FULL PAPER

Continuous Flow Synthesis of Quinolines via a Scalable Tandem Photoisomerization-Cyclization Process

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Abstract: A continuous photochemical process is presented that renders a series of quinoline products via an alkene isomerization and cyclocondensation cascade. It is demonstrated that a high-power LED lamp generates the desired targets with higher productivity and efficiency than a medium-pressure Hg-lamp. The scope of this tandem process is established and allows for the generation of various substituted quinolines in high yields and with throughputs of greater than one gram per hour. Finally, this effective flow process is coupled with a telescoped hydrogenation reaction to render a series of tetrahydroquinolines including the antimalarial natural product galipinine.

Introduction

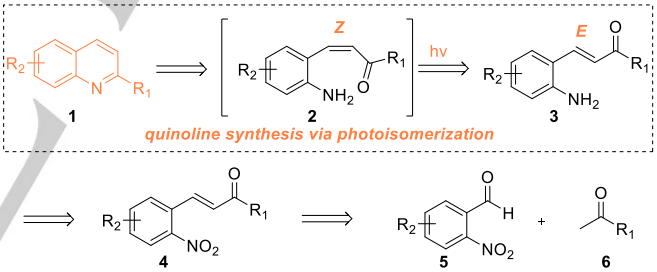
Quinolines are amongst the most prevalent bioactive heterocycles and thus are frequently encountered entities in alkaloid natural products and medicines alike.[1] In recent years interest in quinoline-based drug candidates has further increased due to their potential as antimalarial[2] and anti-inflammatory[3] agents. In addition, chemists can draw from a rich history of classical and contemporary quinoline syntheses[4] that have been exploited extensively for the preparation of quinoline-based drugs and related scaffolds.[5]

In order to provide more efficient access towards valuable target structures, recent years have witnessed a steady uptake of new enabling technologies to enrich the organic chemist's toolbox and facilitate synthetic efforts. Amongst those, continuous flow synthesis stands out as one of the most powerful techniques due to its inherent benefits that have enabled widespread uptake across academia and industry.[6]

Consequently, flow chemistry has become a method of choice in various fields including multi-step[7] and API[8] synthesis as well as natural product[9] chemistry, use of harmful reagents and reaction conditions,[10] organometallic chemistry,[11] polymer chemistry,[12] photochemistry[13] and most recently, electrochemistry.[14]

In view of the value of both quinoline-based compounds and continuous flow processing, we wished to merge these fields and evaluate the merits of developing a continuous flow synthesis of quinolines. More specifically, we decided to implement a strategic photochemical approach that would garner the target compounds under mild and green reaction conditions. This seemed particularly appropriate as light is not only considered a clean and traceless reagent, but moreover the use of light-driven transformations benefits from continuous flow processing due to short pathlengths (narrow tubing diameter) and uniform irradiation profiles thus minimizing decomposition due to over-irradiation.[13,15] Finally, we planned for demonstrating the scalability of such a continuous photochemical approach that should give rise to gram quantities per hour.

To this end we decided to exploit a variation of the Friedländer quinoline synthesis[16] in which a *Z*-configured enone undergoes intramolecular cyclocondensation with a pendent amine group (Scheme 1). Importantly, this approach requires the isomerization of the *E*-configured enone (**3**) in a process that can either be achieved under acidic[17] or photochemical[18] conditions. As we were targeting the latter approach, we identified 2-aminophenyl-enones (**3**) as key intermediates, which would be generated from their corresponding nitro-precursors (**4**). A simple aldol condensation was considered to access these nitro-precursors from readily available 2-nitrobenzaldehyde derivatives (**5**) and methyl ketones (**6**).

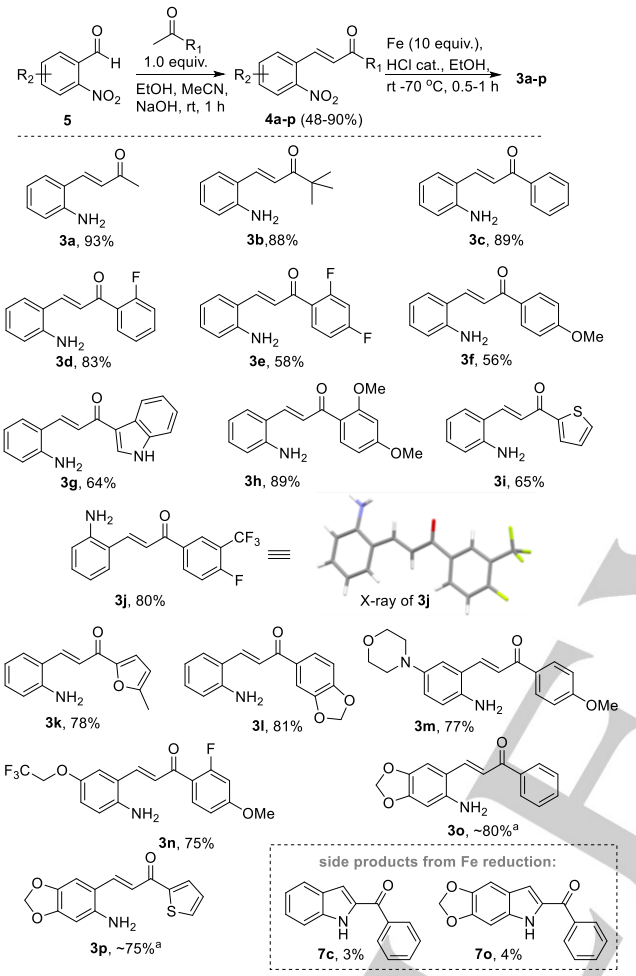


Scheme 1. Synthesis route towards quinoline targets.

Results and Discussion

We commenced our studies by accessing a set of suitable enone species (**3**) following literature precedent, i.e. a base-mediated aldol condensation between 2-nitrobenzaldehyde and selected methyl ketones (see SI for full details).[18a] The corresponding aldol products were obtained in generally high yield and allowed for further elaboration of the nitro group into the desired amine species. To achieve this chemoselective reduction we opted to employ iron powder (~10 equiv.) in the presence of catalytic amounts of acid (HCl aq.) in hot ethanol,[18a] which provided the target compounds not only in a simple and short procedure, but moreover in generally high yield as the *E*-isomer (see SI for full details). Interestingly, our studies also identified small amounts (<5%) of 2-acylindole species (e.g. **7c**, **7o**, Scheme 2) as separable side products that were not recognized in previous reports on this reaction, although indole species have been prepared from analogous nitro substrates under different reducing conditions.[19] As outlined in Scheme 2 this approach allowed for

quickly providing access to a number of different enone substrates including those bearing substitution patterns on the aniline moiety as well as aromatic and aliphatic motifs on the ketone part. Whilst the resulting amino enones were in most cases found to be isolable and stable entities, we decided to directly use product solutions bearing a methylenedioxy moiety on the aniline ring (e.g. **3o** and **3p**) as concentrating these crude reaction mixtures was found to trigger further reactions.



Scheme 2. Preparation of amino enone substrates **3a**-**p**, [a] yield estimated by HPLC without isolating amine product.

Next, we embarked on the key transformation which would render the quinoline targets via a photoisomerization of the enone moiety (*E* to *Z*) followed by an intramolecular cyclocondensation reaction. It is worth mentioning that this process has desirable characteristics: it does not require any additives or catalysts and produces water as the sole by-product. To effectively execute this light-mediated tandem process we made use of a Vapourtec E-series flow reactor system in combination with different light sources. The reactor coil (10 mL volume, FEP tubing) is thereby placed around the light source within a closed compartment. The chosen set-ups included the established UV150 module[20] which is based on a tunable medium-pressure Hg-lamp (75-150 W, complemented with exchangeable broad band filters) as well as a high-power LED system emitting light at 365 nm (50-100 W, see Table 1). The availability and use of these two light sources were furthermore felt advantageous as it allowed for a detailed comparison with respect to efficiency, selectivity and throughput for such a continuous photochemical process which is scarcely reported in the literature.

Table 1. Comparison between light sources used.

	UV150 Hg lamp	High-power LED
Power range	75-150 W adjustable (with cooling)	50-100 W adjustable (with cooling)
Emission range	UV, visible and IR[a], [b]	UV-A: 365 nm

[a] see SI for emission spectra. [b] broadband filters available.

To conduct this comparative study, we selected phenyl substituted amino-enone (**3c**) as model substrate. Ethanol was identified as best solvent, however our studies indicated that alternative solvents (such as acetone, EtOAc and MeCN) can be used. We next defined both concentration and residence time as key variables, whilst keeping the internal reactor temperature constant at ~30 °C. For all experiments reported in Table 2 this allowed to further establish the reaction throughput (defined as mmol quinoline product per hour) as a measure for the efficiency and potential scalability of this process.

Table 2. Comparative study of light sources on the efficiency of the quinoline formation (**3c** to **1c**).

	light source	c [mM]	residence time [min]	^{1}H-NMR yield[c]	throughput [mmol/h][d]
1	Hg-lamp[a]	20	60	98	0.20
2	Hg-lamp[a]	20	20	87	0.52
3	Hg-lamp[a]	100	20	36[e]	1.20
4	UV-LED[b]	20	60	85	0.17
5	UV-LED[b]	20	20	94	0.56
6	UV-LED[b]	100	20	93	2.79
7	UV-LED[b]	150[f]	20	96	4.32
8	UV-LED[b]	100	15	95[g]	3.80
9	UV-LED[b]	100	10	94	5.64
10	UV-LED[b]	100	7.5	90	7.18

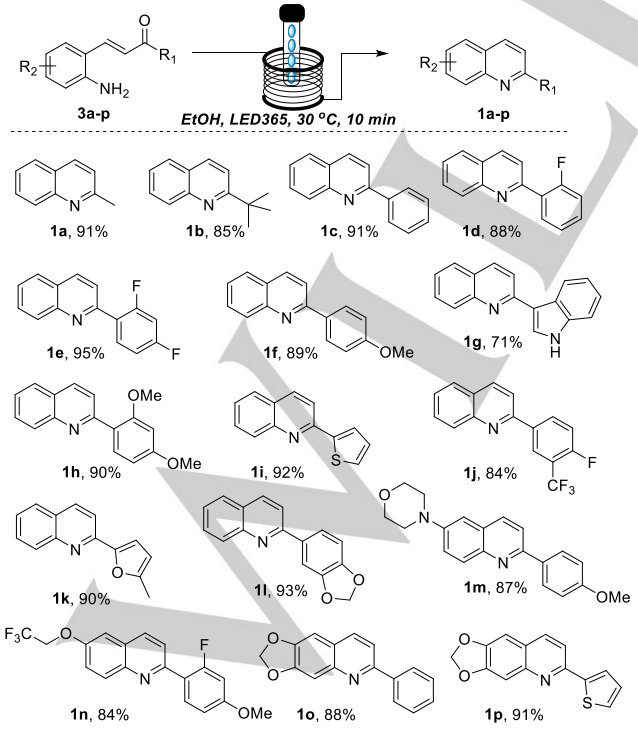
[a] Operating at 110 W in combination with a low-pass filter (see SI). [b] Operating at 75 W. [c] Using 1,3,5-trimethoxybenzene as internal standard (^{1}H relaxation time: 25 s). [d] With respect to quinoline product **1c**. [e] Remaining substrate: 62%. [f] Using 10% acetone as co-solvent in ethanol. [g] Isolated yield: 91%.

The data in Table 2 reveal that the medium-pressure Hg-lamp combined with a low-pass filter performs well at low concentrations (20 mM) giving full conversion of substrate and high ^{1}H-NMR yields for residence times of 60 and 20 min,

respectively (entries 1 and 2). Most notably, upon increasing the concentration to 100 mM a significant drop in conversion is observed with the medium-pressure Hg-lamp giving only 36% of the quinoline product (entry 3). While the high-power LED lamp shows a similar performance at low concentration (20 mM, entries 4 and 5), it is superior at higher concentration (100 mM), where a high yield of 93% is maintained (entry 6). Further increase of concentration to 150 mM (using 10% acetone as co-solvent with ethanol) allows for 96% yield and a throughput of 4.3 mmol/h (entry 7). Next, the reduction of residence time was studied for the LED lamp while maintaining the concentration at 100 mM. This indicated a constant yield of above 90% (entries 8, 9 and 10) that was mirrored by an isolated yield of 91% for entry 8. Importantly, this allows for significantly increasing the throughput, reaching 7.18 mmol/h for entry 10, which is equal to 1.47 g/h for this quinoline product (**1c**).

In summary, this study indicates that the high-power LED lamp outperforms the medium-pressure Hg-lamp in this application as it allows for greater efficiency and yield at higher concentrations. This observation is paralleled by a distinctly lighter color of the exiting product solution for the LED lamp compared to the Hg-lamp, which may indicate higher selectivity due to near-monochromatic light being used.[21] Thus, it can be stated that the high-power LED was found to be superior to the Hg-lamp in terms of performance (yield and throughput), selectivity (avoiding colored impurities) and energy efficiency (LED: 75 W input power vs. Hg-lamp: 110 W).

Having established the advantages of the high-power LED module, we next turned our attention to studying the scope of this continuous quinoline synthesis. We employed the LED module (75 W, ~30 °C) in combination with a residence time of 10-15 minutes and substrate concentrations of 100 mM (EtOH, solubility permitting). Pleasingly, it was found that all enone substrates **3a-p** underwent the desired photochemical tandem process and rendered the desired quinoline products in high yield (Scheme 3).



Scheme 3. Quinoline product scope.

Thus, incorporation of various substituents at the 2-position of the quinoline scaffold was readily achieved including alkyl, aryl and heteroaryl moieties. Furthermore, substitution on the 6- and 7-position was tolerated for incorporating amino as well as various ether groups. The connectivity of the quinoline structures was furthermore verified via single crystal X-ray diffraction experiments on selected products (Figure 1).

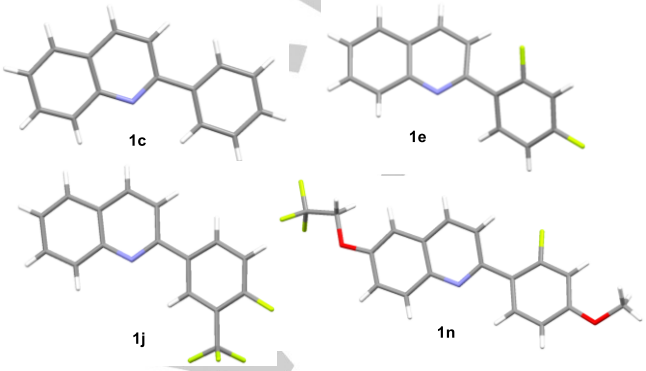
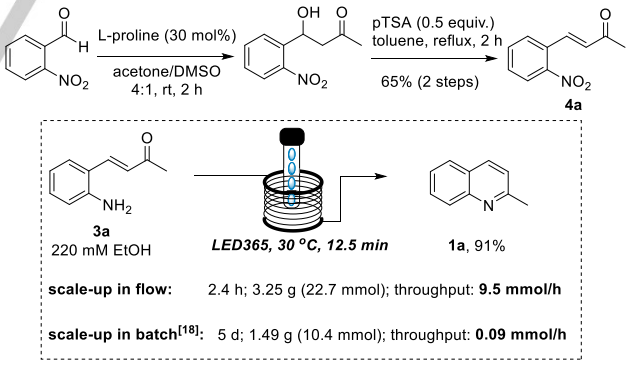


Figure 1: X-ray structures of quinolines **1c**, **1e**, **1j** and **1n**.

In view of the effectiveness of this flow process we next wished to evaluate its scalability over a period of several hours. We selected substrate **3a** for this study as a previous report[18a] had evaluated its scaled preparation in a photochemical batch operation yielding 1.49 g of the desired quinoline product (**1a**, 10.4 mmol, 93% yield) over a period of 5 days using a blue LED lamp (5 W power). To generate sufficient quantities of substrate **3a** we opted to use a modified 2-step approach as reported by List[22] to avoid the formation of indigo dye as a consequence of a competing Baeyer-Drewson reaction.[23] This batch process generated the aldol adduct, which was subsequently dehydrated under acidic conditions (pTSA) as outlined in Scheme 4.



Scheme 4. Scaled flow synthesis of quinoline **1a**.

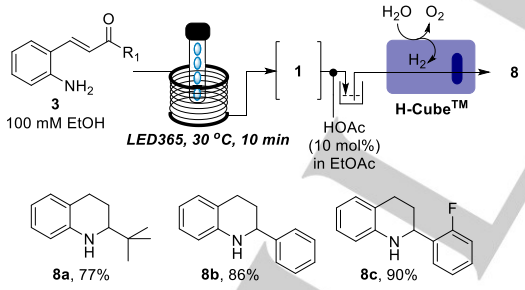
Next, we prepared a stock solution of substrate **3a** (220 mM in EtOH) matching the concentration previously reported[18a] and processed this solution through the flow system (LED, 75 W, 0.8 mL/min, 12.5 min residence time, ~30 °C) over a period of 2.4 hours. After evaporation of the solvent and passing the crude product over a plug of silica (eluent 5% EtOAc/hexanes) 3.25 g of the pure quinoline product was isolated as a yellow oil. This renders a throughput of 9.5 mmol/h which is ~110-fold higher than the reported batch throughput and clearly demonstrates the value of this photochemical flow process in rapidly generating

significant amounts of target product that would not be achievable in batch mode.

As stated earlier, it was noted that this flow process is not only remarkably efficient, but moreover generates the quinoline targets in high yield and purity without recourse to using additives in the form of photocatalysts or sensitizers. The high purity of the quinoline solution exiting the LED reactor system further prompted us to investigate the possibility of directly telescoping a subsequent chemical reaction to diversify the heterocyclic products in a streamlined manner.

In view of this we decided to evaluate the conversion of the quinoline products into tetrahydroquinolines via a telescoped flow hydrogenation process. This was additionally fueled by the therapeutic value of tetrahydroquinolines that have been popular bioactive targets of flow-based transformations before.[24]

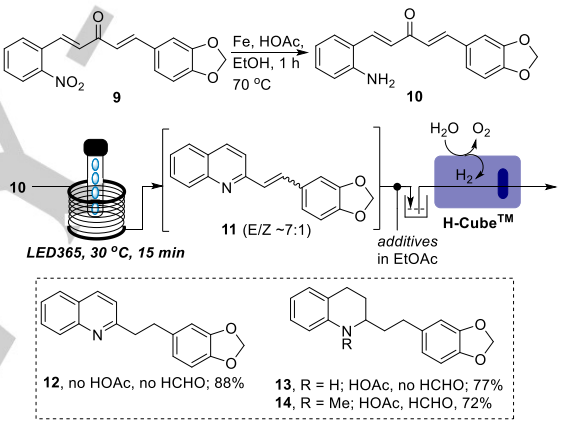
We thus decided to pass the quinoline solution exiting the LED reactor directly into an H-Cube Mini™ equipped with a catalyst cartridge containing a Pd-catalyst (10% Pd/C, 70 mm length). Precedent from the literature reports this approach as a powerful means to achieve the saturation of various azacyclic aromatic substrates.[25] A set of test reactions using quinoline **1c** as a model substrate demonstrated that suitable reaction conditions were based on lowered concentration (20-50 mM EtOH, containing 0.1 equiv. HOAc) with a flow rate of 1 mL/min while the catalyst cartridge was maintained at 50 °C under a pressure of 15 bar. The telescoped process was subsequently realized by firstly diluting the quinoline stream with EtOAc (1-4 mL/min, cat. HOAc) prior to transferring the solution (now 20-50 mM) via a holding reservoir[26] into the H-Cube™ Pd-cartridge (50 °C, 15 bar, 1 mL/min). Pleasingly, this set of conditions proved effective in generating the desired tetrahydroquinoline products **8** in high yields with residence times for the hydrogenation of less than 1 min. Scheme 5 summarizes the reaction set-up and the tetrahydroquinolines accessed via this telescoped flow process.



Scheme 5. Telescoped flow synthesis of tetrahydroquinolines **8**.

The success of this telescoped flow sequence enabled us to furthermore apply our method to the synthesis of a target structure, namely the antimalarial natural product galipinine (**14**) which has seen considerable interest by the synthetic community in recent years.[27] We envisioned that a suitable dienone precursor (**9**) prepared by a sequential aldol condensation process from 2-nitrobenzaldehyde, acetone and piperonal could be subjected to the iron-mediated nitro-reduction to render the required amine building block (**10**) for our telescoped reaction sequence. Indeed, precursor **9** was prepared uneventfully and successfully underwent the chemoselective nitro reduction under the previously established conditions (Scheme 6).

A solution of **10** (50 mM, EtOH) was then passed through the LED reactor (residence time 15 min) cleanly generating the corresponding quinoline (**11**) bearing an alkene moiety in the 2-position (alkene mixture ~7:1). Initially, this alkene mixture was subjected to flow hydrogenation conditions in the absence of acid (EtOH, 1 mL/min, 10% Pd/C, rt, 15 bar) providing quinoline derivative **12** as the sole product. It is of note that this structure has been reported as a natural product with molluscicide activity previously.[28] In contrast, when performing this hydrogenation in the presence of acid (HOAc), the formation of the corresponding tetrahydroquinoline product is observed (**13**, *des*-methyl galipinine). Furthermore, upon addition of formaldehyde (2 equiv. HCHO aq.) the alkene hydrogenation is coupled with both the formation of the tetrahydroquinoline and the *N*-methylation thus directly furnishing galipinine **14** in racemic form.[29] Finally, the optimized flow sequence comprising of the photochemical quinoline synthesis and the hydrogenation cascade was performed in a telescoped manner as before producing galipinine in 72% yield from amine precursor **10** (Scheme 6).



Scheme 6. Telescoped flow synthesis of galipinine **14**.

Conclusion

In summary we have developed a continuous photochemical quinoline synthesis that exploits readily available amino enones and renders the target heterocycles in high yield and efficiency. A new high-power LED light source was thereby identified as a more effective means than an alternative medium-pressure Hg-lamp.[30] Scalability via this optimized set-up was demonstrated providing quinoline products at a rate greater 1 g/h. The high purity of the quinoline stream furthermore allowed for telescoping the photochemical synthesis into a subsequent Pd-catalyzed hydrogenation stage to deliver a set of tetrahydroquinolines. Finally, this process was applied to the telescoped flow synthesis of the antimalarial alkaloid galipinine that was generated in high yield and purity showcasing the value of utilizing this new high-power LED lamp for continuous photochemical transformations.

Experimental Section

Unless otherwise stated, all solvents were purchased from Fisher Scientific and used without further purification. Substrates and reagents were purchased from Fluorochem or Sigma Aldrich and used as received. ^{1}H-NMR spectra were recorded on the indicated instruments and are reported relative to residual solvent: $CHCl_3$ (δ 7.26 ppm) or DMSO (δ 2.50 ppm). ^{13}C-NMR spectra were recorded on the same instruments and are reported relative to $CHCl_3$ (δ 77.16 ppm) or DMSO (δ 39.52 ppm). Data for ^{1}H-NMR are reported as follows: chemical shift (δ/ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br. s = broad singlet, app = apparent. Data for ^{13}C-NMR are reported in terms of chemical shift (δ/ ppm) and multiplicity (C, CH, CH_2 or CH_3). Data for ^{19}F-NMR were recorded at a frequency of 376 MHz using $CFCl_3$ as external standard. DEPT-135, COSY, HSQC, HMBC and NOESY experiments were used in the structural assignment. IR spectra were obtained by use of a Bruker Platinum spectrometer (neat, ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal). High-resolution mass spectrometry was performed using the indicated techniques on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine-enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass. Melting points were recorded on a Stuart SMP10 melting point system and are uncorrected. Flow chemistry experiments were performed with a Vapourtec E-series system in combination with the UV150 photochemistry module (medium-pressure Hg lamp or high-power LED).

Procedure for the preparation of aldol product 4a' and 4a:

L-Proline (0.3 equiv.) was added to a mixture of DMSO/acetone (1:4 by volume, 0.2 M) and the suspension was left to stir for 15-20 min at room temperature. While stirring, 2-nitrobenzaldehyde (1 equiv.) was added to the suspension. The reaction was monitored by TLC (EtOAc/Hex, 25:75). After competition, a saturated aqueous solution of NH_4Cl was added and the product was extracted with EtOAc. After evaporation of the solvent, the product was dissolved in toluene (0.1 M) containing pTSA (50 mol%). The solution was left to stir for 2 h at 120 °C. After competition, a saturated aqueous solution of $NaHCO_3$ was added and the organic layer was separated and evaporated. The brown oil obtained was purified through trituration from Hex/EtOAc (9:1) generating an off-white powder.

4-Hydroxy-4-(2-nitrophenyl)butan-2-one, (4a'):[31] brown oil. Yield: 84% (1.75 g, 8.4 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 7.97 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.91 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.68 (td, *J* = 8.1, 1.0 Hz, 1H), 7.45 (td, *J* = 8.4, 1.4 Hz, 1H), 5.69 (dt, *J* = 9.5, 2.4 Hz, 1H), 3.74 (d, *J* = 3.0 Hz, 1H), 3.15 (dd, *J* = 17.8, 2.1 Hz, 1H), 2.74 (dd, *J* = 17.8, 9.4 Hz, 1H), 2.25 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 208.8 (C), 147.2 (C), 138.3 (C), 133.8 (CH), 128.3 (CH), 128.2 (CH), 124.4 (CH), 65.7 (CH), 51.0 (CH_2), 30.5 (CH_3). IR (neat) v/cm^{-1}: 3411 (broad, w), 2962 (w), 1707 (m), 1521 (s), 1343 (s), 1259 (m), 1064 (m), 790 (m), 742 (m). HR-MS (TOF ES): calculated for $C_{10}H_{11}NO_4Na$ 232.0586, found 232.0584 (M+Na).

(*E*)-4-(2-Nitrophenyl)but-3-en-2-one, (4a):[31] off-white solid. Melting range 59-61 °C. Yield: 78% (570 mg, 3.0 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.06 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 16.2 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.54 (ddd, *J* = 8.6, 6.7, 2.2 Hz, 1H), 6.55 (d, *J* = 16.2 Hz, 1H), 2.41 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 198.0 (C), 148.3 (C), 138.9 (CH), 133.7 (CH), 131.9 (CH), 130.8 (C), 130.4 (CH), 129.1 (CH), 125.0 (CH), 27.0 (CH_3). IR (neat) v/cm^{-1}: 3067 (w), 1685 (s), 1605 (s), 1515 (s), 1342 (s), 1293 (s), 1183 (s), 975 (s), 859 (m), 783 (m), 734 (s), 560 (m). HR-MS (TOF ES): calculated for $C_{10}H_{10}NO_3$ 192.0661, found 192.0656 (M+H+).

General procedure for the preparation of 4b-p and 9a,b: To a solution of a 2-nitrobenzaldehyde derivative (1 equiv.) and methyl ketone (1 equiv.) in acetonitrile (1 M) was added a solution of NaOH (1.0 equiv, 1 M water/ethanol, 50/50 by volume) dropwise at room temperature. Upon stirring the desired aldol condensation product precipitated within 60 minutes and was collected by filtration. After washing with cold ethanol/water (~50/50 by volume) und drying under suction the desired product was isolated as a coloured solid, which can be recrystalized from hot ethyl acetate.

(*E*)-4,4-Dimethyl-1-(2-nitrophenyl)pent-1-en-3-one, (4b):[32] yellow oil. Yield: 83% (385 mg, 1.6 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.06 (d, *J* = 15.5 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.56 – 7.51 (m, 1H), 7.01 (d, *J* = 15.5 Hz, 1H), 1.24 (s, 9H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 203.2 (C), 148.7 (CH), 138.1 (CH), 133.3 (CH), 131.4 (C), 130.0 (CH), 129.2 (CH), 125.6 (CH), 124.9 (CH), 43.3 (C), 26.1 ($3CH_3$). IR (neat) v/cm^{-1}: 2955 (w), 1680 (m), 1600 (m), 1523 (s), 1469 (m), 1335 (s), 1291 (m), 1082 (s), 984 (s), 751 (s), 567 (m). HR-MS (TOF ES): calculated for $C_{13}H_{16}NO_3$ 234.1130, found 234.1141 (M+H+).

(*E*)-3-(2-Nitrophenyl)-1-phenylprop-2-en-1-one, (4c):[33] white solid. Melting range 120-121 °C. Yield: 85% (430 mg, 1.7 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.15 (d, *J* = 15.7 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 7.2 Hz, 1H), 8.02 (s, 1H), 7.76 (d, *J* = 7.3 Hz, 1H), 7.70 (t, *J* = 7.3 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 15.7 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 190.4 (C), 148.5 (C), 140.1 (CH), 137.4 (C), 133.6 (CH), 133.1 (CH), 131.3 (C), 130.3 (CH), 129.2 (CH), 128.8 (2CH), 128.7 (2CH), 127.3 (CH), 125.0 (CH). IR (neat) v/cm^{-1}: 1667 (m), 1602 (m), 1510 (s), 1445 (m), 1339 (s), 1288 (s), 1214 (m), 1010 (m), 858 (m), 740 (s), 682 (s). HR-MS (TOF ES): calculated for $C_{15}H_{12}NO_3$ 254.0817, found 254.0806 (M+H+).

(*E*)-1-(2-Fluorophenyl)-3-(2-nitrophenyl)prop-2-en-1-one, (4d): off-white solid. Melting range 128-131 °C. Yield: 91% (2.47 g, 9.1 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.08 (dd, *J* = 15.9, 1.7 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.81 (td, *J* = 7.6, 1.9 Hz, 1H), 7.72 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.28 – 7.21 (m, 2H), 7.14 (dd, *J* = 10.9, 8.2 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 188.4 (d, *J* = 2 Hz, C), 161.3 (d, *J* = 253 Hz, CF), 148.6 (C), 139.9 (CH), 134.4 (d, *J* = 8 Hz, CH), 133.6 (CH), 131.1 (d, *J* = 2 Hz, CH), 130.9 (C), 130.5 (CH), 130.1 (d, *J* = 6 Hz, CH), 129.2 (CH), 126.3 (d, *J* = 13 Hz, C), 124.9 (CH), 124.6 (d, *J* = 4 Hz, CH), 116.6 (d, *J* = 23 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -110.7. IR (neat) v/cm^{-1}: 1664 (m), 1602 (m), 1512 (s), 1474 (m), 1451 (m), 1199 (m), 1018 (m), 966 (m), 745 (s), 726 (m) HR-MS (TOF ES): calculated for $C_{15}H_{11}FNO_3$ 272.0717, found 272.0719 ($M+H^+$).

(*E*)-1-(2,4-Difluorophenyl)-3-(2-nitrophenyl)prop-2-en-1-one, (4e): orange solid. Melting range 100-103 °C. Yield: 68% (984 mg, 3.4 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.12 (dd, *J* = 15.6, 1.6 Hz, 1H), 8.04 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.90 (td, *J* = 8.6, 6.6 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.66 (td, *J* = 7.3, 0.8 Hz, 1H), 7.55 (td, *J* = 7.9, 7.4, 1.6 Hz, 1H), 7.27 - 7.19 (m, 1H), 7.03 – 6.96 (m, 1H), 6.89 (ddd, *J* = 11.0, 8.7, 2.4 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 186.7 (d, *J* = 3 Hz, C), 165.6 (dd, *J* = 258, 12 Hz, CF), 162.1 (dd, *J* = 258, 12 Hz, CF), 148.6 (C), 140.2 (CH), 133.5 (CH), 133.1 (dd, *J* = 11, 4 Hz, CH), 130.9 (C), 130.5 (CH), 129.7 (d, *J* = 7 Hz, CH), 129.2 (CH), 125.0 (CH), 122.8 (dd, *J* = 13, 3 Hz, C), 112.4 (dd, *J* = 22, 3 Hz, CH), 104.8 (dd, *J* = 27 26 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -101.7, -105.7. IR (neat) v/cm^{-1}: 3076 (w), 1660 (m), 1601 (s), 1521 (s), 1422 (m), 1281 (s), 1229 (s), 1097 (s), 989 (s), 867 (m), 754 (s), 554 (w). HR-MS (TOF ES): calculated for $C_{15}H_9NO_3F_2Na$ 312.0448, found 312.0437 (M+H+).

(*E*)-1-(4-Methoxyphenyl)-3-(2-nitrophenyl)prop-2-en-1-one, (4f):[34] light green solid. Melting range 92-94 °C. Yield: 48% (137 mg, 0.48 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.11 (d, *J* = 15.7 Hz, 1H), 8.06 (dd, *J* = 8.2, 1.1 Hz, 1H), 8.04 (app. d, *J* = 8.9 Hz, 2H), 7.74 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 15.7 Hz, 1H), 6.99 (app. d, *J* = 8.9 Hz, 2H), 3.90 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 188.7 (C), 163.7 (C), 148.6 (C), 139.2 (CH), 133.5 (CH), 131.6 (C), 131.2 (2CH), 130.3 (C), 130.1 (CH), 129.3 (CH), 127.4 (CH), 125.0 (CH), 114.0 (2CH), 55.5 (CH_3). IR (neat) v/cm^{-1}: 2839 (w), 1651 (m), 1592 (s), 1512 (s), 1338 (m), 1259 (s), 1180 (s), 977 (s), 835 (s), 756 (s), 572 (m). HR-MS (TOF ES): calculated for $C_{16}H_{14}NO_4$ 284.0923, found 284.0908 (M+H+).

(*E*)-1-(1*H*-Indol-3-yl)-3-(2-nitrophenyl)prop-2-en-1-one, (4g): dark yellow solid. Melting range ~190 °C (decomposition). Yield: 71% (250 mg, 0.86 mmol). ^{1}H-NMR (500 MHz, DMSO-d_6) δ/ppm 12.19 (s, 1H), 8.75 (d, *J* = 2.7 Hz, 1H), 8.33 (d, *J* = 7.2 Hz, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 15.4 Hz, 1H), 7.84 (d, *J* = 15.4 Hz, 1H), 7.82 (t, *J* = 6.9 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.25 (m, 2H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ/ppm 183.3 (C), 149.3 (C), 137.4 (C), 135.9 (CH), 134.2 (CH), 133.9 (CH), 130.9 (CH), 130.5 (C), 129.6 (CH), 129.5 (CH), 126.2 (C), 125.0 (CH), 123.8 (CH), 122.5 (CH), 122.2 (CH), 118.0 (C), 112.7 (CH). IR (neat) v/cm^{-1}: 3221 (w), 1641 (m), 1586 (m), 1515 (s), 1440 (s), 1342 (m), 1239 (m), 1153 (m), 962 (m), 744 (s), 584 (m), 422 (m). HR-MS (TOF ES): calculated for $C_{17}H_{13}N_2O_3$ 293.0921, found 293.0926 (M+H+).

(*E*)-1-(2,4-Dimethoxyphenyl)-3-(2-nitrophenyl)prop-2-en-1-one, (4h):[35] light green solid. Melting range ~146 °C (decomposition). Yield: 84% (2.61 g, 8.4 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.00 – 7.93 (m, 2H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.68 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 1H), 7.49 (ddd, *J* = 8.5, 7.4, 1.5 Hz, 1H), 7.35 (d, *J* = 15.6 Hz, 1H), 6.55 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.47 (d, *J* = 2.3 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 189.8 (C), 164.5 (C), 160.5 (C), 148.7 (C), 136.8 (CH), 133.2 (CH), 133.1 (CH), 131.9 (CH), 131.6 (C), 129.8 (CH), 129.2 (CH), 124.8 (CH), 121.3 (C), 105.4 (CH), 98.6 (CH), 55.7 (CH_3), 55.6 (CH_3). IR (neat) v/cm^{-1}: 3014 (w), 2843 (w), 1649 (m), 1591 (s), 1522 (s), 1421 (s), 1268 (m), 1251 (s), 1012 (s), 965 (s), 823 (s). HR-MS (TOF ES): calculated for $C_{17}H_{16}NO_5$ 314.1023, found 314.1026 (M+H+).

(*E*)-3-(2-Nitrophenyl)-1-(thiophen-2-yl)prop-2-en-1-one, (4i):[36] red solid. Melting range 125-128 °C. Yield: 65% (1.69 g, 6.5 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.19 (d, *J* = 15.5 Hz, 1H), 8.06 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.87 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.73 – 7.65 (m, 3H), 7.55 (ddd, *J* = 8.4, 7.4, 1.6 Hz, 1H), 7.24 (d, *J* = 15.6 Hz, 1H), 7.20 (dd, *J* = 3.8, 1.1 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 181.7 (C), 148.6 (C), 144.6 (C), 139.3 (CH), 134.5 (CH), 133.5 (CH), 132.6 (CH), 131.2 (C), 130.3 (CH), 129.3 (CH), 128.3 (CH), 126.9 (CH), 125.0 (CH). IR (neat) v/cm^{-1}: 1650 (m), 1602 (m), 1508 (s), 1411 (m), 1339 (m), 1289 (m), 1234 (m), 1062 (w), 968 (m), 848 (m), 714 (s), 582 (m). HR-MS (TOF ES): calculated for $C_{13}H_{10}NO_3S$ 260.0381, found 260.0378 (M+H$^+$).

(*E*)-1-(4-Fluoro-3-(trifluoromethyl)phenyl)-3-(2-nitrophenyl)prop-2-en-1-one, (4j): beige solid. Melting range 146-148 °C. Yield: 88% (2.98 g, 8.8 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.29 – 8.25 (m, 1H), 8.25 – 8.20 (m, 1H), 8.15 (d, *J* = 15.6 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.58 (ddd, *J* = 8.6, 6.8, 2.0 Hz, 1H), 7.34 (t, *J* = 9.2 Hz, 1H), 7.25 (d, *J* = 15.6 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 187.7 (C), 162.5 (dq, *J* = 263, 2 Hz, CF), 148.5 (C), 141.6 (CH), 134.7 (d, *J* = 10 Hz, CH), 133.7 (CH), 133.7 (C), 130. 9 (C), 130.7 (CH), 129.3 (CH), 128.5 – 128.2 (m, CH), 126.0 (CH), 125.1 (CH), 122.1 (qd, *J* = 273, 2 Hz, CF_3), 119.0 (qd, *J* = 34, 15 Hz, C), 117.6 (d, *J* = 20 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -61.6 (d, *J* = 13 Hz), -106.6 (m). IR (neat) v/cm^{-1}: 3073 (w), 1667 (m), 1618 (m), 1603 (m), 1519 (s), 1323 (s), 1275 (s), 1173 (s), 1128 (s), 1056 (m), 842 (s), 752 (s). HR-MS (TOF ES): calculated for $C_{16}H_{10}F_4NO_3$ 340.0591, found 340.0594 (M+H+).

(*E*)-1-(5-Methylfuran-2-yl)-3-(2-nitrophenyl)prop-2-en-1-one (4k): grey solid. Melting range 126-128 °C. Yield: 85% (2.18 g, 8.5 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 8.09 (dd, *J* = 7.8, 1.4 Hz, 1H), 8.05 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.90 (d, *J* = 15.4 Hz, 1H), 7.82 – 7.76 (m, 2H), 7.66 (td, *J* = 7.9, 1.5 Hz, 1H), 7.62 (d, *J* = 15.5 Hz, 1H), 6.44 (dd, *J* = 3.5, 1.2 Hz, 1H), 2.39 (s, 3H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 175.6 (C), 159.7 (C), 152.0 (C), 149.2 (C), 137.0 (CH), 134.1 (CH), 131.4 (CH), 130.0 (C), 129.7 (CH), 126.8 (CH), 125.1 (CH), 122.9 (CH), 110.2 (CH), 14.2 (CH_3). IR (neat) v/cm^{-1}: 3104 (w), 1651 (s), 1597 (s), 1571 (m), 1505 (s), 1333 (s), 1289 (s), 1067 (m), 1029 (s), 977 (s), 793 (s), 751 (s). HR-MS (TOF ES): calculated for $C_{14}H_{12}NO_4$ 258.0761, found 258.0762 (M+H+).

(*E*)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(2-nitrophenyl)prop-2-en-1-one, (4l): light brown solid. Melting range 106-108 °C. Yield: 90% (2.67 g, 9.0 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.08 (d, *J* = 15.6 Hz, 1H), 8.04 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.71 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.62 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.53 (td, *J* = 7.7, 1.6 Hz, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.27 (d, *J* = 15.6 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.05 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 188.1 (C), 152.0 (C), 148.5 (C), 148.4 (C), 139.4 (CH), 133.5 (CH), 132.2 (C), 131.4 (C), 130.2 (CH), 129.2 (CH), 127.0 (CH), 125.2 (CH), 124.9 (CH), 108.5 (CH), 108.0 (CH), 101.9 (CH_2). IR (neat) v/cm^{-1}: 2906 (w), 1654 (m), 1595 (s), 1523 (s), 1441 (s), 1343 (s), 1245 (s), 1110 (s), 1038 (s), 815 (s), 748 (s). HR-MS (TOF ES): calculated for $C_{16}H_{12}NO_5$ 298.0710, found 298.0712 (M+H+).

(*E*)-1-(4-Methoxyphenyl)-3-(5-morpholino-2-nitrophenyl)prop-2-en-1-one (4m): orange solid. Melting range 159-161 °C. Yield: 86% (1.58 g, 4.3 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 8.15 – 8.08 (m, 3H), 8.04 (d, *J* = 9.4 Hz, 1H), 7.71 (d, *J* = 15.5 Hz, 1H), 7.25 (d, *J* = 2.8 Hz, 1H), 7.07

(m, 3H), 3.84 (s, 3H), 3.73 (t, *J* = 4.9 Hz, 4H), 3.46 (t, *J* = 4.9 Hz, 4H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 187.9 (C), 163.9 (C), 154.4 (C), 141.2 (CH), 137.9 (C), 134.2 (C), 131.6 (2CH), 130.5 (C), 128.0 (CH), 126.2 (CH), 114.5 (2CH), 114.1 (CH), 113.1 (CH), 66.2 ($2CH_2$), 56.1 (CH_3), 47.0 ($2CH_2$). IR (neat) v/cm^{-1}: 2967 (w), 1597 (s), 1568 (m), 1497 (m), 1296 (s), 1252 (s), 1167 (m), 1117 (m), 1042 (m), 904 (m), 815 (s), 750 (m). HR-MS (TOF ES): calculated for $C_{20}H_{21}N_2O_5$ 369.1445, found 369.1450 (M+H+).

(*E*)-1-(2-Fluoro-4-methoxyphenyl)-3-(2-nitro-5-(2,2,2-trifluoroethoxy)-phenyl)prop-2-en-1-one (4n): grey powder. Melting range 136-139 °C. Yield: 84% (1.68 g, 4.2 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 8.13 (d, *J* = 9.2 Hz, 1H), 7.94 (d, *J* = 15.6 Hz, 1H), 7.86 (t, *J* = 8.7 Hz, 1H), 7.54 (d, *J* = 2.9 Hz, 1H), 7.50 (dd, *J* = 15.6, 2.5 Hz, 1H), 7.29 (dd, *J* = 9.1, 2.8 Hz, 1H), 6.95 (dd, *J* = 13.4, 2.4 Hz, 1H), 6.91 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.00 (q, *J* = 8.8 Hz, 2H), 3.84 (s, 3H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 186.8 (d, *J* = 3 Hz, C), 165.0 (d, *J* = 12 Hz, C), 162.9 (d, *J* = 254 Hz, CF), 160.8 (C), 143.0 (C), 138.9 (CH), 133.5 (C), 132.8 (d, *J* = 4 Hz, CH), 130.3 (d, *J* = 5 Hz, CH), 128.0 (CH), 124.1 (q, *J* = 278 Hz, CF_3), 119.1 (d, *J* = 12 Hz, C), 117.2 (CH), 115.1 (CH), 111.6 (d, *J* = 3 Hz, CH), 102.6 (d, *J* = 27 Hz, CH), 65.5 (q, *J* = 35 Hz, CH_2), 56.6 (CH_3). ^{19}F-NMR (376 MHz, DMSO-d_6) δ/ppm -72.5 (t, *J* = 8.8 Hz), -107.8 (ddd, *J* = 12.8, 9.1, 2.6 Hz). IR (neat) v/cm^{-1}: 3106 (w), 1660 (w), 1620 (s), 1597 (s), 1572 (m), 1513 (s), 1240 (s), 1223 (s), 1171 (s), 1154 (s), 1115 (s), 1096 (s), 1017 (m), 960 (m), 860 (s), 832 (m). HR-MS (TOF ES): calculated for $C_{18}H_{14}NO_5F_4$ 400.0808, found 400.0813 ($M+H^+$).

(*E*)-3-(6-Nitrobenzo[d][1,3]dioxol-5-yl)-1-phenylprop-2-en-1-one, (4o): light green solid. Yield: 88% (2.61 g, 8.8 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.10 (d, *J* = 15.5 Hz, 1H), 7.98 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.54 (s, 1H), 7.52 – 7.45 (m, 2H), 7.19 (d, *J* = 15.5 Hz, 1H), 7.07 (s, 1H), 6.16 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 190.6 (C), 152.1 (C), 149.1 (C), 143.3 (C), 140.7 (CH), 137.5 (C), 133.0 (CH), 128.7 (2CH), 128.7 (2CH), 128.0 (C), 126.4 (CH), 107.4 (CH), 105.8 (CH), 103.4 (CH_2). IR (neat) v/cm^{-1}: 3055 (w), 2919 (w), 1657 (m), 1597 (s), 1500 (s), 1481 (s), 1317 (s), 1263 (s), 1211 (s), 1011 (s), 967 (s), 925 (s), 755 (s). HR-MS (TOF ES): calculated for $C_{16}H_{12}NO_5$ 298.0710, found 298.0715 (M+H+).

(*E*)-3-(6-Nitrobenzo[d][1,3]dioxol-5-yl)-1-(thiophen-2-yl)prop-2-en-1-one (4p): yellow powder. Melting range 162-165 °C. Yield: 83% (2.51 g, 8.3 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.17 (d, *J* = 15.4 Hz, 1H), 7.85 (dd, *J* = 3.8, 1.3 Hz, 1H), 7.68 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.53 (s, 1H), 7.17 (dd, *J* = 5.0, 3.7 Hz, 1H), 7.11 (d, *J* = 15.4 Hz, 1H), 7.06 (s, 1H), 6.16 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 181.8 (C), 152.0 (C), 149.1 (C), 144.7 (C), 143.4 (C), 139.7 (CH), 134.4 (CH), 132.4 (CH), 128.3 (CH), 127.8 (C), 125.9 (CH), 107.4 (CH), 105.8 (CH), 103.4 (CH_2). IR (neat) v/cm^{-1}: 3111 (w), 2916 (w), 1644 (m), 1610 (m), 1585 (m), 1503 (s), 1480 (s), 1411 (s), 1266 (s), 1031 (s), 970 (s), 864 (m), 730 (s), 520 (m). HR-MS (TOF ES): calculated for $C_{14}H_{10}NO_5S$ 304.0274, found 304.0276 (M+H+).

(*E*)-4-(Benzo[d][1,3]dioxol-5-yl)but-3-en-2-one, (9a): light yellow powder. Melting range 110-113 °C. Yield: 90% (1.71 g, 9.0 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.40 (d, *J* = 16.1 Hz, 1H), 7.04 – 6.97 (m, 2H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.53 (d, *J* = 16.1 Hz, 1H), 5.99 (s, 2H), 2.33 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 198.2 (C), 149.8 (C), 148.4 (C), 143.2 (CH), 128.8 (C), 125.3 (CH), 124.8 (CH), 108.6 (CH), 106.5 (CH), 101.6 (CH_2), 27.5 (CH_3). IR (neat) v/cm^{-1}: 2905 (w), 1669 (m), 1642 (s), 1622 (s), 1596 (s), 1499 (s), 1441 (s), 1236 (s), 1103 (s), 1036 (s), 977 (s), 926 (s), 803 (s). HR-MS (TOF ES): calculated for $C_{11}H_{11}O_3$ 191.0703, found 191.0704 (M+H+).

(1*E*,4*E*)-1-(Benzo[d][1,3]dioxol-5-yl)-5-(2-nitrophenyl)penta-1,4-dien-3-one, (9b): yellow powder. Melting range 175-177 °C. Yield: 92% (2.67 g, 8.3 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 8.04 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 15.8 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 15.8 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 1.7 Hz, 1H), 7.29 (d, *J* = 15.8 Hz, 1H), 7.23 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.10 (d, *J* = 15.8 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 1H), 6.06 (s, 2H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 188.5 (C), 150.1 (C), 149.1 (C), 148.6 (C), 144.3 (CH), 137.3 (CH), 134.2 (CH), 131.3 (CH), 130.4 (C), 129.8 (CH), 129.6 (CH), 129.4 (C), 126.1 (CH), 125.2 (CH), 124.4 (CH), 109.1 (CH), 107.1 (CH), 102.2 (CH_2). IR (neat) v/cm^{-1}: 2911 (w), 1650 (s), 1593 (s), 1507 (s), 1452 (s), 1341 (s), 1253 (s), 1193 (s), 1034 (s), 975 (s), 931 (s), 862 (s), 799 (s), 747 (m). HR-MS (TOF ES): calculated for $C_{18}H_{14}NO_5$ 324.0866, found 324.0867 (M+H+).

General procedure for the preparation of 3a-p, and 7c,7o,10: To a suspension of aldol product **4** (1 equiv.) in EtOH (0.5 M) was added iron powder (10 equiv.) and HCl (10 mol%, aqueous). The resulting mixture was stirred at 70 °C until TLC indicated full conversion of substrate (~1 h). The resulting mixture was allowed to cool to ambient and diluted with EtOAc (10 mL) before filtering over a pad of celite (~10 cm) to remove residual iron. Further purification was achieved by silica column chromatography using EtOAc/hexanes (20-30%) as eluent allowing isolation of **7c** and **7o**.

(*E*)-4-(2-Aminophenyl)but-3-en-2-one, (3a):[37] orange oil. Yield: 93% (115 mg, 0.77 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.68 (d, *J* = 15.9 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.19 (ddd, *J* = 8.2, 7.3, 1.5 Hz, 1H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.71 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.67 (d, *J* = 15.9 Hz, 1H), 3.97 (s, 2H), 2.37 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 198.1 (C), 145.8 (C), 138.6 (CH), 131.6 (CH), 128.2 (CH), 126.8 (CH), 119.9 (C), 119.1 (CH), 116.9 (CH), 28.0 (CH_3). IR (neat) v/cm^{-1}: 3438 (m), 3243 (w), 1664 (s), 1636 (s), 1590 (s), 1488 (s), 1316 (m), 1248 (s), 1159 (m), 974 (m), 751 (m). HR-MS (TOF ES): calculated for $C_{10}H_{12}NO$ 162.0913, found 162.0916 (M+H+).

(*E*)-1-(2-Aminophenyl)-4,4-dimethylpent-1-en-3-one, (3b):[37] red oil. Yield: 88% (627 mg, 3.1 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.81 (d, *J* = 15.4 Hz, 1H), 7.41 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.15 (ddd, *J* = 8.2, 7.4, 1.5 Hz, 1H), 7.03 (d, *J* = 15.3 Hz, 1H), 6.75 (t, *J* = 7.2 Hz, 1H), 6.68 (dd, *J* = 8.1, 0.9 Hz, 1H), 3.98 (s, 2H), 1.21 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 204.3 (C), 146.0 (C), 138.1 (CH), 131.2 (CH), 127.9 (CH), 120.9 (CH), 120.3 (C), 118.7 (CH), 116.6 (CH), 43.1 (C), 26.4 ($3CH_3$). IR (neat) v/cm^{-1} 3367 (w), 2965 (m), 1672 (m), 1586 (s), 1459 (m), 1330 (s), 1262 (w), 1158 (m), 1077 (s), 1007 (m), 748 (s), 577 (w), 460 (w). HR-MS (TOF ES): calculated for $C_{13}H_{18}NO$ 204.1383, found 204.1386 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-phenylprop-2-en-1-one, (3c):[37] yellow solid. Melting range 121-123 °C. Yield: 89% (382 mg, 1.5 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.04 – 7.95 (m, 3H), 7.60 – 7.43 (m, 5H), 7.19 (ddd, J

= 8.2, 7.3, 1.5 Hz, 1H), 6.78 (t, J = 7.3 Hz, 1H), 6.71 (dd, J = 8.1, 0.9 Hz, 1H), 4.06 (s, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 190.2 (C), 146.2 (C), 140.1 (CH), 138.3 (C), 132.7 (CH), 131.6 (CH), 128.6 (2CH), 128.4 (2CH), 128.1 (CH), 121.8 (CH), 120.3 (C), 118.9 (CH), 116.8 (CH). IR (neat) v/cm^{-1}: 3333 (w), 3222 (w), 3031 (w), 1650 (m), 1569 (s), 1485 (m), 1341 (s), 1211 (s), 1155 (m), 1039 (s), 728 (s), 684 (s). HR-MS (TOF ES) calculated for $C_{15}H_{14}NO$ 224.1075, found 224.1076 ($M+H^+$).

(*E*)-3-(2-Aminophenyl)-1-(2-fluorophenyl)prop-2-en-1-one, (3d): yellow powder. Yield: 83% (1.00 g, 4.2 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 7.95 (dd, *J* = 15.4, 2.0 Hz, 1H), 7.84 (td, *J* = 7.5, 2.0 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.35 (dd, *J* = 15.4, 3.0 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.23 – 7.14 (m, 2H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 4.08 (s, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 188.9 – 188.8 (m, C), 161.3 (d, *J* = 253 Hz, CF), 146.4 (C), 140.2 (CH), 133.9 (d, *J* = 9 Hz, CH), 131.8 (CH), 131.0 (d, *J* = 3 Hz, CH), 128.5 (CH), 127.3 (d, *J* = 13 Hz, C), 125.4 (d, *J* = 7 Hz, CH), 124.5 (d, *J* = 3 Hz, CH), 120.1 (C), 119.0 (CH), 116.8 (CH), 116.5 (d, *J* = 23 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -110.7. IR (neat) v/cm^{-1}: 3346 (br), 3235 (w), 1661 (m), 1610 (s), 1583 (s), 1451 (m), 1340 (s), 1260 (m), 1202 (m), 1157 (m), 774 (m). HR-MS (TOF ES): calculated for $C_{15}H_{13}FNO$ 242.0976, found 242.0978 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(2,4-difluorophenyl)prop-2-en-1-one, (3e): orange solid. Melting range 115-117 °C. Yield: 58% (253 mg, 0.98 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.96 – 7.86 (m, 2H), 7.48 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.31 (dd, *J* = 15.4, 3.2 Hz, 1H), 7.19 (ddd, *J* = 8.2, 7.3, 1.4 Hz, 1H), 7.01 – 6.95 (m, 1H), 6.89 (ddd, *J* = 11.0, 8.8, 2.4 Hz, 1H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.70 (dd, *J* = 8.1, 0.7 Hz, 1H), 4.04 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 187.1 (d, *J* = 4 Hz, C), 165.5 (dd, *J* = 257, 12 Hz, CF), 161.9 (dd, *J* = 257, 12 Hz, CF), 146.4 (C), 140.3 (CH), 132.9 (dd, *J* = 11, 4 Hz, CH), 131.9 (CH), 128.4 (CH), 124.7 (d, *J* = 8 Hz, CH), 123.7 (dd, *J* = 13, 4 Hz, C), 119.9 (C), 118.9 (CH), 116.8 (CH), 112.2 (dd, *J* = 21, 3 Hz, CH), 104.7 (dd, *J* = 28, 26 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -102.8, -105.7. IR (neat) v/cm^{-1}: 3403 (w), 1655 (w), 1590 (s), 1561 (s), 1487 (m), 1340 (m), 1229 (m), 1097 (s), 970 (m), 851 (s), 730 (s). HR-MS (TOF ES): calculated for $C_{15}H_{12}F_2NO$ 260.0881, found 260.0882 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one, (3f):[37] green solid. Melting range 94-96 °C. Yield: 56% (100 mg, 0.4 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.04 (app. d, *J* = 9.0 Hz, 2H), 7.97 (d, *J* = 15.4 Hz, 1H), 7.53 – 7.47(m, 2H), 7.19 (ddd, *J* = 8.2, 7.4, 1.5 Hz, 1H), 6.98 (app. d, *J* = 9.0 Hz, 2H), 6.79 (t, *J* = 7.2 Hz, 1H), 6.72 (dd, *J* = 8.1, 0.9 Hz, 1H), 4.06 (s, 2H), 3.89 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 188.5 (C), 163.4 (C), 146.1 (C), 139.3 (CH), 131.4 (CH), 131.2 (C), 130.7 (2CH), 128.1 (CH), 121.7 (CH), 120.5 (C), 118.8 (CH), 116.7 (CH), 113.8 (2CH), 55.5 (CH_3). IR (neat) v/cm^{-1}: 3337 (w), 1650 (m), 1579 (s), 1458 (m), 1334 (m), 1253 (s), 1214 (s), 1161 (s), 1015 (m), 746 (s). HR-MS (TOF ES): calculated for $C_{16}H_{16}NO_2$ 254.1176, found 254.1175 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(1*H*-indol-3-yl)prop-2-en-1-one, (3g): yellow solid. Melting range ~200 °C (decomposition). Yield: 85% (130 mg, 0.5 mmol). ^{1}H-NMR (600 MHz, DMSO-d_6) δ/ppm 12.00 (s, 1H), 8.63 (d, *J* = 3.0 Hz, 1H), 8.33 (d, *J* = 7.1 Hz, 1H), 7.86 (d, *J* = 15.3 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 15.3 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.19 (m, 2H), 7.05 (t, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.1 Hz, 1H), 6.57 (t, *J* = 7.5 Hz, 1H), 5.53 (s, 2H). ^{13}C-NMR (150 MHz, DMSO-d_6) δ/ppm 184.5 (C), 148.8 (C), 137.2 (C), 136.3 (CH), 134.5 (CH), 131.1 (CH), 127.8 (CH), 126.5 (C), 123.4 (CH), 122.8 (CH), 122.2 (CH), 122.1 (CH), 119.2 (C), 118.2 (C), 116.7 (CH), 116.7 (CH), 112.5 (CH). IR (neat) v/cm^{-1}: 3322 (w), 2928 (w), 1628 (m), 1519 (s), 1442 (s), 1311 (m), 1157 (s), 966 (m), 858 (w), 735 (s), 639 (m), 519 (m), 431 (m). HR-MS (TOF ES): calculated for $C_{17}H_{15}N_2O$ 263.1179, found 263.1183 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(2,4-dimethoxyphenyl)prop-2-en-1-one, (3h): yellow oil. Yield: 89% (1.26 g, 4.45 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.83 (d, *J* = 15.6 Hz, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.44 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.43 (d, *J* = 15.4 Hz, 1H), 7.14 (ddd, *J* = 8.4, 7.4, 1.5 Hz, 1H), 6.75 (td, *J* = 7.6, 7.2, 1.3 Hz, 1H), 6.68 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.54 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.47 (d, *J* = 2.2 Hz, 1H), 4.06 (s, 2H), 3.87 (s, 3H), 3.84 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 190.3 (C), 164.2 (C), 160.4 (C), 146.0 (C), 137.4 (CH), 132.9 (CH), 131.0 (CH), 128.3 (CH), 127.2 (CH), 122.3 (C), 120.8 (C), 118.7 (CH), 116.6 (CH), 105.2 (CH), 98.6 (CH), 55.7 (CH_3), 55.5 (CH_3). IR (neat) v/cm^{-1}: 3446 (m), 3357 (m), 3243 (w), 2940 (w), 1644 (m), 1597 (s), 1572 (s), 1456 (m), 1329 (s), 1288 (s), 1248 (s), 1206 (s), 1159 (s), 1124 (s), 1020 (s), 748 (s), 730 (s). HR-MS (TOF ES): calculated for $C_{17}H_{18}NO_3$ 284.1281, found 284.1285 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(thiophen-2-yl)prop-2-en-1-one, (3i):[37] orange solid. Melting range 138-140 °C. Yield: 65% (447 mg, 1.9 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.02 (d, *J* = 15.3 Hz, 1H), 7.87 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.69 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.53 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.38 (d, *J* = 15.3 Hz, 1H), 7.24 – 7.19 (m, 2H), 6.81 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 4.08 (s, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 182.0 (C), 146.3 (C), 145.7 (C), 139.3 (CH), 133.7 (CH), 131.7 (CH) 131.6 (CH), 128.2 (CH), 128.1 (CH), 121.5 (CH), 120.1 (C), 118.9 (CH), 116.8 (CH). IR (neat) v/cm^{-1}: 3331 (w), 1647 (m), 1574 (s), 1458 (m), 1413 (m), 1218 (m), 977 (m), 857 (w), 746 (m), 696 (s), 593 (w). HR-MS (TOF ES): calculated for $C_{13}H_{12}NOS$ 230.0634, found 230.0633 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(4-fluoro-3-(trifluoromethyl)phenyl)prop-2-en-1-one, (3j): yellow solid. Melting range 117-120 °C. Yield: 80% (1.22 g, 4.0 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.27 (dd, *J* = 6.9, 2.3 Hz, 1H), 8.21 (ddd, *J* = 8.6, 4.7, 2.3 Hz, 1H), 8.03 (d, *J* = 15.3 Hz, 1H), 7.51 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.41 (d, *J* = 15.3 Hz, 1H), 7.30 (t, *J* = 9.1 Hz, 1H), 7.23 – 7.18 (m, 1H), 6.82 – 6.76 (m, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 4.10 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 187.2 (C), 162.2 (dq, *J* = 263, 2 Hz, CF), 146.6 (C), 141.5 (CH), 134.6 (C), 134.2 (d, *J* = 10 Hz, CH), 132.2 (CH), 128.1 (CH), 128.1 – 127.7 (m, CH), 122.2 (qd, *J* = 273, 2 Hz, CF_3), 120.0 (CH), 119.7 (C), 119.0 (CH), 118.5 (qd, *J* = 34, 13 Hz, C), 117.3 (d, *J* = 21 Hz, CH), 117.0 (CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -61.6 (d, *J* = 13 Hz, CF_3), -107.6 (m, CF). IR (neat) v/cm^{-1}: 3367 (m), 3068 (w), 1659 (m), 1616 (s), 1577 (s), 1502 (m), 1322 (s), 1196 (s), 1129 (s), 1055 (m), 755 (m). HR-MS (TOF ES): calculated for $C_{16}H_{12}F_4NO$ 310.0850, found 310.0852 (M+H+). X-ray data (CCDC2013440): for $C_{16}H_{11}NOF_4$; C2/c, α = 90, β = 111.0975(9), γ = 90, a = 20.3756(2), b = 5.12105(5), c = 27.8472(3).

(*E*)-3-(2-Aminophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one, (3k): yellow solid. Melting range 122-124 °C. Yield: 78% (890 mg, 3.9 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.97 (d, *J* = 15.5 Hz, 1H), 7.48 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.27 (d, *J* = 15.6 Hz, 1H), 7.20 (d, *J* = 3.5 Hz, 1H), 7.17 – 7.11 (m, 1H), 6.77 – 6.71 (m, 1H), 6.68 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.17 (d, *J* = 3.6 Hz, 1H), 4.13 (s, 2H), 2.39 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$)

δ/ppm 177.3 (C), 158.1 (C), 152.6 (C), 146.4 (C), 138.5 (CH), 131.5 (CH), 128.0 (CH), 121.0 (CH), 120.1 (C), 119.4 (CH), 118.7 (CH), 116.8 (CH), 109.3 (CH), 14.1 (CH_3). IR (neat) v/cm^{-1}: 3339 (m), 3224 (m), 1638 (s), 1587 (s), 1511 (s), 1345 (s), 1246 (m), 1203 (m), 1038 (m), 1024 (m), 803 (m), 747 (s). HR-MS (TOF ES): calculated for $C_{14}H_{14}NO_2$ 228.1019, found 228.1021 (M+H+).

(*E*)-3-(2-Aminophenyl)-1-(benzo[d][1,3]dioxol-5-yl)prop-2-en-1-one, (3l): yellow powder. Yield: 81% (1.07 g, 4.0 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.94 (d, *J* = 15.3 Hz, 1H), 7.63 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.51 (d, *J* = 1.6 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.41 (d, *J* = 15.3 Hz, 1H), 7.17 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.77 (td, *J* = 7.6, 1.1 Hz, 1H), 6.70 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.04 (s, 2H), 4.06 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 188.1 (C), 151.6 (C), 148.3 (C), 146.2 (C), 139.6 (CH), 133.1 (C), 131.5 (CH), 128.0 (CH), 124.6 (CH), 121.5 (CH), 120.4 (C), 118.8 (CH), 116.7 (CH), 108.4 (CH), 107.9 (CH), 101.8 (CH_2). IR (neat) v/cm^{-1}: 3348 (w), 2901 (w), 1639 (m), 1601 (m), 1566 (s), 1486 (s), 1441 (s), 1335 (m), 1245 (s), 1110 (m), 1036 (m), 807 (m), 748 (s). HR-MS (TOF ES): calculated for $C_{16}H_{14}NO_3$ 268.0968, found 268.0969 (M+H+).

(*E*)-3-(2-Amino-5-morpholinophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (3m): red powder. Yield: 77% (1.04 g, 3.1 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.02 (d, *J* = 9.0 Hz, 2H), 7.93 (d, *J* = 15.4 Hz, 1H), 7.44 (d, *J* = 15.4 Hz, 1H), 7.05 (d, *J* = 2.7 Hz, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 6.89 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 1H), 3.87 (s, 3H), 3.86 (app. s, 4H), 3.81 (br s, 2H), 3.07 – 3.02 (m, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 188.5 (C), 163.4 (C), 144.5 (C), 140.6 (C), 139.7 (CH), 131.2 (C), 130.8 (2CH), 121.9 (CH), 121.7 (CH), 121.2 (C), 118.1 (CH), 115.8 (CH), 113.8 (2CH), 67.0 ($2CH_2$), 55.5 (CH_3), 51.0 ($2CH_2$). IR (neat) v/cm^{-1}: 3353 (m), 2960 (m), 2837 (m), 1650 (m), 1598 (s), 1498 (s), 1311 (m), 1258 (s), 1230 (s), 1164 (s), 1114 (s), 1021 (m), 981 (m), 902 (m), 831 (s), 727 (s). HR-MS (TOF ES): calculated for $C_{20}H_{23}N_2O_3$ 339.1709, found 339.1706 ($M+H^+$).

(*E*)-3-(2-Amino-5-(2,2,2-trifluoroethoxy)phenyl)-1-(2-fluoro-4-methoxyphenyl)prop-2-en-1-one (3n): orange powder. Yield: 75% (1.10 g, 3.0 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.90 – 7.83 (m, 2H), 7.33 (dd, *J* = 15.4, 3.0 Hz, 1H), 7.06 (d, *J* = 3.0 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.66 (d, *J* = 8.9 Hz, 1H), 6.63 (dd, *J* = 13.1, 2.4 Hz, 1H), 4.29 (q, *J* = 8.2 Hz, 2H), 3.90 (br s, 2H), 3.85 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 186.8 (d, *J* = 4 Hz, C), 164.6 (d, *J* = 12 Hz, C), 163.1 (d, *J* = 254 Hz, CF), 150.5 (C), 141.9 (C), 138.4 (CH), 132.6 (d, *J* = 5 Hz, CH), 126.1 (d, *J* = 9 Hz, CH), 123.4 (q, *J* = 279 Hz, CF_3), 121.2 (C), 119.8 (CH), 119.6 (d, *J* = 13 Hz, C), 118.1 (CH), 114.1 (CH), 110.9 (d, *J* = 3 Hz, CH), 101.8 (d, *J* = 28 Hz, CH), 67.1 (q, *J* = 35 Hz, CH_2), 55.8 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -74.1 (t, *J* = 8.3 Hz), -106.5 (ddt, *J* = 13.7, 9.0, 2.7 Hz). IR (neat) v/cm^{-1}: 3372 (w), 2944 (w), 1614 (s), 1585 (m), 1498 (m), 1289 (m), 1238 (s), 1160 (s), 976 (m), 854 (m). HR-MS (TOF ES): calculated for $C_{18}H_{16}NO_3F_4$ 370.1066, found 370.1052 ($M+H^+$).

(1*H*-Indol-2-yl)(phenyl)methanone, (7c):[40] off-white solid. Melting range 143-146 °C. Yield: 3% (35 mg, 0.16 mmol; *side-product*). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 9.48 (s, 1H), 8.02 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.67 – 7.62 (m, 1H), 7.56 (dd, *J* = 8.3, 6.9 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.21 – 7.15 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 187.2 (C), 138.0 (C), 137.6 (C), 134.4 (C), 132.4 (CH), 129.2 (2CH), 128.5 (2CH), 127.8 (C), 126.5 (CH), 123.3 (CH), 121.1 (CH), 112.8 (CH), 112.2 (CH). IR (neat) v/cm^{-1}: 3316 (s), 3060 (w), 1618 (s), 1572 (m), 1519 (s), 1342 (m), 1261 (m), 1127 (m), 728 (m). HR-MS (TOF ES): calculated for $C_{15}H_{12}NO$ 222.0919, found 222.0912 ($M+H^+$).

(5*H*-[1,3]Dioxolo[4,5-f]indol-6-yl)(phenyl)methanone (7o): yellow powder. Yield: 6% (21 mg, 0.08 mmol; *side-product*). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 9.29 (s, 1H), 7.97 – 7.90 (m, 2H), 7.61 – 7.56 (m, 1H), 7.53 – 7.47 (m, 2H), 7.02 (d, *J* = 3.5 Hz, 1H), 6.98 (s, 1H), 6.86 (s, 1H), 5.98 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 185.9 (C), 149.0 (C), 144.4 (C), 138.2 (C), 134.0 (C), 133.7 (C), 132.0 (CH), 129.0 (2CH), 128.4 (2CH), 122.1 (C), 113.3 (CH), 101.2 (CH_2), 100.0 (CH), 91.8 (CH). IR (neat) v/cm^{-1}: 3284 (s), 2904 (w), 1602 (s), 1573 (m), 1497 (s), 1485 (s), 1365 (m), 1290 (s), 1251 (m), 12223 (s), 1175 (m). HR-MS (TOF ES): calculated for $C_{16}H_{12}NO_3$ 266.0817, found 266.0818 ($M+H^+$).

(1*E*,4*E*)-1-(2-Aminophenyl)-5-(benzo[d][1,3]dioxol-5-yl)penta-1,4-dien-3-one, (10): orange powder. Melting range 175-177 °C. Yield: 86% (2.08 g, 7.1 mmol). ^{1}H-NMR (400 MHz, DMSO-d_6) δ/ppm 7.94 (d, *J* = 15.8 Hz, 1H), 7.59 (d, *J* = 15.8 Hz, 1H), 7.50 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.45 (d, *J* = 1.6 Hz, 1H), 7.33 (d, *J* = 15.8 Hz, 1H), 7.23 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.09 – 7.03 (m, 1H), 6.98 – 6.89 (m, 2H), 6.68 (d, *J* = 7.9 Hz, 1H), 6.53 (t, *J* = 7.4 Hz, 1H), 6.06 (s, 2H), 5.74 (s, 2H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ/ppm 188.7 (C), 149.7 (C), 149.2 (C), 148.5 (C), 142.1 (CH), 139.0 (CH), 132.0 (CH), 129.8 (C), 127.5 (CH), 125.6 (CH), 124.9 (CH), 123.5 (CH), 118.2 (C), 116.8 (CH), 116.7 (CH), 109.0 (CH), 107.1 (CH), 102.0 (CH_2). IR (neat) v/cm^{-1}: 3332 (m), 3222 (m), 3020 (w), 1634 (s), 1600 (m), 1566 (s), 1493 (s), 1450 (s), 1346 (s), 1257 (s), 1185 (s), 1031 (s), 921 (s), 736 (s). HR-MS (TOF ES): calculated for $C_{18}H_{16}NO_3$ 294.1125, found 294.1126 (M+H+).

General procedure for the preparation of quinolines 1a-o: A solution of amine **3** (typically 100 mM EtOH) was prepared and pumped through the UV LED unit (10 min residence time, ~30 °C, 75 W power). After evaporating the solvent and silica column chromatography (10% hexanes/EtOAc) the desired quinoline products were isolated in pure form.

2-Methylquinoline, (1a):[37] red oil. Yield: 91% (2.7 g, 18.9 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.03 (m, 2H), 7.77 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.68 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.48 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 2.75 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 159.0 (C), 147.8 (C), 136.2 (CH), 129.4 (CH), 128.5 (CH), 127.5 (CH), 126.5 (C), 125.7 (CH), 122.0 (CH), 25.3 (CH_3). IR (neat) v/cm^{-1}: 3055 (w), 1600 (m), 1504 (m), 1423 (m), 1311 (m), 1220 (m), 1117 (m), 950 (w), 817 (s), 745 (s), 619 (m), 474 (m). HR-MS (TOF ES): calculated for $C_{10}H_{10}N$ 144.0808, found 144.0809 (M+H+).

2-(tert-Butyl)quinoline, (1b):[37] pale yellow oil. Yield: 85% (66 mg, 0.36 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.07 (d, *J* = 8.3 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.66 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.47 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 1.47 (s, 9H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 169.2 (C), 147.4 (C), 135.8 (CH), 129.4 (CH), 128.9 (CH), 127.2 (CH), 126.4 (C), 125.6 (CH), 118.2

(CH), 38.1 (C), 30.1 ($3CH_3$). IR (neat) v/cm^{-1}: 2957 (m), 1619 (m), 1600 (s), 1502 (s), 1363 (m), 1138 (s), 1102 (w), 829 (s), 756 (s), 478 (w). HR-MS (TOF ES): calculated for $C_{13}H_{16}N$ 186.1277, found 186.1280 (M+H+).

2-Phenylquinoline, (1c):[37] off-white solid. Melting range 85-87 °C. Yield: 91% (374 mg, 1.8 mmol). ^{1}H-NMR (300 MHz, $CDCl_3$) δ/ppm 8.25 (d, *J* = 8.7 Hz, 1H), 8.22 – 8.16 (m, 3H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.85 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.75 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.60 – 7.46 (m, 4H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 157.4 (C), 148.3 (C), 139.7 (C), 136.8 (CH), 129.8 (CH), 129.6 (CH), 129.3 (CH), 128.8 (2CH), 127.6 (CH), 127.5 (CH), 127.2 (C), 126.3 (2CH), 119.0 (CH). IR (neat) v/cm^{-1}: 2922 (m), 1595 (m), 1486 (m), 1318 (w), 1123 (w), 1074 (w), 827 (s), 762 (s), 688 (s), 481 (m). HR-MS (TOF ES): calculated for $C_{15}H_{12}N$ 206.0970, found 206.0962 (M+H+). X-ray data (CCDC2013438): for $C_{15}H_{11}N$; Pna21, α = 90, β = 90, γ = 90, a = 16.5745(5), b = 11.1553(4), c = 5.8522(4).

2-(2-Fluorophenyl)quinoline, (1d): off-white solid. Melting range 120-123 °C. Yield: 88% (196 mg, 0.88 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.20 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 8.6 Hz, 1H), 8.09 (td, *J* = 7.8, 1.8 Hz, 1H), 7.88 (dd, *J* = 8.6, 2.7 Hz, 1H), 7.84 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.57 – 7.51 (m, 1H), 7.46 – 7.39 (m, 1H), 7.35 – 7.28 (m, 1H), 7.19 (ddd, *J* = 11.2, 8.2, 1.4 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 160.8 (d, *J* = 251 Hz, CF), 154.0 (C), 148.3 (C), 136.1 (CH), 131.5 (d, *J* = 3 Hz, CH), 130.8 (d, *J* = 8 Hz, CH), 129.7 (CH), 129.6 (CH), 128.0 (d, *J* = 12 Hz, C), 127.5 (CH), 127.2 (C), 126.6 (CH), 124.7 (d, *J* = 4 Hz, CH), 122.4 (d, *J* = 8 Hz, CH), 116.2 (d, *J* = 23 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -117.3. IR (neat) v/cm^{-1}: 3059 (w), 1598 (m), 1505 (m), 1489 (m), 1452 (m), 1206 (m), 831 (m), 761 (s). HR-MS (TOF ES): calculated for $C_{15}H_{11}FN$ 224.0870, found 224.0875 (M+H+).

2-(2,4-Difluorophenyl)quinoline, (1e):[38] white solid. Melting range 94-95 °C. Yield: 95% (42 mg, 0.17 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.17 – 8.10 (m, 3H), 7.83 – 7.79 (m, 2H), 7.71 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 7.03 (dddd, *J* = 8.8, 8.0, 2.5, 0.9 Hz, 1H), 6.93 (ddd, *J* = 11.2, 8.8, 2.5 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 163.4 (dd, *J* = 250, 12 Hz, CF), 160.9 (dd, *J* = 251, 12 Hz, CF), 153.1 (d, *J* = 2 Hz, C), 148.3 (C), 136.4 (CH), 132.7 (dd, *J* = 10, 5 Hz, CH), 129.7 (CH), 129.6 (CH), 127.5 (CH), 127.2 (C), 126.7 (CH), 124.3 (dd, *J* = 12, 4 Hz, C), 122.1 (d, *J* = 9 Hz, CH), 112.1 (dd, *J* = 21, 4 Hz, CH), 104.4 (app. t, *J* = 26, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -108.7, -112.8. IR (neat) v/cm^{-1}: 2921 (w), 1595 (m), 1496 (m), 1416 (m), 1263 (m), 1133 (m), 1095 (m), 968 (m), 833 (s), 755 (s), 468 (m). HR-MS (TOF ES): calculated for $C_{15}H_{10}F_2N$ 242.0776, found 242.0781 (M+H+). X-ray data (CCDC2013437): for $C_{15}H_9NF_2$; 21/n, α = 90, β = 99.775(2), γ = 90, a = 15.5081(3), b = 3.81884(9), c = 18.2055(4).

2-(4-Methoxyphenyl)quinoline, (1f):[37] white solid. Melting range 126-130 °C. Yield: 89% (139 mg, 0.53 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.24 – 8.13 (m, 4H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.82 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.73 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.09 – 7.05 (m, 2H), 3.90 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 160.9 (C), 156.9 (C), 148.2 (C), 136.8 (C), 132.1 (C), 129.7 (C), 129.4 (C), 129.0 (2CH), 127.4 (CH), 126.9 (CH), 126.0 (CH), 118.6 (CH), 114.3 (2CH), 55.4 (CH_3). IR (neat) v/cm^{-1}: 2917 (w), 1594 (m), 1496 (m), 1429 (m), 1288 (w), 1248 (m), 1174 (m), 1027 (m), 815 (s), 788 (m), 745 (m), 482 (w). HR-MS (TOF ES): calculated for $C_{16}H_{14}NO$ 236.1070, found 236.1074 (M+H+).

2-(1*H*-Indol-3-yl)quinoline, (1g):[39] light yellow solid. Yield: 71% (30 mg, 0.12 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.77 (m, 1H), 8.67 (br. s, 1H), 8.19 (d, *J* = 10.7 Hz, 1H), 8.14 (d, *J* = 11.6 Hz, 1H), 7.81 (m, 3H), 7.72 (ddd, *J* = 11.2, 9.2, 2.0 Hz, 1H), 7.49 (ddd, *J* = 10.8, 9.3, 1.6 Hz, 1H), 7.41 (m, 1H), 7.33 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 155.1 (C), 148.5 (C), 137.0 (C), 136.0 (CH), 129.4 (CH), 129.1 (CH), 127.4 (CH), 126.5 (C), 125.8 (C), 125.4 (CH), 125.2 (CH), 122.9 (CH), 122.1 (CH), 121.2 (CH), 119.5 (CH), 117.7 (C), 111.3 (CH). IR (neat) v/cm^{-1}: 3037 (w), 1598 (m), 1539 (s), 1431 (s), 1290 (w), 1238 (m), 1152 (w), 1117 (m), 983 (w), 932 (w), 815 (s), 742 (s), 562 (m), 496 (m), 427 (m). HR-MS (TOF ES): calculated for $C_{17}H_{13}N_2$ 245.1073, found 245.1078 (M+H+).

2-(2,4-Dimethoxyphenyl)quinoline, (1h): colourless oil. Yield: 90% (713 mg, 2.7 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.14 (dd, *J* = 8.6, 1.0 Hz, 1H), 8.08 (d, *J* = 8.7 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.78 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.67 (ddd, *J* = 8.6, 6.8, 1.5 Hz, 1H), 7.51 – 7.45 (m, 1H), 6.66 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.58 (d, *J* = 2.3 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 161.7 (C), 158.4 (C), 156.8 (C), 148.3 (C), 135.0 (CH), 132.4 (CH), 129.5 (CH), 129.1 (CH), 127.3 (CH), 126.9 (C), 125.9 (CH), 123.4 (CH), 122.6 (C), 105.4 (CH), 98.9 (CH), 55.6 (CH_3), 55.5 (CH_3). IR (neat) v/cm^{-1}: 2937 (w), 2835 (w), 1606 (s), 1497 (s), 1456 (s), 1427 (m), 1299 (s), 1277 (s), 1207 (s), 1160 (s), 1060 (m), 1030 (s), 834 (m), 759 (m). HR-MS (TOF ES): calculated for $C_{17}H_{16}NO_2$ 265.1097, found 265.1088 (M+H+).

2-(Thiophen-2-yl)quinoline, (1i):[37] white solid. Melting range 133-135 °C. Yield: 92% (43 mg, 0.2 mmol). ^{1}H-NMR (500 MHz, $CDCl_3$) δ/ppm 8.14 (d, *J* = 8.6 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.75 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.17 (dd, *J* = 5.0, 3.7 Hz, 1H).^{13}C-NMR (125 MHz, $CDCl_3$) δ/ppm 152.3 (C), 148.1 (C), 145.4 (C), 136.6 (CH), 129.8 (CH), 129.3 (CH), 128.6 (CH), 128.0 (CH), 127.5 (CH), 127.2 (C), 126.1 (CH), 125.8 (CH), 117.7 (CH). IR (neat) v/cm^{-1}: 2916 (w), 1592 (m), 1497 (m), 1424 (m), 1315 (m), 1057 (w), 821 (s), 756 (s), 707 (s), 618 (m), 470 (m). HR-MS (TOF ES): calculated for $C_{13}H_{10}NS$ 212.0528, found 212.0533 (M+H+).

2-(4-Fluoro-3-(trifluoromethyl)phenyl)quinoline, (1j): off-white solid. Melting range 104-106 °C. Yield: 84% (244 mg, 0.84 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.45 (dd, *J* = 6.9, 2.3 Hz, 1H), 8.33 (ddd, *J* = 8.6, 4.8, 2.3 Hz, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.74 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.35 – 7.28 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 160.5 (dq, *J* = 257, 2 Hz, CF), 154.5 (C), 148.2 (C), 137.2 (CH), 136.0 (d, *J* = 4 Hz, C), 132.8 (d, *J* = 9 Hz, CH), 130.1 (CH), 129.7 (CH), 127.5 (CH), 127.2 (C), 126.8 (CH), 126.5 – 126.2 (m, CH), 122.6 (qd, *J* = 272, 2 Hz, CF_3), 118.8 (qd, *J* = 33, 13 Hz, C), 118.1 (CH), 117.3 (d, *J* = 21 Hz, CH). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -61.4 (d, *J* = 12 Hz, CF_3), -114 (m). IR (neat) v/cm^{-1}: 3080 (w), 1597 (m), 1499 (m), 1290 (m), 1260 (m), 1242 (m), 1111 (s), 1050 (m), 812 (s), 767 (m), 682 (m). HR-MS (TOF ES): calculated for $C_{16}H_{10}F_4N$ 292.0744, found 292.0745 (M+H+). X-ray data (CCDC2013441): for $C_{16}H_9NF_4$; P21/n, α = 90, β = 101.674(2), γ = 90, a = 7.0848(1), b = 11.7942(2), c = 14.9556(2).

2-(5-Methylfuran-2-yl)quinoline, (1k): off-white solid. Melting range 119-122 °C. Yield: 90% (188 mg, 0.90 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$)

δ/ppm 8.06 – 8.12 (m, 2H), 7.70- 7.80 (m, 2H), 7.66 (ddd, *J* = 8.6, 6.9, 1.4 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.10 (d, *J* = 3.3 Hz, 1H), 6.18 – 6.15 (m, 1H), 2.44 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 154.5 (C), 152.1 (C), 149.2 (C), 148.1 (C), 136.4 (CH), 129.7 (CH), 129.3 (CH), 127.5 (CH), 126.9 (C), 125.8 (CH), 117.3 (CH), 111.5 (CH), 108.6 (CH), 14.0 (CH_3). IR (neat) v/cm^{-1}: 3061 (w), 1593 (m), 1540 (m), 1422 (m), 1201 (m), 1131 (m), 1080 (m), 1014 (s), 832 (s), 795 (s), 766 (s). HR-MS (TOF ES): calculated for $C_{14}H_{12}NO$ 210.0913, found 210.0915 (M+H+).

2-(Benzo[d][1,3]dioxol-5-yl)quinoline, (1l): off-white solid. Melting range 91-93 °C. Yield: 93% (231 mg, 0.93 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.15 – 8.10 (m, 2H), 7.77 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.74 (d, *J* = 1.8 Hz, 1H), 7.69 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.64 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.48 (ddd, *J* = 7.9, 6.7, 1.2 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.02 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 156.6 (C), 148.8 (C), 148.4 (C), 148.2 (C), 136.6 (CH), 134.1 (C), 129.6 (CH), 129.5 (CH), 127.4 (CH), 127.0 (C), 126.0 (CH), 121.7 (CH), 118.6 (CH), 108.4 (CH), 107.9 (CH), 101.3 (CH_2). IR (neat) v/cm^{-1}: 2893 (m), 1594 (s), 1556 (m), 1486 (s), 1443 (s), 1354 (m), 1290 (m), 1251 (s), 1034 (s), 930 (s), 799 (s), 742 (s). HR-MS (TOF ES): calculated for $C_{16}H_{12}NO_2$ 250.0863, found 250.0867 (M+H+).

4-(2-(4-Methoxyphenyl)quinolin-6-yl)morpholine (1m): light brown powder. Yield: 87% (279 mg, 0.87 mmol). ^{1}H-NMR (600 MHz, $CDCl_3$) δ/ppm 8.09 (d, *J* = 8.6 Hz, 2H), 8.03 (app. dd, *J* = 8.9, 4.1 Hz, 2H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.47 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.05 – 7.01 (m, 3H), 3.93 – 3.90 (m, 4H), 3.87 (s, 3H), 3.30 – 3.28 (m, 4H). ^{13}C-NMR (150 MHz, $CDCl_3$) δ/ppm 160.5 (C), 154.5 (C), 148.9 (C), 143.9 (C), 135.4 (CH), 132.5 (C), 130.3 (CH), 128.5 (2CH), 127.9 (C), 122.1 (CH), 118.9 (CH), 114.2 (2CH), 108.9 (CH), 66.9 (2CH_2), 55.4 (CH_3), 49.5 (2CH_2). IR (neat) v/cm^{-1}: 2956 (w), 2855 (m), 1669 (m), 1595 (s), 1512 (m), 1495 (m), 1449 (m), 1247 (s), 1226 (s), 1167 (s), 1116 (s), 1024 (s), 826 (s), 810 (s). HR-MS (TOF ES+) calculated for $C_{20}H_{21}N_2O_2$ 321.1603, found 321.1601 (M+H$^+$).

2-(2-Fluoro-4-methoxyphenyl)-6-(2,2,2-trifluoroethoxy)quinoline (1n): colourless solid. Melting range 113-115 °C. Yield: 84% (295 mg, 0.84 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.10 – 8.04 (m, 3H), 7.85 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.42 (dd, *J* = 9.2, 2.9 Hz, 1H), 7.11 (d, *J* = 3.0 Hz, 1H), 6.86 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.72 (dd, *J* = 13.1, 2.5 Hz, 1H), 4.48 (q, *J* = 8.1 Hz, 2H), 3.86 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 161.7 (d, *J* = 11 Hz, C), 161.5 (d, *J* = 249 Hz, CF), 155.2 (C), 152.5 (C), 144.9 (C), 135.0 (CH), 131.9 (d, *J* = 5 Hz, CH), 131.6 (CH), 127.5 (C), 123.2 (q, *J* = 277 Hz, CF_3), 122.8 (d, *J* = 9 Hz, CH), 121.7 (CH), 120.1 (d, *J* = 12 Hz, C), 110.8 (d, *J* = 3 Hz, CH), 106.9 (CH), 101.9 (d, *J* = 27 Hz, CH), 65.9 (q, *J* = 36 Hz, CH_2), 55.7 (CH_3). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -73.8 (t, *J* = 8.1 Hz), -114.6 (ddd, *J* = 12.7, 9.4, 2.7 Hz). IR (neat) v/cm^{-1}: 2946 (w), 1625 (m), 1497 (m), 1284 (s), 1253 (m), 1225 (m), 1159 (s), 975 (m), 835 (s). HR-MS (TOF ES): calculated for $C_{18}H_{14}NO_2F_4$ 352.0961, found 352.0947 (M+H$^+$). X-ray data (CCDC2013439): for $C_{18}H_{13}NO_2F_4$; P-1, α = 86.5843(8), β = 79.7431(8), γ = 74.8033(8), a = 11.5995(1), b = 12.3325(1), c = 17.0643(2).

6-Phenyl-[1,3]dioxolo[4,5-g]quinoline (1o):[41] colourless solid. Yield: 88% (218 mg, 0.88 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.12 – 8.07 (m, 2H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.44 (s, 1H), 7.44 – 7.39 (m, 1H), 7.05 (s, 1H), 6.10 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 155.3 (C), 150.8 (C), 147.7 (C), 146.5 (C), 139.8 (C), 135.5 (CH), 128.9 (CH), 128.7 (2CH), 127.2 (2CH), 124.1 (C), 117.2 (CH), 106.2 (CH), 102.5 (CH), 101.6 (CH_2). IR (neat) v/cm^{-1}: 2904 (w), 1618 (w), 1489 (m), 1464 (s), 1230 (s), 1174 (m), 1038 (m), 956 (m), 860 (m), 756 (m). HR-MS (TOF ES): calculated for $C_{16}H_{12}NO_2$ 250.0868, found 250.0862 (M+H$^+$).

6-(Thiophen-2-yl)-[1,3]dioxolo[4,5-g]quinoline (1p):[41] colourless solid. Melting range 120-124 °C. Yield: 91% (230 mg, 0.91 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.91 (d, *J* = 8.6 Hz, 1H), 7.64 – 7.63 (m, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.40 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.36 (s, 1H), 7.11 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.00 (s, 1H), 6.08 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 150.9 (C), 150.4 (C), 147.6 (C), 146.3 (C), 145.5 (C), 135.3 (CH), 127.9 (CH), 127.7 (CH), 124.9 (CH), 124.0 (C), 115.8 (CH), 105.8 (CH), 102.7 (CH), 101.6 (CH2). IR (neat) v/cm^{-1}: 3068 (w), 2902 (w), 1617 (w), 1581 (w), 1499 (m), 1466 (s), 1439 (s), 1258 (m), 1240 (m), 1218 (m), 1173 (m), 1037 (m), 852 (m), 706 (m). HR-MS (TOF ES): calculated for $C_{14}H_{10}NO_2S$ 256.0427, found 256.0429 (M+H+).

General procedure for the preparation of tetrahydroquinolines 8a-c: The flow stream exiting the photochemical reactor (**1**, 100 mM EtOH, 1 mL/min) was continuously diluted by adding a with a stream of EtOAc (4 mL/min) via a T-piece. The resulting mixture was directed into a holding reservoir and pumped from this into an H-Cube™ Mini (1 mL/min) equipped with a catalyst cartridge containing 10% Pd/C (70 mm length, maintained at 50 °C). Upon evaporation of the volatile products **8a-c** were isolated and purified on silica (10% EtOAc/hexanes).

2-(tert-Butyl)-1,2,3,4-tetrahydroquinoline, (8a):[42] colourless oil. Yield: 77% (73 mg, 0.38 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.90 – 6.99 (m, 2H), 6.57 (td, *J* = 7.4, 1.2 Hz, 1H), 6.48 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.79 (s, 1H), 2.95 (dd, *J* = 10.9, 2.6 Hz, 1H), 2.86 – 2.76 (m, 1H), 2.72 (ddd, *J* = 16.1, 5.3, 2.7 Hz, 1H), 1.96 (ddt, *J* = 12.7, 5.4, 2.7 Hz, 1H), 1.64 – 1.54 (m, 1H), 0.96 (s, 9H). ^{13}C-NMR (100 MHz,) δ/ppm 145.4 (C), 128.9 (CH), 126.7 (CH), 121.5 (C), 116.7 (CH), 114.0 (CH), 60.9 (CH), 33.4 (C), 27.4 (CH_2), 26.0 (3CH_3), 23.1 (CH_2). IR (neat) v/cm^{-1}: 3420 (m), 2960 (s), 2868 (m), 1607 (m), 1504 (m), 1486 (s), 1311 (m), 1261 (m), 1116 (m), 744 (s). HR-MS (TOF ES): calculated for $C_{13}H_{20}N$ 190.1590, found 190.1590 (M+H+).

2-Phenyl-1,2,3,4-tetrahydroquinoline, (8b):[42] colourless oil. Yield: 86% (90 mg, 0.43 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.43 – 7.34 (m, 4H), 7.33 – 7.27 (m, 1H), 7.00 – 7.09 (m, 2H), 6.70 – 6.64 (m, 1H), 6.58 – 6.53 (m, 1H), 4.45 (dd, *J* = 9.4, 3.4 Hz, 1H), 4.04 (s, 1H), 2.94 (ddd, *J* = 16.2, 10.6, 5.5 Hz, 1H), 2.75 (dt, *J* = 16.3, 4.8 Hz, 1H), 2.19 – 2.09 (m, 1H), 2.07 – 1.96 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 144.8 (C), 144.7 (C), 129.3 (CH), 128.6 (2CH), 127.4 (CH), 126.9 (CH), 126.5 (2CH), 120.9 (C), 117.2 (CH), 114.0 (CH), 56.3 (CH), 31.0 (CH_2), 26.4 (CH_2). IR (neat) v/cm^{-1}: 3400 (w), 3024 (w), 2921 (w), 2840 (w), 1606 (m), 1478 (s), 1308 (m), 1272 (m), 1251 (m), 1111 (m), 743 (s), 714 (s). HR-MS (TOF ES): calculated for $C_{15}H_{16}N$ 210.1277, found 210.1279 (M+H+).

2-(2-Fluorophenyl)-1,2,3,4-tetrahydroquinoline, (8c):[43] colourless oil. Yield: 90% (163 mg, 0.72 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.46 (td, *J* = 7.7, 1.8 Hz, 1H), 7.26 – 7.20 (m, 1H), 7.10 (td, *J* = 7.4, 1.3 Hz, 1H),

7.06 – 6.97 (m, 3H), 6.65 (td, *J* = 7.4, 1.3 Hz, 1H), 6.56 (dd, *J* = 7.9, 1.3 Hz, 1H), 4.84 (dd, *J* = 8.1, 3.6 Hz, 1H), 3.98 (s, 1H), 2.88 (ddd, *J* = 15.4, 9.4, 5.3 Hz, 1H), 2.68 (dt, *J* = 16.4, 5.4 Hz, 1H), 2.16 (dtd, *J* = 12.9, 5.5, 3.4 Hz, 1H), 2.07 – 1.94 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 160.0 (d, *J* = 246 Hz, CF), 144.5 (C), 131.6 (d, *J* = 14 Hz, C), 129.3 (CH), 128.6 (d, *J* = 8 Hz, CH), 127.8 (d, *J* = 5 Hz, CH), 126.9 (CH), 124.2 (d, *J* = 4 Hz, CH), 120.8 (C), 117.3 (CH), 115.3 (d, *J* = 23 Hz, CH), 114.0 (CH), 48.7 (d, *J* = 3 Hz, CH), 28.8 (CH_2), 25.7 (CH_2). ^{19}F-NMR (376 MHz, $CDCl_3$) δ/ppm -120.3. IR (neat) ν/cm^{-1}: 3407 (w), 3017 (w), 2927 (w), 1607 (m), 1585 (m), 1483 (s), 1311 (m), 1273 (m), 1230 (m), 750 (s). HR-MS (TOF ES): calculated for $C_{15}H_{15}FN$ 228.1183, found 228.1182 (M+H+).

Procedures for the preparation of galipinine 11-14: A solution of amine **10** (100 mM EtOH) was prepared and pumped through the UV LED unit (15 min residence time, ~30 °C, 75 W power) producing quinoline **11** as a ~7:1 mixture of alkene isomers.

2-(2-(Benzo[d][1,3]dioxol-5-yl)vinyl)quinoline, (alkene mixture, 11 (major isomer)): yellow oil. Yield: 90% (246 mg, 0.9 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.04 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.73 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.68 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 1H), 6.87 – 6.78 (m, 3H), 6.76 (d, *J* = 12.5 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 5.92 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 157.0 (C), 148.2 (C), 147.5 (C), 147.4 (C), 135.3 (CH), 134.1 (CH), 130.5 (C), 129.7 (CH), 129.5 (CH), 129.1 (CH), 127.5 (CH), 126.9 (C), 126.3 (CH), 123.6 (CH), 122.2 (CH), 109.2 (CH), 108.2 (CH), 101.0 (CH_2). HR-MS (TOF ES): calculated for $C_{18}H_{14}NO_2$ 276.1019, found 276.1021 (M+H+).

After continuously diluting the above reaction mixture (**11**, 100 mM EtOH, 1 mL/min) with a stream of EtOAc (4 mL/min) the resulting mixture was directed into a holding reservoir and pumped from this into an H-Cube™ Mini (1 mL/min) equipped with a catalyst cartridge containing 10% Pd/C (maintained at 50 °C). Upon evaporation of the volatiles product **12** was isolated and purified on silica (10% EtOAc/hexanes).

2-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)quinoline, (12):[41] colourless oil. Yield: 88% (244 mg, 0.88 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 8.07 – 8.00 (m, 2H), 7.76 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.68 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.20 (d, *J* = 8.3 Hz, 1H), 6.74 (d, *J* = 1.7 Hz, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.66 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.90 (s, 2H), 3.23 (dd, *J* = 9.5, 6.3 Hz, 2H), 3.07 (dd, *J* = 9.5, 6.5 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 161.7 (C), 148.0 (C), 147.5 (C), 145.7 (C), 136.2 (CH), 135.3 (C), 129.4 (CH), 128.9 (CH), 127.5 (CH), 126.8 (C), 125.8 (CH), 121.5 (CH), 121.3 (CH), 109.0 (CH), 108.1 (CH), 100.7 (CH_2), 41.2 (CH_2), 35.6 (CH_2). IR (neat) ν/cm^{-1}: 3042 (w), 2893 (m), 1600 (m), 1502 (s), 1488 (s), 1442 (m), 1244 (s), 1039 (s), 929 (m), 815 (m). HR-MS (TOF ES): calculated for $C_{18}H_{16}NO_2$ 278.1176, found 278.1176 (M+H+).

When adding 2 equivalents of HOAc in the diluting stream (EtOAc) in the above procedure, tetrahydroquinoline **13** was obtained as the hydrogenation product after purification on silica (10% EtOAc/hexanes). Further addition of 2 equivalents of formaldehyde (aqueous formalin) to the EtOAc solution and increasing the temperature of the Pd/C cartridge to 70 °C rendered racemic galipinine **14**, which was isolated in pure form after silica chromatography (5% EtOAc/hexanes).

2-(2-(Benzo[d][1,3]dioxol-5-yl)ethyl)-1,2,3,4-tetrahydroquinoline, (13):[42] colourless oil. Yield: 77% (215 mg, 0.77 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 6.99 – 6.90 (m, 2H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.68 (d, *J* = 1.7 Hz, 1H), 6.64 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.58 (td, *J* = 7.4, 1.2 Hz, 1H), 6.46 – 6.41 (m, 1H), 5.91 (s, 2H), 3.74 (s, 1H), 3.27 (dtd, *J* = 9.4, 6.3, 3.0 Hz, 1H), 2.75 (tp, *J* = 16.5, 5.2 Hz, 2H), 2.67 – 2.60 (m, 2H), 1.97 (dddd, *J* = 12.9, 5.5, 4.4, 3.0 Hz, 1H), 1.81 – 1.72 (m, 2H), 1.64 (dddd, *J* = 12.8, 10.4, 9.2, 5.6 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 147.6 (C), 145.7 (C), 144.5 (C), 135.6 (C), 129.2 (CH), 126.7 (CH), 121.3 (C), 121.0 (CH), 117.0 (CH), 114.1 (CH), 108.7 (CH), 108.2 (CH), 100.8 (CH_2), 50.9 (CH), 38.5 (CH_2), 31.8 (CH_2), 27.9 (CH_2), 26.2 (CH_2). IR (neat) ν/cm^{-1}: 3390 (w), 2922 (m), 1606 (m), 1488 (s), 1444 (m), 1246 (s), 1038 (s), 928 (m), 810 (m), 749 (m). HR-MS (TOF ES): calculated for $C_{18}H_{20}NO_2$ 282.1489, found 282.1489 (M+H+).

Galipinine (rac), (14):[44] colourless oil. Yield: 72% (105 mg, 0.36 mmol). ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm 7.06 (t, *J* = 8.2 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 1.7 Hz, 1H), 6.61 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.60 – 6.54 (m, 1H), 6.51 (d, *J* = 8.1 Hz, 1H), 5.90 (s, 2H), 3.25 (dq, *J* = 8.5, 4.2 Hz, 1H), 2.89 (s, 3H), 2.82 (ddd, *J* = 17.6, 11.6, 6.7 Hz, 1H), 2.67 (dt, *J* = 15.1, 3.6 Hz, 1H), 2.64 – 2.57 (m, 1H), 2.48 (ddd, *J* = 13.9, 10.0, 6.6 Hz, 1H), 1.95 – 1.81 (m, 3H), 1.74 – 1.62 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ/ppm 147.6 (C), 145.6 (C), 145.3 (C), 135.8 (C), 128.6 (CH), 127.1 (CH), 121.7 (C), 120.9 (CH), 115.4 (CH), 110.6 (CH), 108.7 (CH), 108.1 (CH), 100.7 (CH_2), 58.2 (CH), 38.0 (CH_3), 33.1 (CH_2), 32.0 (CH_2), 24.3 (CH_2), 23.5 (CH_2). IR (neat) ν/cm^{-1}: 2937 (m), 2889 (m), 1602 (m), 1501 (s), 1442 (m), 1245 (s), 1040 (m), 937 (m), 809 (m), 746 (m). HR-MS (TOF ES): calculated for $C_{19}H_{22}NO_2$ 296.1645, found 296.1635 (M+H+).

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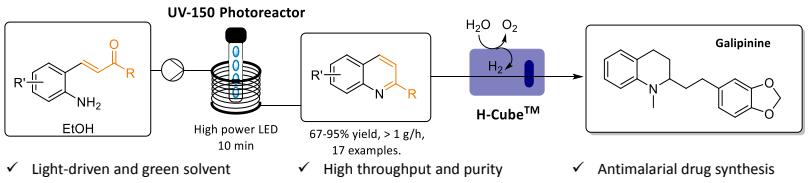

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