9,10-Phenanthrenedione as Visible-Light Photoredox Catalyst: A Green Methodology for the Functionalization of 3,4-Dihydro-1,4-Benzoxazin-2-Ones through a Friedel-Crafts Reaction

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Abstract: A visible-light photoredox functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones through a Friedel-Crafts reaction with indoles using an inexpensive organophotoredox catalyst is described. The reaction uses a dual catalytic system that is formed by a photocatalyst simple and cheap, 9,10-phenanthrenedione, and a Lewis acid, Zn(OTf)₂. 5W white LEDs are used as visible-light source and oxygen from air as a terminal oxidant, obtaining the corresponding products with good yields. The reaction can be extended to other electron-rich arenes. Our methodology represents one of the most valuable and sustainable approach for the functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones, as compared to the reported procedures. Furthermore, several transformations were carried out, such as the synthesis of the natural product cephalandole A and a tryptophol derivative.

Keywords: visible-light photocatalysis; organophotoredox catalysis; Friedel-Crafts reaction; indoles; 1,4-benzoxazin-2-ones

1. Introduction

Visible-light (sunlight) is a safe, renewable, abundant, inexpensive, and non-polluting source of energy, which means that sunlight is the most “green” energy source that we can use. Therefore, the development of methodologies using visible-light has become one of the greatest challenges in the scientific community in the last century [1,2]. In this context, the development of methodologies to increase the use of visible-light to control chemical reactivity and achieve molecular complexity with higher levels of efficiency have become a hot topic in the last years and many challenging organic reactions have been described [3–9]. For this purpose, intensive research has been devoted to develop photoredox catalysts that are capable of absorbing visible light and transfer this energy to the organic molecules. Many elegant works on photocatalysis have been reported using transition metal ruthenium or iridium polypyridyl complexes as efficient photosensitizers [10–13]. However, these transition metals are expensive and they have potential toxicity that has limited their usefulness. Therefore, for the development of more sustainable visible-light photoredox methodologies the use of organic dyes is more convenient due to the low cost, high availability, and low toxicity that offer this kind of catalyst. However, some of the organophotoredox catalysts are expensive, such as pyrilium [14–18] or acridinium [19–24] salts (Figure 1). Organic dyes, such as Rose Bengal and Eosin Y, are more convenient due to their lower cost [25–31]. Nevertheless, the development of new methodologies using simpler organophotoredox catalysts that improve the sustainability of the “green” chemical
process is highly desirable. In this context, α-diketones represent a class of compounds that can exhibit absorption bands in the visible range and that have been used for photochemical processes [32–34]. For example, 9,10-phenanthrene diione is an inexpensive organic compound with very low molecular weight (Figure 1) when compared with other organophotoredox catalysts. This α-diketone has absorption bands in the visible region (412 and 505 nm in acetonitrile, see Supplementary Materials for further details) and therefore could be excited by visible-light. However, it has been rarely used in visible-light photochemical processes [35–37].

![Figure 1. Comparison of commercially available common visible-light photoredox catalysts and 9,10-phenanthrene diione (source: Sigma-Aldrich (2018)).](image)

On the other hand, tertiary amines represent an important class of compounds in organic synthesis, where functionalization is of great interest for the chemical community, medicinal chemistry, pharmaceutical, and agrochemical industry. In this context, the combination of visible-light catalysis and C-H bond functionalization adjacent to a tertiary amine has been successfully developed in the last years [38–41]. Normally, this sp3-C-H functionalization involves the oxidation of the amine to iminium ion, which can be attacked by various kind of nucleophiles. Nonetheless, the major number of examples are regarded to the functionalization of N-aryl tetrahydroisoquinolines [42–52], N,N-dimethyl anilines [53–57], and N-aryl glycine derivatives [58–62]. Hence, exploring other substrates is highly desirable. In this context, 1,4-dibenzoxazinone skeleton is present in a wide number of compounds with biological activities and its functionalization could be significant and interesting for medicinal chemistry [63–69]. Very recently, Huo described the iron catalyzed sp3-C-H functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones [70,71] using as a terminal oxidant tert-Butyl hydroperoxide (TBHP) [70] or 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) [71]. We envisioned that this functionalization could be achieved by a visible-light photochemical process. Herein, continuing with our interest in the synthesis of multisubstituted 1,4-dihydrobenzoxazin-2-ones [72] and the Friedel-Crafts reactions with indoles [73–75], we described the visible-light photoredox Friedel-Crafts reaction of indoles with benzoxazin-2-ones using as catalyst a simple and cheap diketone such as the 9,10-phenanthrene diione, and oxygen as terminal oxidant. During our experimental work and the preparation of manuscript, a photoredox functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones was reported [76,77]. In both cases, the expensive Ru(bpy)$_2$Cl$_2$ was used as photocatalyst. Besides, unlike the photoredox catalytic system described earlier [76], the results that were obtained with our method are not affected by the steric hindrance around the C3 carbon atom of the indole skeleton. The second paper [77] deals with the functionalization of 3,4-dihydro-1,4-quinolinoxin-2(1H)-one skeleton and only one example of 3,4-dihydro-1,4-benzoxazin-2-ones was reported with low yield (44%).
2. Results

Initially, we choose the Friedel-Crafts reaction between indole 1a and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one 2a in acetonitrile at room temperature under air atmosphere and the irradiation of white LEDs (5W). Under these conditions, a survey of photocatalyst were screened, and the results are summarized in Table 1. In a preliminary study of the photocatalyst (entries 1–6), Ru(bpy)$_2$Cl$_2$ (A), Rose Bengal (B), Fukuzumi photocatalyst (E), and 9,10-phenanthrenedione (F) afforded product 3aa with similar yields, around 30%, after 24 h. With these catalysts, we decided to change the molar ratio of 1a:2a from 0.15:0.1 to 0.1:0.15 (entries 7–10). The best yield for compound 3aa was obtained when Rose Bengal (B) and 9,10-phenanthrenedione (F) were used as photocatalyst (53% yield in both cases). In view of the good performance of the photocatalyst F, we decided to carry out the reaction using another α-diketone, such as benzyl (G), however the yield of 3aa drop to only 15%. In view of the results, we decided to continue the optimization of the reaction conditions using 9,10-phenanthrenedione as a photocatalyst, due to its low molecular weight and its lower price in relation to the other photocatalysts tested.

![Table 1. Preliminary optimization of the reaction conditions a.](image)

| Entry | Photocatalyst (mol%) | 1a (mmol) | 2a (mmol) | t (h) | Yield of 3aa (%) b |
|-------|----------------------|-----------|-----------|------|-------------------|
| 1     | A (1%)               | 0.15      | 0.1       | 24   | 28                |
| 2     | B (5%)               | 0.15      | 0.1       | 27   | 38                |
| 3     | C (5%)               | 0.15      | 0.1       | 46   | 27                |
| 4     | D (5%)               | 0.15      | 0.1       | 48   | 13                |
| 5     | E (5%)               | 0.15      | 0.1       | 48   | 35                |
| 6     | F (10%)              | 0.15      | 0.1       | 25   | 33                |
| 7     | A (1%)               | 0.1       | 0.15      | 24   | 48                |
| 8     | B (5%)               | 0.15      | 0.15      | 24   | 53                |
| 9     | E (5%)               | 0.1       | 0.15      | 48   | 27                |
| 10    | F (10%)              | 0.1       | 0.15      | 24   | 53                |
| 11    | G (10%)              | 0.1       | 0.15      | 24   | 15                |

a Reaction conditions: 1a, 2a, x mol% of photocatalyst in 1 mL of CH$_3$CN at rt under white LEDs 5W irradiation and air atmosphere. b Isolated yield of 3aa.

In order to improve the yield of 3aa, we decided to investigate a dual catalytic protocol combining Brønsted or Lewis acid catalysis and visible-light photoredox catalysis [58] (Table 2). For this purpose, different Brønsted acids, such as PhCO$_2$H or AcOH, were tested, however product 3aa was obtained with lower yield (entries 2 and 3, respectively). After we decided to test Zn salts as Lewis acid, obtaining an improvement of the catalytic performance when we used 10 mol% of Zn(OTf)$_2$. In these conditions, the functionalized benzooxazinone 3aa was obtained in 76% after 9 h (entry 5). Other Lewis acids, such as Fe(OTf)$_2$, Cu(OTf)$_2$, and Sc(OTf)$_3$ were evaluated (entries 6–8), obtaining lower yields for the corresponding product 3aa. The lowering of the catalyst loading of Zn(OTf)$_2$ to 5 mol% did not influence in the yield of product 3aa (entry 10). Subsequently, different solvents such as toluene, CH$_2$Cl$_2$, DMF, THF, or MeOH were screened (entries 11–14), obtaining the functionalized benzooxazinone 3aa with much lower yields. We could diminish the photocatalyst and Lewis acid loadings maintaining the yield of product 3aa (entries 15 and 16). Finally, some control experiments
were carried out. Thus, in the absence of visible-light (entry 19) or 9,10-phenanthrenedione (entry 20), the product 3aa was not detected or the conversion was very low.

With the optimized reaction conditions in hand (entry 13, Table 2), the scope of the Friedel-Crafts reaction was explored with a range of indoles 1 using indole 1a as nucleophile (Scheme 2). An assortment of derivatives with different groups on the benzyl moiety reacted smoothly in the optimized reaction conditions, obtaining the corresponding products 3na–3pa with high yields (54–80%) independently of the position or the electronic character of the substituents. Moreover, disubstituted indoles, such as 1n–1p, afforded the corresponding products 3na–3pa, with high yields (up to 77%). It is interesting to note the good results that were obtained with 2- and 4-substituted indoles, despite the steric hindrance around the reactive carbon atom. Thus, for example, 2-methyl- and 4-methylindol gave the corresponding reaction products with yields of 58% and 64%, respectively (versus 13% and 26% described in the literature [76]). Also 2-phenyl-, 4-fluoro-, and 1,2-dimethylindole give yields of 80%, 79%, and 70%, respectively.

Afterwards, we examined the scope of the Friedel-Crafts alkylation with a range of 3,4-dihydro-1,4-benzoxazin-2-ones 2 using indole 1a as nucleophile (Scheme 2). An assortment of derivatives with different groups on the benzyl moiety reacted smoothly in the optimized reaction conditions, obtaining the corresponding products 3ab–3ad with good yields (56–88%). A thienylmethyl group on the nitrogen of the benzoxazinone 1e could be used in the Friedel-Crafts reaction obtaining the corresponding product 3ae with a high yield (77%). Additionally, 3,4-dihydro-1,4-benzoxazin-2-ones 1g and 1h, with methyl substituents at 6 and 7 positions worked well in this Friedel-Crafts reaction.

### Table 2. Optimization of the reaction conditions

| Entry | Photocat. (mol%) | Additive (mol%) | Solvent | t (h) | Yield of 3aa (%) |
|-------|------------------|----------------|---------|-------|-----------------|
| 1     | F (10%)          | -              | CH3CN   | 24    | 53              |
| 2     | F (10%)          | PhCO2H (10 mol%) | CH3CN   | 24    | 36              |
| 3     | F (10%)          | AcOH (10 mol%)  | CH3CN   | 24    | 26              |
| 4     | F (10%)          | Zn(OAc)2 (10 mol%) | CH3CN   | 24    | 37              |
| 5     | F (10%)          | Zn(OTf)2 (10 mol%) | CH3CN   | 9     | 76              |
| 6     | F (10%)          | Fe(OTf)2 (10 mol%) | CH3CN   | 20    | 22              |
| 7     | F (10%)          | Cu(OTf)2 (10 mol%) | CH3CN   | 17    | 19              |
| 8     | F (10%)          | Sc(OTf)3 (10 mol%) | CH3CN   | 19    | 16              |
| 9     | F (10%)          | Zn(OTf)2 (5 mol%)  | CH3CN   | 9     | 74              |
| 10    | F (10%)          | Zn(OTf)2 (5 mol%)  | Toluene | 8     | 40              |
| 11    | F (10%)          | Zn(OTf)2 (5 mol%)  | CH2Cl2  | 20    | 30              |
| 12    | F (10%)          | Zn(OTf)2 (5 mol%)  | DMF     | 72    | 12              |
| 13    | F (10%)          | Zn(OTf)2 (5 mol%)  | THF     | 9     | 34              |
| 14    | F (10%)          | Zn(OTf)2 (5 mol%)  | MeOH    | 17    | 22              |
| 15    | F (5%)           | Zn(OTf)2 (5 mol%)  | CH3CN   | 10    | 74              |
| 16    | F (5%)           | Zn(OTf)2 (2.5 mol%) | CH3CN   | 10    | 75              |
| 17    | B (5%)           | Zn(OTf)2 (2.5 mol%) | CH3CN   | 17    | 38              |
| 18    | F (5%)           | Zn(OTf)2 (2.5 mol%) | CH3CN   | 15    | 45              |
| 19    | F (5%)           | Zn(OTf)2 (2.5 mol%) | CH3CN   | 72    | n.d. e          |
| 20    | -                | Zn(OTf)2 (2.5 mol%) | CH3CN   | 72    | <5 e           |

a Reaction conditions: 1a (0.1 mmol), 2a (0.15 mmol), x mol% of photocatalyst, x mol% of additive in 1 mL of solvent at rt under white LEDs 5W irradiation and air atmosphere; b Isolated yield of 3aa; c 0.12 mmol of 2a was used; d Reaction performed under darkness; e Conversion to product 3aa by 1H NMR of the crude reaction mixture. N.d. = not detected.
We also extended our methodology to other electron-rich arenes, such as pyrrole (4a), N-methylpyrrole (4b), and 1,3,5-trimethoxybenzene (5) (Scheme 3), which were reacted with 3,4-dihydro-1,4-benzoxazin-2-ones 2a under the optimized reaction conditions, obtaining the corresponding functionalized benzoxazinones 6a, 6b, and 7 with good yields (55–83%). Again, it is interesting to note the good result obtained with 1,3,5-trimethoxybenzene, a starting material with a large steric hindrance. The reaction product was obtained with a yield of 83% (versus 23% described in the literature [76]).
Tryptophols are a class of indoles bearing a 3-(hydroxyethyl) side chain. These class of compounds have been isolated from a variety of natural sources, and some of them possess biological activity [79–82].

Furthermore, in order to demonstrate the sustainability of our visible-light photoredox methodology, the reaction was performed using sun-light (Scheme 4). Therefore, when the Friedel-Crafts reaction was placed outdoors under sun-light irradiation, the corresponding product 3aa was obtained with 87% yield in 5 h.

Based on previous literature reports [3,70] and control experiments (see Supplementary Materials for further details) a possible mechanism for the reaction is proposed in Scheme 5. Initially, under visible-light irradiation, 9,10-phenanthrenedione F is excited to F*. Subsequently, this excited state, by a single-electron transfer (SET), transforms 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one 2a into a nitrogen radical cation I, with the consequent reduction of F* to the radical anion F*, which can be oxidized by molecular oxygen (O2) regenerating the photocatalyst F. On the other hand, deprotonation of the nitrogen radical cation I can generate the α-amino radical II, which can be further oxidized to the iminium ion III. After the nucleophilic attack of indole 1a to the iminium ion III, product 3aa is obtained. The radical mechanism was confirmed by an experiment control using a radical scavenger (TEMPO). Under these conditions, a trace amount of product 3aa was observed by 1H NMR of the crude reaction mixture and the corresponding adduct formed from radical II and TEMPO was detected by HRMS. In this mechanism, the O2 is the terminal oxidant that is reduced in H2O2. The role of molecular oxygen was also studied in a control experiment. When we performed the photocatalyzed Friedel-Crafts reaction under argon atmosphere, the conversion to product 3aa was very low (12%). However, the role of Zn(OTf)2 is not clear, with this Lewis acid, the reaction is accelerated, activating either the electrophile or the nucleophile, or both.

To showcase the utility of our catalytic protocol, we performed several synthetic transformations (Scheme 6). Compound 3aa was catalytically deprotected using H2 and 10% Pd/C in THF/EtOH, and then the addition of 1 equivalent of DDQ for 1 h, allowed us to obtain the natural product cephalandole A [78] (8) in 91% yield in a one-pot reaction. Moreover, compounds 3 can be used to prepare tryptophol derivatives by a reduction of the carbonyl group of the benzoxazin-2-one. Tryptophols are a class of indoles bearing a 3-(hydroxyethyl) side chain. These class of compounds have been isolated from a variety of natural sources, and some of them possess biological activity [79–82].
Therefore, compound 3aa has been reduced with LiAlH₄ affording tryptophol derivative 9 with 57% yield.

![Scheme 5](image)

**Scheme 5.** Pausible mechanism for the visible-light photoredox Friedel-Crafts alkylation of 1a with 2a.

![Scheme 6](image)

**Scheme 6.** Synthetic transformations. Isolated yields after column chromatography.

### 3. Materials and Methods

#### 3.1. General Information

Reactions were carried out in 5 mL vials under air, unless otherwise indicated. Commercial reagents were used as purchased. Reactions were monitored by thin-layer chromatography (TLC) analysis using Merck Silica Gel 60 F-254 (Sigma-Aldrich, St. Louis, MO, USA) thin layer plates and these are visualized using both an UV lamp (254 nm) and then a CAM solution (an aqueous solution of ceric ammonium molybdate). Flash column chromatography was performed on Merck Silica Gel 60 (Sigma-Aldrich, St. Louis, MO, USA), 0.040–0.063 mm. NMR (Nuclear Magnetic Resonance) spectra were run in a Bruker DPX300 spectrometer (Bruker, Billerica, MA, USA) at 300 MHz for ¹H and 75 MHz for ¹³C using residual nondeuterated solvent as internal standard (CHCl₃: δ 7.26 and δ 77.00 ppm, respectively, MeOH: δ 3.34 ppm and δ 49.87 ppm, respectively, Acetone: δ 2.05 ppm and δ 29.84 ppm, respectively). Chemical shifts are given in ppm. The carbon multiplicity was established by DEPT (Distortionless Enhancement by Polarization Transfer) experiments. High resolution mass spectra (HRMS-ESI) were recorded on a TRIPLETOFT5600 spectrometer (AB Sciex, Warrington, UK), equipped with an electrospray source with a capillary voltage of 4.5 kV (ESI).

All photocatalysts, indoles, and related arenes were commercially available. 3,4-dihydro-benzoxazin-2-ones derivatives 2a, 2b, and 2c were synthesized according to a procedure that was published in the literature and the spectroscopic data (¹H-NMR and ¹³C-NMR) match with those reported. 3,4-dihydro-benzoxazin-2-ones derivatives 2d, 2e, 2f, 2g, and 2h were synthesized according to the same procedure and were characterized by ¹H-NMR, ¹³C-NMR, and HRMS (see Supplementary Materials for further details).
3.2. General Procedure: Friedel-Crafts Reaction between 4-Benzyl-3,4-Dihydro-1,4-Benzoxazin-2-Ones and Indoles, Pyrroles and 1,3,5-Trimethoxybenzene

In a 5 mL vial were placed the proper aromatic compound (1, 4, or 5, 0.10 mmol), the proper 4-benzyl-3,4-dihydro-1,4-benzoxazin-2-one (2, 0.15 mmol), Zn(OTf)\(_2\) (1.0 mg, 0.0025 mmol, 2.5 mol%), and 9,10-phenanthredione (F, 1.0 mg, 0.005 mmol, 5 mol%). Subsequently, the mixture was dissolved in non-dried acetonitrile (1 mL) and was placed at two centimetres from the white LEDs. The reaction was monitored by TLC and was stopped when the corresponding indole was consumed (NOTE: It is important to analyse frequently the conversion and to stop the reaction in the precise moment to avoid product decomposition. The reaction should not be left overnight under irradiation conditions). The resulted reaction mixture was purified by column chromatography using hexane:EtOAc mixtures (from 95:5 to 85:15) to afford pure product 3, 6, or 7.

3.3. Characterization Data for Compounds 3, 6 and 7

4-Benzyl-3-(1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3aa)

Using indole (1a, 11.7 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3aa was obtained (26.6 mg, 0.075 mmol, 75% yield) after 10 h as a colourless oil. \(\text{\(^1H\) NMR (300 MHz, CDCl}_3\)) \(\delta\) 8.12 (s, 1H), 7.51 (d, \(J = 7.9\) Hz, 1H), 7.38–7.27 (m, 5H), 7.24–7.17 (m, 1H), 7.16–7.04 (m, 1H), 6.91 (td, \(J = 7.7, 1.4\) Hz, 1H), 6.72 (d, \(J = 2.6\) Hz, 1H), 5.41 (s, 1H), 4.62 (d, \(J = 14.9\) Hz, 1H), 4.15 (d, \(J = 14.8\) Hz, 1H); \(\text{\(^{13}C\) NMR (75 MHz, CDCl}_3\)} \(\delta\) 164.56 (C), 141.84 (C), 136.08 (C), 135.78 (C), 134.13 (C), 128.81 (CH), 127.77 (CH), 126.05 (C), 125.37 (CH), 122.87 (CH), 122.79 (CH), 120.41 (CH), 119.85 (CH), 119.09 (CH), 116.53 (CH), 113.87 (CH), 111.27 (CH), 108.69 (CH), 55.86 (CH), 51.55 (CH\(_2\)). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(1-methyl-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ba)

Using N-methylindole (1b, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ba was obtained (21.2 mg, 0.058 mmol, 58% yield) after 15 h as a white solid. \(\text{\(^1H\) NMR (300 MHz, CDCl}_3\)} \(\delta\) 7.48 (dt, \(J = 8.0, 1.0\) Hz, 1H), 7.38–7.21 (m, 7H), 7.16–7.10 (m, 2H), 7.10–7.04 (m, 1H), 6.92 (td, \(J = 7.7, 1.5\) Hz, 1H), 6.82 (dd, \(J = 8.0, 1.4\) Hz, 1H), 6.59 (d, \(J = 0.6\) Hz, 1H), 5.40 (d, \(J = 0.6\) Hz, 1H), 4.61 (d, \(J = 14.9\) Hz, 1H), 4.16 (d, \(J = 14.9\) Hz, 1H), 3.64 (s, 3H); \(\text{\(^{13}C\) NMR (75 MHz, CDCl}_3\)} \(\delta\) 164.5 (C), 141.8 (C), 136.7 (C), 136.2 (C), 134.1 (C), 128.8 (CH), 127.8 (CH), 127.7 (CH), 127.2 (CH), 126.7 (C), 125.3 (CH), 122.4 (CH), 120.0 (CH), 119.8 (CH), 119.2 (CH), 116.6 (CH), 113.8 (CH), 109.4 (CH), 107.1 (C), 55.8 (CH), 51.5 (CH\(_2\)), 32.9 (CH\(_3\)). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(2-methyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ca)
Using 2-methylindole (1c, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ca was obtained (21.2 mg, 0.058 mmol, 58% yield) after 11 h as a white solid. $^{1}$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.98 (bs, 1H), 7.29–7.22 (m, 4H), 7.18 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.16–7.03 (m, 5H), 6.95 (ddd, $J = 8.1, 1.4, 1.1$ Hz, 1H), 6.89 (td, $J = 7.7, 1.4$ Hz, 1H), 6.80 (ddd, $J = 8.1, 1.4$ Hz, 1H), 5.34 (s, 1H), 4.95 (d, $J = 16.1$ Hz, 1H), 3.98 (d, $J = 16.1$ Hz, 1H), 2.02 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 141.8 (C), 138.2 (d, $J_{\text{C-F}} = 3.9$ Hz, 1H), 125.3 (CH), 123.1 (CH), 119.8 (CH), 116.4 (CH), 115.2 (d, $J_{\text{C-F}} = 19.4$ Hz, 1H), 114.7 (CH), 107.7 (d, $J_{\text{C-F}} = 3.9$ Hz, C), 107.6 (d, $J_{\text{C-F}} = 3.8$ Hz, CH), 105.8 (d, $J_{\text{C-F}} = 19.6$ Hz, CH), 56.8 (d, $J_{\text{C-F}} = 3.2$ Hz, CH), 51.7 (d, $J_{\text{C-F}} = 1.5$ Hz, CH$_2$); HRMS (ESI) m/z: 373,1342 [M + H]$^+$, C$_{23}$H$_{18}$FN$_2$O$_2$ required 373,1347.

Using 4-fluoroindole (1e, 13.5 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ea was obtained (29.4 mg, 0.079 mmol, 79% yield) after 14 h as a colourless oil. $^{1}$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.28 (s, 1H), 7.14 (dd, $J = 7.9, 1.6$ Hz, 1H), 7.11–7.08 (m, 2H), 7.00 (td, $J = 7.7, 1.6$ Hz, 1H), 6.89 (td, $J = 7.7, 1.5$ Hz, 1H), 6.85–6.77 (m, 1H), 6.74–6.63 (m, 2H), 5.71 (s, 1H), 4.46 (d, $J = 15.5$ Hz, 1H), 4.35 (d, $J = 15.5$ Hz, 1H); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -121.20 (s); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.9 (C), 141.8 (C), 138.2 (d, $J_{\text{C-F}} = 10.9$ Hz, C), 136.5 (C), 133.7 (C), 128.7 (CH), 127.4 (CH), 125.3 (CH), 123.3 (d, $J_{\text{C-F}} = 7.9$ Hz, CH), 123.1 (CH), 119.8 (CH), 116.4 (CH), 115.2 (d, $J_{\text{C-F}} = 19.4$ Hz, C), 114.7 (CH), 107.7 (d, $J_{\text{C-F}} = 3.9$ Hz, C), 107.6 (d, $J_{\text{C-F}} = 3.8$ Hz, CH), 105.8 (d, $J_{\text{C-F}} = 19.6$ Hz, CH), 56.8 (d, $J_{\text{C-F}} = 3.2$ Hz, CH), 51.7 (d, $J_{\text{C-F}} = 1.5$ Hz, CH$_2$); HRMS (ESI) m/z: 373,1342 [M + H]$^+$, C$_{23}$H$_{18}$FN$_2$O$_2$ required 373,1347.
Using 5-methylindole (1f, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3fa was obtained (23.2 mg, 0.063 mmol, 63% yield) after 11 h as a brown oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.01 (bs, 1H), 7.73–7.23 (m, 5H), 7.11–7.02 (m, 2H), 6.89 (td, $J = 7.7, 1.4$ Hz, 1H), 6.86–6.79 (m, 2H), 6.76 (dd, $J = 8.7, 2.3$ Hz, 1H), 6.67 (d, $J = 2.5$ Hz, 1H), 5.28 (s, 1H), 4.60 (d, $J = 14.9$ Hz, 1H), 4.12 (d, $J = 14.9$ Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.7 (C), 154.6 (C), 141.8 (C), 136.1 (C), 134.3 (C), 130.8 (C), 128.8 (CH), 127.8 (CH), 126.4 (C), 125.5 (CH), 123.7 (CH), 119.8 (CH), 116.6 (CH), 113.7 (CH), 113.6 (CH), 112.1 (CH), 108.7 (C), 100.3 (CH), 55.8 (CH), 55.7 (CH$_3$), 51.3 (CH$_2$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(5-methoxy-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ga)

Using 5-methoxyindole (1g, 14.7 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ga was obtained (26.1 mg, 0.068 mmol, 68% yield) after 11 h as a white solid. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.43–7.26 (m, 6H), 7.16–7.07 (m, 2H), 7.06 (td, $J = 26.1$ Hz, 1H), 7.03 (d, $J = 14.9$ Hz, 1H), 4.62 (dd, $J = 2.5$ Hz, 1H), 5.37 (d, $J = 14.9$ Hz, 1H), 4.12 (d, $J = 14.9$ Hz, 1H), 2.41 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.7 (C), 154.6 (C), 141.8 (C), 136.1 (C), 134.3 (C), 130.8 (C), 128.8 (CH), 127.9 (CH), 127.8 (CH), 126.4 (C), 125.3 (CH), 124.4 (CH), 122.9 (CH), 119.8 (CH), 118.7 (CH), 116.5 (CH), 113.9 (CH), 110.9 (CH), 108.2 (C), 55.8 (CH), 51.5 (CH$_2$), 21.4 (CH$_3$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(5-hydroxy-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ha)

Using 5-hydroxyindole (1h, 13.3 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ha was obtained (24.4 mg, 0.066 mmol, 66% yield) after 11 h as a colourless oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.38–7.23 (m, 5H), 7.13 (d, $J = 8.7$ Hz, 1H), 7.11–7.02 (m, 2H), 6.89 (td, $J = 7.7, 1.4$ Hz, 1H), 6.86–6.79 (m, 2H), 6.76 (dd, $J = 8.7, 2.3$ Hz, 1H), 6.67 (d, $J = 2.5$ Hz, 1H), 5.28 (s, 1H), 4.60 (d, $J = 14.9$ Hz, 1H), 4.12 (d, $J = 14.9$ Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.7 (C), 150.1 (C), 141.7 (C), 136.1 (C), 134.1 (C), 131.0 (C), 128.8 (CH), 127.8 (CH), 126.7 (C), 125.4 (CH), 123.8 (CH), 119.8 (CH), 116.6 (CH), 113.9 (CH), 112.8 (CH), 112.0 (CH), 108.0 (C), 103.6 (CH), 56.0 (CH), 51.6 (CH$_2$); HRMS (ESI) m/z: 371,1393 [M + H]$^+$, C$_{23}$H$_{19}$N$_2$O$_3$ required 371,1390.

4-Benzyl-3-(5-bromo-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ia)
Using 5-bromoindole (1i, 19.6 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ia was obtained (23.4 mg, 0.054 mmol, 54% yield) after 14 h as a white solid. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.21 (s, 1H), 7.54 (d, $J$ = 1.8 Hz, 1H), 7.40–7.32 (m, 3H), 7.32–7.24 (m, 3H), 7.17 (d, $J$ = 8.6 Hz, 1H), 7.15–7.05 (m, 2H), 6.93 (td, $J$ = 7.7, 1.4 Hz, 1H), 6.84 (dd, $J$ = 8.0, 1.3 Hz, 1H), 6.71 (d, $J$ = 2.6 Hz, 1H), 5.29 (s, 1H), 4.62 (d, $J$ = 14.6 Hz, 1H), 4.06 (d, $J$ = 14.6 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.46 (C), 141.84 (C), 135.73 (C), 134.39 (C), 134.02 (C), 128.89 (CH), 127.95 (CH), 127.73 (CH), 126.45 (C), 125.75 (CH), 125.51 (CH), 124.02 (CH), 121.78 (CH), 120.15 (CH), 116.60 (CH), 114.07 (CH), 113.75 (C), 112.73 (CH), 108.37 (C), 55.32 (CH), 51.54 (CH$_2$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(6-methyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ja)

Using 6-methylindole (1j, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ja was obtained (28.3 mg, 0.077 mmol, 77% yield) after 14 h as a white solid. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.98 (bs, 1H), 7.43–7.26 (m, 6H), 7.16–7.07 (m, 2H), 7.06 (td, $J$ = 7.7, 1.6 Hz, 1H), 6.96 (dd, $J$ = 8.2, 1.4 Hz, 1H), 6.91 (td, $J$ = 7.7, 1.5 Hz, 1H), 6.81 (dd, $J$ = 8.0, 1.4 Hz, 1H), 6.66 (d, $J$ = 2.5 Hz, 1H), 5.37 (d, $J$ = 0.7 Hz, 1H), 4.61 (d, $J$ = 14.8 Hz, 1H), 4.15 (d, $J$ = 14.8 Hz, 1H), 2.44 (s, 3H): $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.6 (C), 141.9 (C), 136.3 (C), 136.1 (C), 134.2 (C), 132.7 (C), 128.8 (CH), 127.8 (CH), 127.7 (CH), 125.3 (CH), 123.9 (C), 122.3 (CH), 119.8 (CH), 118.7 (CH), 116.5 (CH), 113.8 (C), 111.2 (CH), 108.6 (C), 56.0 (CH), 51.5 (CH$_2$), 21.6 (CH$_3$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(7-methyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ka)

Using 7-methylindole (1k, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ka was obtained (26.1 mg, 0.071 mmol, 71% yield) after 14 h as a yellow oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.03 (s, 1H), 7.33 (m, 6H), 7.12 (dd, $J$ = 7.9, 1.5 Hz, 1H), 7.09–6.98 (m, 2H), 6.91 (td, $J$ = 7.7, 1.4 Hz, 1H), 6.81 (dd, $J$ = 8.1, 1.4 Hz, 1H), 6.73 (d, $J$ = 2.6 Hz, 1H), 5.39 (d, $J$ = 0.7 Hz, 1H), 4.61 (d, $J$ = 14.9 Hz, 1H), 4.16 (d, $J$ = 14.9 Hz, 1H), 2.42 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.5 (C), 141.9 (C), 136.1 (C), 135.4 (C), 134.2 (C), 128.8 (CH), 127.8 (CH), 127.5 (C), 125.3 (CH), 123.3 (CH), 122.6 (CH), 120.7 (CH), 120.5 (C), 119.8 (CH), 116.8 (CH), 116.5 (CH), 113.9 (CH), 109.2 (C), 56.0 (CH), 51.6 (CH$_2$), 16.4 (CH$_3$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(7-chloro-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3la)

Using 7-chloroindole (1l, 15.2 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3la was obtained (22.9 mg, 0.059 mmol, 59% yield) after 16 h as a white solid. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.29 (bs, 1H), 7.39
Using 2-phenylindole (1m, 19.3 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ma was obtained (34.4 mg, 0.080 mmol, 80% yield) after 14 h as a yellow oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.27 (bs, 1H), 7.54–7.46 (m, 2H), 7.42–7.32 (m, 4H), 7.22–7.14 (m, 3H), 7.11–7.05 (m, 3H), 6.96–6.91 (m, 2H), 6.69 (dd, $J = 8.1$, 1.4 Hz, 1H), 5.57 (s, 1H), 4.42 (d, $J = 16.2$ Hz, 1H), 3.87 (d, $J = 16.3$ Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 166.2 (C), 140.5 (C), 139.4 (C), 136.4 (C), 135.9 (C), 134.2 (C), 131.3 (C), 129.0 (C), 128.9 (C), 128.7 (C), 128.4 (C), 127.0 (C), 126.9 (C), 126.3 (C), 125.5 (C), 122.9 (C), 120.7 (C), 120.0 (C), 118.9 (C), 116.9 (C), 113.1 (C), 111.1 (C), 107.6 (C), 56.1 (CH), 50.0 (CH$_2$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(1,2-dimethyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3na)

Using 1,2-dimethylindole (1n, 14.5 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3na was obtained (26.7 mg, 0.070 mmol, 70% yield) after 12 h as a brown oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.31–7.22 (m, 4H), 7.19–7.14 (m, 3H), 7.14–7.08 (m, 2H), 7.05 (ddd, $J = 8.1$, 7.4, 1.6 Hz, 1H), 6.96 (ddd, $J = 8.0$, 6.9, 1.1 Hz, 1H), 6.88 (ddd, $J = 7.9$, 7.5, 1.4 Hz, 1H), 6.78 (dd, $J = 8.1$, 1.4 Hz, 1H), 5.38 (d, $J = 0.5$ Hz, 1H), 4.57 (d, $J = 16.2$ Hz, 1H), 3.99 (d, $J = 16.2$ Hz, 1H), 3.63 (s, 3H), 2.12 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 166.1 (C), 140.9 (C), 140.7 (C), 137.0 (C), 136.8 (C), 134.6 (C), 128.7 (C), 127.2 (C), 127.1 (C), 125.8 (C), 125.5 (C), 121.3 (CH), 120.0 (CH), 119.0 (C), 118.6 (CH), 117.0 (CH), 113.2 (CH), 109.0 (CH), 105.3 (C), 56.2 (CH), 49.9 (CH$_2$), 29.6 (CH$_3$), 10.3 (CH$_3$). The spectroscopic data match with those reported in the literature [70].

4-Benzyl-3-(5-methoxy-7-methyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3oa)

Using 5-methoxy-7-methylindole (1o, 16.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3oa was obtained (27.9 mg, 0.070 mmol, 70% yield) after 11 h as a colourless oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.98 (bs, 1H), 7.40–7.27 (m, 5H), 7.13 (dd, $J = 7.9$, 1.5 Hz, 1H), 7.07 (td, $J = 7.7$, 1.5 Hz, 1H), 6.91
(td, J = 7.7, 1.4 Hz, 1H), 6.82 (dd, J = 8.1, 1.3 Hz, 1H), 6.74–6.62 (m, 3H), 5.33 (s, 1H), 4.61 (d, J = 14.8 Hz, 1H), 4.10 (d, J = 14.7 Hz, 1H), 3.71 (s, 3H), 2.36 (s, 3H); $^1$C NMR (75 MHz, CDCl$_3$) δ 164.7 (C), 154.7 (C), 141.8 (C), 136.1 (C), 134.3 (C), 130.6 (C), 128.8 (CH), 127.9 (CH), 127.8 (CH), 125.8 (C), 125.4 (CH), 123.3 (CH), 121.6 (C), 119.8 (CH), 116.5 (CH), 114.1 (CH), 113.8 (CH), 109.1 (C), 97.8 (CH), 55.8 (CH), 55.6 (CH$_3$), 51.2 (CH$_2$), 16.4 (CH$_3$). HRMS (ESI) m/z: 399,1708 [M + H]$^+$, C$_{25}$H$_{21}$N$_2$O$_3$ required 399,1703.

3-(1H-benzo[g]indol-3-yl)-4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3pa)

Using 1H-benzo[g]indole (1p, 16.7 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3pa was obtained (31.0 mg, 0.077 mmol, 77% yield) after 14 h as a brown solid. $^1$H NMR (300 MHz, Acetone) δ 11.25 (bs, 1H), 8.27 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.58–7.29 (m, 8H), 7.18–7.02 (m, 2H), 6.99–6.87 (m, 3H), 5.68 (d, J = 0.6 Hz, 1H), 4.68 (d, J = 15.1 Hz, 1H), 4.40 (d, J = 15.1 Hz, 1H); $^1$C NMR (75 MHz, Acetone) δ 165.05 (C), 143.02 (C), 138.04 (C), 135.22 (C), 131.87 (C), 131.47 (C), 129.52 (CH), 129.40 (CH), 128.60 (CH), 128.32 (CH), 126.48 (CH), 126.08 (CH), 125.02 (CH), 123.09 (C), 122.00 (C), 122.23 (CH), 121.56 (CH), 121.12 (CH), 120.64 (CH), 119.68 (CH), 116.95 (CH), 115.37 (CH), 110.99 (C), 57.46 (CH), 52.53 (CH$_2$); HRMS (ESI) m/z: 405,1592 [M + H]$^+$, C$_{27}$H$_{21}$N$_2$O$_2$ required 405,1598.

3-(1H-indol-3-yl)-4-(4-methoxybenzyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ab)

Using indole (1a, 11.7 mg, 0.1 mmol) and 4-(4-methoxybenzyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2b, 40.4 mg, 0.15 mmol), in accordance with General Procedure, the product 3ab was obtained (21.5 mg, 0.056 mmol, 56% yield) after 10 h as a white solid. $^1$H NMR (300 MHz, CDCl$_3$) δ 8.09 (bs, 1H), 7.50 (d, J = 7.9 Hz, 1H), 7.35–7.30 (m, 1H), 7.24–7.16 (m, 3H), 7.16–7.04 (m, 3H), 6.92 (d, J = 7.7, 1.4 Hz, 1H), 6.90–6.83 (m, 3H), 6.71 (d, J = 2.4 Hz, 1H), 5.37 (d, J = 0.4 Hz, 1H), 4.57 (d, J = 14.4 Hz, 1H), 4.07 (d, J = 14.3 Hz, 1H), 3.82 (s, 3H); $^1$C NMR (75 MHz, CDCl$_3$) δ 164.54 (C), 159.22 (C), 141.93 (C), 135.76 (C), 134.29 (C), 129.22 (CH), 127.80 (C), 126.10 (C), 125.34 (CH), 122.79 (CH), 122.76 (CH), 120.40 (CH), 119.81 (CH), 119.20 (CH), 116.50 (CH), 114.21 (CH), 113.86 (CH), 111.21 (CH), 108.75 (C), 55.30 (CH), 50.90 (CH$_2$). The spectroscopic data match with those reported in the literature [70].

4-(4-cyanobenzyl)-(3-(1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ac)

Using indole (1a, 11.7 mg, 0.1 mmol) and 4-(4-cyanobenzyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2c, 39.6 mg, 0.15 mmol), in accordance with General Procedure, the product 3ac was obtained (33.4 mg, 0.088 mmol, 88% yield) after 13 h as a white solid. $^1$H NMR (300 MHz, CDCl$_3$) δ 8.15 (bs, 1H), 7.66–7.59
(m, 2H), 7.52 (d, J = 7.9 Hz, 1H), 7.41 (d, J = 8.5 Hz, 2H), 7.35 (d, J = 8.1 Hz, 1H), 7.26–7.19 (m, 1H), 7.18–7.11 (m, 2H), 7.04 (td, J = 7.7, 1.6 Hz, 1H), 6.94 (td, J = 7.7, 1.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 6.65 (dd, J = 8.0, 1.4 Hz, 1H), 5.39 (s, 1H), 4.60 (d, J = 16.0 Hz, 1H), 4.27 (d, J = 16.0 Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.1 (C), 142.1 (C), 141.9 (C), 135.8 (C), 133.4 (C), 132.7 (CH), 128.1 (CH), 126.0 (C), 125.4 (CH), 123.1 (CH), 122.9 (CH), 120.7 (CH), 120.6 (CH), 118.9 (CH), 118.6 (C), 116.8 (CH), 113.9 (CH), 111.6 (C), 111.4 (CH), 108.5 (C), 57.0 (CH), 51.7 (CH$_2$); HRMS (ESI) $m/z$: 380,1398 [M + H]$^+$, C$_{24}$H$_{18}$N$_3$O$_2$ required 380,1394.

4-(3-(bromobenzyl)-3-(1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ad)

Using indole (1a, 11.7 mg, 0.1 mmol) and 4-(3-bromobenzyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2d, 47.7 mg, 0.15 mmol), in accordance with General Procedure, the product 3ad was obtained (25.5 mg, 0.059 mmol, 59% yield) after 13 h as a brown oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.13 (s, 1H), 7.54–7.49 (m, 1H), 7.46–7.41 (m, 2H), 7.35–7.31 (m, 1H), 7.25–7.18 (m, 3H), 7.17–7.11 (m, 2H), 7.05 (dd, $J = 7.9, 1.6$ Hz, 1H), 6.93 (td, $J = 7.7, 1.4$ Hz, 1H), 6.81–6.69 (m, 2H), 5.39 (d, $J = 0.5$ Hz, 1H), 4.54 (d, $J = 15.2$ Hz, 1H), 4.12 (d, $J = 15.3$ Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.4 (C), 142.0 (C), 139.3 (C), 133.7 (C), 130.9 (CH), 130.7 (CH), 130.4 (CH), 126.2 (CH), 126.0 (C), 125.4 (CH), 122.9 (C), 122.9 (CH), 120.6 (CH), 120.2 (CH), 119.0 (CH), 116.7 (CH), 113.9 (CH), 111.3 (CH), 108.6 (C), 56.3 (CH), 51.2 (CH$_2$); HRMS (ESI) $m/z$: 433,0539 [M + H]$^+$, C$_{23}$H$_{18}$BrN$_2$O$_2$ required 433,0546.

3-(1H-indol-3-yl)-4-(thiophen-2-ylmethyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3ae)

Using indole (1a, 11.7 mg, 0.1 mmol) and 4-(thiophen-2-ylmethyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2e, 36.8 mg, 0.15 mmol), in accordance with General Procedure, the product 3ae was obtained (27.8 mg, 0.077 mmol, 77% yield) after 24 h as a brown solid. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.13 (bs, 1H), 7.56 (d, $J = 7.9$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.27 (dd, $J = 5.0, 1.0$ Hz, 1H), 7.25–7.17 (m, 1H), 7.17–7.06 (m, 2H), 6.99–6.90 (m, 4H), 6.74 (d, $J = 2.4$ Hz, 1H), 5.45 (s, 1H), 4.77 (d, $J = 15.1$ Hz, 1H), 4.35 (d, $J = 15.4$ Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.6 (C), 142.0 (C), 139.3 (C), 135.8 (C), 133.7 (C), 126.9 (CH), 126.6 (CH), 126.0 (C), 125.7 (CH), 125.4 (CH), 123.2 (CH), 122.8 (CH), 120.4 (CH), 120.3 (CH), 119.1 (CH), 116.7 (CH), 114.0 (CH), 111.3 (CH), 108.5 (C), 55.5 (CH), 46.7 (CH$_2$); HRMS (ESI) $m/z$: 361,1008 [M + H]$^+$, C$_{24}$H$_{17}$N$_2$O$_2$S required 361,1005.

3-(1H-indol-3-yl)-4-(3-phenylpropyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (3af)

Using indole (1a, 11.7 mg, 0.1 mmol) and 4-(3-phenylpropyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2f, 40.1 mg, 0.15 mmol), in accordance with General Procedure, the product 3af was obtained (28.3 mg, 0.074 mmol, 74% yield) after 24 h as a colourless oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.07 (bs, 1H), 7.66...
Using indole (1a, 11.7 mg, 0.1 mmol) and 4-benzyl-7-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2g, 38.0 mg, 0.15 mmol), in accordance with General Procedure, the product 3ag was obtained (25.4 mg, 0.069 mmol, 69% yield) after 16 h as a yellow oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.11 (bs, 1H), 7.52 (d, $J = 7.9$ Hz, 1H), 7.38–7.26 (m, 6H), 7.16–7.10 (m, 1H), 6.93 (d, $J = 1.4$ Hz, 1H), 6.86 (ddd, $J = 8.1$, 1.9, 0.6 Hz, 1H), 6.73 (d, $J = 2.5$ Hz, 1H), 6.70 (d, $J = 8.2$ Hz, 1H), 5.37 (d, $J = 0.4$ Hz, 1H), 4.56 (d, $J = 14.8$ Hz, 1H), 4.12 (d, $J = 14.8$ Hz, 1H), 2.31 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.8 (C), 141.9 (C), 136.3 (C), 135.8 (C), 131.7 (C), 129.9 (C), 128.9 (CH), 127.8 (CH), 127.7 (CH), 126.2 (C), 125.7 (CH), 122.8 (CH), 122.8 (CH), 120.4 (CH), 119.2 (CH), 117.1 (CH), 114.0 (CH), 111.2 (CH), 108.8 (C), 56.0 (CH), 51.8 (CH$_2$), 20.5 (CH$_3$). The spectroscopic data match with those reported in the literature [70].

Using indole (1a, 11.7 mg, 0.1 mmol) and 6-methyl-4-(3-phenylpropyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2h, 38.0 mg, 0.15 mmol), in accordance with General Procedure, the product 3ah was obtained (23.8 mg, 0.060 mmol, 60% yield) after 16 h as a colourless oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.07 (bs, 1H), 8.11 (bs, 1H), 7.71–7.61 (m, 1H), 7.39–7.25 (m, 3H), 7.24–7.09 (m, 5H), 6.93 (d, $J = 8.1$ Hz, 1H), 6.72 (d, $J = 2.3$ Hz, 1H), 6.64 (ddd, $J = 8.1$, 1.8, 0.6 Hz, 1H), 6.50 (d, $J = 1.5$ Hz, 1H), 5.37 (d, $J = 0.6$ Hz, 1H), 3.41 (ddd, $J = 13.9$, 8.0, 5.8 Hz, 1H), 3.13–2.98 (m, 1H), 2.68 (td, $J = 7.4$, 3.1 Hz, 2H), 2.30 (s, 3H), 2.10–1.88 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.4 (C), 141.1 (C), 139.6 (C), 135.9 (C), 135.0 (C), 133.4 (C), 128.5 (CH), 128.4 (CH), 126.1 (CH), 126.0 (C), 122.9 (CH), 122.7 (CH), 120.4 (CH), 119.6 (CH), 119.1 (CH), 116.2 (CH), 113.5 (CH), 111.3 (CH), 109.5 (C), 56.9 (CH), 47.2 (CH$_2$), 32.9 (CH$_2$), 28.3 (CH$_2$), 21.4 (CH$_3$); HRMS (ESI) $m/z$: 397,1918 [M + H]$^+$, C$_{26}$H$_{25}$N$_2$O$_2$ required 397,1911.

Using pyrrole (4a, 7 µL, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 6a was obtained (16.7 mg, 0.055 mmol, 55% yield) after 12 h as a brown oil. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.95 (bs, 1H), 7.45–7.27 (m, 5H), 7.37–7.25 (m, 5H), 7.25–7.11 (m, 5H), 7.11–7.04 (m, 2H), 6.86 (ddd, $J = 8.1$, 1.9, 0.6 Hz, 1H), 6.73 (d, $J = 2.5$ Hz, 1H), 6.70 (d, $J = 8.2$ Hz, 1H), 6.64 (ddd, $J = 8.1$, 1.8, 0.6 Hz, 1H), 5.37 (d, $J = 1.5$ Hz, 1H), 5.37 (d, $J = 0.6$ Hz, 1H), 3.41 (ddd, $J = 13.9$, 8.0, 5.8 Hz, 1H), 3.13–2.98 (m, 1H), 2.68 (td, $J = 7.4$, 3.1 Hz, 2H), 2.30 (s, 3H), 2.10–1.88 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 164.4 (C), 141.1 (C), 139.6 (C), 135.9 (C), 135.0 (C), 133.4 (C), 128.5 (CH), 128.4 (CH), 126.1 (CH), 126.0 (C), 122.9 (CH), 122.7 (CH), 120.4 (CH), 119.6 (CH), 119.1 (CH), 116.2 (CH), 113.5 (CH), 111.3 (CH), 109.5 (C), 56.9 (CH), 47.2 (CH$_2$), 32.9 (CH$_2$), 28.3 (CH$_2$), 21.4 (CH$_3$); HRMS (ESI) $m/z$: 419,2060 [M + H]$^+$, C$_{26}$H$_{25}$N$_2$O$_2$ required 419,2060.
Using N-methylpyrrole (4b, 9 μL, 0.1 mmol) and 4-benzyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (2a, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product 6b was obtained (18.4 mg, 0.058 mmol, 58\% yield) after 11 h as a yellow oil. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.37-7.30\) (m, 5H), 7.10 (dd, \(J = 7.9, 1.5\) Hz, 1H), 7.06–7.00 (m, 1H), 6.89 (dd, \(J = 7.7, 1.5\) Hz, 1H), 6.76 (dd, \(J = 8.0, 1.3\) Hz, 1H), 6.42 (t, \(J = 2.5\) Hz, 1H), 6.31 (t, \(J = 2.0\) Hz, 1H), 5.75 (dd, \(J = 2.6, 1.9\) Hz, 1H), 4.93 (s, 1H), 4.55 (d, \(J = 14.5\) Hz, 1H), 4.07 (d, \(J = 14.5\) Hz, 1H), 3.53 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta 165.64\) (C), 141.93 (C), 136.25 (C), 134.19 (C), 128.80 (CH), 127.96 (CH), 127.70 (CH), 125.17 (CH), 122.33 (CH), 120.54 (CH), 119.68 (CH), 116.36 (CH), 115.67 (C), 113.82 (CH), 107.83 (CH), 56.93 (CH), 51.18 (CH\(_2\)), 36.24 (CH\(_3\)). The spectroscopic data match with those reported in the literature [70].
3-(1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (Cephalandole A, 8)

Bright yellow solid; $^1$H NMR (300 MHz, Acetone) $\delta$ 11.04 (s, 1H), 8.88–8.82 (m, 1H), 8.78 (t, $J = 1.5$ Hz, 1H), 7.87–7.83 (m, 1H), 7.57–7.49 (m, 1H), 7.49–7.35 (m, 2H), 7.35–7.28 (m, 1H), 7.28–7.21 (m, 2H); $^{13}$C NMR (75 MHz, Acetone) $\delta$ 153.00 (C), 149.05 (C), 146.22 (C), 137.86 (C), 134.58 (CH), 133.20 (C), 129.58 (CH), 128.88 (CH), 127.36 (C), 126.12 (CH), 124.18 (CH), 124.10 (CH), 122.47 (CH), 116.75 (CH), 112.77 (CH), 112.37 (C). The spectroscopic data match with those reported in the literature [70].

3.5. Synthesis and Characterization of Compound 9

In a 10 mL round bottomed flask was placed compound 3aa (15.5 mg, 0.044 mmol) and it was purged with N$_2$. Afterwards, dry THF (1 mL) was added via syringe and the resulted solution was cooled down to 0 °C. After 5 min, LiAlH$_4$ (0.08 mL 1 M in THF, 0.087 mmol, two equivalents) was added via syringe and the mixture was stirred for 1.5 h at 0 °C. Subsequently, the reaction was stopped with the addition of saturated aqueous NH$_4$Cl solution (1 mL) and saturated aqueous Rochelle Salt solution (5 mL). The resulting mixture was extracted with EtOAc (three times), washed with brine, and dried over anhydrous MgSO$_4$. The solvent was removed by reduced pressure and the resulting residue was purified by column chromatography using hexane: EtOAc as eluent (from 90:10 to 60:40) to afford compound 9 (9.0 mg, 0.025 mmol, 57% yield) as a colourless oil.

2-(Benzyli(2-hydroxy-1-(1H-indol-3-yl)ethyl)amino)phenol (9)

Brown oil; $^1$H NMR (300 MHz, CDCl$_3$:CD$_3$OD) $\delta$ 8.59 (bs, 1H), 7.42 (d, $J = 8.0$ Hz, 1H), 7.36–7.27 (m, 5H), 7.25–7.20 (m, 1H), 7.11 (t, $J = 7.6$ Hz, 2H), 7.03–6.95 (m, 2H), 6.70 (d, $J = 7.8$ Hz, 2H), 6.55 (d, $J = 7.9$ Hz, 1H), 4.29–4.21 (m, 3H), 4.12 (dd, $J = 10.8$, 6.1 Hz, 1H), 4.01 (dd, $J = 10.8$, 7.7 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 144.42 (C), 138.92 (C), 136.28 (C), 128.45 (CH), 127.68 (CH), 127.16 (CH), 126.90 (C), 121.85 (CH), 121.77 (CH), 120.18 (CH), 119.32 (CH), 119.08 (CH), 116.17 (C), 116.10 (C), 114.15 (CH), 112.24 (CH), 111.08 (CH), 111.03 (CH), 66.23 (CH$_2$), 48.79 (CH$_2$), 44.63 (CH); HRMS (ESI) $m/z$: 359,1757 [M + H]$^+$, C$_{23}$H$_{23}$N$_2$O$_2$ required 359,1754.

4. Conclusions

In summary, we have described a visible-light functionalization of 3,4-dihydro-1,4-benzoazin-2-ones with indoles and other electron-rich arenes using a dual catalytic system that was formed by a Lewis acid (Zn(OTf)$_2$) and 9,10-phenanthredione as photocatalyst. Under our reaction conditions, the corresponding products are obtained with good yields. Unlike the photoredox catalytic system described earlier [76], the results that were obtained with our method are not affected by the steric hindrance around the reactive carbon atom. Thus, 2- and 4-substituted indoles and 1,3,5-trimethoxybenzene give the corresponding reaction products with good yields. Besides our method uses one of the cheapest, simple, and commercially available organophotocatalyst (9,10-phenanthredione) and oxygen from air as oxidant, providing a valuable contribution for the development of more “green” chemical synthesis. Moreover, several transformations have been carried out with the reaction products. Studies to further extend the scope of this reaction are currently underway in our laboratory.
Supplementary Materials: The following materials are available online at http://www.mdpi.com/2073-4344/8/12/653/s1, Complete experimental procedures and characterization of new products, $^1$H and $^{13}$C NMR spectra for all compounds.

Author Contributions: C.V. and J.R.-B. conceived and designed the experiments; J.R.-B. performed the experiments; J.R.-B. and C.V. analyzed the data; G.B. contributed reagents/materials/analysis tools; C.V. and J.R.P. wrote the paper. All authors read, revised and approved the final manuscript.

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References

1. Ciamician, G. The Photochemistry of the Future. Science 1912, 36, 385–394. [CrossRef] [PubMed]
2. Albani, A.; Fagnoni, M. Green chemistry and photochemistry were born at the same time. Green Chem. 2004, 6, 1–6. [CrossRef]
3. Ravelli, D.; Protti, S.; Fagnoni, M. Carbon–Carbon Bond Forming Reactions via Photogenerated Intermediates. Chem. Rev. 2016, 116, 9850–9913. [CrossRef] [PubMed]
4. Lang, X.; Zhao, J.; Chen, X. Cooperative photoredox catalysis. Chem. Soc. Rev. 2016, 45, 3026–3038. [CrossRef] [PubMed]
5. Yoon, T.P. Photochemical Stereocontrol Using Tandem Photoredox–Chiral Lewis Acid Catalysis. Acc. Chem. Res. 2016, 49, 2307–2315. [CrossRef]
6. Narayanan, J.M.R.; Stephenson, C.R.J. Visible light photoredox catalysis: Applications in organic synthesis. Chem. Soc. Rev. 2011, 40, 102–113. [CrossRef]
7. Chen, J.-R.; Hu, X.-Q.; Lu, L.-Q.; Xiao, W.-J. Visible light photoredox-controlled reactions of N-radicals and radical ions. Chem. Soc. Rev. 2016, 45, 2044–2056. [CrossRef]
8. Shaw, M.H.; Twilton, J.; MacMillan, D.W.C. Photoredox Catalysis in Organic Chemistry. J. Org. Chem. 2016, 81, 6898–6926. [CrossRef]
9. Fabry, D.C.; Rueping, M. Merging Visible Light Photoredox Catalysis with Metal Catalyzed C–H Activations: On the Role of Oxygen and Superoxide Ions as Oxidants. Acc. Chem. Res. 2016, 49, 1969–1979. [CrossRef]
10. Prier, C.K.; Rankic, D.A.; MacMillan, D.W.C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. Chem. Rev. 2013, 113, 5322–5363. [CrossRef]
11. Arias-Rotondo, D.M.; McCusker, J.K. The photophysics of photoredox catalysis: A roadmap for catalyst design. Chem. Soc. Rev. 2016, 45, 5803–5820. [CrossRef] [PubMed]
12. Tucker, J.W.; Stephenson, C.R.J. Shining Light on Photoredox Catalysis: Theory and Synthetic Applications. J. Org. Chem. 2012, 77, 1617–1622. [CrossRef] [PubMed]
13. Tellis, J.C.; Kelly, C.B.; Primer, D.N.; Jouffroy, M.; Patel, N.R.; Molander, G.A. Single-Electron Transmetalation via Photoredox/Nickel Dual Catalysis: Unlocking a New Paradigm for sp3–sp2 Cross-Coupling. Acc. Chem. Res. 2016, 49, 1429–1439. [CrossRef] [PubMed]
14. Alfonso, E.; Alfonso, F.S.; Beeler, A.B. Redesign of a Pyrylium Photoredox Catalyst and Its Application to the Generation of Carbonyl Ylides. Org. Lett. 2017, 19, 2989–2992. [CrossRef] [PubMed]
15. Wang, K.; Meng, L.-G.; Wang, L. Visible-Light-Promoted [2 + 2 + 2] Cyclization of Alkynes with Nitriles to Pyridines Using Pyrylium Salts as Photoredox Catalysts. Org. Lett. 2017, 19, 1958–1961. [CrossRef]
16. Kottisch, V.; Michaudel, Q.; Forst, B.P. Cationic Polymerization of Vinyl Ethers Controlled by Visible Light. J. Am. Chem. Soc. 2016, 138, 15353–15358. [CrossRef]
17. Perkowski, A.J.; You, W.; Nicewicz, D.A. Visible Light Photoinitiated Metal-Free Living Cationic Polymerization of 4-Methoxystyrene. J. Am. Chem. Soc. 2015, 137, 7580–7583. [CrossRef]
18. Perkowski, A.J.; Cruz, C.L.; Nicewicz, D.A. Ambient-Temperature Newman–Kwart Rearrangement Mediated by Organic Photoredox Catalysis. J. Am. Chem. Soc. 2015, 137, 15684–15687. [CrossRef]
43. Chen, C.-C.; Hong, B.-C.; Li, W.-S.; Chang, T.-T.; Lee, G.-H. Synthesis of Biologically Active Bis(indolyl)Methane Derivatives by Bisindole Alkylation of Tetrahydroisoquinolines with Visible-Light Induced Ring-Opening Fragmentation. Asian J. Org. Chem. 2017, 6, 426–431. [CrossRef]

44. Li, Q.-Y.; Ma, Z.; Zhang, W.-Q.; Xu, J.-L.; Wei, W.; Lu, H.; Zhao, X.; Wang, X.-J. AIE-active tetraphenylethene functionalized metal–organic framework for selective detection of nitroaromatic explosives and organic photocatalysis. Chem. Commun. 2016, 52, 11284–11287. [CrossRef] [PubMed]

45. Wang, B.; Shelar, D.P.; Han, X.; Li, T.; Guan, X.; Lu, W.; Liu, K.; Chen, Y.; Fu, W.; Che, C. Long-Lived Excited States of Zwiterionic Copper(I) Complexes for Photoinduced Cross-Dehydrogenative Coupling Reactions. Chem. Eur. J. 2015, 21, 1184–1190. [CrossRef] [PubMed]

46. Zhong, J.; Wu, C.; Meng, Q.; Gao, X.; Lei, T.; Tung, C.; Wu, L. A Cascade Cross-Coupling and in Situ Hydrogenation Reaction by Visible Light Catalysis. Adv. Synth. Catal. 2014, 356, 2846–2852. [CrossRef]

47. Wu, C.-J.; Zhong, J.-J.; Meng, Q.-Y.; Lei, T.; Gao, X.-W.; Tung, C.-H.; Wu, L.-Z. Cobalt-Catalyzed Cross-Dehydrogenative Coupling Reaction in Water by Visible Light. Org. Lett. 2015, 17, 884–887. [CrossRef]

48. Zhong, J.-J.; Meng, Q.-Y.; Liu, B.; Li, X.-B.; Gao, X.-W.; Lei, T.; Wu, C.-J.; Li, Z.-J.; Tung, C.-H.; Wu, L.-Z. Cross-Coupling Hydrogen Evolution Reaction in Homogeneous Solution without Noble Metals. Org. Lett. 2014, 16, 1988–1991. [CrossRef]

49. Meng, Q.-Y.; Zhong, J.-J.; Liu, Q.; Gao, X.-W.; Zhang, H.-H.; Lei, T.; Li, Z.-J.; Feng, K.; Chen, B.; Tung, C.-H.; et al. A Cascade Cross-Coupling Hydrogen Evolution Reaction by Visible Light Catalysis. J. Am. Chem. Soc. 2013, 135, 19052–19055. [CrossRef]

50. Zhong, J.-J.; Meng, Q.-Y.; Wang, G.-X.; Liu, Q.; Chen, B.; Feng, K.; Tung, C.-H.; Wu, L.-Z. A Highly Efficient and Selective Aerobic Cross-Dehydrogenative-Coupling Reaction Photocatalyzed by a Platinum(II) Terpyridyl Complex. Chem. Eur. J. 2013, 19, 6443–6450. [CrossRef]

51. Freeman, D.B.; Forst, L.; Condle, A.G.; Stephenson, C.R.J. Functionally Diverse Nucleophilic Trapping of Iminium Intermediates Generated Utilizing Visible Light. Org. Lett. 2012, 14, 94–97. [CrossRef] [PubMed]

52. Han, X.; He, X.; Sun, L.; Han, X.; Zhan, W.; Xu, J.; Wang, X.; Chen, J. Increasing Effectiveness of Photogenerated Carriers by in Situ Anchoring of Cu2O Nanoparticles on a Nitrogen-Doped Porous Carbon Yolk–Shell Cuboctahedral Framework. ACS Catal. 2018, 8, 3348–3356. [CrossRef]

53. Hefnburn, H.B.; Melchiorre, P. Bronsted acid-catalyzed conjugate addition of photochemically generated α-amino radicals to alkenylpyridines. Chem. Commun. 2016, 52, 3520–3523. [CrossRef] [PubMed]

54. Murphy, J.J.; Bastida, D.; Paria, S.; Fagnonia, M.; Melchiorre, P. Asymmetric catalytic formation of quaternary carbons by iminium ion trapping of radicals. Nature 2016, 532, 218–222. [CrossRef] [PubMed]

55. Ju, X.; Li, D.; Li, W.; Yu, W.; Bian, F. The Reaction of Tertiary Anilines with Maleimides under Visible Light. Adv. Synth. Catal. 2012, 354, 3561–3567. [CrossRef]

56. Uruguchi, D.; Kinoshita, N.; Kizu, T.; Ooi, T. Synergistic Catalysis of Ionic Bronsted Acid and Photosensitizer for a Redox Neutral Asymmetric α-Coupling of N-Arylaminothiophenemethanes with Aldimines. J. Am. Chem. Soc. 2015, 137, 13768–13771. [CrossRef] [PubMed]

57. Zhu, S.; Das, A.; Bui, L.; Zhou, H.; Curran, D.P.; Rueping, M. Oxygen Switch in Visible-Light Photoredox Catalysis: Radical Additions and Cyclizations and Unexpected C–C-Bond Cleavage Reactions. J. Am. Chem. Soc. 2013, 135, 1832–1829. [CrossRef] [PubMed]

58. Zhu, S.; Rueping, M. Merging visible-light photoredox and Lewis acid catalysis for the functionalization and arylation of glycine derivatives and peptides. Chem. Commun. 2012, 48, 11960–11962. [CrossRef] [PubMed]

59. Wang, Z.-Q.; Hu, M.; Huang, X.-C.; Gong, L.-B.; Xie, Y.-X.; Li, J.-H. Direct α-Arylation of α-Amino Carbonyl Compounds with Indoles Using Visible Light Photoredox Catalysis. J. Org. Chem. 2012, 77, 8705–8711. [CrossRef] [PubMed]

60. He, Y.-H.; Xiang, Y.; Yang, D.-C.; Guan, Z. Combining enzyme and photoredox catalysis for aminoalkylation of indoles via a relay catalysis strategy in one pot. Green Chem. 2016, 18, 5325–5330. [CrossRef]

61. Gao, X.-W.; Meng, Q.-Y.; Li, J.-X.; Zhong, J.-J.; Lei, T.; Li, X.-B.; Tung, C.-H.; Wu, L.-Z. Visible Light Catalysis Assisted Site-Specific Functionalization of Amino Acid Derivatives by C–H Bond Activation without Oxidant: Cross-Coupling Hydrogen Evolution Reaction. ACS Catal. 2015, 5, 2391–2396. [CrossRef]
64. Achari, B.; Mandal, S.B.; Duttaa, P.K.; Chowdhury, C. Perspectives on 1,4-Benzodioxins, 1,4-Benzoxazines and their 2,3-Dihydro Derivatives. *Syndett 2004*, 2449–2467. [CrossRef]

65. Patel, M.; McHush, R.J.; Cordova, B.C.; Klabe, R.M.; Erickson-Viitanen, S.; Trainor, G.L.; Rodgers, J.D. Synthesis and evaluation of quinoxalinones as HIV-1 reverse transcriptase inhibitors. *Bioorg. Med. Chem. Lett. 2000*, 10, 1729–1731. [CrossRef]

66. Pamerla, M.; Reddy, D.R.S.; Battula, S.; Bodipati, N.; Murthy, Y.L.N. Antimicrobial evaluation of 1,4-benzoxazine derivatives. *Med. Chem. Res. 2015*, 24, 611–615. [CrossRef]

67. Bouyssou, T.; Casarosa, P.; Naline, E.; Pestel, S.; Konetzki, I.; Devillier, P.; Schnapp, A. Pharmacological characterization of olodaterol, a novel inhaled beta2-adrenoceptor agonist exerting a 24-h-long duration of action in preclinical models. *J. Pharmacol. Exp. Ther. 2010*, 334, 53–62. [CrossRef]

68. Liu, C.; Tan, J.L.; Xiao, S.Y.; Liao, J.F.; Zou, G.R.; Ai, X.X.; Chen, J.B.; Xiang, Y.; Yang, Q.; Zuo, H. 1,4-Benzoxazine-3(4H)-ones as Potent Inhibitors of Platelet Aggregation: Design, Synthesis and Structure–Activity Relations. *Chem. Pharm. Bull. 2014*, 62, 915–920. [CrossRef]

69. Zidar, N.; Kikelj, D. A convenient synthesis of 3,4-dihydro-1,4-benzoxazin-2-ones. *Tetrahedron 2008*, 64, 5756–5761. [CrossRef]

70. Huo, C.; Dong, J.; Su, Y.; Tang, J.; Chen, F. Iron-catalyzed oxidative sp carbon–hydrogen bond functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones. *Chem. Commun. 2016*, 52, 13341–13344. [CrossRef]

71. Dong, J.; Min, W.; Li, H.; Quan, Z.; Yang, C.; Huo, C. Iron-Catalyzed C(sp3)–C(sp3) Bond Formation in 3,4-Dihydro-1,4-benzoxazin-2-ones. *Adv. Synth. Catal. 2017*, 359, 3940–3944. [CrossRef]

72. De Munck, L.; Vila, C.; Pons, C.; Pedro, J.R. Synthesis of Multisubstituted 1,4-Dihydrobenzoxazin-2-ones through a One-Pot Nucleophilic N-Alkylation/C-Alkylation of Cyclic α-Mino Esters. *Synthesis 2017*, 49, 2683–2690. [CrossRef]

73. Blay, G.; Fernández, I.; Muñoz, M.C.; Pedro, J.R.; Vila, C. Highly Enantioselective Friedel–Crafts Alkylation with β-Trifluoromethyl-α,β-enediones. *Chem. Eur. J. 2010*, 16, 9117–9122. [CrossRef] [PubMed]

74. Blay, G.; Fernández, I.; Monleón, A.; Muñoz, M.C.; Pedro, J.R.; Vila, C. Synthesis of Functionalized Indoles with an α-Stereogenic Ketone Moiety Through an Enantioselective Friedel–Crafts Alkylation with (E)-1,4-Diaryl-2-buten-1-ones Catalyzed by an (BINOLate–Hafnium(IV))–3,3′-Bis(2,2′-Bipyridine)–Hafnium(IV) Complex. *Adv. Synth. Catal. 2018*, 360, 2334–2340. [CrossRef]

75. Akula, P.S.; Hong, B.-C.; Lee, G.-H. Visible-light-induced C(sp3)–H activation for a C–C bond forming reaction of 3,4-dihydroquinolin-2(1H)-one with nucleophiles using oxygen with a photoredox catalyst or under catalyst-free conditions. *RSC Adv. 2018*, 8, 19580–19584. [CrossRef]

76. Mason, J.J.; Bergman, J.; Janosik, T. Synthetic Studies of Cephalandole Alkaloids and the Revised Structure of Cephalandole A. *J. Nat. Prod. 2008*, 71, 1447–1450. [CrossRef]

77. Cornford, E.M.; Crane, P.D.; Braun, L.D.; Bocash, W.D.; Nyerges, A.M.; Oldendorf, W.H. Reduction in Brain Glucose Utilization Rate after Tryptophol (3-Indole Ethanol) Treatment. *J. Neurochem. 1981*, 36, 1758–1765. [CrossRef]

78. Khaledkar, V.; Tillack, A.; Michalik, M.; Beller, M. Convenient synthesis of tryptophols and tryptophol homologues by hydroamination of alkynes. *Tetrahedron 2005*, 61, 7622–7631. [CrossRef]

79. Fernando, I.N.; Francis, P.L.; Smith, I. Acyltryptophols reversibly inhibit muscle contractions caused by the actions of acetylcholine and raised potassium ion concentrations. *J. Neural. Transm. 1983*, 56, 33–41. [CrossRef] [PubMed]

80. Blay, G.; Fernandez, I.; Muñoz, M.C.; Pedro, J.R.; Vila, C. Enantioselective Friedel–Crafts Alkylation of Indoles with (E)-1-Aryl-4-benzoxazoylbut-2-en-1-ones Catalyzed by an (R)-3,3′-Br2BINOLate–Hafnium(IV) Complex. *Eur. J. Org. Chem. 2013*, 1902–1907. [CrossRef]