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Medy C Nongbe, Abollé Abollé, Vincent Coeffard, François-xavier Felpin. Rose Bengal Immobilized on Cellulose Paper for Sustainable Visible-Light Photocatalysis. *ChemPlusChem*, 2022, 87 (9), 10.1002/cplu.202200242 . hal-04025898

HAL Id: hal-04025898

<https://nantes-universite.hal.science/hal-04025898>

Submitted on 13 Mar 2023

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Rose Bengal Immobilized on Cellulose Paper for Sustainable Visible-Light Photocatalysis

Medy C. Nongbe,^[a, b] Abollé Abollé,^[c] Vincent Coeffard,^[a] and François-Xavier Felpin*^[a]

This work reports the heterogenization of Rose Bengal dye on simple cellulose paper sheets (Cell-RB) through copper-catalyzed azide-alkyne click ligation. The photocatalytic properties of Cell-RB under green LED irradiation were evaluated in a series of dehydrogenative transformations for the functionaliza-

tion of *N*-aryltetrahydroisoquinolines and quinoxalin-2(1*H*)-ones. The excellent photocatalytic activities observed, associated to the ease of recovery with simple tweezers, highlight the strong assets of Cell-RB with respect to traditional homogeneous organic photocatalysts.

Introduction

Visible-light-driven organic photocatalysis has emerged as a powerful sustainable and cost-effective approach for the elaboration of high-value molecular architectures.^[1–5] The low cost of visible light associated with the wide commercial availability of organic photocatalysts which prevents the use of expensive and toxic transition-metal complexes are key features for the development of green chemistry processes. In the tool box of synthetic chemists, Rose Bengal (RB) is one of the most relevant organic photocatalyst for developing sustainable transformations as it is non-toxic, metal-free and strongly absorbs in the green region of the visible spectrum (480–550 nm).^[6–8] While many contributions highlighted its assets as organic photocatalyst for various transformations,^[9] RB is a hydrophilic dye prone to form aggregates under aqueous or hydrophilic solvents, leading to diminished quantum yields and photobleaching.^[10] This drawback associated to the difficult removal of RB from crude mixtures that can result in further undesired side reactions are severe limitations in the context of sustainable synthesis.^[11]

The immobilization of RB onto a suitable insoluble carrier can address both of these issues as this allows to recover the immobilized photocatalyst from the crude mixture by simple

filtration and prevents aggregation through the creation of isolated active sites.^[12–14] Recent approaches reported in the literature mostly rely on the covalent anchoring of Rose Bengal to silica-based materials.^[11,15–19] However, the modest stability of siloxane bonds under strongly hydrolytic conditions can result in a significant leaching of the dye. The covalent anchoring of Rose Bengal to polymers such as polystyrene resins is another strategy which proved to be efficient for photooxidation reactions.^[20–23] For the development of more sustainable processes, the immobilization of Rose Bengal on biopolymers is a more appealing strategy that has surprisingly been mostly overlooked. Wool^[24] and natural cotton fibers^[25] have been used as biosourced supports for the immobilization of Rose Bengal through physisorption and ionic interactions, respectively. The covalent immobilization of Rose Bengal on chitosan is another strategy which increases the robustness of the photocatalytic material.^[26] However, the high solubility of chitosan in water complicates the removal of the photocatalytic material when reactions are carried out in aqueous conditions.

Cellulose is the most abundant renewable biopolymer on earth with an almost inexhaustible annual bioproduction of 10¹² tons. Cellulose is one of the most relevant material for the development of sustainable heterogeneous catalysis as it is non-toxic, biocompatible, inexpensive, robust and highly hydrophilic but not soluble in water. It consists of linear chains of β (1–4) linked D-glucose units strongly involved in a dense hydrogen bond network. Cellulose exists under various forms such as pulp, micro- or nanocrystalline powder and paper. While micro- and nano-cellulose are the preferred forms as supports for the immobilization of catalysts,^[27–31] catalysis on paper is an emerging field of research featuring several assets.^[32–35] The removal of the catalytic paper from the crude mixture can be done with simple tweezers without any filtration, simplifying the work-up procedure. Moreover, the evolution of the heterogeneous catalyst (structure, color...) can be easily monitored by visual inspection.

In the current contribution we describe a straightforward strategy for the covalent immobilization of Rose Bengal on cellulose paper through a copper-catalyzed Huisgen click ligation. The resulting catalytic Cell-RB material was further

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Supporting information for this article is available on the WWW under <https://doi.org/10.1002/cplu.202200242>

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evaluated for the C–H functionalization of tertiary amines under sustainable conditions.

Results and Discussion

Immobilization of Rose Bengal on cellulose paper

The immobilization of Rose Bengal stands on the use of a copper-catalyzed Huisgen azide-alkyne 1,3-dipolar cycloaddition between cellulose paper functionalized with azide functions (Cell-N₃) and Rose Bengal bearing a terminal alkyne group (Scheme 1). Cell-N₃ was prepared in two steps from mercerized pristine cellulose paper through the activation of C-6 alcohols as tosylate derivatives followed by the nucleophilic displacement of the tosylate leaving groups with sodium azide (NaN₃).^[36] The efficiency of this two-step procedure was evaluated through the determination of the degree of substitution (DS) of Cell-N₃. A DS of 0.38–0.40 was calculated by elemental analysis, meaning that an average of four C-6 alcohols were azidated every ten glucose units. Reaching higher DS under more demanding conditions is possible but not recommended as the resulting Cell-N₃ paper loses its physical integrity due to hydrogen bond cleavage and solubilizes in water and polar solvents (DMF, THF...)

The click ligation between Cell-N₃ and Rose Bengal derivative **1** was carried out in refluxing aqueous THF using CuSO₄ as copper catalyst and sodium ascorbate as reducing agent. The conversion was conveniently monitored by Fourier-transform infrared (FTIR) spectroscopy at different reaction times through the progressive disappearance of the characteristic vibration band $\nu_{as}(N_3)$ at 2108 cm⁻¹ together with the apparition of a band at 1738 cm⁻¹ attributed to the C=O stretching frequency of the ester function (Figure 1).

New bands at 1330, 1450 and 1546 cm⁻¹, corresponding to the C=C stretching vibrations of the aromatic structure of Rose Bengal, also attest to the successful grafting of RB on the cellulose matrix. The surface composition of cellulose papers was also analyzed by X-ray photoelectron spectroscopy (XPS) analysis (Figure 2).

The full scan spectrum of Cell-RB shows the apparition of chlorine and iodine elements identified as the hallmark of the Rose Bengal moiety. The high resolution spectrum of the C1s region of Cell-RB shows a sharp increase of the peak at 285.0 eV

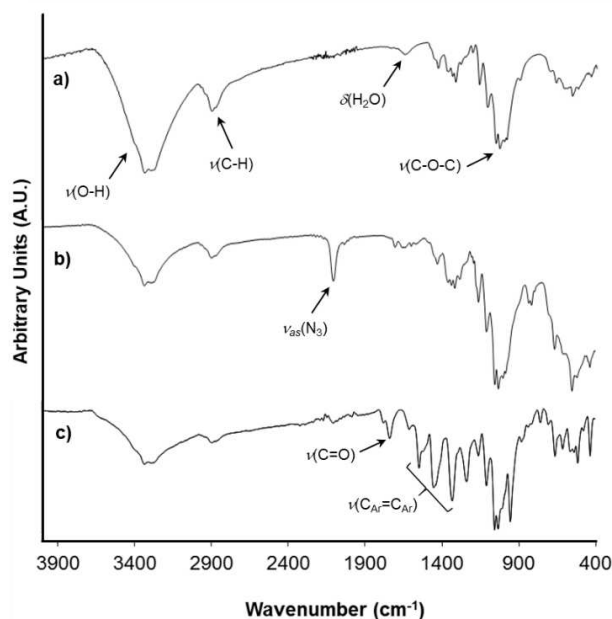
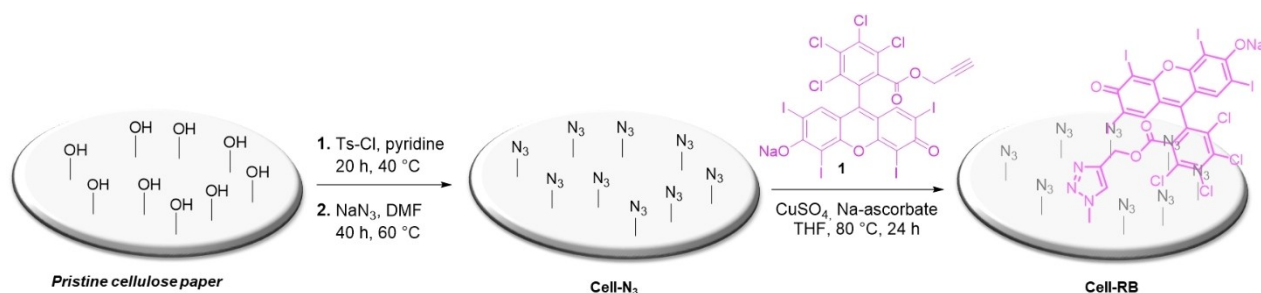


Figure 1. FTIR spectra of (a) pristine cellulose, (b) Cell-N₃ and (c) Cell-RB.

corresponding to C–C bonds while the N1s region photoemission curve reveals two peaks at 400.3 and 402.0 eV. The loss of peak at ca. 404–405 eV accounting for the electron-deficient nitrogen atom of the azide function, confirms the ligation of RB through the [3+2]-cycloaddition. Scanning electron microscopy (SEM) images reported in Figure S1 show a filamentous aspect of the fiber surface after chemical grafting likely due to the marginal loss of hemicellulose but without significant modification of the fiber size, in the range of 5–20 μm, and without paper wrinkling.

Photocatalytic properties of Cell-RB

We evaluated the activity of Cell-RB as the photocatalyst with the benchmark Cell-RB photoredox-catalyzed reaction of *N*-phenyltetrahydroisoquinoline **2a** with nitromethane **3a** under green LEDs irradiation (525 nm) and air atmosphere (Table 1). We initially performed the reaction in MeNO₂ (190 equivalents) acting as the solvent and the nucleophile, as described in many



Scheme 1. Preparation of the photocatalytic paper Cell-RB.

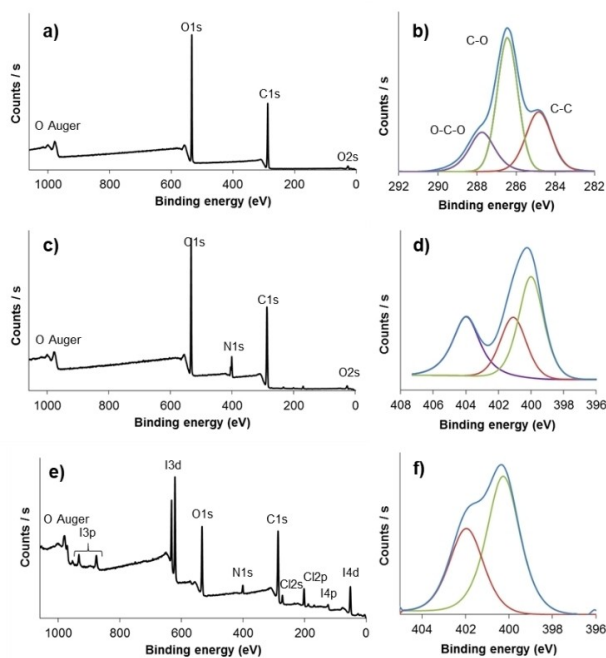
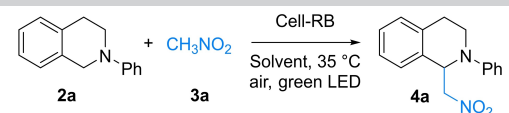


Figure 2. Survey scan spectra of a) pristine cellulose, c) Cell- N_3 and e) Cell-RB. High resolution b) C1s spectrum of Cell, d) N1s spectrum of Cell- N_3 and f) N1s spectrum of Cell-RB.

Table 1. Optimization of reaction conditions.				
				
Entry	Cell-RB [mol %]	Solvent	Time [h]	Conversion [%] ^[a]
1 ^[b]	20	CH ₃ NO ₂	10	> 95
2 ^[b]	10	CH ₃ NO ₂	15	> 95
3 ^[b]	5	CH ₃ NO ₂	24	> 95
4 ^[c]	5	EtOH	24	> 95 (84)
5 ^[c]	5	EtOH	12	85
6 ^[d]	5	EtOH	24	85
7 ^[c]	0	EtOH	24	16
8 ^[c,f]	5	EtOH	24	17
9 ^[c,e]	5	EtOH	24	40
10 ^[c,g]	5	EtOH	24	90
11 ^[c,h]	5	EtOH	24	> 95

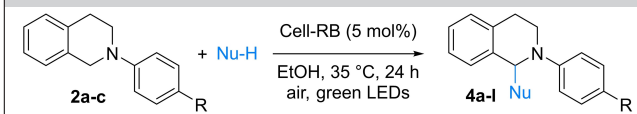
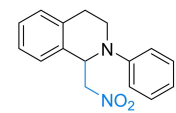
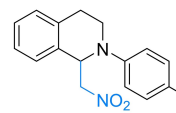
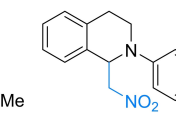
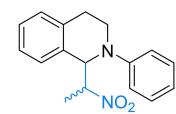
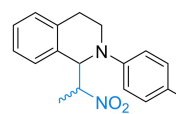
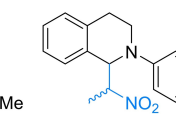
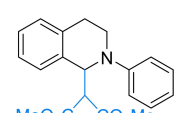
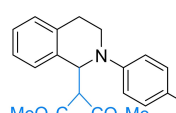
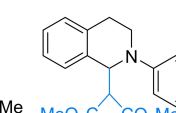
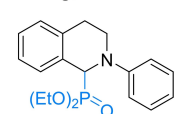
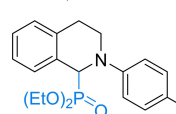
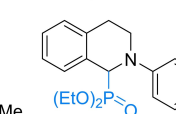
[a] Conversion determined by ¹H NMR using 1,3,5-trimethylbenzene as internal standard. Isolated yield in brackets. [b] Reaction conditions: **2a** (0.2 mmol), **3a** (2 mL), Cell-RB (see table), 35 °C, open flask. [c] Reaction conditions: **2a** (0.2 mmol), **3a** (1 mmol, 5 equiv.), EtOH (1 mL), Cell-RB (see table), 35 °C. [d] 2.5 equivalents of **3a** (0.5 mmol) were used. [e] Reaction carried out under Ar. [f] Reaction carried out in the dark. [g] Reaction conducted with Cell-RB reused three times. [h] Cell-RB stored five months on the bench at room temperature.

previous reports (entries 1–3).^[37–39] While full conversions were reached under these conditions, we reasoned that the use of an environmentally friendly and biodegradable solvent could increase the sustainability of the procedure and save expensive MeNO₂. Interestingly, a full conversion for **4a** was observed with EtOH as the solvent and MeNO₂ only acting as the reactant (5 equivalents) under otherwise identical experimental con-

ditions (entry 4). An eroded conversion (85%) was obtained when further decreasing the reaction time (entry 5) or the stoichiometry of MeNO₂ to 2.5 equivalents (entry 6). Avoiding the use of either the photocatalyst, the green LEDs irradiation or the presence of oxygen severely compromised the conversion and confirmed a true Cell-RB photoredox-catalyzed process (entries 7–9). Cell-RB maintained its high reactivity after three reuses but further recycling is not recommended due to the fragility of the reused paper material (entry 10). Cell-RB can be stored at room temperature for months on the bench without noticeable decrease of its reactivity (entry 11).

With the optimized conditions in hand, we further explored the oxidative functionalization of *N*-aryltetrahydroisoquinolines with various nucleophiles using Cell-RB as the heterogeneous organophotocatalyst (Table 2). The use of nitroalkanes as nucleophiles provides the corresponding alkylated *N*-aryltetrahydroisoquinolines in high yields ranging from 80 to 98%, which are comparable or even superior to literature precedents using immobilized Rose Bengal photocatalysts on related substrates (compounds **4a–f**).^[18,25, 40] The use of dimethylmalonate **3c** as the nucleophile smoothly provides constrained precursors of β -aminoacids in good to excellent yields (compounds **4g–i**). The successful creation of C–C bonds prompted us to also explore the formation of C–P bonds. In this

Table 2. Substrate scope for the Cell-RB photoredox-catalyzed functionalization of *N*-aryltetrahydroisoquinolines.^[a]

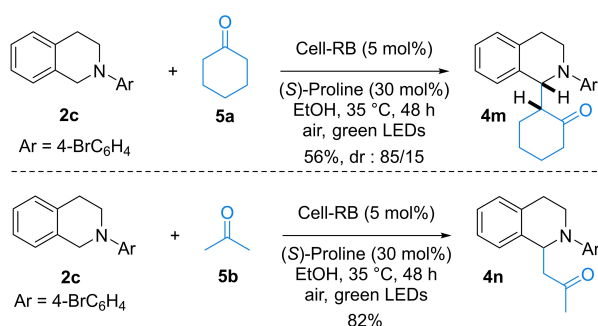
		
NuH = 3a - CH ₃ NO ₂ 3c - CH ₂ (CO ₂ Me) ₂ 3b - C ₂ H ₅ NO ₂ 3d - HPO(OEt) ₂ R = H, OMe, Br		
		
4a , 94%	4b , 98%	4c , 99%
		
4d , 80%, 65/35 dr	4e , 98%, 67/33 dr	4f , 81%, 65/35 dr
		
4g , 75%	4h , 67%	4i , 71%
		
4j , 89%	4k , 83%	4l , 93%

[a] Reaction conditions: **2a–c** (0.2 mmol), **3a–d** (1 mmol, 5 equiv.), Cell-RB (5 mol %), 35 °C, 24 h, open flask. Isolated yields are reported.

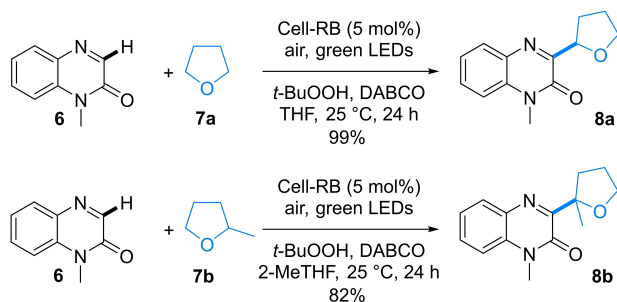
frame, we applied our process to the synthesis of α -amino phosphonates through the Cell-RB-catalyzed phosphorylation of *N*-aryltetrahydroisoquinolines **2a–c** with diethylphosphite **3d**. The remarkable efficiency of this transformation allowed the preparation of α -amino phosphonates **4j–l** in high yields (83–93%). α -Amino phosphonates have a prominent place in medicinal chemistry as antagonists of α -amino acids to inhibit enzymes and modify the physiological activity of cell.^[41]

Following this success, we studied the photocatalyzed dehydrogenative Mannich reaction between *N*-aryltetrahydroisoquinolines **2c** and ketones **5a–b** (Scheme 2). Dehydrogenative Mannich reactions has the potential to outperform the traditional Mannich reaction as the reactive iminium intermediate is generated in situ from the corresponding amine and does not need any extra step. Dehydrogenative Mannich reactions between tertiary amines and ketones usually give modest yields as ketones are poor nucleophiles.^[37,39] In our hand, the dehydrogenative Mannich reaction of *N*-aryltetrahydroisoquinolines **2c** with cyclohexanone **5a** or acetone **5b** using a combination of Cell-RB and (*S*)-proline under green LED irradiation furnished the expected coupled products in modest to good yields (56–82%) considering the mild conditions and experimental simplicity of the methodology without any expensive transition metal.

The α -C–H functionalization of ethers under mild and metal-free conditions is an attractive and appealing but still underexplored strategy to assemble complex structural motifs.^[42–47] In our hands, Cell-RB successfully catalyzed the coupling of 1-methylquinoxalin-2(1*H*)-one **6** with THF **7a** and 2-methyl-THF **7b** in the presence of *t*-BuOOH as the oxidant and



Scheme 2. Cell-RB photoredox-catalyzed dehydrogenative Mannich reactions.



Scheme 3. Cell-RB photoredox-catalyzed cross-dehydrogenative coupling of 1-methylquinoxalin-2(1*H*)-one **6** with THF and 2-methyl-THF.

DABCO as the base at room temperature (Scheme 3). With 2-methyl-THF, the α -C–H functionalization occurred on the most substituted position presumably due to the higher stability of the corresponding radical intermediate.

Conclusion

In summary, we have developed a new paper-based heterogeneous photocatalyst by grafting Rose Bengal dye on cellulose paper. This material showed excellent photocatalytic activities for a variety of cross-dehydrogenative couplings. The immobilization of Rose Bengal on cellulose paper, significantly simplifies the reaction work-up as the heterogeneous catalyst can be recovered from the reaction mixture with simple tweezers without any tedious filtration procedure. In addition, Cell-RB can be recycled three times without compromising the catalytic activity. We believe that such heterogeneous catalysts benefiting from the bio-compatibility and low cost of cellulose paper as support will become widely used standards for the development of sustainable processes.

Experimental Section

General information: All reagents, starting materials and solvents were obtained from commercial suppliers and used as such without further purification, unless otherwise noted. High-field ¹H and ¹³C NMR spectra were recorded at 300 or 400 and 75 or 100 MHz, respectively. ¹H and ¹³C NMR spectra were referenced to the internal deuterated solvent (CDCl₃) at 7.26 and 77.16 ppm, respectively and coupling constants were measured in Hertz. All chemical shifts were quoted in ppm, relative to TMS, using the residual solvent peak as a reference standard. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. FTIR spectra were recorded in the ATR mode. Wavelengths of maximum absorbance (ν_{\max}) are shown in wavenumbers (cm⁻¹). High resolution mass spectrometry (HRMS) was recorded on a Xevo G2-XS QTOF spectrometer equipped with orthogonal electrospray interface (ESI). An atmospheric solid analysis probe (ASAP) was used for the direct analysis of samples by atmospheric pressure ionization (ASAP+ or ASAP-). Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm pre-coated silica gel plates (60 F254), and visualization was accomplished with UV light at 254 nm. Flash column chromatography was performed using silica gel 60 (40–63 μ m).

Procedure for the pretreatment of cellulose papers.^[36] Five pieces of cellulose filter papers (approximately 750 mg) were dispersed in 250 mL of a freshly prepared 10% (w/w) NaOH aqueous solution. This mixture was then shaken 20 h on an orbital agitator. The cellulose samples were washed 6 times with 50 mL of EtOH and stored in EtOH.

Preparation of the tosylated cellulose papers: A piece of cellulose paper (145 mg, 0.81 mmol) was immersed in pyridine (10 mL) and treated with *p*-toluenesulfonyl chloride (464 mg, 2.44 mmol). The resulting mixture was then shaken for 20 h at 40 °C on an orbital agitator. Tosylated cellulose was sonicated three times in 20 mL of DMF and stored in DMF for the next step (DS = 0.45).

Preparation of the azidated cellulose paper (Cell-N₃): A piece of Cell-Ts (0.81 mmol of glucose units) was immersed in DMF (10 mL)

and treated with NaN_3 (526 mg, 8.10 mmol). The resulting mixture was then shaken for 40 h at 60 °C on an orbital agitator. Cell- N_3 was successively sonicated with 20 mL of H_2O (3 times), CH_3COCH_3 (10 mL), EtOH (10 mL) and CH_2Cl_2 (10 mL) and dried under vacuum ($DS = 0.40$).

Preparation of Cell-RB: A piece of Cell- N_3 (0.20 mmol of glucose units) was immersed in a mixture of THF (3 mL) and H_2O (2 mL) and treated with Rose Bengal alkyne $1^{[46]}$ (207 mg, 0.20 mmol, 1 equiv.), CuSO_4 (3.2 mg, 10 mol%) and sodium ascorbate (39.6 mg, 0.20 mmol, 1 equiv.). The resulting mixture was then shaken for 24 h at 80 °C on an orbital agitator. Cell-RB was successively sonicated with 10% aqueous EDTA solution (20 mL), CH_3COCH_3 (2 × 10 mL) and CH_2Cl_2 (10 mL) and dried under vacuum.

General procedure for the preparation of N-arylated 1,2,3,4-tetrahydroisoquinoline: To a solution of 1,2,3,4-tetrahydroisoquinoline (3.00 g, 22.5 mmol, 1.5 equiv.) and ethylene glycol (2.80 g, 30.0 mmol, 2.0 equiv.) in *i*-PrOH (15 mL) at 23 °C, were successively added the required 4-iodoarene (15.0 mmol, 1.0 equiv.), K_3PO_4 (9.56 g, 30.0 mmol, 2.0 equiv.) and CuI (0.429 g, 1.50 mmol, 0.1 equiv.). The resulting mixture was stirred at 80 °C for 24 h. After completion, the reaction medium was diluted with Et_2O (50 mL) and filtered through a pad of Celite®. The filtered solution was diluted with water (100 mL) and extracted with diethyl ether (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried over anhydrous MgSO_4 and concentrated under reduced pressure. Crude residues were purified by flash column chromatography to give the corresponding products (**2a–c**) as white solids.

2-phenyl-1,2,3,4-tetrahydroisoquinoline (2a): Purification by flash chromatography on silica gel (5% EtOAc-hexane) gave **2a** as a white solid (2.64 g, 84%). mp = 189 °C. IR (ATR) ν 3024, 2917, 2811, 1596, 1498, 740 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz) δ 7.41–7.46 (m, 2H), 7.28–7.33 (m, 4H), 7.11–7.14 (m, 2H), 6.96–7.01 (m, 1H), 4.54 (s, 2H), 3.66–3.70 (m, 2H), 3.11 (br s, 2H). ^{13}C NMR (CDCl_3 , 100 MHz) δ 150.5, 134.9, 134.6, 129.3, 128.6, 126.6, 126.4, 126.1, 118.7, 115.2, 50.8, 46.6, 29.2. HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{16}\text{N}$ 210.1283; Found 210.1290.

2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (2b): Purification by flash chromatography on silica gel (10% EtOAc-hexane) gave **2b** as a white solid (2.75 g, 76%). mp 92.5–93 °C. IR (ATR) ν 2996, 2921, 2808, 1507, 1238, 1034, 820, 752 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz) δ 7.13–7.19 (m, 4H), 6.99 (dm, 2H, $J = 9.1$ Hz), 6.88 (dm, 2H, $J = 9.1$ Hz), 4.31 (s, 2H), 3.79 (s, 3H), 3.46 (t, 2H, $J = 5.8$ Hz), 2.88 (t, 2H, $J = 5.8$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz) δ 153.7, 145.5, 134.8, 134.7, 128.8, 126.7, 126.4, 126.1, 118.2, 114.8, 55.8, 52.8, 48.6, 29.3. HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{18}\text{NO}$ 240.1388; Found 240.1382.

2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinoline (2c): Purification by flash chromatography on silica gel (5% EtOAc-hexane) gave **2c** as a white solid (3.72 g, 86%). mp 72–72.5 °C. IR (ATR) ν 3033, 2947, 2839, 1585, 1490, 802, 736 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz) δ 7.35 (dm, 2H, $J = 8.8$ Hz), 7.15–7.20 (m, 4H), 6.83 (dm, 2H, $J = 9.0$ Hz), 4.38 (s, 2H), 3.53 (t, 2H, $J = 5.8$ Hz), 2.98 (t, 2H, $J = 5.8$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz) δ 149.6, 134.9, 134.2, 132.1, 128.6, 126.7, 126.3, 116.6, 110.6, 50.6, 46.5, 29.1. HRMS (ASAP+) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{15}\text{NBr}$ 288.0388; Found 288.0388.

General procedure for the functionalization of N-arylated 1,2,3,4-tetrahydroisoquinoline 2a–c with nucleophiles 3a–d (Table 2): To a solution of N-arylated 1,2,3,4-tetrahydroisoquinoline **2a–c** (0.2 mmol) and Cell-RB (5 mol%) in EtOH (1 mL) was added nucleophiles **3a–d** (1 mmol). The resulting mixture was stirred on an orbital agitator at room temperature for 24 h under green LED irradiation ($\lambda_{\text{max}} = 525$ nm). Cell-RB was removed, washed with EtOH

and volatiles were removed under reduced pressure. Crude residues were purified by flash column chromatography to give the corresponding products (**4a–l**).

1-(Nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4a): Purification by flash chromatography on silica gel (8% EtOAc-hexane) gave **4a** as an orange oil (50.4 mg, 94%). IR (ATR) ν 3026, 2917, 1546, 1496, 1378, 750 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 7.07–7.24 (m, 6H), 6.94 (d, 2H, $J = 8.2$ Hz), 6.81 (t, 1H, $J = 7.3$ Hz), 5.51 (t, 1H, $J = 7.2$ Hz), 4.81 (dd, 1H, $J = 7.9$, 11.8 Hz), 4.50 (dd, 1H, $J = 6.6$, 11.8 Hz), 3.56–3.62 (m, 2H), 2.99–3.09 (m, 1H), 2.73 (dt, 1H, $J = 4.9$, 16.4 Hz). ^{13}C NMR (CDCl_3 , 100 MHz) δ 148.6, 135.4, 133.1, 129.6, 129.3, 128.2, 127.1, 126.8, 119.6, 115.3, 78.9, 58.3, 42.2, 26.6. HRMS (ASAP+) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}_2$ 269.1290; Found 269.1293.

2-(4-Methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (4b): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4b** as a yellow oil (58.4 mg, 98%). IR (ATR) ν 2932, 2834, 1548, 1507, 1240, 1031, 825, 752 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 7.14–7.25 (m, 4H), 6.93 (dm, 2H, $J = 9.2$ Hz), 6.83 (dm, 2H, $J = 9.2$ Hz), 5.40 (dd, 1H, $J = 5.9$, 8.6 Hz), 4.83 (dd, 1H, $J = 8.6$, 11.9 Hz), 4.56 (dd, 1H, $J = 5.8$, 11.9 Hz), 3.76 (s, 3H), 3.55–3.60 (m, 2H), 2.97–3.08 (m, 1H), 2.70 (dt, 1H, $J = 4.0$, 16.6 Hz). ^{13}C NMR (CDCl_3 , 100 MHz) δ 154.1, 143.2, 135.5, 133.0, 129.6, 128.0, 127.0, 126.7, 119.0, 114.8, 79.1, 59.0, 55.7, 43.3, 25.9. HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_3$ 299.1396; Found 299.1390.

2-(4-Bromophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (4c): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4c** as a yellow oil (68.0 mg, 98%). IR (ATR) ν 2914, 1547, 1490, 1215, 805, 737 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz) δ 7.32 (dm, 2H, $J = 9.1$ Hz), 7.10–7.24 (m, 4H), 6.82 (dm, 2H, $J = 9.1$ Hz), 5.47 (t, 1H, $J = 7.3$ Hz), 4.82 (dd, 1H, $J = 8.0$, 11.9 Hz), 4.54 (dd, 1H, $J = 6.4$, 11.9 Hz), 3.54–3.64 (m, 2H), 3.01–3.08 (m, 1H), 2.76 (dt, 1H, $J = 4.8$, 16.4 Hz). ^{13}C NMR (CDCl_3 , 100 MHz) δ 147.7, 135.2, 132.6, 132.4, 129.4, 128.4, 127.1, 127.0, 117.0, 111.7, 78.8, 58.2, 42.3, 26.4. HRMS (ASAP+) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_2\text{Br}$ 347.0395; Found 347.0398.

1-(1-Nitroethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4d): Purification by flash chromatography on silica gel (15% EtOAc-hexane) gave **4d** as an orange oil. **4d** is a mixture of two unseparable diastereoisomers (45.1 mg, 80%, 65:35 diastereoisomeric ratio). IR (ATR) ν 2920, 1596, 1545, 1497, 748 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz) δ 7.07–7.23 (m, 6H), 6.93–6.96 (m, 2H), 6.74–6.79 (m, 1H), 5.17–5.22 (m, 1H), 4.98–5.03 (m, 1H × 0.65), 4.81–4.87 (m, 1H × 0.35), 3.74–3.83 (m, 2H × 0.35), 3.50–3.58 (m, 2H × 0.65), 1.65 (d, 3H × 0.35, $J = 9.2$ Hz), 1.49 (d, 3H × 0.65, $J = 9.2$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz) δ 149.3 (0.35), 149.0 (0.65), 135.8 (0.65), 134.9 (0.35), 134.0 (0.35), 132.2 (0.65), 129.6 (0.35), 129.4 (0.65), 129.2 (0.65), 128.9 (0.35), 128.5 (0.35), 128.3 (0.65), 127.4 (0.65 + 0.35), 126.7 (0.35), 126.3 (0.65), 119.5 (0.65), 119.0 (0.35), 115.6 (0.65), 114.7 (0.35), 89.1 (0.35), 85.6 (0.65), 62.9 (0.65), 61.3 (0.35), 43.7 (0.35), 42.9 (0.65), 26.9 (0.35), 26.6 (0.65), 17.5 (0.35), 16.5 (0.65). HRMS (ASAP+) m/z $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_2$ 283.1447; Found 283.1443.

2-(4-Methoxyphenyl)-1-(1-nitroethyl)-1,2,3,4-tetrahydroisoquinoline (4e): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4e** as a yellow oil. **4e** is a mixture of two unseparable diastereoisomers (61.1 mg, 98%, 67:33 diastereoisomeric ratio). IR (ATR) ν 2933, 2833, 1547, 1507, 1242, 1033, 820, 752 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz) δ 7.11–7.26 (m, 3H + 1H × 0.67), 7.02–7.05 (m, 1H × 0.33), 6.93 (d, 2H, $J = 9.1$ Hz), 6.83 (m, 2H × 0.33), 6.79 (m, 2H × 0.67), 5.01–5.09 (m, 1H + 1H × 0.67), 4.85–4.91 (m, 1H × 0.33), 3.75–3.83 (m, 1H), 3.76 (s, 3H × 0.33), 3.74 (s, 3H × 0.67), 3.49–3.53 (m, 1H), 2.95–3.00 (m, 1H), 2.79–2.85 (m, 1H), 1.68 (d, 3H × 0.33, $J = 6.8$ Hz), 1.54 (d, 3H × 0.67, $J = 6.8$ Hz). ^{13}C NMR (CDCl_3 , 100 MHz)

δ 153.8 (0.67), 153.6 (0.33), 143.9 (0.33), 143.5 (0.67), 135.9 (0.67), 135.1 (0.33), 133.7 (0.33), 132.1 (0.67), 129.3 (0.67), 129.0 (0.33), 128.4 (0.67), 128.1 (0.67), 128.0 (0.33), 127.2 (0.33), 126.5 (0.33), 126.1 (0.67), 118.9 (0.67), 118.3 (0.33), 114.7 (0.33), 114.6 (0.67), 88.9 (0.33), 85.8 (0.67), 63.5 (0.67), 62.2 (0.33), 55.6 (0.33), 55.6 (0.67), 45.20 (0.33), 44.0 (0.67), 26.3 (0.33), 26.1 (0.67), 17.1 (0.33), 16.6 (0.67). HRMS (ASAP+) m/z $[M+H]^+$ Calcd for $C_{18}H_{21}N_2O_3$ 313.1552; Found 313.1553.

2-(4-Bromophenyl)-1-(1-nitroethyl)-1,2,3,4-tetrahydroisoquinoline (4f): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4f** as a yellow oil. **4f** is a mixture of two unseparable diastereoisomers (58.5 mg, 81%, 65:35 diastereoisomeric ratio). IR (ATR) ν 2918, 1587, 1545, 1490, 806, 755 cm^{-1} . 1H NMR ($CDCl_3$, 400 MHz) δ 7.11–7.36 (m, 6H), 6.84–6.87 (m, 2H), 5.20 (d, 1H, $J=8.8$ Hz), 5.15 (d, 1H, $J=8.8$ Hz), 4.96–5.03 (m, 1H, $J=8.8$ Hz), 4.83–4.90 (m, 1H, $J=8.8$ Hz), 3.77–3.83 (m, 1H, $J=8.8$ Hz), 3.45–3.60 (m, 1H, $J=8.8$ Hz), 1.54 (d, 3H, $J=6.8$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.3 (0.35), 148.1 (0.65), 135.5 (0.65), 137.7 (0.35), 133.6 (0.35), 132.3 (0.65), 132.2 (0.35), 131.9 (0.35), 129.3 (0.65), 128.9 (0.35), 128.6 (0.65), 128.5 (0.65), 128.5 (0.65), 127.4 (0.35), 126.9 (0.35), 126.4 (0.65), 117.2 (0.65), 116.2 (0.35), 111.6 (0.65), 111.0 (0.35), 88.9 (0.35), 85.6 (0.65), 62.9 (0.65), 61.2 (0.35), 43.9 (0.35), 42.9 (0.65), 26.8 (0.35), 26.4 (0.65), 17.5 (0.35), 16.7 (0.65). HRMS (ASAP+) m/z $[M+H]^+$ Calcd for $C_{17}H_{18}N_2O_2Br$ 361.0552; Found 361.0552.

Dimethyl 2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (4g): Purification by flash chromatography on silica gel (15% EtOAc-hexane) gave **4g** as a colorless oil (50.8 mg, 75%). IR (ATR) ν 2955, 1732, 1436, 1143, 1023, 753 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 7.11–7.25 (m, 6H), 7.01 (d, 2H, $J=7.9$ Hz), 6.77 (t, 1H, $J=7.3$ Hz), 5.74 (d, 1H, $J=9.4$ Hz), 3.98 (d, 1H, $J=9.4$ Hz), 3.76–3.67 (m, 2H), 3.67 (s, 3H), 3.56 (s, 3H), 3.03–3.14 (ddd, 1H, $J=6.3, 8.8, 16.4$ Hz), 2.84–2.93 (dt, 1H, $J=5.1, 16.4$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4, 167.5, 148.9, 135.8, 134.9, 129.2, 129.2, 127.7, 127.2, 126.2, 118.8, 115.4, 59.2, 58.3, 52.6, 52.6, 42.3, 26.2. HRMS (ASAP+) m/z $[M+H]^+$ Calcd for $C_{20}H_{22}NO_4$ 340.1549; Found 340.1545.

Dimethyl 2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (4h): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4h** as a colorless oil (49.5 mg, 67%). IR (ATR) ν 2951, 2835, 1731, 1508, 1433, 1242, 1137, 1032, 824 cm^{-1} . 1H NMR ($CDCl_3$, 400 MHz) δ 7.15–7.21 (m, 2H), 7.09–7.12 (m, 2H), 6.91 (dm, 2H, $J=9.1$ Hz), 6.77 (dm, 2H, $J=9.1$ Hz), 5.49 (d, 1H, $J=9.3$ Hz), 3.95 (d, 1H, $J=9.3$ Hz), 3.73 (s, 3H), 3.64–3.70 (m, 1H), 3.63 (s, 3H), 3.60 (s, 3H), 3.51–3.57 (m, 1H), 2.96–3.05 (m, 1H), 2.73–2.79 (dt, 1H, $J=4.4, 16.7$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4, 167.7, 153.5, 143.6, 135.5, 135.0, 129.3, 127.6, 127.2, 126.1, 118.5, 114.6, 59.3, 55.7, 52.6, 52.6, 43.2, 25.7. HRMS (ASAP+) m/z $[M+H]^+$ Calcd for $C_{21}H_{24}NO_5$ 370.1654; Found 370.1648.

Dimethyl 2-(2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (4i): Purification by flash chromatography on silica gel (25% EtOAc-hexane) gave **4i** as a colorless oil (57.5 mg, 71%). IR (ATR) ν 2956, 1732, 1437, 1145, 1022 cm^{-1} . 1H NMR ($CDCl_3$, 400 MHz) δ 7.28 (d, 2H, $J=9.1$ Hz), 7.18–7.21 (m, 2H), 7.10–7.15 (m, 2H), 6.85 (d, 2H, $J=9.1$ Hz), 5.64 (d, 1H, $J=9.4$ Hz), 3.90 (d, 1H, $J=9.4$ Hz), 3.66 (s, 3H), 3.63–3.70 (m, 1H), 3.55 (s, 3H), 3.52–3.58 (m, 1H), 3.02–3.09 (m, 1H), 2.88–2.94 (dt, 1H, $J=5.5, 16.4$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 167.4, 147.9, 135.6, 134.7, 132.0, 129.1, 128.0, 127.2, 126.4, 116.6, 110.6, 59.2, 58.2, 52.8, 52.7, 42.6, 26.2. HRMS (ASAP+) m/z $[M+H]^+$ Calcd for $C_{20}H_{21}NO_4Br$ 418.0654; Found 418.0653.

Diethyl (2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (4j): Purification by flash chromatography on silica gel (45% EtOAc-hexane) gave **4j** as a colorless oil (61.4 mg, 89%). IR (ATR) ν

2980, 1736, 1597, 1498, 1018, 959, 747 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 7.36–7.39 (m, 1H), 7.17–7.29 (m, 5H), 6.99 (d, 2H, $J=8.3$ Hz), 6.80 (t, 1H, $J=7.3$ Hz), 5.19 (d, 1H, $J=20.0$ Hz), 3.86–4.14 (m, 5H), 3.60–3.67 (dt, 1H, $J=5.4, 12.6$ Hz), 2.99–3.10 (m, 2H), 1.26 (t, 3H, $J=7.1$ Hz), 1.15 (t, 3H, $J=7.1$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.5 (d, $J_{C-P}=5.7$ Hz), 136.5 (d, $J_{C-P}=5.5$ Hz), 130.8, 129.2, 128.8 (d, $J_{C-P}=2.4$ Hz), 128.2 (d, $J_{C-P}=4.6$ Hz), 127.5 (d, $J_{C-P}=3.4$ Hz), 125.9 (d, $J_{C-P}=2.6$ Hz), 118.5, 114.9, 63.3 (d, $J_{C-P}=7.3$ Hz), 62.4 (d, $J_{C-P}=7.7$ Hz), 58.9 (d, $J_{C-P}=159.6$ Hz), 43.6, 26.9, 16.5 (d, $J_{C-P}=5.7$ Hz), 16.4 (d, $J_{C-P}=6.1$ Hz). ^{31}P NMR ($CDCl_3$, 162 MHz) δ 22.2 (s). HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{24}NO_3NaP$ 368.1391; Found 368.1389.

Diethyl (2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (4k): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4k** as a colorless oil (60.6 mg, 83%). IR (ATR) ν 2979, 2904, 2833, 1509, 1240, 1017, 743 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 7.37–7.41 (m, 1H), 7.11–7.20 (m, 3H), 6.92 (d, 2H, $J=9.1$ Hz), 6.81 (d, 2H, $J=9.1$ Hz), 5.02 (d, 1H, $J=21.5$ Hz), 3.90–4.15 (m, 5H), 3.74 (s, 3H), 3.50–3.58 (dt, 1H, $J=5.0, 12.7$ Hz), 2.90–2.95 (m, 2H), 1.25 (t, 3H, $J=7.1$ Hz), 1.16 (t, 3H, $J=7.1$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.2, 144.3 (d, $J_{C-P}=8.3$ Hz), 136.5 (d, $J_{C-P}=5.8$ Hz), 130.7, 129.0 (d, $J_{C-P}=2.4$ Hz), 128.3 (d, $J_{C-P}=4.5$ Hz), 127.4 (d, $J_{C-P}=3.4$ Hz), 125.9 (d, $J_{C-P}=2.8$ Hz), 117.7, 114.6, 63.4 (d, $J_{C-P}=7.2$ Hz), 62.3 (d, $J_{C-P}=7.6$ Hz), 59.6 (d, $J_{C-P}=158.6$ Hz), 55.7, 44.8, 26.3, 16.5 (d, $J_{C-P}=5.5$ Hz), 16.4 (d, $J_{C-P}=5.9$ Hz). ^{31}P NMR ($CDCl_3$, 162 MHz) δ 22.2 (s). HRMS (ASAP-) m/z $[M-H]^-$ Calcd for $C_{20}H_{25}NO_4P$ 374.1521; Found 374.1510.

Diethyl (2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (4l): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4l** as a colorless oil (78.9 mg, 93%). IR (ATR) ν 2982, 2903, 2857, 1587, 1496, 1235, 1027, 945, 782 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 7.18–7.34 (m, 6H), 6.85 (d, 2H, $J=9.1$ Hz), 5.11 (d, 1H, $J=19.1$ Hz), 3.83–4.11 (m, 5H), 3.49–3.57 (m, 1H), 3.11–3.20 (m, 1H), 2.93–3.02 (m, 1H), 1.23 (t, 3H, $J=7.1$ Hz), 1.14 (t, 3H, $J=7.1$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4 (d, $J_{C-P}=4.8$ Hz), 136.4 (d, $J_{C-P}=7.4$ Hz), 131.9, 130.5, 128.7 (d, $J_{C-P}=2.7$ Hz), 128.2 (d, $J_{C-P}=4.9$ Hz), 127.7 (d, $J_{C-P}=3.5$ Hz), 126.1 (d, $J_{C-P}=2.6$ Hz), 116.2, 110.4, 63.3 (d, $J_{C-P}=7.4$ Hz), 62.5 (d, $J_{C-P}=7.8$ Hz), 58.8 (d, $J_{C-P}=158.0$ Hz), 43.7, 27.0, 16.5 (d, $J_{C-P}=5.4$ Hz), 16.4 (d, $J_{C-P}=5.9$ Hz). ^{31}P NMR ($CDCl_3$, 162 MHz) δ 21.8 (s). HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{23}NO_3NaBrP$ 446.0497; Found 446.0498.

2-(2-(4-Bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)cyclohexan-1-one (4m): Purification by flash chromatography on silica gel (20% EtOAc-hexane) gave **4m** as a pale yellow oil. **4m** is a mixture of two unseparable diastereoisomers (43.0 mg, 56%, 85:15 diastereoisomeric ratio). IR (ATR) ν 2933, 2859, 1701, 1585, 1491, 733 cm^{-1} . 1H NMR ($CDCl_3$, 400 MHz) δ 7.29 (d, 2H, $J=9.2$ Hz), 7.27 (d, 2H, $J=9.2$ Hz), 7.12–7.17 (m, 4H), 6.79 (d, 2H, $J=9.2$ Hz), 6.68 (d, 2H, $J=9.2$ Hz), 5.61 (d, 1H, $J=8.5$ Hz), 5.57 (d, 1H, $J=8.5$ Hz), 5.57 (d, 1H, $J=4.5$ Hz), 3.64–3.71 (m, 1H, $J=8.5$ Hz), 3.43–3.56 (m, 1H, $J=8.5+2H \times 0.15$), 2.82–3.06 (m, 3H, $J=8.5+2H \times 0.15$), 2.68–2.74 (m, 1H, $J=8.5$), 2.43–2.49 (m, 1H, $J=8.5$), 2.17–2.35 (m, 1H, $J=8.5+1H \times 0.15$), 2.04–2.11 (m, 1H, $J=8.5$), 1.80–1.97 (m, 3H), 1.52–1.73 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5 (0.15), 148.4 (0.85), 140.1 (0.15), 135.7 (0.85), 134.9 (0.85), 134.4 (0.15), 132.1 (0.85), 131.9 (0.15), 128.8 (0.85), 128.1 (0.85), 127.9 (0.15), 127.3 (0.15), 126.9 (0.85), 126.6 (0.15), 126.0 (0.85), 116.6 (0.85), 114.0 (0.15), 110.2 (0.85), 108.3 (0.15), 59.4 (0.15), 56.5 (0.85), 55.2 (0.85), 54.2 (0.15), 43.9 (0.15), 43.2 (0.15), 42.7 (0.85), 41.6 (0.85), 32.9 (0.15), 30.4 (0.85), 28.7 (0.15), 27.8 (0.15), 27.4 (0.85), 27.3 (0.85), 25.8 (0.15), 24.1 (0.85). HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{21}H_{23}NOBr$ 384.0963; Found 384.0962.

1-(2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (4n): Purification by flash chromatography on silica gel (50% EtOAc-hexane) gave **4n** as an orange oil (55.0 mg, 82%). IR (ATR) ν

2915, 2837, 1707, 1586, 1491, 1337, 1149, 807, 754 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 7.31 (d, 2H, *J* = 9.2 Hz), 7.12–7.22 (m, 4H), 6.81 (d, 2H, *J* = 9.2 Hz), 5.35 (app t, 1H, *J* = 6.6 Hz), 3.47–3.64 (m, 2H), 3.00–3.09 (m, 2H), 2.85–2.87 (m, 1H), 2.79–2.82 (m, 1H), 2.09 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ 207.1, 148.0, 138.0, 134.3, 132.2, 128.8, 127.1, 126.9, 126.5, 116.3, 110.2, 54.8, 50.3, 42.3, 31.2, 27.2. HRMS (ASAP+) *m/z* [M+H]⁺ Calcd for C₁₈H₁₉NO⁷⁹Br 344.0650; Found 344.0656.

1-Methylquinoxalin-2(1H)-one (6):^[49] A suspension of 1,2-diaminobenzene (108 mg, 1 mmol, 1 equiv.) in EtOH (10 mL) was treated with ethyl glyoxylate (102 mg, 1 mmol, 1 equiv.) and the resulting mixture was stirred for 1 h at 80 °C and 14 h at room temperature. The solid formed was filtered, washed with EtOH and dried under vacuum to give the corresponding quinoxalinone. The latter was dissolved in DMF (10 mL) in the presence of K₂CO₃ (138 mg, 1.2 mmol, 1.2 equiv.) and iodomethane (100 μL, 1.6 mmol, 1.6 equiv.) and stirred for 14 h at room temperature. The resulting mixture was quenched with water (100 mL) and extracted with EtOAc (3 × 100 mL). The collected organic phases were washed with brine (2 × 100 mL), dried over anhydrous MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography on silica gel (100% EtOAc) gave **6** as a pale yellow solid (138 mg, 86%). mp 114.5–115 °C [Lit.^[50] 120–121 °C]. IR (ATR) ν 3044, 2987, 2941, 1653, 1464, 1312, 1064, 949, 745 cm⁻¹. ¹H NMR (CDCl₃, 400 MHz) δ 8.31 (s, 1H), 7.87–7.90 (m, 1H), 7.58–7.64 (m, 1H); 7.34–7.40 (m, 2H); 3.70 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ 155.2, 150.4, 133.6, 133.5, 131.2, 130.7, 123.9, 113.9, 28.9. HRMS (ASAP+) *m/z* [M+H]⁺ Calcd for C₉H₉N₂O 161.0715; Found 161.0721.

1-Methyl-3-(tetrahydrofuran-2-yl)quinoxalin-2(1H)-one (8a): To a mixture of 1-methylquinoxalinone **5** (32 mg, 0.2 mmol, 1 equiv.) and Cell-RB (5 mol%) in THF (2 mL) was added *tert*-butylhydroperoxide (28 μL, 0.2 mmol, 1 equiv., 70% in water) and DABCO (22.4 mg, 0.2 mmol, 1 equiv.). The resulting mixture was stirred on an orbital agitator at room temperature for 24 h under green LED irradiation (λ_{max} = 525 nm). Purification by flash chromatography on silica gel (100% EtOAc) gave **8a** as a colorless oil (63.6 mg, 95%). IR (ATR) ν 2949, 2873, 1648, 1467, 1067, 752 cm⁻¹. ¹H NMR (CDCl₃, 400 MHz) δ 7.94 (dd, 1H, *J* = 1.4, 8.0 Hz), 7.51–7.55 (m, 1H), 7.28–7.35 (m, 2H), 5.37 (dd, 1H, *J* = 6.0, 7.6 Hz), 4.19–4.24 (m, 1H), 3.97–4.02 (m, 1H), 3.68 (s, 3H), 2.42–2.52 (m, 1H), 2.00–2.09 (m, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ 159.6, 154.2, 133.3, 132.6, 130.6, 130.2, 123.7, 113.6, 77.7, 69.3, 30.6, 28.9, 25.8. HRMS (ASAP+) *m/z* [M+H]⁺ Calcd for C₁₃H₁₅N₂O₂ 213.1134; Found 213.1134.

1-Methyl-3-(2-methyltetrahydrofuran-2-yl)quinoxalin-2(1H)-one (8b): To a mixture of 1-methylquinoxalinone **5** (32 mg, 0.2 mmol, 1 equiv.) and Cell-RB (5 mol%) in Me-THF (2 mL) was added *tert*-butylhydroperoxide (28 μL, 0.2 mmol, 1 equiv., 70% in water) and DABCO (22.4 mg, 0.2 mmol, 1 equiv.). The resulting mixture was stirred on an orbital agitator at room temperature for 24 h under green LED irradiation (λ_{max} = 525 nm). Purification by flash chromatography on silica gel (100% EtOAc) gave **8b** as a yellow oil (56.3 mg, 82%). IR (ATR) ν 2931, 2874, 1647, 1590, 1469, 1075, 751 cm⁻¹. ¹H NMR (CDCl₃, 400 MHz) δ 7.97 (dd, 1H, *J* = 1.4, 8.0 Hz), 7.52–7.56 (m, 1H), 7.28–7.35 (m, 2H), 4.10–3.99 (m, 2H), 3.69 (s, 3H), 2.53–2.60 (m, 1H), 2.12–2.19 (m, 1H), 2.00–2.07 (m, 1H), 1.84–1.90 (m, 1H), 1.72 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ 161.4, 153.7, 133.6, 132.3, 130.8, 130.3, 123.6, 113.5, 85.1, 68.1, 36.3, 29.0, 25.8, 24.9. HRMS (ASAP+) *m/z* [M+H]⁺ Calcd for C₁₄H₁₇N₂O₂ 245.1290; Found 245.1300.

Acknowledgements

We gratefully acknowledge Nantes Université and the “Centre National de la Recherche Scientifique” (CNRS) for financial support. M.C. Nongbe thanks the “Ministère de l’Enseignement Supérieur et de la Recherche Scientifique de Côte d’Ivoire” for a visiting grant in France. We acknowledge Christine Labrugère (PLACAMAT, University of Bordeaux), and Denis Loquet (CEISAM UMR CNRS 6230, Nantes Université) for XPS and elemental analyses, respectively. The authors greatly acknowledge J. Hémez and L. Arzel (AMaCC platform, CEISAM UMR CNRS 6230, Nantes Université) for their mass spectrometry analytical contributions to this work. This work includes NMR experiments carried out on the CEISAM NMR platform.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: cellulose · heterogeneous photocatalyst · photocatalysis · rose bengal · visible-light

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Manuscript received: July 18, 2022

Revised manuscript received: August 18, 2022

Accepted manuscript online: August 22, 2022