "metal-free" photoredox catalysts involve difficult synthetic procedures. In an effort to avoid the need for structural modification, very recently, unmodified fluorescein has been used as a photocatalytic system for the synthesis of benzimidazoles in organic media using a blue LED as the source of radiation (Scheme 1).[30]

Received: August 14, 2020

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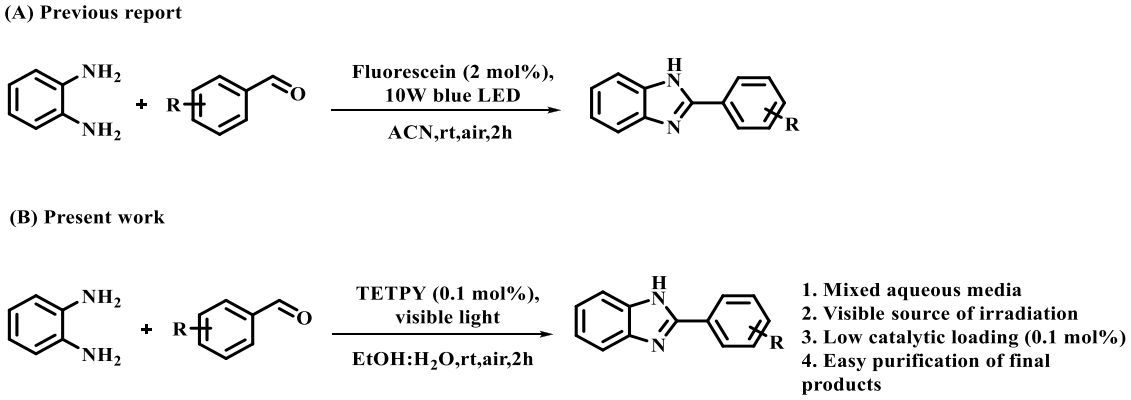
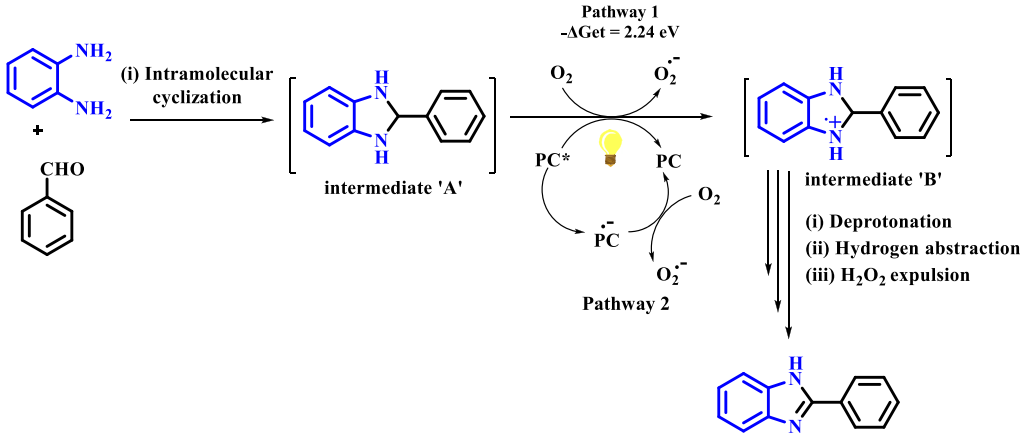
Scheme 1. Comparison of Previous and Present Protocols for the Synthesis of 2-Benzimidazoles



Scheme 2. Possible Mechanistic Pathway for the Synthesis of Benzimidazoles[a]



[a]Pathway 1: PET from intermediate **A** to O_2. Pathway 2: PET from intermediate **A** to the photocatalyst (PC).

Although the requirement of high energy radiation and organic solvents for acceleration of the reaction is not cost-effective and eco-friendly, the approach is inspiring. This study motivated us to develop a "metal-free" easy-to-synthesize photocatalytic system that could work efficiently under mild reaction conditions such as low-energy visible light irradiation, mixed aqueous media, low catalytic loading, and air as an oxidant.

A look at the mechanistic cycle proposed on the basis of literature reports in the case of photocatalyzed reactions between diamines and aldehydes showed that the *in situ* generation of radical cation intermediate **B** through the oxidation of intermediate **A** is a vital preliminary step as shown in Scheme 2. For the feasibility of the next reaction steps (deprotonation, proton abstraction, etc.) under base/inert atmosphere/additional oxidant-free conditions, *in situ* generation of reactive oxygen species (superoxide species) through reduction of aerial oxygen is a prerequisite.

As part of our initial investigation, we explored the possibility of activation of aerial oxygen by intermediate **A** through a photoinduced electron transfer (PET) process. We calculated the free energy change ($-\Delta G_{et}$) for this step from the available literature data,[30,31] and the value comes out to be 2.24 eV (Scheme 2, pathway 1). Surprisingly, despite the decently favorable ΔG_{et} value, the insignificant progress of the reaction observed under "catalyst-free" conditions may be attributed to very weak absorption of reactants and intermediate **A** in the visible region (*vide infra*).

Based on our preliminary investigation and proposed mechanistic cycle (Scheme 2), to catalyze the synthesis of benzimidazoles under metal/base/oxidant/inert atmosphere-free conditions, the hypothesized photocatalyst aside from having strong absorption in the visible region should also have good transportability and reduction potential to assist the electron transfer for the generation of intermediate **B** and for the reduction of aerial oxygen (Scheme 2, pathway 2).

Recently, from our lab, we reported the preparation of a pyrazine-based donor−acceptor system (TETPY, Figure 1), which exhibited high efficiency in various oxidative organic transformations facilitated by *in situ* generation of reactive oxygen species (ROS).[32]

The nanoassemblies of TETPY exhibited sufficient reduction potential to generate superoxide species from molecular oxygen under visible light irradiation in mixed aqueous media. In view of the favorable properties of TETPY, we examined the catalytic efficiency of the nanoassemblies of TETPY for the synthesis of benzimidazoles under "metal/base/additive/argon-free" conditions in mixed aqueous media using visible light at room temperature.

The test reaction proceeded very well at 0.1 mol % catalytic loading of nanoassemblies of TETPY and furnished the final product in an excellent yield of 96%. We further examined the potential of the nanoassemblies of TETPY to catalyze the reaction between *o*-phenylenediamine/substituted diamines and a variety of aliphatic/heterocyclic/aromatic aldehydes bearing electron-withdrawing/electron-releasing groups. To

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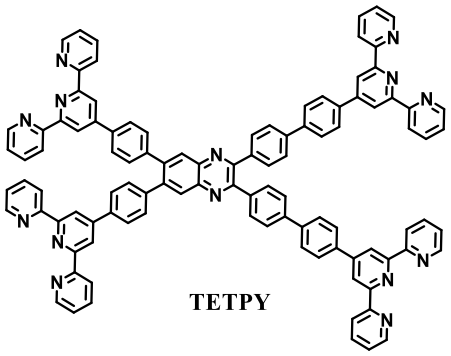


Figure 1. Structure of the pyrazine-based donor–acceptor system TETPY.

our pleasure, all the reactions worked well to furnish the desired products in good to excellent yields with high TONs and TOFs. In comparison to other reported catalytic systems, TETPY nanoassemblies exhibited high catalytic efficiency to synthesize 2-substituted benzimidazoles under mild reaction conditions such as mixed aqueous media, visible light irradiation, room temperature, and air using molecular oxygen as the sole oxidant (Table S1, Supporting Information). Interestingly, TETPY nanoassemblies also exhibited high efficiency in catalyzing the synthesis of 2-benzothiazoles with a good substrate scope. Further, the photoredox catalytic system also exhibited high efficiency for the gram-scale synthesis of benzimidazole/benzothiazole. The efficiency of TETPY nanoassemblies has also been demonstrated for the preparation of 2-substituted quinazolines. Unprecedentedly, this report reveals the potential of TETPY assemblies in photocatalyzing the synthesis of 2-benzimidazole/benzothiazole/quinazolines under "metal/oxidant/inert atmosphere-free" conditions in mixed aqueous media.

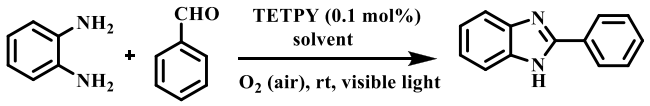
RESULTS AND DISCUSSION

Photophysical Properties of TETPY. The derivative TETPY is synthesized by Suzuki–Miyaura coupling following the procedure reported in the literature.[32] The donor–acceptor TETPY system showed strong absorption in the visible region and formed supramolecular nanoassemblies in mixed aqueous media due to its intramolecular charge transfer (ICT) and aggregation-induced emission enhancement (AIEE) characteristics as already reported.[32] The nanoassemblies of TETPY showed good photostability under continuous irradiation of visible light for 36 h. Furthermore, due to the sufficient ground-state reduction potential (−1.76 V), the donor–acceptor-based TETPY system exhibited high potential to reduce molecular oxygen (E_{red} = −0.89 V) to generate superoxide species.[32]

VISIBLE LIGHT-INDUCED PHOTOCATALYTIC SYNTHESIS OF 2-BENZIMIDAZOLES

For the initial optimization, we examined the coupling of *o*-phenylenediamine (**1a**) with benzaldehyde (**2a**) in EtOH as the reaction media in the presence of the isolated form of TETPY as a photocatalyst under visible light irradiation using air as an oxidant. The reaction gave the desired product in 80% yield (Table 1, entry 1). Interestingly, upon switching the isolated form of TETPY with the as-prepared assembled form, the desired product was furnished in 96% yield using mixed aqueous media (EtOH/H_2O, 1:1) (Table 1, entry 2), which may be attributed to the potential of TETPY assemblies to generate ROS more efficiently in mixed aqueous media.[32] Further, we believe that the carbonyl oxygen of aldehyde (**2a**) and NH_2 hydrogen of *o*-phenylenediamine (**1a**) are activated in the presence of water as the co-solvent through cooperative hydrogen bonding. These studies clearly indicate the importance of TETPY nanoassemblies as the photocatalyst. To understand the influence of the intensity of light irradiation

Table 1. Optimizations of the Reaction Conditions for the Synthesis of 2-Benzimidazoles[a]



1a 2a 3a

entry	photocatalyst (nanoassemblies)	additive/base	solvent	time (h)	yield (%)
1[b]	TETPY		EtOH	2	80
2	TETPY		EtOH/H_2O (1:1)	2	96
3[c]	TETPY		EtOH/H_2O (1:1)	1.5	96
4	TETPY		DMSO/H_2O (1:1)	2	60
5	TETPY		THF	2	40
6	TETPY		ACN	2	70
7	TETPY		DMF	2	30
8	TETPY		MeOH	2	78
9	TETPY		H_2O	2	10
10	TETPY	Na_2CO_3 as base	EtOH/H_2O (1:1)	2	96
11[d]	TETPY		EtOH/H_2O (1:1)	2	traces
12			EtOH/H_2O (1:1)	2	traces
13[e]	TETPY		EtOH/H_2O (1:1)	2	traces
14[f]	TETPY		EtOH/H_2O (1:1)	2	96

[a]Reaction conditions (unless otherwise noted): **1a** (0.5 mmol), **2a** (0.5 mmol), solvent (2 mL), assemblies of TETPY (4.0 mg of TETPY dissolved in 800 μL of DMSO and 1200 μL of distilled water). The resulting solution (500 μL) was used as the photocatalyst for each reaction: 16 W white LED as the irradiation source, room temperature, 2 h, in aerial conditions. [b]Isolated form of TETPY (1 mg). [c]5W blue LED as source of irradiation; [d]Dark. [e]Inert atmosphere. [f]Reaction condition: **1a** (0.5 mmol) and **2a** (1 mmol).

https://dx.doi.org/10.1021/acs.joc.0c01965
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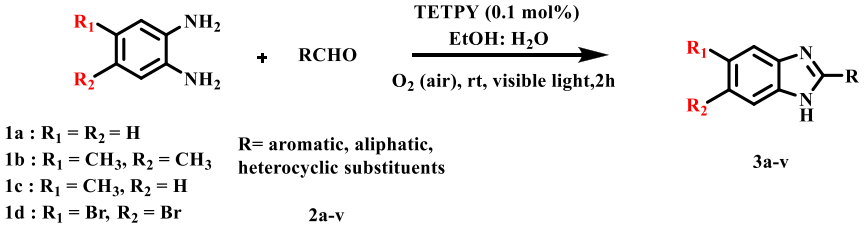
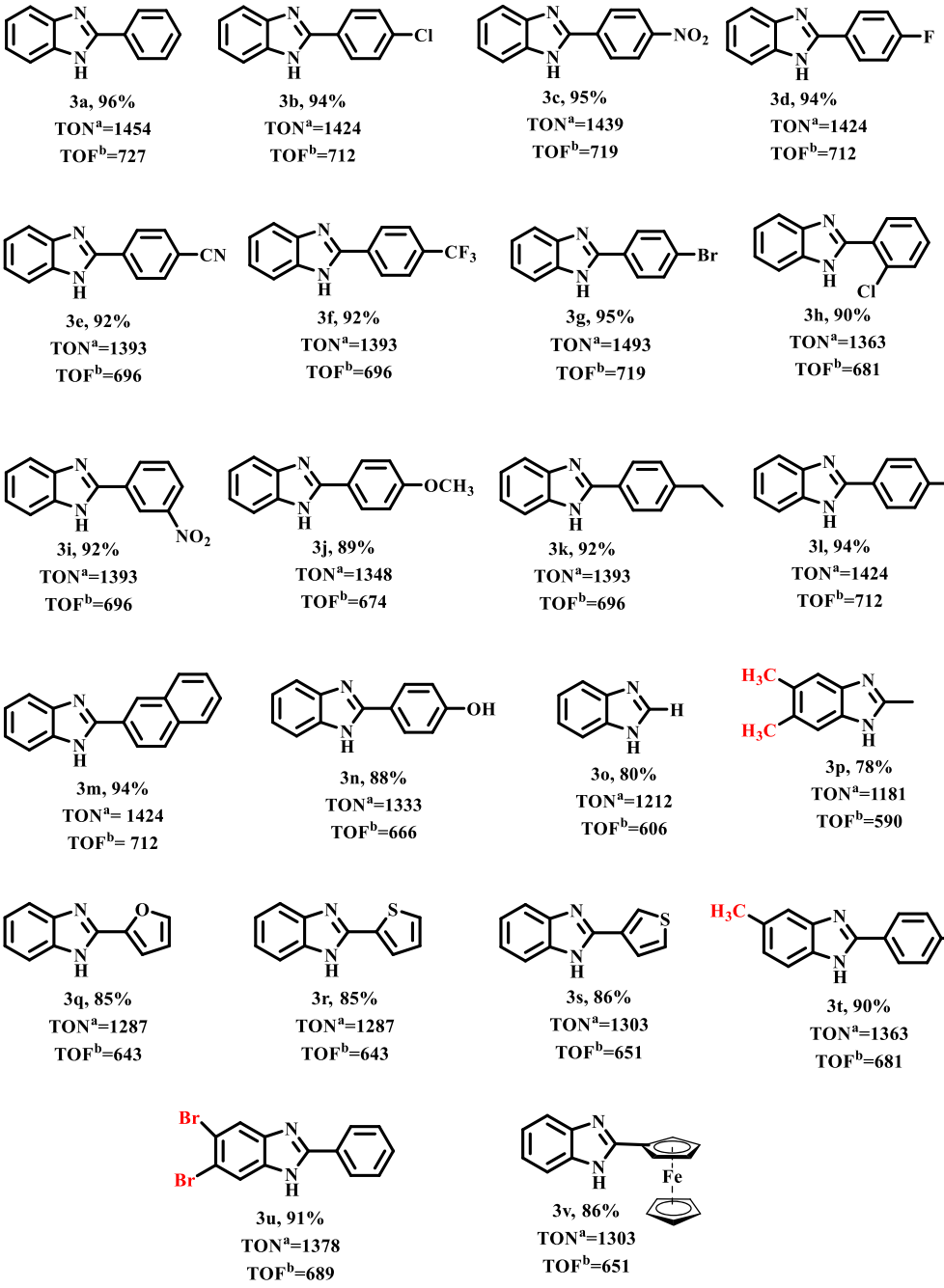
Table 2. Substrate Scope for the Synthesis of 2-Benzimidazoles Using Supramolecular Nanoassemblies of TETPY





[a]The moles of 2-substituted benzimidazole formed per unit catalyst. [b]The rate of formation of 2-substituted benzimidazole per unit catalyst per unit time (2 h).

on the reaction, we examined the model reaction using a blue LED as the source of irradiation. The desired product was obtained in 96% yield in 1.5 h (Table 1, entry 3). Although the reaction time was shortened, we preferred "more green" low-energy white light irradiation for carrying out further reactions. The effect of the other solvents such as DMSO/H_2O, THF,

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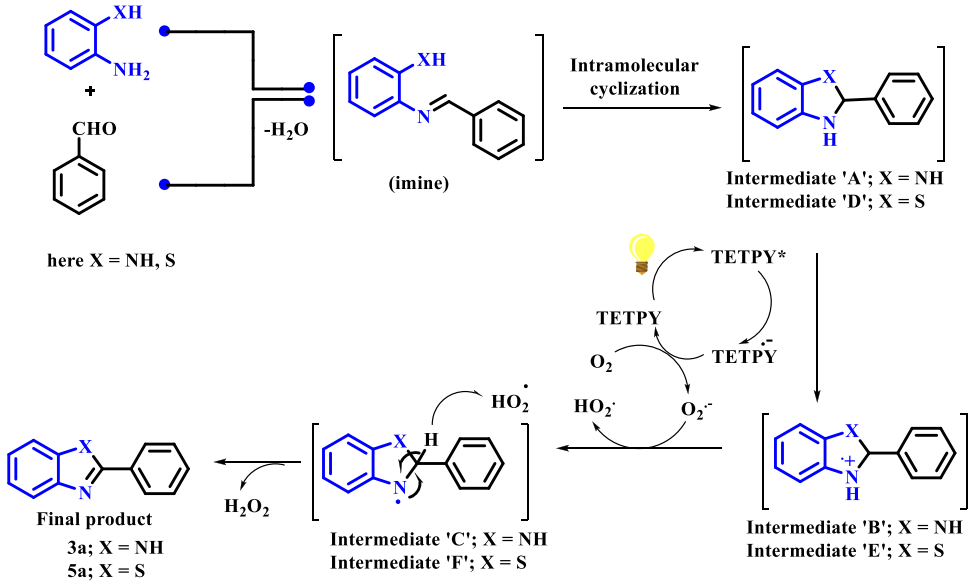
Scheme 3. Proposed Reaction Mechanism for the Synthesis of 2-Benzimidazoles/Benzothiazoles Using Supramolecular Nanoassemblies of TETPY



ACN, DMF, MeOH, and H_2O were also examined in the model reaction using supramolecular nanoassemblies of TETPY as the photocatalyst (Table 1, entries 4−9). All these studies clearly show that in the presence of polar protic solvents except in the case of H_2O, the desired product is obtained in higher yield. The insolubility of the reactants in aqueous medium may be the reason behind the insignificant progress of the reaction in H_2O. Based upon these optimization experiments, EtOH/H_2O (1:1) was chosen as the reaction solvent for the preparation of benzimidazole derivatives. Next, we examined the role of the presence/absence of a base on the yield/kinetics of the reaction under the optimized reaction conditions; the product was obtained in traces, which clearly shows the insignificant role of the base in catalyzing the synthesis of 2-benzimidazoles (Table 1, entry 10). To understand the contribution of each reaction condition, i.e., visible light irradiation, assemblies of TETPY, and air, toward the progress of the reaction, we performed different control experiments. In the first control reaction, the model reaction between **1a** and **2a** was allowed to proceed in the dark in the presence of nanoassemblies of TETPY, and the desired product was obtained in traces. Next, upon irradiating the reaction mixture in the absence of assemblies of TETPY, the desired product was again obtained in traces. When the model reaction was repeated under inert atmosphere conditions, the formation of the desired product was detected in traces. All these experiments demonstrate the importance of assemblies of TETPY, visible light irradiation, and aerial conditions for the synthesis of 2-benzimidazoles (Table 1, entries 11−13). To ascertain the product selectivity of the TETPY-catalyzed system in terms of formation of 2-substituted/1,2-disubstituted benzimidazoles, the control experiment was performed using higher equivalents (1 mmol) of the benzaldehyde (**2a**) under the optimized reaction conditions (Table 1, entry 14). The formation of 1,2-disubstituted benzimidazole was not detected even in traces, which confirms the high selectivity of the supramolecular nanoassemblies of TETPY for the preparation of monosubstituted benzimidazoles. In the next part of the investigation, we explored the substrate scope of the condensation of *o*-phenylenediamine (**1a**)/substituted diamines (**1b−d**) with regard to various substituted aldehydes (**2a−v**) bearing aliphatic, aromatic, and heterocyclic groups using supramolecular assemblies of TETPY as the catalytic system (Table 2).

The aromatic aldehydes bearing electron-withdrawing/donating groups were allowed to react, and the desired products were furnished in excellent yield (Table 2, products **3b−n**). Next, we examined the catalytic efficiency of TETPY in a reaction involving aliphatic aldehydes such as formaldehyde (**2o**) and acetaldehyde (**2p**) as one of the coupling partners, and the desired benzimidazoles were obtained in good yields (Table 2, products **3o−p**). Substituted diamines (**1b−d**) irrespective of the substitution on them were also found to be reactive with aromatic/aliphatic aldehydes and gave the desired products in excellent yield (Table 2, products **3p**, **3t**, and **3u**). Next, the catalytic efficiency of TETPY assemblies in reaction with regard to heterocyclic aldehydes such as furfuraldehdye (**2q**), 2-thienylcarboxaldehyde (**2r**), and 3-thienylcarboxaldehyde (**2s**) was also explored and the desired benzimidazoles were furnished in over 85% yields (Table 2, products **3q−s**). Ferrocene-2-carboxaldehyde (**2v**) also proved as a successful partner for the synthesis of ferrocene-substituted benzimidazole (Table 2, product **3v**). In general, all the aliphatic/heterocyclic/aromatic aldehydes bearing electron-withdrawing/releasing groups furnished the desired benzimidazoles derivatives in good to excellent yields. However, the aldehydes having electron-withdrawing groups furnished the desired product in a slightly higher yield. Since the first step of the reaction involves the nucleophilic attack of diamines on the aldehydes, we believe that in the case of the electron deficient aldehydes, the nucleophilic attack is more favored.[33] All the products (Table 2, products **3a−v**) were purified by recrystallization. The calculated TONs and TOFs for all the synthesized 2-benzimidazoles are quite high, which support the excellent efficiency of the supramolecular nanoassemblies of TETPY in these reactions.

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Mechanistic Studies. Various control reactions clearly highlighted the important role of visible light irradiation, aerial conditions, and TETPY assemblies in the completion of the reaction in a short reaction time and high product yield. To understand it further, we monitored the model reaction using absorption spectroscopy. The UV−vis spectra of *o*-phenylenediamine (**1a**) and benzaldehyde (**2a**) did not show absorption in the visible region; however, an absorption band appeared at 368 nm after irradiating the reaction mixture for 20 min (Figure S1, Supporting Information). Since the target compound (**3a**) absorbs at 318 nm,[34] this study confirms that the reaction proceeds through intermediate **A** having absorption in the visible region (368 nm). Further, the value of free energy change ($-\Delta G_{et}$) for the electron transfer from intermediate **A** to TETPY assemblies (Scheme 3) comes out to be 1.37 eV which confirms the spontaneity of the process (detailed calculations in the Supporting Information).[30,32] On the basis of these results, we propose that the first step of the reaction involves the condensation of reactants to form an imine derivative and generation of photoexcited TETPY* species upon irradiating the reaction mixture. Further, intramolecular cyclization of the imine derivative led to the generation of intermediate **A**, which serves as an electron donor and transfers an electron to TETPY* assemblies to generate $TETPY^{\cdot-}$, which in turn activates the oxygen to furnish superoxide species before returning to the ground state. Subsequently, the oxidation of intermediate **A** results in the formation of intermediate **B**. In the next step, the deprotonation of intermediate **B** by superoxide radical anion species generates species **C**, which after hydrogen abstraction by hydroperoxyl radical furnishes the final product (Scheme 3). The potential of TETPY assemblies to transfer a single electron was confirmed by their absorption studies in the presence of methyl viologen (MV^{2+}) as the acceptor and triethanolamine (TEOA) as the sacrificial donor. The absorption studies indicated the presence of the reduced form of methyl viologen, which is attributed to the transfer of electrons from the sacrificial donor (TEOA) to the acceptor (MV^{2+}) by TETPY assemblies[32] (Figure S2, Supporting Information).

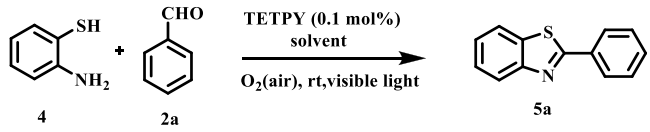
The *in situ* generation of superoxide species by TETPY assemblies was also supported by absorption studies using *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine (TMPD) as an indicator.[32] The studies suggest the TMPD oxidation and formation of radical cations of TMPD mediated by *in situ* release of superoxide species (Figure S3, Supporting Information). In this reaction mechanism (Scheme 3), the generation of H_2O_2 as the side product is confirmed by iodometric experiments (Figures S4 and S5, Supporting Information).[35]

Unfortunately, all our attempts to isolate the intermediate **A** under lab conditions failed due to its high reactivity. We believe that the high transport ability and sufficient reduction potential of TETPY assemblies in the ground state contributed significantly toward catalyzing the progress of the reaction in a much shorter time to furnish the target products in high yields.

VISIBLE LIGHT-INDUCED PHOTOCATALYTIC SYNTHESIS OF 2-BENZOTHIAZOLES

Encouraged by the high photoredox catalytic activity of assemblies of TETPY for the synthesis of 2-benzimidazoles, we planned to examine their potential in the synthesis of 2-benzothiazoles. The model reaction was carried out between *o*-aminothiophenol (**4**) and benzaldehyde (**2a**) under visible light irradiation using supramolecular nanoassemblies of TETPY in EtOH/H_2O (1:1) as the reaction media, and interestingly, the desired benzothiazole product was furnished in 97% yield in 40 min (Table 3, entry 1). On the other hand,

Table 3. Optimization Reaction Conditions for the Synthesis of 2-Benzothiazoles[a]



4 2a 5a

entry	photocatalyst (Assemblies)	solvent	time (min)	yield (%)
1	TETPY	EtOH/H_2O (1:1)	40	97
2[b]	TETPY	EtOH	40	80
3	TETPY	DMSO/H_2O (1:1)	40	55
4	TETPY	MeOH	40	70
5	TETPY	ACN	40	72
6	TETPY	H_2O	40	10
7	TETPY	DMF	40	42
8	TETPY	THF	40	40
9		EtOH/H_2O (1:1)	40	traces
10[c]	TETPY	EtOH/H_2O (1:1)	40	traces
11[d]	TETPY	EtOH/H_2O (1:1)	40	traces

[a]Reaction conditions (unless otherwise noted): **4** (0.5 mmol), **2a** (0.5 mmol), solvent (2 mL), TETPY (0.1 mol %, 4.0 mg of TETPY dissolved in 800 μL of DMSO and 1200 μL of distilled water). The resulting solution (500 μL) was used as the photocatalyst for each reaction: 16 W white LED as the irradiation source, room temperature, 40 min, in aerial conditions. [b]Isolated form of TETPY (1 mg). [c]Dark. [d]Inert atmosphere.

while repeating the same reaction using TETPY in its isolated form using EtOH as the reaction media, the target product was obtained in 80% yield after 40 min (Table 3, entry 2). We also examined the model reaction using different solvents such as DMSO/H_2O, MeOH, ACN, H_2O, DMF, and THF (Table 3, entries 3−8), and the highest efficiency was observed in the presence of EtOH/H_2O (1:1) as the reaction media. In the optimization reaction, when the model reaction was carried out in the absence of supramolecular assemblies of TETPY, the product was obtained in traces. The formation of products was also not observed in the absence of light and inert atmospheric conditions (Table 3, entries 9−11). These optimization experiments highlight the prudent role of supramolecular assemblies of TETPY, visible light irradiation, and aerial oxygen in the synthesis of 2-benzothiazoles. To widen the substrate scope of the reaction with this protocol, several aromatic/aliphatic aldehydes (**2a−m**, **2w**, **2y**, **2o**) were allowed to react with *o*-aminothiophenol (**4**) under optimized reaction conditions (Table 4).

In the case of substituted benzaldehydes having electron-withdrawing/donating groups, the desired products were furnished in good to excellent yields with excellent TONs and TOFs (Table 4, products **5b−m**, **5w**, **5x**). The catalytic efficiency of TETPY assemblies is also found to be excellent in the case of aliphatic aldehyde, and the desired product is obtained in very good yield (Table 4, product **5o**). All the products (Table 4, products **5a−m**, **5w**, **5x**, **5o**) were purified by column chromatography. We also examined the catalytic efficiency of TETPY assemblies for catalyzing the reaction at

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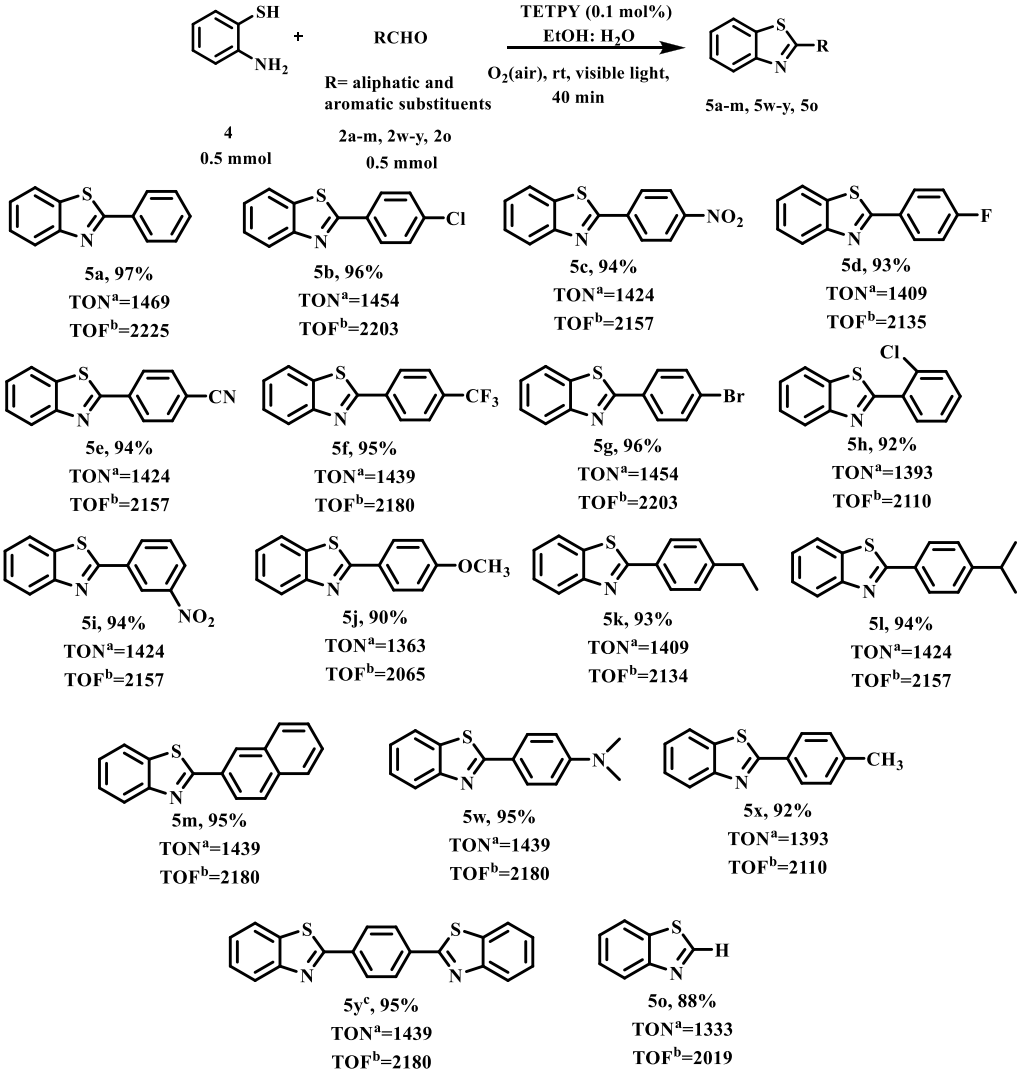
Table 4. Substrate Scope for the Synthesis of 2-Benzothiazoles Using Supramolecular Nanoassemblies of TETPY



[a]Moles of 2-substituted benzothiazole formed per unit catalyst. [b]Rate of formation of 2-substituted benzothiazole per mole catalyst per unit time (40 min). [c]**4** (1 mmol).

two sites simultaneously. Terephthalaldehdye (**2y**) was chosen as the reacting partner, and the desired product (1,4-diphenylbenzothiazole)[43] was furnished in 95% yield under optimized reaction conditions (Table 4, product **5y**). The product **5y** was purified by crystallization.

Mechanistic Studies. Literature reports showed the synthesis of benzothiazole in low yield (23%) in the absence of the photocatalyst through photoinduced electron transfer from intermediate **D** to aerial oxygen.[36] On the other hand, the presence of supramolecular TETPY nanoassemblies has a huge impact on the reaction rate due to their excellent transportability to form desired benzothiazole products in excellent yield in a shorter time.

We believe that the reaction proceeds through the formation of intermediate **D** after the condensation of reactants. Generation of intermediate **E** is facilitated by intermediate **D** as well as photoexcited TETPY* assemblies through a photoinduced electron transfer process. Subsequently, supramolecular TETPY assemblies assisted the deprotonation and proton abstraction of intermediate **F** to furnish the final product through formation of superoxide species as proposed in Scheme 3.

To confirm the formation of intermediate **D**, we monitored the reaction using FT-IR spectroscopy. The model reaction was performed using optimized reaction conditions under an inert atmosphere, and after 20 min, a peak corresponding to N−H stretching appeared at 2950 cm^{-1} in the FT-IR spectrum.[26] The FT-IR spectrum of the final product (**5a**) did not show the presence of any peak at 2950 cm^{-1}, which confirmed the formation of intermediate **D** during the reaction process (Figure S6, Supporting Information). The generation of H_2O_2 in the proposed reaction pathway (Scheme 3) is confirmed by iodometric and KI/CH_3COOH experimental tests (Figures S7 and S8, Supporting Information).[35a,37]

GRAM-SCALE SYNTHESIS OF 3A AND 5A

Further, to check the potential of the assemblies of TETPY, the photocatalytic reaction for the synthesis of benzimidazole (**3a**) and benzothiazole (**5a**) was repeated using gram-scale (1.5 g) of the reactants under optimized reaction conditions.

https://dx.doi.org/10.1021/acs.joc.0c01965
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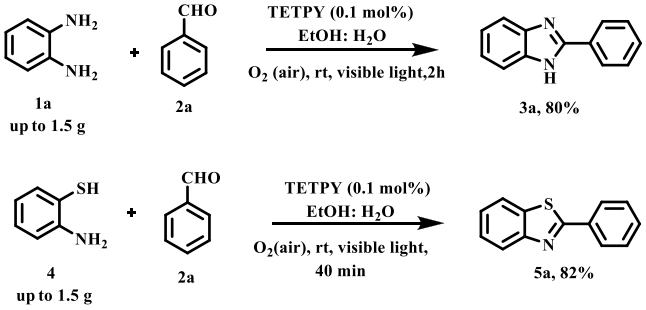
To our delight, the final products **3a** and **5a** were furnished in 80 and 82% yields (Scheme 4). The product **3a** was isolated by a recrystallization process, and the product **5a** was isolated by column chromatography. Therefore, the catalytic system works well for the synthesis of benzimidazoles and benzothiazoles on a gram scale.

Scheme 4. Gram-Scale Photocatalytic Synthesis of 2-Benzimidazole (3a) and 2-Benzothiazole (5a) Using Supramolecular Nanoassemblies of TETPY



VISIBLE LIGHT-INDUCED PHOTOCATALYTIC SYNTHESIS OF 2-SUBSTITUTED QUINAZOLINES

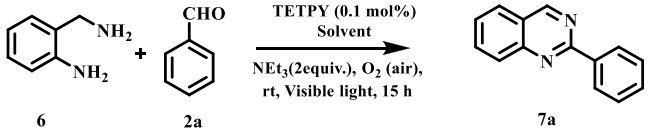
Encouraged by the high efficiency of the assemblies of TETPY in catalyzing the condensation of various aromatic/aliphatic aldehydes with substituted diamines (**1a–d**)/*o*-aminothiophenol (**4**), we planned to examine the potential of the catalytic system for the synthesis of 2-substituted quinazolines. Earlier, base-promoted metal-free[38a]/metal-based,[38b,c] and commercially available dye[39a,b]-based catalytic systems have been used for the synthesis of quinazolines with good yields but the requirement of a longer reaction time and thermal heating is still a limitation.

For the model reaction, we chose 2-aminobenzylamine (**6**) and benzaldehyde (**2a**) as coupling partners in EtOH/H_2O solvent media under the same optimization conditions of benzimidazoles and benzothiazoles in the presence of nanoassemblies of TETPY for 15 h. To our delight, the product was obtained in 70% yield (Table 5, entry 1). Further, the role of NEt_3 as the base was checked based on the kinetics of the reaction, and it was observed that upon using 2 equiv of the base, the yield of the final product was furnished in 93% yield (Table 5, entry 2). The reaction efficiency was also determined with the isolated form of TETPY, and the product was obtained in 80% yield (Table 5, entry 3). The model reaction was allowed to proceed in the absence of visible light and assemblies of TETPY and under inert reaction conditions (Table 5, entries 4–6). In all the cases, the desired product was obtained in traces, which highlighted the role of visible light, nanoassemblies of TETPY, and aerial conditions. In a nutshell, for the successful transformation to quinazolines, the presence of a light source, nanoassemblies of TETPY, aerial conditions, and presence of a base are necessary. After the optimization of the reaction conditions for the photocatalytic synthesis of quinazolines, we explored the efficiency of the catalyst with a range of substituted aldehydes. In all the cases, the desired products (Table 6, products **7a–d**) were obtained in excellent yields.

Mechanistic Studies. To gain insight into the mechanism, control experiments were performed by setting up the reaction between 2-aminobenzylamine (**6**) and benzaldehyde (**2a**) in EtOH/H_2O as the solvent media (Scheme 5). After 2 h, intermediate **8a** was obtained in 85% yield and was subjected to further reaction by adding NEt_3 (2 equiv) and supramolecular nanoassemblies of TETPY. Finally, the product **7a** was observed in 93% yield. This experiment confirmed the *in situ* formation of intermediate **8a** as a condensation product of 2-aminobenzylamine (**6**) and benzaldehyde (**2a**).

On the basis of these observations, the mechanistic cycle for the synthesis of quinazolines is proposed as shown in Scheme 6. The first step involves the condensation of 2-aminobenzylamine (**6**) and benzaldehyde (**2a**) to form 2-phenyl-1,2,3,4-tetrahydroquinazoline (**8a**). With the help of NEt_3, **8a** was deprotonated to generate intermediate **G**, which transfers the electron to the TETPY system and gives intermediate **H** and $TETPY^{\cdot-}$. Subsequently, $TETPY^{\cdot-}$ transfers the electron to molecular oxygen to give superoxide radical anion ($O_2^{\cdot-}$) before returning to the ground state. The formed intermediate **H** gave intermediate **I** after the deprotonation step and H_2O_2 as a side product. Subsequently, after similar steps, intermediate **I** gave the target product. The *in situ* formation of H_2O_2 was confirmed by iodometric experiments (Figure S9, Supporting Information).[35a]

Table 5. Optimization Reaction Conditions for the Synthesis of Quinazolines[a]



entry	photocatalyst (assemblies)	solvent	base	time (h)	yield (%)
1	TETPY	EtOH/H_2O (1:1)		15	70
2	TETPY	EtOH/H_2O (1:1)	NEt_3	15	93
3[b]	TETPY	EtOH	NEt_3	15	80
4		EtOH/H_2O (1:1)	NEt_3	15	traces
5[c]	TETPY	EtOH/H_2O (1:1)	NEt_3	15	traces
6[d]	TETPY	EtOH/H_2O (1:1)	NEt_3	15	traces

[a]Reaction conditions (unless otherwise noted): **6** (0.5 mmol), **2a** (0.5 mmol), solvent (2 mL), TETPY (0.1 mol %, 4.0 mg of TETPY dissolved in 800 μL of DMSO and 1200 μL of distilled water). The resulting solution (500 μL) was used as the photocatalyst for each reaction: 16 W white LED as the radiation source, room temperature, 15 h, in aerial conditions. [b]Isolated form of TETPY (1 mg). [c]Dark. [d]Inert atmosphere.

CONCLUSIONS

To sum up, AIEE-ICT-active TETPY assemblies exhibited excellent potential for photocatalyzing the synthesis of 2-benzimidazoles/benzothiazoles/quinazolines under aerial conditions in mixed aqueous media. Due to their sufficient ground-state reduction potential and good transportation ability, TETPY assemblies could efficiently generate vital reaction intermediates without requiring any additional oxidant. Moreover, all the products were obtained in high yield and their purification was not troublesome.

EXPERIMENTAL SECTION

General Experimental Methods and Materials.[40] All the reagents/chemicals were purchased from Aldrich and were used without any further purification. HPLC-grade solvents were used in UV–vis experimental studies. UV–vis spectra were recorded on a

https://dx.doi.org/10.1021/acs.joc.0c01965
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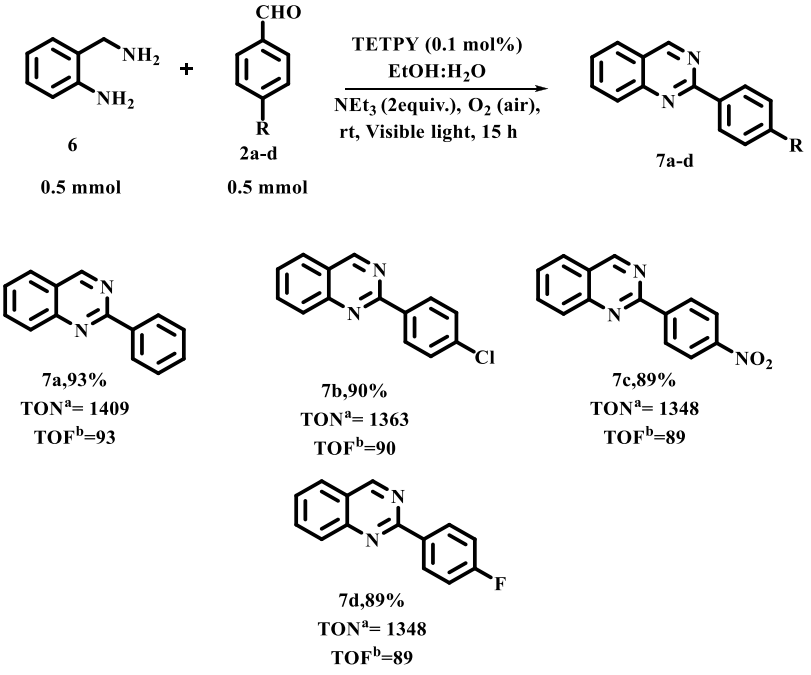
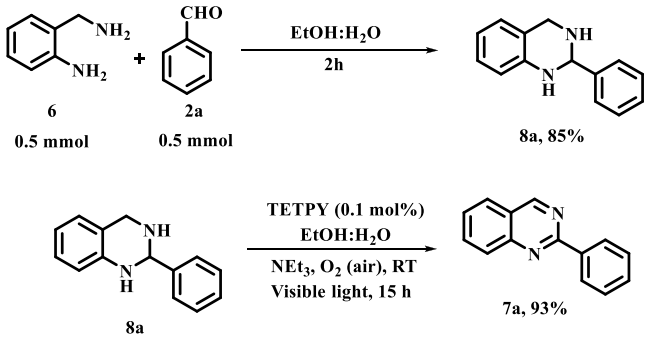
Table 6. Substrate Scope for the Synthesis of 2-Quinazolines Using Supramolecular Nanoassemblies of TETPY



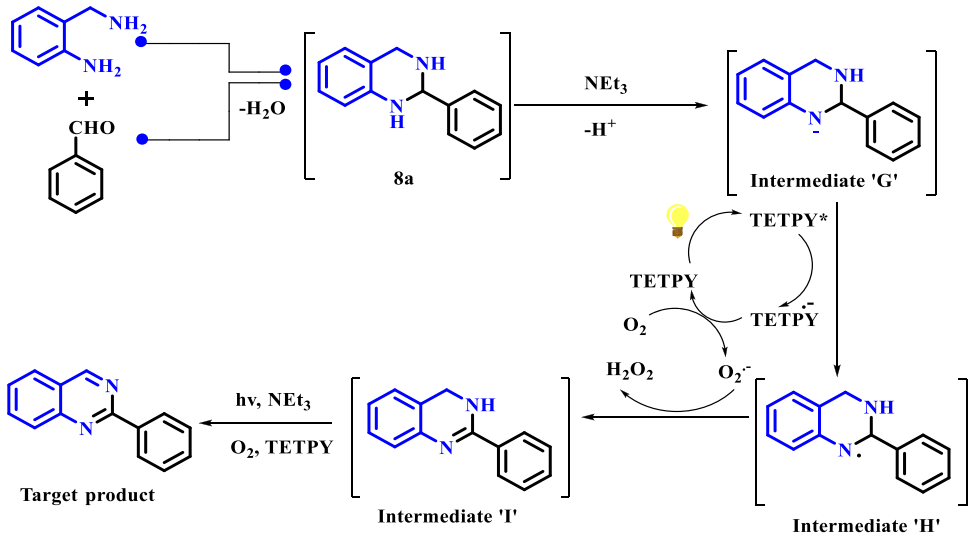
[a]Moles of quinazoline formed per unit catalyst. [b]Rate of formation of quinazoline per mole catalyst per unit time (15 h).

Scheme 5. Control Experiment



SHIMADZU UV-2450 spectrophotometer with a quartz cuvette (path length of 1 cm). To record FT-IR, a Varian 660 IR spectrometer was used. Melting points were measured on Stuart melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Avance III HD 500 MHz with $CDCl_3$ and DMSO-d_6 as solvents and tetramethylsilane and $SiMe_4$ as internal standards. Data is reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quintet, m = multiplet, br = broad), coupling constants J (Hz). For the light promoted reactions, 16 W white LEDs purchased from Philips (Manufacturer: Signify Innovations India Limited, Model Number: 929001818814_2, λ > 410 nm, spectral distribution: 380−760 nm, intensity: 1440 lm) were used. All the reactants and catalysts were added to a 10 mL borosilicate round-bottom flask and irradiated with the mentioned light source (distance app. of 7−9 cm) without the use of any filters. Blue LEDs (5 W) were purchased from Aluxcia

Scheme 6. Proposed Reaction Mechanism for the Synthesis of Quinazolines Using Supramolecular Nanoassemblies of TETPY



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(manufacturer: Aluxcia LED Co., Ltd., part no. ALC1020-Bx2-US-5W, λ > 455 nm) and used without any filters.

Preparation of the Photocatalyst (Supramolecular Nanoassemblies of TETPY).[32] A 500 μL mixture of 4.0 mg of TETPY dissolved in 800 μL of DMSO and 1200 μL of distilled water was used as the photocatalyst for each photocatalytic reaction.

General Procedure for the Synthesis of 2-Benzimidazole/Benzothiazole/Quinazolines Using the Isolated Form of TETPY as the Photocatalytic System. For 2-benzimidazole and benzothiazole synthesis, a mixture of *o*-phenylenediamine (**1a**)/*o*-aminothiophenol (**4**) (0.5 mmol) and benzaldehyde (**2a**) (0.5 mmol) in EtOH (2 mL) as the solvent in a 10 mL round-bottom flask in the presence of the isolated form of TETPY (1 mg) as the photocatalyst was stirred at room temperature for 2 h/40 min, respectively, under visible light irradiation (16 W white LED) and aerial conditions. For 2-quinazoline synthesis, a mixture of 2-aminobenzylamine (**6**) (0.5 mmol), benzaldehyde (**2a**) (0.5 mmol), and NEt_3 (2 equiv) in EtOH (2 mL) as the solvent mixture in a 10 mL round-bottom flask in the presence of the isolated form of TETPY (1 mg) as the photocatalyst was stirred at room temperature for 15 h under visible light irradiation (16 W white LED) and aerial conditions. The reaction mixture in a reaction vessel was dipped in a continuous flow water bath to avoid photoheating effects. The progress of the reaction was monitored by TLC. After completion of the reaction, the final product (**3a**) was isolated after recrystallization ($CHCl_3$/MeOH) and products **5a** and **7a** were isolated by column chromatography. All the products were identified by ^{1}HNMR spectroscopy (Figures S10, S32, and S50, Supporting Information).

General Procedure for the Synthesis of 2-Benzimidazoles/Benzothiazoles Using Supramolecular Nanoassemblies of TETPY as the Photocatalytic System. For 2-benzimidazole derivative synthesis, a mixture of diamines (**1a−d**) (0.5 mmol) and substituted aldehyde (**2a−v**) (0.5 mmol) in EtOH/H_2O (1:1) (2 mL) in a 10 mL round-bottom flask in the presence of supramolecular nanoassemblies of TETPY (0.1 mol %) as the photocatalyst was stirred at room temperature for 2 h under visible light irradiation (16 W white LED) and aerial conditions. For 2-benzothiazole derivative synthesis, a mixture of *o*-aminothiophenol (**4**) (0.5 mmol) and substituted aldehyde (**2a−m**, **2w−x**, **2o**) (0.5 mmol) in EtOH/H_2O (1:1) (2 mL) in a 10 mL round-bottom flask in the presence of supramolecular nanoassemblies of TETPY (0.1 mol %) as the photocatalyst was stirred at room temperature for 40 min under visible light irradiation (16 W white LED) and aerial conditions. The reaction mixtures in reaction vessels were dipped in a continuous flow water bath to avoid photoheating effects. The progress of the reaction was monitored with TLC. After completion of the reaction, the final products of benzimidazoles derivatives (**3a−v**) were purified after recrystallization ($CHCl_3$/MeOH). All the products (**3a−v**) were identified by^{1}HNMR spectroscopy (Figures S10−S31, Supporting Information). For benzothiazoles products, the combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The products (**5a−m**, **5w−x**, **5o**) were purified by column chromatography using EtOAc/hexane as the eluent. All the products (**5a−m**, **5w−x**, **5o**) were identified by ^{1}H NMR spectroscopy (Figures S32−S46 and S49, Supporting Information).

General Procedure for the Synthesis of 1,4-Diphenylbenzothiazole (5y) Using Supramolecular Nanoassemblies of TETPY as the Photocatalytic system.[43] A mixture of *o*-aminothiophenol (**4**) (1 mmol) and terephthalaldehyde (**2y**) (0.5 mmol) in EtOH/H_2O (1:1) (2 mL) in a 10 mL round-bottom flask in the presence of supramolecular nanoassemblies of TETPY (0.1 mol %) as the photocatalyst was stirred at room temperature for 40 min under visible light irradiation (16 W white LED) and aerial conditions. The reaction mixture in a reaction vessel was dipped in a continuous flow water bath to avoid photoheating effects. The insoluble product was then filtered and washed properly with ethanol. It was also characterized by ^{1}HNMR spectroscopy (Figure S47, Supporting Information). FT-IR (ν/cm^{-1}): 1480, 1432, 1495, 1310, 1225, 965, 842, 762, 724, 686, 624 (Figure S48, Supporting Information).

Gram-Scale Synthesis Procedure for the Synthesis of 3a And 5a Using Supramolecular Nanoassemblies of TETPY as the Photocatalytic System. For the gram-scale synthesis of **3a**, a mixture of *o*-phenylenediamine (**1a**) (13.8 mmol) and benzaldehyde (**2a**) (13.8 mmol) in EtOH/H_2O (1:1) (30 mL) in a 50 mL round-bottom flask in the presence of supramolecular nanoassemblies of TETPY (0.1 mol %) as the photocatalyst was stirred at room temperature for 2 h under visible light irradiation (16 W white LED) and aerial conditions. For the gram-scale synthesis of **5a**, a mixture of *o*-aminothiophenol (**4**) (12 mmol) and benzaldehyde (**2a**) (12 mmol) in EtOH/H_2O (1:1) (30 mL) in a 50 mL round-bottom flask in the presence of supramolecular nanoassemblies of TETPY (0.1 mol %) as the photocatalyst was stirred at room temperature for 40 min under visible light irradiation (16 W white LED) and aerial conditions. The reaction mixtures in reaction vessels were dipped in a continuous flow water bath to avoid photoheating effects. The progress of the reaction was monitored by TLC. After completion of the reaction, the final product (**3a**) was isolated after recrystallization ($CHCl_3$/MeOH) and the product **5a** was isolated by column chromatography. Both the products were identified by ^{1}HNMR spectroscopy (Figures S10 and S32, Supporting Information).

General Procedure for the Synthesis of 2-Quinazolines Using Supramolecular Nanoassemblies of TETPY as the Photocatalytic System. A mixture of 2-aminobenzylamine (**6**) (0.5 mmol), substituted aldehyde (**2a−d**) (0.5 mmol), and NEt_3 (2 equiv) in EtOH/H_2O (1:1) (2 mL) in a 10 mL round-bottom flask in the presence of supramolecular nanoassemblies of TETPY (0.1 mol %) as the photocatalyst was stirred at room temperature for 15 h under visible light irradiation (16 W white LED) and aerial conditions. The reaction mixture in a reaction vessel was dipped in a continuous flow water bath to avoid photoheating effects. The progress of the reaction was monitored by TLC. After completion of the reaction, the organic part was extracted with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The products were purified by column chromatography using EtOAc/hexane as the eluent. All the products (**7a−d**) were identified by ^{1}H NMR spectroscopy (Figures S50−S53, Supporting Information).

General Procedure for the Synthesis of 2-Phenyl-1,2,3,4-tetrahydroquinazoline (8a). A mixture of 2-aminobenzylamine (**6**) (0.5 mmol) and benzaldehyde (**2a**) (0.5 mmol) in EtOH/H_2O (1:1) (2 mL) in a 10 mL round-bottom flask was stirred for 2 h. The progress of the reaction was monitored with TLC. After completion of the reaction, the organic part was extracted with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The products were purified by column chromatography using EtOAc/hexane as the eluent. The product (**8a**) was identified by ^{1}H NMR spectroscopy (Figure S54, Supporting Information).

^{1}H NMR Characterization. *2-Phenyl-1H-benzimidazole (**3a**).*[41] White solid (93 mg, 96% yield). m.p. 289−292 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.90 (br s, 1H), 8.17 (d, J = 5 Hz, 2H), 7.66 (d, J = 5 Hz, 1H), 7.57−7.48 (m, 4H), 7.24−7.17 (m, 2H).

*2-(4-Chlorophenyl)-1H-benzimidazole (**3b**).*[42] White solid (107 mg, 94% yield). m.p. 291 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.99 (br s, 1H), 8.17 (d, J = 5 Hz, 2H), 7.67−7.62 (m, 3H), 7.53 (d, J = 5 Hz, 1H), 7.21 (t, J = 5 Hz, 2H).

*2-(4-Nitrophenyl)-1H-benzimidazole (**3c**).*[43] Off-white solid (113 mg, 95% yield). m.p. 328−329 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 13.31 (br s, 1H), 8.42 (s, 4H), 7.73 (d, J = 10 Hz, 1H), 7.59 (d, J = 10 Hz, 1H), 7.31−7.23 (m, 2H).

*2-(4-Fluorophenyl)-1H-benzimidazole (**3d**).*[41] Pale yellow solid (99 mg, 94% yield). m.p. 247−249 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.92 (br s, 1H), 8.23−8.20 (m, 2H), 7.59 (d, J = 60 Hz, 2H), 7.40 (t, J = 10 Hz, 2H), 7.21 (s, 2H).

*4-(1H-Benzimidazol-2-yl)benzonitrile (**3e**).*[17] White solid (100 mg, 92% yield). m.p. 264−265 °C.^{1}H NMR (500 MHz, DMSO-d_6): δ

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(ppm) 8.34 (d, J = 10 Hz, 2H), 8.03 (d, J = 10 Hz, 2H), 7.65 (s, 2H), 7.27 (s, 2H).

2-(4-Trifluoromethylphenyl)-1H-benzimidazole (**3f**).[21] White solid (92 mg, 92% yield). m.p. 265−266 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 13.17 (br s, 1H), 8.38 (d, J = 5 Hz, 2H), 7.93 (d, J = 10 Hz, 2H), 7.71 (d, J = 10 Hz, 1H), 7.57 (d, J = 10 Hz, 1H), 7.28−7.21 (m, 2H).

2-(4-Bromophenyl)-1H-benzimidazole (**3g**).[10] White solid (128 mg, 95% yield). m.p. 283−284 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 13.03 (br s, 1H), 8.11 (d, J = 10 Hz, 2H), 7.76 (d, J = 5 Hz, 2H), 7.54 (m, 2H), 7.18 (m, 2H).

2-(2-Chlorophenyl)-1H-benzimidazole (**3h**).[5] Brown solid (102 mg, 90% yield). m.p. 232−234 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.73 (br s, 1H), 7.90 (d, J = 10 Hz, 1H), 7.67 (dd, J = 25 Hz, 2H), 7.57−7.51 (m, 3H), 7.27−7.21 (m, 2H).

2-(3-Nitrophenyl)-1H-benzimidazole (**3i**).[43] White solid (109 mg, 92% yield). m.p. 203 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 13.31 (br s, 1H), 9.02 (s, 1H), 8.61 (d, J = 5 Hz, 1H), 8.33 (d, J = 5 Hz, 1H), 7.86 (t, J = 10 Hz, 1H), 7.65 (d, J = 55 Hz, 2H), 7.26 (s, 2H).

2-(4-Methoxyphenyl)-1H-benzimidazole (**3j**).[5] White solid (99 mg, 89% yield). m.p. 220 °C.^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.11 (d, J = 10 Hz, 2H), 7.55 (s, 2H), 7.18−7.16 (m, 2H), 7.11 (d, J = 10 Hz, 2H), 3.84 (s, 3H).

2-(4-Ethylphenyl)-1H-benzimidazole (**3k**).[44] White solid (102 mg, 92% yield). m.p. 143−145 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.84 (br s, 1H), 8.08 (d, J = 10 Hz, 2H), 7.63 (d, J = 5 Hz, 1H), 7.51 (d, J = 10 Hz, 1H), 7.39 (d, J = 10 Hz, 2H), 7.22−7.16 (m, 2H), 2.67 (q, J = 10 Hz, 2H), 1.22 (t, J = 10 Hz, 3H).

2-(4-Isopropylphenyl)-1H-benzimidazole (**3l**).[10] White solid (110 mg, 94% yield). m.p. 249−250 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.85 (br s, 1H), 8.09 (d, J = 10 Hz, 2H), 7.64 (d, J = 10 Hz, 1H), 7.51 (d, J = 10 Hz, 1H), 7.42 (d, J = 10 Hz, 2H), 7.22−7.14 (m, 2H), 2.99−2.93 (m, 1H), 1.24 (d, J = 5 Hz, 6H).

2-(Naphthalen-2-yl)-1H-benzimidazole (**3m**).[11] White solid (114 mg, 94% yield). m.p. 220−221 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 8.84 (s, 1H), 8.27−8.23 (m, 2H), 8.14−8.07 (m, 2H), 7.87−7.85 (m, 2H), 7.76−7.71 (m, 2H), 7.57−7.55 (m, 2H).

4-(1H-Benzimidazol-2-yl) Phenol (**3n**).[45] White solid (92 mg, 88% yield). m.p. 254 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 10.08 (s, 1H), 8.00 (d, J = 10 Hz, 2H), 7.57−7.55 (m, 2H), 7.21−7.20 (m, 2H), 6.93 (d, J = 10 Hz, 2H).

1H-Benzimidazole (**3o**).[26] White solid (47 mg, 80% yield). m.p. 170−172 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.41 (br s, 1H), 8.20 (s, 1H), 7.58 (s, 2H), 7.18 (s, 2H).

2,5,6-Trimethyl-1H-benzimidazole (**3p**).[46] Yellow solid (62 mg, 78% yield). m.p. 229−231 °C.^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 7.19 (s, 2H), 2.42 (s, 3H), 2.26 (s, 6H).

2-(Furan-2-yl)-1H-benzimidazole (**3q**).[12] Yellow solid (78 mg, 85% yield). m.p. 284−286 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.92 (br s, 1H), 7.94 (s, 1H), 7.62 (d, J = 10 Hz, 1H), 7.49 (d, J = 10 Hz, 1H), 7.23−7.17 (m, 3H), 6.73−6.72 (m, 1H).

2-(Thiophen-2-yl)-1H-benzimidazole (**3r**).[47] Yellow solid (85 mg, 85% yield). m.p. 330−331 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.94 (br s, 1H), 7.82 (d, J = 5 Hz, 1H), 7.72 (d, J = 5 Hz, 1H), 7.60 (d, J = 5 Hz, 1H), 7.49 (d, J = 5 Hz, 1H), 7.24−7.16 (m, 3H).

2-(Thiophen-3-yl)-1H-benzimidazole (**3s**).[47] Off-white solid (89 mg, 86% yield). m.p. 347 °C (decomposition). ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.80 (br s, 1H), 8.23 (s, 1H), 7.77 (d, J = 5 Hz, 1H), 7.73−7.72 (m, 1H), 7.62 (d, J = 10 Hz, 1H), 7.50 (d, J = 10 Hz, 1H), 7.22−7.15 (m, 2H).

2-(4-Chlorophenyl)-5-methyl-1H-benzimidazole (**3t**).[14] White solid (108 mg, 90% yield). m.p. 223−224 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 12.83 (d, J = 25 Hz, 1H), 8.16 (d, J = 10 Hz, 2H), 7.61 (d, J = 5 Hz, 2H), 7.54−7.31 (m, 2H), 7.06−7.01 (m, 1H), 2.42 (d, J = 10 Hz, 3H).

5,6-Dibromo-2-phenyl-1H-benzimidazole (**3u**).[48] White solid (159 mg, 91% yield). m.p. 177 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 13.26 (br s, 1H), 8.15 (d, J = 5 Hz, 2H), 8.07 (s, 1H), 7.90 (s, 1H), 7.59−7.53 (m, 3H).

Ferrocene Benzimidazole (**3v**).[26] Yellow solid (129 mg, 86% yield). m.p. 235−236 °C (decomposition). ^{1}HNMR (500 MHz, DMSO-d_6): δ (ppm) 12.34 (br s, 1H), 7.49 (d, J = 50 Hz, 2H), 7.13 (s, 2H), 5.04 (s, 2H), 4.47 (s, 2H), 4.10 (s, 5H).

2-Phenylbenzothiazole (**5a**).[49] Pale yellow solid (102 mg, 97% yield). m.p. 112 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.11−8.07 (m, 3H), 7.91 (d, J = 5 Hz, 1H), 7.51−7.49 (m, 4H), 7.39 (t, J = 10 Hz, 1H).

2-(4-Chlorophenyl) Benzothiazole (**5b**).[50] White solid (117 mg, 96% yield). m.p. 115−116 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.07 (d, J = 10 Hz, 1H), 8.03 (d, J = 10 Hz, 2H), 7.91 (d, J = 10 Hz, 1H), 7.52−7.47 (m, 3H), 7.40 (t, J = 10 Hz, 1H).

2-(4-Nitrophenyl) Benzothiazole (**5c**).[43] Yellow solid (120 mg, 94% yield). m.p. 233 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.36 (d, J = 10 Hz, 2H), 8.27 (d, J = 5 Hz, 2H), 8.13 (d, J = 5 Hz, 1H), 7.96 (d, J = 5 Hz, 1H), 7.56 (t, J = 10 Hz, 1H), 7.46 (t, J = 5 Hz, 1H).

2-(4-Fluorophenyl) Benzothiazole (**5d**).[50] White solid (106 mg, 93% yield). m.p. 102 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.11−8.06 (m, 3H), 7.91 (d, J = 10 Hz, 1H), 7.50 (t, J = 10 Hz, 1H), 7.39 (t, J = 5 Hz, 1H), 7.21−7.17 (m, 2H).

4-(Benzothiazole-2-yl) Benzonitrile (**5e**).[50] White solid (110 mg, 94% yield). m.p. 169−170 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.19 (d, J = 5 Hz, 2H), 8.11 (d, J = 10 Hz, 1H), 7.94 (d, J = 10 Hz, 1H), 7.78 (d, J = 10 Hz, 2H), 7.54 (t, J = 10 Hz, 1H), 7.44 (t, J = 5 Hz, 1H).

2-(4-Trifluoromethylphenyl) Benzothiazole (**5f**).[51] White solid (102 mg, 95% yield). m.p. 162−164 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.21 (d, J = 10 Hz, 2H), 8.11 (d, J = 10 Hz, 1H), 7.94 (d, J = 10 Hz, 1H), 7.76 (d, J = 10 Hz, 2H), 7.53 (t, J = 10 Hz, 1H), 7.43 (t, J = 5 Hz, 1H).

2-(4-Bromophenyl) Benzothiazole (**5g**).[50] White solid (138 mg, 96% yield). m.p. 132 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.07 (d, J = 10 Hz, 1H), 7.96 (d, J = 5 Hz, 2H), 7.91 (d, J = 10 Hz, 1H), 7.63 (d, J = 10 Hz, 2H), 7.50 (t, J = 5 Hz, 1H), 7.40 (t, J = 5 Hz, 1H).

2-(2-Chlorophenyl) Benzothiazole (**5h**).[49] Pale yellow solid (112 mg, 92% yield). m.p. 85 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.23−8.20 (m, 1H), 8.14 (d, J = 10 Hz, 1H), 7.96 (d, J = 10 Hz, 1H), 7.56−7.52 (m, 2H), 7.46−7.40 (m, 3H).

2-(3-Nitrophenyl) Benzothiazole (**5i**).[49] Yellow solid (119 mg, 94% yield). m.p. 183 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.94 (s, 1H), 8.41 (d, J = 10 Hz, 1H), 8.34 (d, J = 10 Hz, 1H), 8.12 (d, J = 10 Hz, 1H), 7.94 (d, J = 10 Hz, 1H), 7.69 (d, J = 10 Hz, 1H), 7.54 (t, J = 5 Hz, 1H), 7.45 (t, J = 5 Hz, 1H).

2-(4-Methoxyphenyl) Benzothiazole (**5j**).[51] White solid (108 mg, 90% yield). m.p. 123−125 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.05−8.02 (m, 3H), 7.88 (d, J = 10 Hz, 1H), 7.47 (t, J = 10 Hz, 1H), 7.35 (t, J = 5 Hz, 1H), 7.01 (d, J = 10 Hz, 2H), 3.89 (s, 3H).

2-(4-Ethylphenyl) Benzothiazole (**5k**).[50] Pale yellow solid (111 mg, 93% yield). m.p. 63 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.06 (d, J = 5 Hz, 1H), 8.01 (d, J = 5 Hz, 2H), 7.89 (d, J = 5 Hz, 1H), 7.48 (t, J = 5 Hz, 1H), 7.37 (t, J = 10 Hz, 1H), 7.33 (d, J = 10 Hz, 2H), 2.72 (q, J = 10 Hz, 2H), 1.28 (t, J = 5 Hz, 3H).

2-(4-Isopropylphenyl) Benzothiazole (**5l**).[50] White solid (118 mg, 94% yield). m.p. 78−80 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.06 (d, J = 5 Hz, 1H), 8.02 (d, J = 10 Hz, 2H), 7.90 (d, J = 10 Hz, 1H), 7.48 (t, J = 5 Hz, 1H), 7.39−7.35 (m, 3H), 2.97 (septet, J = 10 Hz, 1H), 1.30 (d, J = 10 Hz, 6H).

2-(Naphthalen-2-yl) Benzothiazole (**5m**).[36] White solid (123 mg, 95% yield). m.p. 129 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.58 (s, 1H), 8.22 (d, J = 10 Hz, 1H), 8.12 (d, J = 10 Hz, 1H), 7.99−7.93 (m, 3H), 7.90−7.88 (m, 1H), 7.58−7.50 (m, 3H), 7.41 (t, J = 10 Hz, 1H).

4-(Benzothiazol-2-yl)-N,N-dimethylaniline (**5w**).[51] Yellow solid (119 mg, 95% yield). m.p. 128−130 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.99−7.95 (m, 3H), 7.84 (d, J = 10 Hz, 1H), 7.43 (t, J = 10 Hz, 1H), 7.30 (t, J = 10 Hz, 1H), 6.75 (d, J = 10 Hz, 2H), 3.06 (s, 6H).

https://dx.doi.org/10.1021/acs.joc.0c01965
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*2-(4-Methylphenyl) Benzothiazole (**5x**).*[50] White solid (103 mg, 92% yield). m.p. 85−86 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.06 (d, *J* = 10 Hz, 1H), 7.99 (d, *J* = 10 Hz, 2H), 7.89 (d, *J* = 5 Hz, 1H), 7.48 (t, *J* = 10 Hz, 1H), 7.37 (t, *J* = 10 Hz, 1H), 7.30 (d, *J* = 10 Hz, 2H), 2.43 (s, 3H).

*1,4-Diphenylbenzothiazole (**5y**).*[43] Off-white solid (163 mg, 95% yield). m.p. 261−263 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.24 (s, 4H), 8.12 (d, *J* = 10 Hz, 2H), 7.94 (d, *J* = 5 Hz), 7.53 (t, *J* = 10 Hz, 2H), 7.42 (t, *J* = 5 Hz, 2H).

*Benzothiazole (**5o**).*[26] Yellow oil (59 mg, 88% yield). b.p. 227−229 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.96 (s, 1H), 8.12 (d, *J* = 10 Hz, 1H), 7.92 (d, *J* = 5 Hz, 1H), 7.49 (t, *J* = 10 Hz, 1H), 7.40 (d, *J* = 5 Hz, 1H).

*2-Phenylquinazoline (**7a**).*[38] White solid (95 mg, 93% yield). m.p. 101−103 °C. ^{1}HNMR (500 MHz, $CDCl_3$): δ (ppm) 9.48 (s, 1H), 8.61 (d, *J* = 5 Hz, 2H), 8.10 (d, *J* = 10 Hz, 1H), 7.94−7.90 (m, 2H), 7.62 (t, *J* = 10 Hz, 1H), 7.56−7.50 (m, 3H).

*2-(4-Chlorophenyl) Quinazoline (**7b**).*[38] White solid (108 mg, 90% yield). m.p. 136−138 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.46 (s, 1H), 8.57 (d, *J* = 10 Hz, 2H), 8.08 (d, *J* = 10 Hz, 1H), 7.95−7.91 (m, 2H), 7.63 (t, *J* = 5 Hz, 1H), 7.50 (d, *J* = 5 Hz, 2H).

*2-(4-Nitrophenyl) Quinazoline (**7c**).*[38] White solid (111 mg, 89% yield). m.p. 222−234 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.52 (s, 1H), 8.83 (d, *J* = 10 Hz, 2H), 8.38 (d, *J* = 10 Hz, 2H), 8.14 (d, *J* = 10 Hz, 1H), 8.01−7.97 (m, 2H), 7.71 (d, *J* = 10 Hz, 1H).

*2-(4-Fluorophenyl) Quinazoline (**7d**).*[38] White solid (99 mg, 89% yield). m.p. 131−133 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.45 (s, 1H), 8.65−8.61 (m, 2H), 8.07 (d, *J* = 10 Hz, 1H), 7.94−7.89 (m, 2H), 7.61 (t, *J* = 5 Hz, 1H), 7.21 (t, *J* = 10 Hz, 2H).

*2-Phenyl-1,2,3,4-tetrahydroquinazoline (**8a**).*[38] Brown solid (89 mg, 85% yield). m.p. 101−103 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.52 (d, *J* = 10 Hz, 2H), 7.41−7.34 (m, 3H), 7.05 (t, *J* = 10 Hz, 1H), 6.94 (d, *J* = 5 Hz, 1H), 6.72 (t, *J* = 5 Hz, 1H), 6.59 (d, *J* = 10 Hz, 1H), 5.25 (s, 1H), 4.29−4.20 (m, 1H), 3.99 (d, *J* = 15 Hz, 1H), 1.83 (br s, 1H).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01965.

> FAIR Data is available as Supporting Information for Publication and includes the primary NMR FID files for compounds **3a−3v**, **5a−m**, **5w**, **5y**, **5o**, **7a**, and **8a−8d**, detection of H_2O_2, FT-IR spectra, UV−vis studies, and table of comparison of present manuscript with previous reports (PDF)

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Author Contributions

All the experiments were performed and compiled by S.D. V.B. and M.K. supervised the work and led the project.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

V.B. is thankful to SERB, New Delhi (ref. no. CRG/2018/001274), CSIR New Delhi (No. 02(0358/19/EMR-II) and RUSA 2.0 for the financial support. S.D. is thankful to DST-INSPIRE (New Delhi) for Senior Research Fellowship (SRF).

■ ABBREVIATIONS

AIEE, aggregation-induced emission enhancement; ICT, intramolecular charge transfer; PC, photocatalyst; TON, turnover number; TOF, turnover frequency

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