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Article

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 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.

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 capable to absorb 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 have potential toxicity that have 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 catalysts. 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 Eosyn Y are more convenient due to their lower cost. [25-31] Nevertheless, is highly desirable the development of new methodologies using simpler organophotoredox catalysts that improve the sustainability of the "green" chemical process. 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-phenanthrenedione is an inexpensive organic compound with very low molecular weight (Figure 1) compared with other organophotoredox catalyst. This α-diketone has absorption bands in the visible region (412 and 505 nm in acetonitrile) [35] and therefore could be excited by visible-light. However, it has been rarely used in visible-light photochemical processes. [36-38]

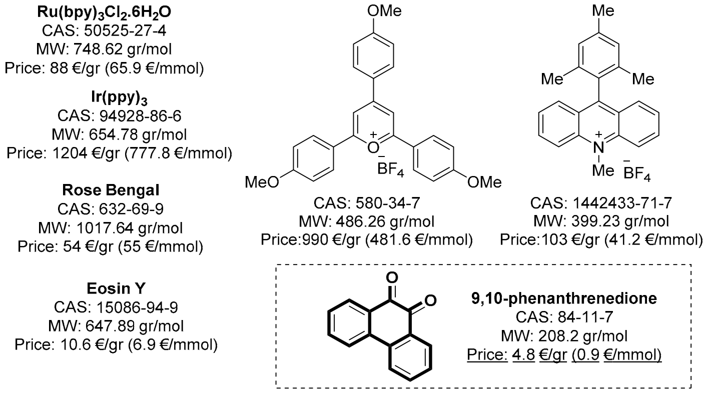


Figure 1. Comparison of commercially available common visible-light photoredox catalysts and 9,10-phenanthrenedione (source: Sigma-Aldrich (2018)).

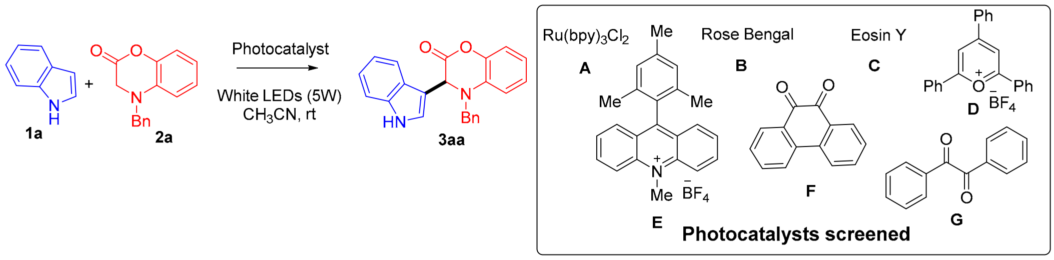
On the other hand, tertiary amines represent an important class of compounds in organic synthesis, which functionalization is of great interest for the chemical community, medicinal chemistry, pharmaceutical and agrochemical industry. In this context, the combination of visible-light catalysis and C–H bond functionalization adjacent to a tertiary amine has been successfully developed in the last years. [39-42] Normally, this sp^3-C-H functionalization involves the oxidation of the amine to iminium ion, that can be attacked by various kind of nucleophiles. Nonetheless, the major number of examples are regarded to the functionalization of *N*-aryl tetrahydroisoquinolines, [43-53] *N,N*-dimethylanilines[54-58] and *N*-aryl glycine derivatives.[59-63] 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. [64-70] Very recently, Huo described the iron catalyzed sp^3-C-H functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones[71-72] using as a terminal oxidant TBHP[71] or DDQ[72]. 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[73] and the Friedel-Crafts reactions with indoles,[74-76] 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-phenanthrenedione, and oxygen as terminal oxidant.[77-78]

2. Results

Initially, we choose the Friedel-Crafts reaction between indole **1a** and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one **2a** in acetonitrile at room temperature under air atmosphere and 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), $Ru(bpy)_2Cl_2$ (**A**), Rose Bengal (**B**), Fukuzumi photocatalyst (**E**) and 9,10-phenanthrenedione (**F**) afforded product **3aa** with similar yields, around 30%, after 24 hours. 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 photocatalyst, due to its low molecular weight and its lower price in relation to the other photocatalysts tested.

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 [59] (Table 2). For this purpose, different Brønsted acid such as $PhCO_2H$ 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 benzoxazinone **3aa** was obtained in 76% after 9 hours (entry 5). The lowering of the catalyst loading of $Zn(OTf)_2$ to 5 mol% did not influenced in the yield of product **3aa** (entry 6). Subsequently, different solvents such as toluene, CH_2Cl_2, DMF, THF or MeOH were screened (entries 7-11), obtaining the functionalized benzoxazinone **3aa** with much lower yields. We could diminish the photocatalyst and Lewis acid loadings maintaining the yield of product **3aa** (entries 12 and 13). Finally, some control experiments were carried out. So, in the absence of visible-light (entry 15) or 9,10-phenanthrenedione (entry 16), the product **3aa** was not detected or the conversion was very low.

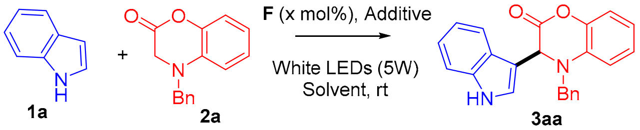
Table 1 Preliminary optimization of the reaction conditions.[a]



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 %)	0.1	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_3CN at rt under white LEDs 5W irradiation and air atmosphere. [b] Isolated yield of **3aa**.

Table 2. Optimization of the reaction conditions.

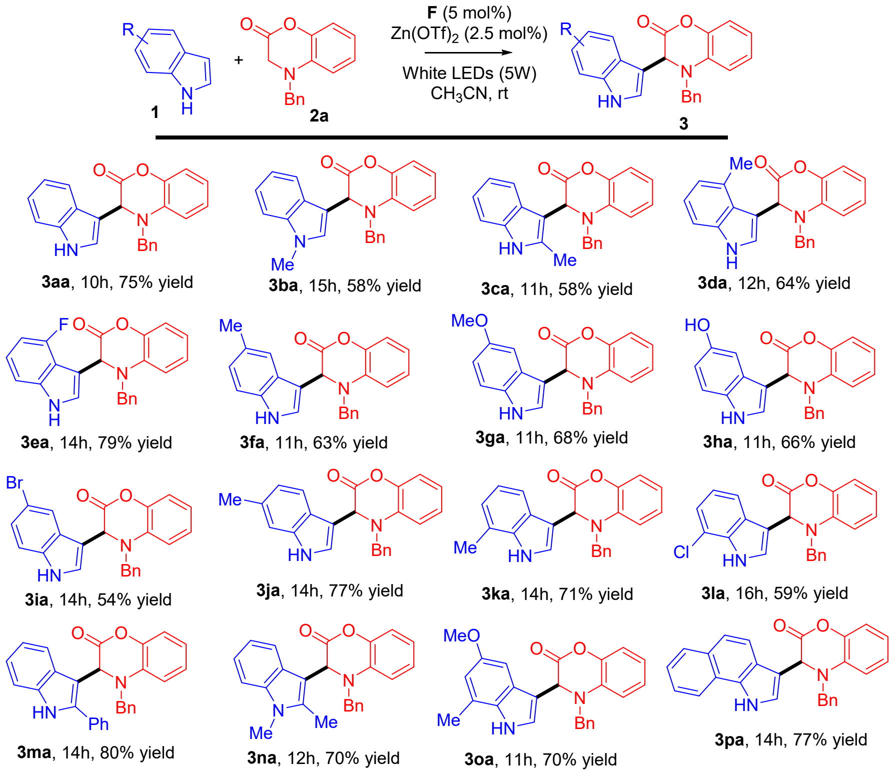


Entry	Photocat. (mol %)	Additive (mol%)	Solvent	t (h)	Yield of **3aa** (%)[b]
1	**F** (10 %)	-	CH_3CN	24	53
2	**F** (10 %)	$PhCO_2H$ (10 mol%)	CH_3CN	24	36
3	**F** (10 %)	AcOH (10 mol%)	CH_3CN	24	26
4	**F** (10 %)	$Zn(OAc)_2$ (10 mol%)	CH_3CN	24	37
5	**F** (10 %)	$Zn(OTf)_2$ (10 mol%)	CH_3CN	9	76
6	**F** (10 %)	$Zn(OTf)_2$ (5 mol%)	CH_3CN	9	74
7	**F** (10 %)	$Zn(OTf)_2$ (5 mol%)	Toluene	8	40
8	**F** (10 %)	$Zn(OTf)_2$ (5 mol%)	CH_2Cl_2	20	30

9	**F** (10 %)	Zn(OTf)$_2$ (5 mol%)	DMF	72	12
10	**F** (10 %)	Zn(OTf)$_2$ (5 mol%)	THF	9	34
11	**F** (10 %)	Zn(OTf)$_2$ (5 mol%)	MeOH	17	22
12	**F** (5 %)	Zn(OTf)$_2$ (5 mol%)	CH$_3$CN	10	74
13	**F** (5 %)	Zn(OTf)$_2$ (2.5 mol%)	CH$_3$CN	10	75
14[c]	**F** (5 %)	Zn(OTf)$_2$ (2.5 mol%)	CH$_3$CN	15	45
15[d]	**F** (5 %)	Zn(OTf)$_2$ (2.5 mol%)	CH$_3$CN	72	n.d.[e]
16	-	Zn(OTf)$_2$ (2.5 mol%)	CH$_3$CN	72	<5[e]

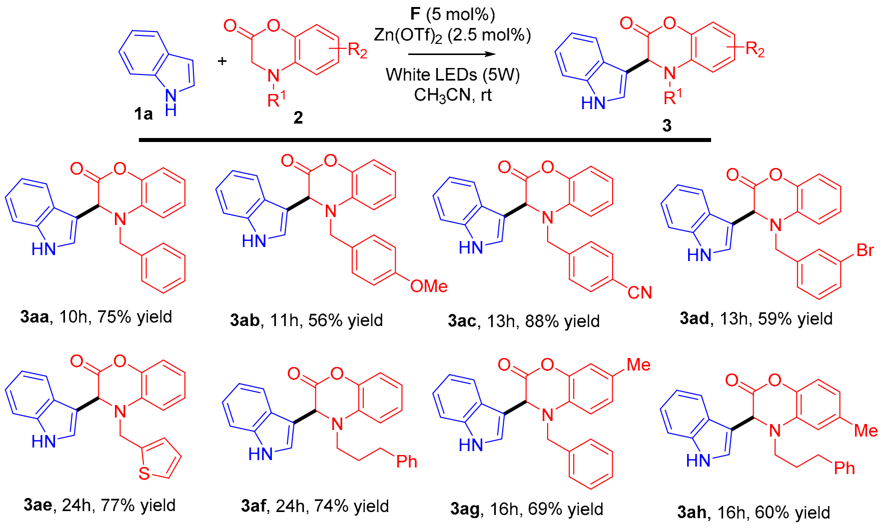
[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), x mol% of photocatalyst, x mol% of additive in 1 mL of solvent at rt under white LEDs 5W irradiation and air atmosphere; [b] Isolated yield of **3aa**; [c] 0.12 mmol of **2a** was used; [d] Reaction performed under darkness; [e] Conversion to product **3aa** by ^{1}H NMR of the crude reaction mixture. N.d.= not detected.

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** with several substituents in different positions (Scheme 1). Indoles bearing electron-donating (Me, Ph, OMe, OH) or electron-withdrawing (F, Cl, Br) groups furnished the corresponding functionalized benzoxazinones **3** in 54-80% yield, 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 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 [77]). Also 2-phenyl-, 4-fluoro- and 1,2-dimethylindole give yields of 80%, 79% and 70% respectively.



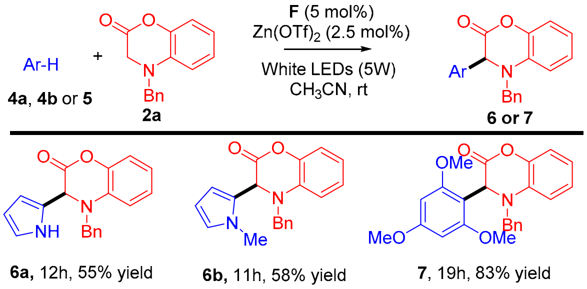
Scheme 1. Scope of the Friedel-Crafts reaction with different indoles **1** and **2a**. Reaction conditions: **1** (0.1 mmol), **2a** (0.15 mmol), **F** (5 mol%) and Zn(OTf)$_2$ (2.5 mol%) in 1 mL of CH$_3$CN at rt under white LEDs irradiation. Isolated yields after column chromatography.

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.



Scheme 2. Scope of the Friedel-Crafts reaction with indole **1a** and different benzoxazinones **2**. Reaction conditions: **1a** (0.1 mmol), **2** (0.15 mmol), **F** (5 mol%) and $Zn(OTf)_2$ (2.5 mol%) in 1 mL of CH_3CN at rt under white LEDs irradiation. Isolated yields after column chromatography.

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 [77]).



Scheme 3. Scope of the Friedel-Crafts reaction with other electron-rich arenes and benzoxazinone **2a**. Reaction conditions: arene (0.1 mmol), **2a** (0.15 mmol), **F** (5 mol%) and $Zn(OTf)_2$ (2.5 mol%) in 1 mL of CH_3CN at rt under white LEDs irradiation. Isolated yields after column chromatography.

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

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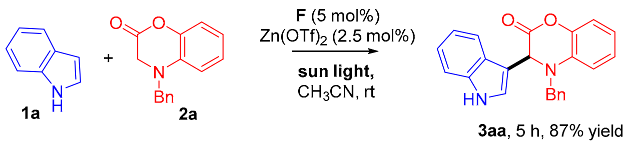
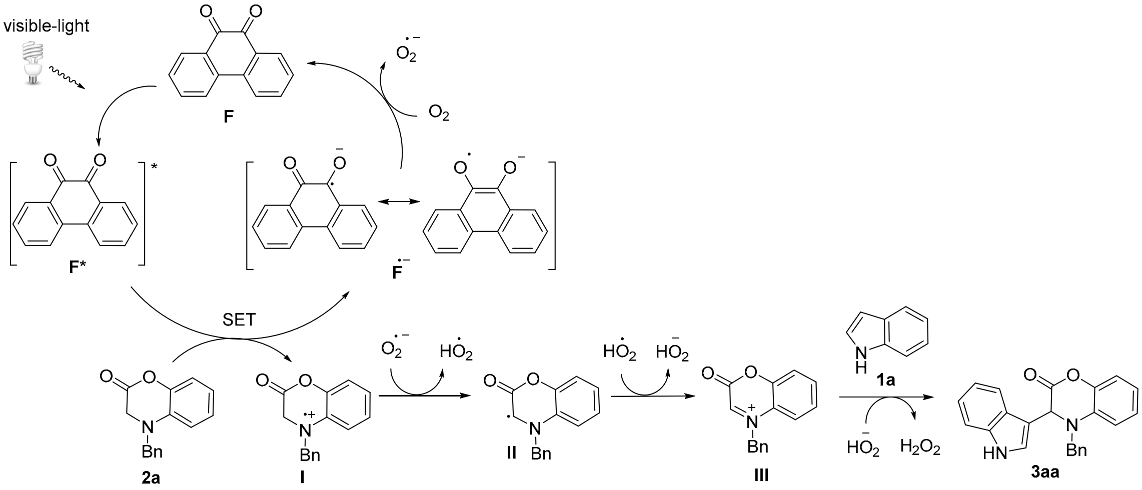


Scheme 4. Friedel-Crafts alkylation of indole **1a** with benzoxazinone **2a** using sun-light irradiation. Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), **F** (5 mol%) and $Zn(OTf)_2$ (2.5 mol%) in 1 mL of CH_3CN at rt under sun-light irradiation. Isolated yield after column chromatography.

Based on previous literature reports[3,71] and control experiments,[35] a possible mechanism for the reaction is proposed in the 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-2*H*-benzo[*b*][1,4]oxazin-2-one **2a** into a nitrogen radical cation **I**, with the consequent reduction of **F*** to the radical anion $F^{\cdot-}$, which can be oxidized by molecular oxygen (O_2) 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 trace amount of product **3aa** was observed by ^{1}H NMR of the crude reaction mixture and the corresponding adduct formed from radical **II** and TEMPO was detected by HRMS. In this mechanism, the O_2 is the terminal oxidant that is reduced in H_2O_2. 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.



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

To showcase the utility of our catalytic protocol we performed several synthetic transformations (Scheme 6). Compound **3aa** was catalytically deprotected using H_2 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 [79] (**8**) in 91% yield in a one-pot reaction. Moreover, compounds **3** can be used to prepare tryptophol derivatives by 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.[80-83] Therefore, compound **3aa** has been reduced with $LiAlH_4$ affording tryptophol derivative **9** with 57% yield.

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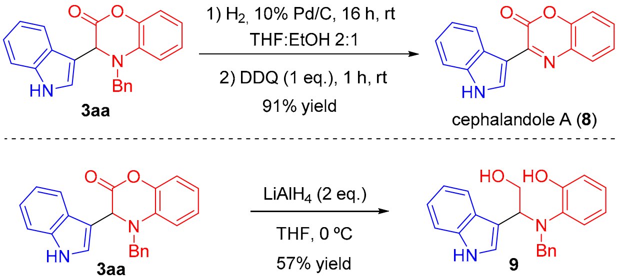


Scheme 6. Synthetic transformations. Isolated yields after column chromatography.

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 TLC analysis using Merck Silica Gel 60 F-254 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, 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 ^{1}H and 75 MHz for ^{13}C using residual nondeuterated solvent as internal standard ($CHCl_3$: 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 TRIPLETOF^{T}5600 spectrometer (AB Sciex, Warrington, UK) equipped with an electrospray source with a capillary voltage of 4.5 kV (ESI).

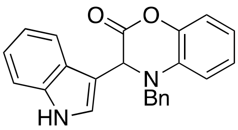
All photocatalysts, indoles and related arenes were commercially available. 3,4-dihydro-benzoxazin-2-ones derivatives **2a**, **2b** and **2c** were synthesized according to a procedure published in the literature and the spectroscopic data (^{1}H-NMR and ^{13}C-NMR) match with those reported. 3,4-dihydro-benzoxazin-2-ones derivatives **2d**, **2e**, **2f**, **2g** and **2h** were synthesized according to the same procedure and were characterized by ^{1}H-NMR, ^{13}C-NMR and HRMS.[35]

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-phenanthrenedione (**F**, 1.0 mg, 0.005 mmol, 5 mol %). Then, 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**.

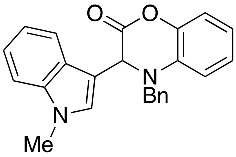
*3.3. Characterization Data for Compounds **3**, **6** and **7**.*

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



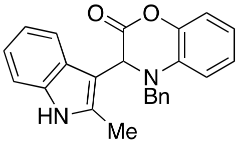
Using indole (**1a**, 11.7 mg, 0,1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3aa** was obtained (26.6 mg, 0.075 mmol, 75% yield) after 10 h as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 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, 3H), 6.91 (td, *J* = 7.7, 1.4 Hz, 1H), 6.82 (dd, *J* = 8.0, 1.2 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 (C), 55.86 (CH), 51.55 (CH_2). The spectroscopic data match with those reported in the literature.[71]

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



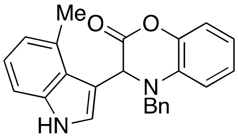
Using *N*-methylindole (**1b**, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ba** was obtained (21.2 mg, 0.058 mmol, 58% yield) after 15 h as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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. [71]

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-2*H*-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. ^1H NMR (300 MHz, $CDCl_3$) δ 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, 6.9, 1.1 Hz, 1H), 6.89 (td, *J* = 7.7, 1.4 Hz, 1H), 6.80 (dd, *J* = 8.1, 1.4 Hz, 1H), 5.34 (s, 1H), 4.59 (d, *J* = 16.1 Hz, 1H), 3.98 (d, *J* = 16.1 Hz, 1H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (C), 140.7 (C), 136.6 (C), 135.4 (C), 135.2 (C), 134.6 (C), 128.7 (CH), 127.3 (CH), 127.2 (CH), 126.5 (C), 125.5 (CH), 121.7 (CH), 120.2 (CH), 119.1 (CH), 118.7 (CH), 117.0 (CH), 113.2 (CH), 110.5 (CH), 106.0 (C), 55.8 (CH), 49.9 (CH_2), 11.6 (CH_3). The spectroscopic data match with those reported in the literature. [71]

4-benzyl-3-(4-methyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**3da**)



Using 4-methylindole (**1d**, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3da** was obtained (23.6 mg, 0.064 mmol, 64% yield) after 12 h as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (bs, 1H), 7.34 – 7.29 (m, 3H), 7.21 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.19 – 7.04 (m, 4H), 6.97 – 6.83 (m, 3H), 6.64 (d, *J* = 2.5 Hz, 1H), 5.70 (s, 1H), 4.63 (d, *J* = 14.4 Hz, 1H), 4.07 (d, *J* = 14.4 Hz, 1H),

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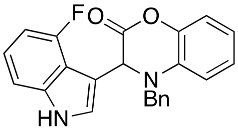
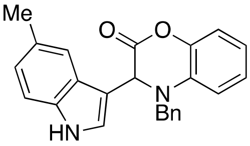
2.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8 (C), 141.5 (C), 136.0 (C), 135.7 (C), 134.6 (C), 130.8 (C), 128.8 (CH), 128.1 (CH), 127.8 (CH), 125.4 (CH), 124.8 (C), 122.7 (CH), 122.6 (C), 122.4 (CH), 119.7 (CH), 116.5 (CH), 113.4 (CH), 110.2 (C), 109.2 (CH), 55.3 (CH), 51.0 (CH_2), 20.5 (CH_3). The spectroscopic data match with those reported in the literature. [71]

4-benzyl-3-(4-fluoro-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**3ea**)



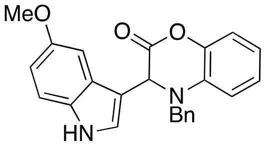
Using 4-fluoroindole (**1e**, 13.5 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ea** was obtained (29.4 mg, 0.079 mmol, 79% yield) after 14 h as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ -121.20 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9 (C), 156.6 (d, J_{C-F} = 246.6 Hz, C), 141.8 (C), 138.2 (d, J_{C-F} = 10.9 Hz, C), 136.5 (C), 133.7 (C), 128.7 (CH), 127.4 (CH), 127.2 (CH), 125.3 (CH), 123.3 (d, J_{C-F} = 7.9 Hz, CH), 123.1 (CH), 119.8 (CH), 116.4 (CH), 115.2 (d, J_{C-F} = 19.4 Hz, C), 114.7 (CH), 107.7 (d, J_{C-F} = 3.9 Hz, C), 107.6 (d, J_{C-F} = 3.8 Hz, CH), 105.8 (d, J_{C-F} = 19.6 Hz, CH), 56.8 (d, J_{C-F} = 3.2 Hz, CH), 51.7 (d, J_{C-F} = 1.5 Hz, CH_2); HRMS (ESI) *m*/*z*: 373,1342 $[M + H]^+$, $C_{23}H_{18}FN_2O_2$ required 373,1347.

4-benzyl-3-(5-methyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**3fa**)



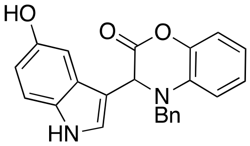
Using 5-methylindole (**1f**, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3fa** was obtained (23.2 mg, 0.063 mmol, 63% yield) after 11 h as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (bs, 1H), 7.37 – 7.27 (m, 5H), 7.24 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.20 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.12 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.04 (ddd, *J* = 9.4, 8.0, 1.6 Hz, 2H), 6.92 (td, *J* = 7.7, 1.5 Hz, 1H), 6.82 (dd, *J* = 8.0, 1.4 Hz, 1H), 6.67 (d, *J* = 2.5 Hz, 1H), 5.37 (d, *J* = 0.7 Hz, 1H), 4.61 (d, *J* = 14.8 Hz, 1H), 4.12 (d, *J* = 14.8 Hz, 1H), 2.41 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6 (C), 141.9(C), 136.1 (C), 134.3 (C), 134.1 (C), 129.7 (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. [71]

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



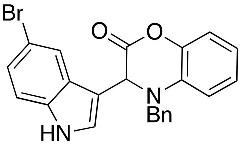
Using 5-methoxyindole (**1g**, 14.7 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ga** was obtained (26.1 mg, 0.068 mmol, 68% yield) after 11 h as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (bs, 1H), 7.40 – 7.27 (m, 5H), 7.19 (dd, *J* = 8.8, 0.7 Hz, 1H), 7.13 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.08 (ddd, *J* = 8.0, 7.5, 1.5 Hz, 1H), 6.91 (ddd, *J* = 7.5, 1.5 Hz, 1H), 6.88 – 6.79 (m, 3H), 6.72 (dd, *J* = 2.6, 0.6 Hz, 1H), 5.34 (d, *J* = 0.6 Hz, 1H), 4.62 (dd, *J* = 14.7, 0.8 Hz, 1H), 4.10 (d, *J* = 14.7 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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), 125.5 (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. [71]

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



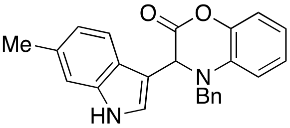
Using 5-hydroxyindole (**1h**, 13.3 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ha** was obtained (24.4 mg, 0.066 mmol, 66% yield) after 11 h as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (bs, 1H), 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, $CDCl_3$) δ 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 $[M + H]^+$, $C_{23}H_{19}N_2O_3$ required 371,1390.

4-benzyl-3-(5-bromo-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**3ia**)



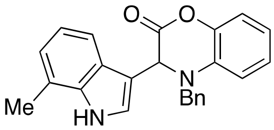
Using 5-bromoindole (**1i**, 19.6 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ia** was obtained (23.4 mg, 0.054 mmol, 54% yield) after 14 h as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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. [71]

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



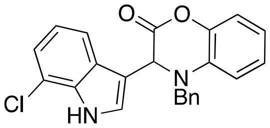
Using 6-methylindole (**1j**, 13.1 mg, 0,1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ja** was obtained (28.3 mg, 0.077 mmol, 77% yield) after 14 h as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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), 122.2 (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. [71]

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



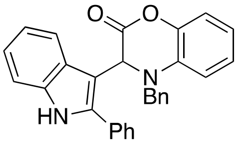
Using 7-methylindole (**1k**, 13.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ka** was obtained (26.1 mg, 0.071 mmol, 71% yield) after 14 h as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.33 (m, 6H), 7.12 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.09 – 6.98 (m, 3H), 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, $CDCl_3$) δ 164.5 (C), 141.9 (C), 136.1 (C), 135.4 (C), 134.2 (C), 128.8 (CH), 127.8 (CH), 127.8 (CH), 125.7 (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. [71]

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



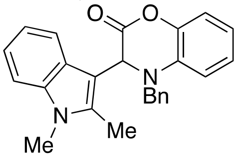
Using 7-chloroindole (**1l**, 15.2 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3la** was obtained (22.9 mg, 0.059 mmol, 59% yield) after 16 h as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (bs, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.36 – 7.24 (m, 5H), 7.21 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.15 – 7.02 (m, 3H), 6.92 (td, *J* = 7.7, 1.4 Hz, 1H), 6.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.80 (d, *J* = 2.6 Hz, 1H), 5.35 (s, 1H), 4.64 (d, *J* = 14.7 Hz, 1H), 4.12 (d, *J* = 14.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.20 (C), 141.83 (C), 135.83 (C), 134.00 (C), 133.15 (C), 128.87 (CH), 127.88 (CH), 127.45 (C), 125.48 (CH), 123.41 (CH), 122.22 (CH), 121.29 (CH), 120.13 (CH), 117.93 (CH), 116.76 (C), 116.64 (CH), 113.92 (CH), 110.01 (C), 55.73 (CH), 51.63 (CH_2). The spectroscopic data match with those reported in the literature. [71]

4-benzyl-3-(2-phenyl-1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**3ma**)



Using 2-phenylindole (**1m**, 19.3 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-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, $CDCl_3$) δ 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), 7.04 – 6.96 (m, 2H), 6.96 – 6.91 (m, 2H), 6.90 – 6.82 (m, 1H), 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, $CDCl_3$) δ 166.2 (C), 140.5 (C), 139.4 (C), 136.4 (C), 135.9 (C), 134.2 (C), 131.3 (C), 129.0 (CH), 128.9 (CH), 128.7 (CH), 128.4 (CH), 127.0 (CH), 126.9 (CH), 126.3 (C), 125.5 (CH), 122.9 (CH), 120.7 (CH), 120.0 (CH), 118.9 (CH), 116.9 (CH), 113.1 (CH), 111.1 (CH), 107.6 (C), 56.1 (CH), 50.0 (CH_2). The spectroscopic data match with those reported in the literature. [71]

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-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the

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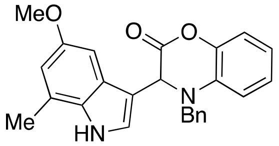
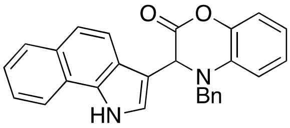
product **3na** was obtained (26.7 mg, 0.070 mmol, 70% yield) after 12 h as a brown oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.31 – 7.22 (m, 4H), 7.19 – 7.14 (m, 3H), 7.14 – 7.08 (m, 2H), 7.05 (ddd, *J* = 8.1, 7.4, 1.6 Hz, 1H), 6.96 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 6.88 (ddd, *J* = 7.9, 7.5, 1.4 Hz, 1H), 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$_3$) δ 166.1 (C), 140.9 (C), 140.7 (C), 137.0 (C), 136.8 (C), 134.6 (C), 128.7 (CH), 127.2 (CH), 127.1 (CH), 125.8 (C), 125.5 (CH), 121.3 (CH), 120.0 (CH), 119.0 (CH), 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. [71]

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



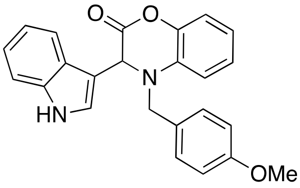
Using 5-methoxy-7-methylindole (**1o**, 16.1 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3oa** was obtained (27.9 mg, 0.070 mmol, 70% yield) after 11 h as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 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); ^{13}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$_{23}$N$_2$O$_3$ required 399,1703.

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



Using 1*H*-benzo[*g*]indole (**1p**, 16.7 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-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); ^{13}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), 123.00 (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-2*H*-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 (dd, *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

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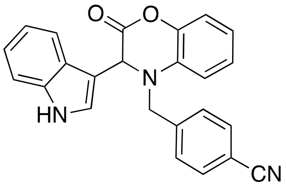
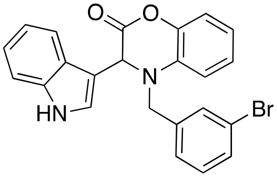
Hz, 1H), 4.57 (d, *J* = 14.4 Hz, 1H), 4.07 (d, *J* = 14.3 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.54 (C), 159.22 (C), 141.93 (C), 135.76 (C), 134.29 (C), 129.22 (CH), 127.80 (C), 126.10 (C), 125.34 (CH), 122.79 (CH), 122.76 (CH), 120.40 (CH), 119.81 (CH), 119.20 (CH), 116.50 (CH), 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. [71]

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



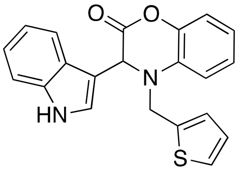
Using indole (**1a**, 11.7 mg, 0.1 mmol) and 4-(4-cyanobenzyl)-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2c**, 39.6 mg, 0.15 mmol), in accordance with General Procedure, the product **3ac** was obtained (33.4 mg, 0.088 mmol, 88% yield) after 13 h as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) 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, $CDCl_3$) δ 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]$^+$, $C_{24}H_{18}N_3O_2$ 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-2*H*-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, $CDCl_3$) δ 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, $CDCl_3$) δ 164.4 (C), 141.9 (C), 138.7 (C), 135.8 (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), 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]$^+$, $C_{23}H_{18}BrN_2O_2$ 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-2*H*-benzo[*b*][1,4]oxazin-2-one (**2e**, 36.8 mg, 0.15 mmol), in accordance with General Procedure, the product **3ad** was obtained (27.8 mg, 0.077 mmol, 77% yield) after 24 h as a brown solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, 3H), 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, $CDCl_3$) δ 164.6 (C), 142.0 (C),

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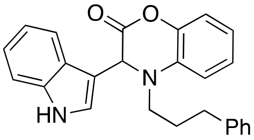
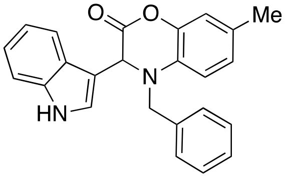
139.3 (C), 135.8 (C), 133.7 (C), 126.9 (CH), 126.6 (CH), 126.0 (C), 125.7 (CH), 125.4 (CH), 123.2 (CH), 122.8 (CH), 120.4 (CH), 120.3 (CH), 119.1 (CH), 116.7 (CH), 114.0 (CH), 111.3 (CH), 108.5 (C), 55.5 (CH), 46.7 (CH$_2$); HRMS (ESI) *m*/*z*: 361,1008 [M + H]$^+$, C$_{21}$H$_{17}$N$_2$O$_2$S required 361,1005.

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



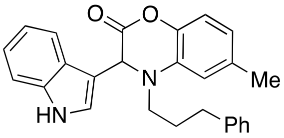
Using indole (**1a**, 11.7 mg, 0.1 mmol) and 4-(3-phenylpropyl)-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2f**, 40.1 mg, 0.15 mmol), in accordance with General Procedure, the product **3af** was obtained (28.3 mg, 0.074 mmol, 74% yield) after 24 h as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.07 (bs, 1H), 7.66 (dd, *J* = 7.7, 0.5 Hz, 1H), 7.33 – 7.25 (m, 3H), 7.25 – 7.11 (m, 5H), 7.11 – 7.04 (m, 2H), 6.86 (ddd, *J* = 8.1, 7.4, 1.4 Hz, 1H), 6.75 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.69 (d, *J* = 2.2 Hz, 1H), 5.40 (d, *J* = 0.7 Hz, 1H), 3.50 – 3.36 (m, 1H), 3.16 – 3.00 (m, 1H), 2.68 (t, *J* = 7.4 Hz, 2H), 2.09 – 1.94 (m, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 164.3 (C), 141.6 (C), 141.1 (C), 135.9 (C), 133.8 (C), 128.5 (CH), 128.4 (CH), 126.1 (CH), 125.9 (C), 125.3 (CH), 122.8 (CH), 122.8 (CH), 120.5 (CH), 119.1 (CH), 119.1 (CH), 116.6 (CH), 112.9 (CH), 111.3 (CH), 109.4 (C), 56.8 (CH), 47.3 (CH$_2$), 32.9 (CH$_2$), 28.3 (CH$_2$); HRMS (ESI) *m*/*z*: 383,1759 [M + H]$^+$, C$_{25}$H$_{23}$N$_2$O$_2$ required 383,1754.

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



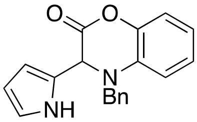
Using indole (**1a**, 11.7 mg, 0.1 mmol) and 4-benzyl-7-methyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2g**, 38.0 mg, 0.15 mmol), in accordance with General Procedure, the product **3ag** was obtained (25.4 mg, 0.069 mmol, 69% yield) after 16 h as a yellow oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.11 (bs, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.38 – 7.26 (m, 6H), 7.24 – 7.17 (m, 1H), 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$_3$) δ 164.8 (C), 141.9 (C), 136.3 (C), 135.8 (C), 131.7 (C), 129.9 (C), 128.8 (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. [71]

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



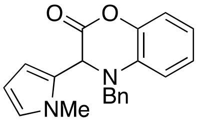
Using indole (**1a**, 11.7 mg, 0.1 mmol) and 6-methyl-4-(3-phenylpropyl)-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2h**, 38.0 mg, 0.15 mmol), in accordance with General Procedure, the product **3ah** was obtained (23.8 mg, 0.060 mmol, 60% yield) after 16 h as a colourless oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.08 (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$_3$) δ 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.

4-benzyl-3-(1H-pyrrol-2-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**6a**)



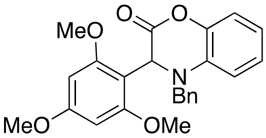
Using pyrrole (**4a**, 7 µL, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **6a** was obtained (16.7 mg, 0.055 mmol, 55% yield) after 12 h as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (bs, 1H), 7.45 – 7.27 (m, 5H), 7.15 – 7.07 (m, 2H), 6.97 – 6.87 (m, 2H), 6.67 (td, J = 2.7, 1.5 Hz, 1H), 6.06 (dd, J = 6.1, 2.7 Hz, 1H), 5.92 – 5.83 (m, 1H), 5.03 (s, 1H), 4.65 (d, J = 14.3 Hz, 1H), 4.08 (d, J = 14.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.15 (C), 141.39 (C), 135.58 (C), 133.73 (C), 128.96 (CH), 128.12 (CH), 128.04 (CH), 127.73 (CH), 125.67 (CH), 123.09 (C), 120.34 (CH), 119.12 (CH), 116.79 (CH), 113.85 (CH), 108.87 (CH), 56.86 (CH), 51.60 (CH_2). The spectroscopic data match with those reported in the literature.[71]

4-benzyl-3-(1-methyl-1H-pyrrol-2-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**6b**)



Using *N*-methylpyrrole (**4b**, 9 µL, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-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, $CDCl_3$) δ 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, $CDCl_3$) δ 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. [71]

4-benzyl-3-(2,4,6-trimethoxyphenyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (**7**)



Using 1,3,5-trimethoxybenzene (**5**, 16.8 mg, 0.1 mmol) and 4-benzyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-2-one (**2a**, 35.8 mg, 0.15 mmol), in accordance with General Procedure, the product **7** was obtained (33.6 mg, 0.083 mmol, 83% yield) after 19 h as a yellowish solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 2H), 7.21 – 7.15 (m, 3H), 7.04 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.88 (ddd, *J* = 8.0, 7.6, 1.5 Hz, 1H), 6.70 (td, *J* = 7.7, 1.4 Hz, 1H), 6.50 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.04 (s, 2H), 5.87 (s, 1H), 4.37 (d, *J* = 16.6 Hz, 1H), 4.22 (d, *J* = 16.6 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 6H);^{13}C NMR (75 MHz, $CDCl_3$) δ 167.51 (C), 161.76 (C), 159.31 (C), 140.98 (C), 137.86 (C), 133.86 (C), 128.35 (CH), 126.80 (CH), 126.53 (CH), 124.63 (CH), 117.37 (CH), 115.70 (CH), 111.83 (CH), 106.70 (C), 90.68 (CH), 55.51 (CH_3), 55.33 (CH), 53.89 (CH_3), 50.71 (CH_2). The spectroscopic data match with those reported in the literature. [71]

3.4. Synthesis and characterization of Cephalandole A (8).

In a 25 mL round bottomed flask were placed compound **3aa** (30 mg, 0.085 mmol) and Pd/C 10% w/w (18.1 mg, 0.017 mmol, 20 mol %). Then, THF (2 mL) and EtOH (1 mL) were added and the resulting suspension was bubbled with H_2. After this, the reaction mixture was stirred at room temperature for 16 h with a H_2 balloon. The reaction was monitored by TLC and, when compound **3aa** was consumed, DDQ (19.3 mg, 0.085 mmol) was added directly to the reaction mixture. After 1 h, the reaction mixture was filtered through a pad of Celite, the solvents were removed by reduced

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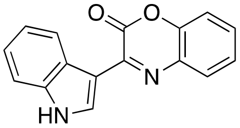
pressure and the resulting residue was purified by column chromatography using a hexane:EtOAc 95:5 mixture as eluent to afford Cephalandole A, **8** (20.3 mg, 0.077 mmol, 92% yield) as a bright yellow solid.

3-(1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (Cephalandole A, **8**)

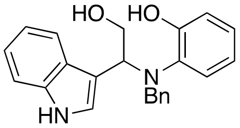


Bright yellow solid; ^{1}H NMR (300 MHz, Acetone) δ 11.04 (s, 1H), 8.88 – 8.82 (m, 1H), 8.78 (t, *J* = 1.5 Hz, 1H), 7.87 – 7.83 (m, 1H), 7.57 – 7.49 (m, 1H), 7.49 – 7.35 (m, 2H), 7.35 – 7.28 (m, 1H), 7.28 – 7.21 (m, 2H); ^{13}C NMR (75 MHz, Acetone) δ 153.00 (C), 149.05 (C), 146.22 (C), 137.86 (C), 134.58 (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. [71]

3.4. Synthesis and characterization of compound **9**

In a 10 mL round bottomed flask was placed compound **3aa** (15.5 mg, 0.044 mmol) and was purgued with N_2. Then, dry TFH (1 mL) was added via syringe and the resulted solution was cooled down to 0 °C. After 5 minutes, $LiAlH_4$ (0.08 mL 1M in THF, 0.087 mmol, 2 equivalents) was added via syringe and the mixture was stirred for 1.5 h at 0 ºC. Then, the reaction was stopped with the addition of saturated aqueous NH_4Cl solution (1 mL) and saturated aqueous Rochelle Salt solution (5 mL). The resulting mixture was extracted with EtOAc (3 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 mixtures 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-(benzyl(2-hydroxy-1-(1H-indol-3-yl)ethyl)amino)phenol (**9**)



Brown oil; ^{1}H NMR (300 MHz, $CDCl_3$:CD_3OD) δ 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, $CDCl_3$) δ 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 $[M + H]^+$, $C_{23}H_{23}N_2O_2$ required 359,1754.

4. Conclusions

In summary, we have described a visible-light functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones with indoles and other electron-rich arenes using a dual catalytic system formed by a Lewis acid ($Zn(OTf)_2$) and 9,10-phenanthrenedione as photocatalyst. Under our reaction conditions, the corresponding products are obtained with good yields. Unlike the photoredox catalytic system described earlier[77], the results 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-phenanthrenedione) 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.

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Supplementary Materials: The following materials are available online at www.mdpi.com/xxx/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, DOI: 10.1126/science.36.926.385.
2. Albani, A.; Fagnoni, M. Green chemistry and photochemistry were born at the same time. *Green Chem*. **2004**, *6*, 1-6, DOI: 10.1039/B309592D.
3. Ravelli, D.; Protti, S.; Fagnoni, M. Carbon–Carbon Bond Forming Reactions via Photogenerated Intermediates. *Chem. Rev*., **2016**, *116*, 9850-9913, DOI: 10.1021/acs.chemrev.5b00662.
4. Lang, X.; Zhao, J.; Chen, X. Cooperative photoredox catalysis. *Chem. Soc. Rev*. **2016**, *45*, 3026-3038, DOI: 10.1039/C5CS00659G.
5. Yoon, T. P. Photochemical Stereocontrol Using Tandem Photoredox–Chiral Lewis Acid Catalysis. *Acc. Chem. Res.*, **2016**, *49*, 2307-2315, DOI: 10.1021/acs.accounts.6b00280.
6. Narayanam, J. M. R.; Stephenson, C. R. J. Visible light photoredox catalysis: applications in organic synthesis. *Chem. Soc. Rev*., **2011**, *40*, 102-113, DOI: 10.1039/B913880N.
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, DOI: 10.1039/C5CS00655D.
8. Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. Photoredox Catalysis in Organic Chemistry. *J. Org. Chem*., **2016**, *81*, 6898-6926, DOI: 10.1021/acs.joc.6b01449.
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, DOI: 10.1021/acs.accounts.6b00275.
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, DOI: 10.1021/cr300503r.
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, DOI: 10.1039/C6CS00526H.
12. Tucker, J. W.; Stephenson, C. R. J. Shining Light on Photoredox Catalysis: Theory and Synthetic Applications. *J. Org. Chem*., **2012**, *77*, 1617-1622, DOI: 10.1021/jo202538x.
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, DOI: 10.1021/acs.accounts.6b00214.
14. Alfonzo, 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, DOI: 10.1021/acs.orglett.7b01222.
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, DOI: 10.1021/acs.orglett.7b00292.
16. Kottisch, V.; Michaudel, Q.; Fors, B. P. Cationic Polymerization of Vinyl Ethers Controlled by Visible Light. *J. Am. Chem. Soc*., **2016**, *138*, 15535-15538, DOI: 10.1021/jacs.6b10150.
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, DOI: 10.1021/jacs.5b03733.

Peer-reviewed version available at Catalysts 2018, 8, 653; doi:10.3390/catal8120653

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, DOI: 10.1021/jacs.5b11800.
19. Fukuzumi, S.; Ohkubo, K. Organic synthetic transformations using organic dyes as photoredox catalysts. *Org. Biomol. Chem.* **2014**, *12*, 6059-6071, DOI: 10.1039/C4OB00843J.
20. Margrey, K. A.; Nicewicz, D. A. A General Approach to Catalytic Alkene Anti-Markovnikov Hydrofunctionalization Reactions via Acridinium Photoredox Catalysis. *Acc. Chem. Res.*, **2016**, *49*, 1997-2006, DOI: 10.1021/acs.accounts.6b00304.
21. Fukuzumi, S.; Kotani, H.; Ohkubo, K.; Ogo, S.; Tkachenko, N. V.; Lemmetyinen, H. Electron-Transfer State of 9-Mesityl-10-methylacridinium Ion with a Much Longer Lifetime and Higher Energy Than That of the Natural Photosynthetic Reaction Center. *J. Am. Chem. Soc.*, **2004**, *126*, 1600-1601, DOI: 10.1021/ja038656q.
22. Xuan, J.; Xia, X.-D.; Zeng, T.-T.; Feng, Z.-J.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. Visible-Light-Induced Formal [3+2] Cycloaddition for Pyrrole Synthesis under Metal-Free Conditions. *Angew. Chem. Int. Ed.*, **2014**, *53*, 5653-5656, DOI: 10.1002/anie.201400602.
23. Hamilton, D. S.; Nicewicz, D. A. Direct Catalytic Anti-Markovnikov Hydroetherification of Alkenols. *J. Am. Chem. Soc*. **2012**, *134*, 18577-18580, DOI: 10.1021/ja309635w.
24. Romero, N. A.; Margrey, K. A.; Tay, N. E.; Nicewicz, D. A. Site-selective arene C-H amination via photoredox catalysis. *Science*, **2015**, *349*, 1326-1330, DOI: 10.1126/science.aac9895.
25. Romero, N. A.; Nicewicz, D. A.; Organic Photoredox Catalysis. *Chem. Rev.*, **2016**, *116*, 10075-10166, DOI: 10.1021/acs.chemrev.6b00057.
26. Ravelli, D.; Fagnoni, M. Dyes as Visible Light Photoredox Organocatalysts. *ChemCatChem* **2012**, *4*, 169-171, DOI: 10.1002/cctc.201100363.
27. Haria, D. P.; König, B. Synthetic applications of eosin Y in photoredox catalysis. *Chem. Commun.*, **2014**, *50*, 6688-6699, DOI: 10.1039/C4CC00751D.
28. Srivastava, V.; Singh, P. P. Eosin Y catalysed photoredox synthesis: a review. *RSC Adv.*, **2017**, *7*, 31377-31392, DOI: 10.1039/C7RA05444K.
29. Pan, Y.; Kee, C. W.; Chen, L.; Tan, C.-H. Dehydrogenative coupling reactions catalysed by Rose Bengal using visible light irradiation. *Green Chem*. **2011**, *13*, 2682-2685, DOI: 10.1039/C1GC15489C.
30. Neumann, M.; Füldner, S.; König, B.; Zeitler, K. Metal-Free, Cooperative Asymmetric Organophotoredox Catalysis with Visible Light. *Angew. Chem. Int. Ed.* **2011**, *50*, 951-954, DOI: 10.1002/anie.201002992.
31. Hari, D. P.; Hering, T.; König, B. The Photoredox-Catalyzed Meerwein Addition Reaction: Intermolecular Amino-Arylation of Alkenes. *Angew. Chem. Int. Ed.* **2014**, 53, 725-728, DOI: 10.1002/anie.201307051.
32. Yang, N. C.; Yang, D.-D. H. Photochemical Reactions of Ketones in Solution. *J. Am. Chem. Soc.*, **1958**, *80*, 2913-2914, DOI: 10.1021/ja01544a092.
33. Coyle, J. D.; Carless, H. A. Selected aspects of photochemistry. I Photochemistry of carbonyl compounds. *Chem. Soc. Rev.*, **1972**, *1* (4), 465-480.
34. Hoffmann, N. Photochemical Reactions as Key Steps in Organic Synthesis. *Chem. Rev.*, **2008**, *108*, 1052-1103, DOI: 10.1021/cr0680336.
35. See Supporting Information for further details.
36. Jana, S.; Verma, A.; Kadu, R.; Kumar, S. Visible-light-induced oxidant and metal-free dehydrogenative cascade trifluoromethylation and oxidation of 1,6-enynes with water. *Chem. Sci*., **2017**, *8*, 6633-6644, DOI: 10.1039/C7SC02556D.
37. Li, L.; Mu, X.; Liu, W.; Wang, Y.; Mi, Z.; Li, C.-J. Simple and Clean Photoinduced Aromatic Trifluoromethylation Reaction. *J. Am. Chem. Soc*., **2016**, *138*, 5809-5812, DOI: 10.1021/jacs.6b02782.
38. Li, J.; Caiuby, C. A. D.; Paixão, M. W.; Li, C.-J. Synthesis of 6-Trifluoromethylphenanthridines through Radical Trifluoromethylation of Isocyanides with Sodium Triflinate under Visible Light. *Eur. J. Org. Chem*., **2018**, 2498-2512, DOI: 10.1002/ejoc.201701487.
39. Beatty, J. W.; Stephenson, C. R. J. Amine Functionalization via Oxidative Photoredox Catalysis: Methodology Development and Complex Molecule Synthesis. *Acc. Chem. Res*., **2015**, *48*, 1474-1484, DOI: 10.1021/acs.accounts.5b00068.
40. Shi, L.; Xia, W. Photoredox functionalization of C–H bonds adjacent to a nitrogen atom. *Chem. Soc. Rev.,* **2012**, *41*, 7687-7697, DOI: 10.1039/C2CS35203F.

41. Nakajima, K.; Miyake, Y.; Nishibayashi, Y. Synthetic Utilization of α-Aminoalkyl Radicals and Related Species in Visible Light Photoredox Catalysis. *Acc. Chem. Res.*, **2016**, *49*, 1946-1956, DOI: 10.1021/acs.accounts.6b00251.
42. Hu, J.; Wang, J.; Nguyen, T. H.; Zheng, N. The chemistry of amine radical cations produced by visible light photoredox catalysis. *Beilstein J. Org. Chem.* **2013,** *9*, 1977-2001, DOI: 10.3762/bjoc.9.234.
43. Han, X.; He, X.; Wang, F.; Chen, J.; Xu, J.; Wang, X.; Han, X. Engineering an N-doped Cu2O@N–C interface with long-lived photo-generated carriers for efficient photoredox catalysts. *J. Mater. Chem. A*, **2017**, *5*, 10220-10226, DOI: 10.1039/C7TA01909B.
44. 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, DOI: 10.1002/ajoc.201600415.
45. 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, DOI: 10.1039/C6CC04997D.
46. 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 Zwitterionic Copper(I) Complexes for Photoinduced Cross-Dehydrogenative Coupling Reactions. *Chem. Eur. J.*, **2015**, *21*, 1184-1190, DOI: 10.1002/chem.201405356.
47. 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, DOI: 10.1002/adsc.201400588.
48. 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, DOI: 10.1021/ol503744a.
49. 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, DOI: 10.1021/ol500534w.
50. 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.; Wu, L.-Z. A Cascade Cross-Coupling Hydrogen Evolution Reaction by Visible Light Catalysis. *J. Am. Chem. Soc.* **2013**, *135*, 19052-19055, DOI: 10.1021/ja408486v.
51. 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, DOI: 10.1002/chem.201204572.
52. Freeman, D. B.; Furst, L., Condie, A. G.; Stephenson, C. R. J. Functionally Diverse Nucleophilic Trapping of Iminium Intermediates Generated Utilizing Visible Light. *Org. Lett.*, **2012**, *14*, 94-97, DOI: 10.1021/ol202883v.
53. 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 Cu_2O Nanoparticles on a Nitrogen-Doped Porous Carbon Yolk–Shell Cuboctahedral Framework. *ACS Catal*. **2018**, *8*, 3348-3356, DOI: 10.1021/acscatal.7b04219.
54. Hepburn, H. B.; Melchiorre, P. Brønsted acid-catalysed conjugate addition of photochemically generated α-amino radicals to alkenylpyridines. *Chem. Commun.* **2016**, *52*, 3520-3523, DOI: 10.1039/C5CC10401G.
55. 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, DOI: 10.1038/nature17438.
56. Ju, X.; Li, D.; Li, W.; Yu, W.; Bian, F. The Reaction of Tertiary Anilines with Maleimides under Visible Light Redox Catalysis. *Adv. Synth. Catal*. **2012**, *354*, 3561-3567, DOI: 10.1002/adsc.201200608.
57. Uraguchi, D.; Kinoshita, N.; Kizu, T.; Ooi, T. Synergistic Catalysis of Ionic Brønsted Acid and Photosensitizer for a Redox Neutral Asymmetric α-Coupling of N-Arylaminomethanes with Aldimines. *J. Am. Chem. Soc*. **2015**, *137*, 13768-13771, DOI: 10.1021/jacs.5b09329.
58. 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*, 1823-1829, DOI: 10.1021/ja309580a.
59. 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, DOI: 10.1039/C2CC36995H.

60. 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, DOI: 10.1021/jo301691h.
61. 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, DOI: 10.1039/C6GC00550K.
62. 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, DOI: 10.1021/acscatal.5b00093.
63. Zhang, G.-Y.; Xiang, Y.; Guan, Z.; He, Y.-H. Enzyme and photoredox sequential catalysis for the synthesis of 1,3-oxazine derivatives in one pot. *Catal. Sci. Technol.*, **2017**, *7*, 1937-1942, DOI: 10.1039/C6CY02682F.
64. Ilaš, J.; Anderluh, P. Š.; Dolenc, M. S.; Kikelj, D. Recent advances in the synthesis of 2H-1,4-benzoxazin-3-(4H)-ones and 3,4-dihydro-2H-1,4-benzoxazines. *Tetrahedron* **2005**, *61*, 7325-7348, DOI: 10.1016/j.tet.2005.05.037.
65. Achari, B.; Mandal, S. B.; Duttaand, P. K.; Chowdhury, C. Perspectives on 1,4-Benzodioxins, 1,4-Benzoxazines and their 2,3-Dihydro Derivatives. *Synlett* **2004**, 2449-2467, DOI: 10.1055/s-2004-834816.
66. 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, DOI: 10.1016/S0960-894X(00)00321-8.
67. 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, DOI: 10.1007/s00044-014-1159-x.
68. 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-hour-long duration of action in preclinical models. *J. Pharmacol. Exp. Ther*. **2010**, *334*, 53-62, DOI: 10.1124/jpet.110.167007.
69. 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(4*H*)-ones as Potent Inhibitors of Platelet Aggregation: Design, Synthesis and Structure–Activity Relations. *Chem. Pharm. Bull*. **2014**, *62*, 915-920, DOI: 10.1248/cpb.c14-00330.
70. Zidar, N.; Kikelj, D. A convenient synthesis of 3,4-dihydro-1,4-benzoxazin-2-ones. *Tetrahedron*, **2008**, *64*, 5756-5761, DOI: 10.1016/j.tet.2008.04.010.
71. Huo, C.; Dong, J.; Su, Y.; Tang, J.; Chen, F. Iron-catalyzed oxidative sp^3 carbon–hydrogen bond functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones. *Chem. Commun*. **2016**, *52*, 13341-13344, DOI: 10.1039/C6CC05885J.
72. Dong, J.; Min, W.; Li, H.; Quan, Z.; Yang, C.; Huo, C. Iron-Catalyzed $C(sp^3)-C(sp^3)$ Bond Formation in 3,4-Dihydro-1,4-benzoxazin-2-ones. *Adv. Synth. Catal*. **2017**, *359*, 3940-3944, DOI: 10.1002/adsc.201700816.
73. 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-Imino Esters. *Synthesis*, **2017**, *49*, 2683-2690, DOI: 10.1055/s-0036-1588742.
74. Blay, G.; Fernández, I.; Muñoz, M. C.; Pedro, J. R.; Vila, C. Synthesis of Functionalized Indoles with a Trifluoromethyl-Substituted Stereogenic Tertiary Carbon Atom Through an Enantioselective Friedel–Crafts Alkylation with β-Trifluoromethyl-α,β-enones. *Chem. Eur. J.* **2010**, *16*, 9117-9122, DOI: 10.1002/chem.201000568.
75. 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-butene-1,4-diones. *Adv. Synth. Catal.* **2009**, *351*, 2433-2440, DOI: 10.1002/adsc.200900357.
76. Blay, G.; Fernández, I.; Pedro, J. R.; Vila, C. Highly Enantioselective Friedel−Crafts Alkylations of Indoles with Simple Enones Catalyzed by Zirconium(IV)−BINOL Complexes. *Org. Lett*. **2007**, *9*, 2601-2604, DOI: 10.1021/ol0710820.
77. During our experimental work and preparation of manuscript a photoredox functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones using the expensive $Ru(bpy)_2Cl_2$ photocatalyst was reported, see: Zhang, G.-Y.; Yu, K.-K.; Zhang, C.; Guan, Z.; He, Y.-H. Oxidative Cross-Dehydrogenative-Coupling Reaction of 3,4-Dihydro-1,4-Benzoxazin-2-ones through Visible-Light Photoredox Catalysis. *Eur. J. Org. Chem*. **2018**, 525-531, DOI: 10.1002/ejoc.201701683.

78. During the preparation of the manuscript, a photoredox functionalization of 3,4-dihydro-1,4-benzoxazin-2-ones was described using the expensive Ru(bpy)$_2$Cl$_2$ photocatalyst was reported. In this case only one example, leading to compound **3aa** with 44% yield, was reported. Akula, P. S. Hong, B.-C.; Lee, G.-H. Visible-light-induced C(sp^3)–H activation for a C–C bond forming reaction of 3,4-dihydroquinoxalin-2(1*H*)-one with nucleophiles using oxygen with a photoredox catalyst or under catalyst-free conditions. *RSC Adv*. **2018**, *8*, 19580-19584, DOI: 10.1039/C8RA03259A.
79. 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, DOI: 10.1021/np800334j.
80. 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, DOI: 10.1111/j.1471-4159.1981.tb00428.x.
81. Khedekar, V.; Tillack, A.; Michalik, M.; Beller, M. Convenient synthesis of tryptophols and tryptophol homologues by hydroamination of alkynes. *Tetrahedron* **2005**, *61*, 7622-7631, DOI: 10.1016/j.tet.2005.05.093.
82. 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, DOI: 10.1007/BF01243372.
83. For an example of synthesis of tryptophol derivatives from our group, see: Blay, G.; Fernandez, I.; Muñoz, M. C.; Pedro, J. R.; Vila, C. Enantioselective Friedel–Crafts Alkylation of Indoles with (*E*)-1-Aryl-4-benzyloxybut-2-en-1-ones Catalyzed by an (*R*)-3,3′-Br$_2$BINOLate–Hafnium(IV) Complex. *Eur. J. Org. Chem*. **2013**, 1902-1907, DOI: 10.1002/ejoc.201201636.