DOI: 10.1002/adsc.201600735

Advanced Synthesis & Catalysis

One-Pot Directing Group Formation/C–H Bond Functionalization *via* Copper(I) and Ruthenium(II) Catalysis

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Received: July 10, 2016; Revised: September 22, 2016; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201600735.

Abstract: A copper(I)-catalyzed oxidation leading to the formation of 2-pyridyl ketone directing groups has been efficiently coupled with a ruthenium(II)-catalyzed C(sp^2)–H bond arylation transformation without performing any intermediate work-up. This sustainable approach was further extended to sequential three-step transition metal-catalyzed transformations in which up to four new bonds (C–O, C–C, C–H and O–H) are formed in a one-pot fashion. This is the first example in which two different transition metal catalysts are sequentially employed for the directing group formation and the C–H bond functionalization, respectively.

Keywords: C–H bond activation; copper; oxidation; pyridine; ruthenium

Introduction

Progress in C–H bond functionalization has evolved in such a way that nowadays multiple catalytic systems are able to perform extremely selective transformations in a very efficient manner.[1] Most of the catalysts employed in C–H bond functionalization reactions are derived from transition metals such as rhodium, palladium, ruthenium and more recently, cobalt.[2] Since the ultimate goal of catalysis is the straightforward production of complex molecules from readily available starting materials, C–H bond functionalization reactions have been successfully coupled with other chemical transformations without the isolation of intermediates.[3,4] Such a one-pot approach is particularly appealing since it reduces the time and costs devoted to work-up and purification processes, and also diminishes chemical wastes.[5]

In this context, one of the major drawbacks in the field of transition metal-catalyzed C–H bond functionalization is the synthetic effort required for the introduction of the directing group. Interestingly, the directing group synthesis is known to be compatible, under certain circumstances, with the reaction conditions imposed by the further C–H bond transformation, which enables one-pot processes involving these two important transformations (Figure 1). As such, C–H bond functionalization reactions have been proven compatible with purely (non-catalyzed) organic transformations that generate the directing group [Eq. (1), Figure 1].[6] From an atom- and cost-economy point of view, an interesting alternative is the utilization of a single transition metal catalyst for the formation of the directing group and for the C–H bond functionalization step [Eq. (2), Figure 1). This strategy has been elegantly demonstrated for ruthe-

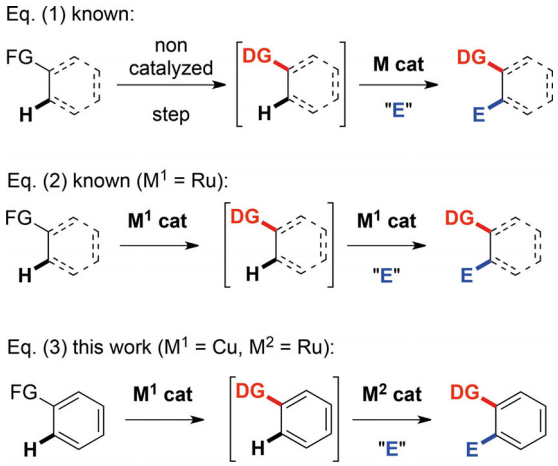
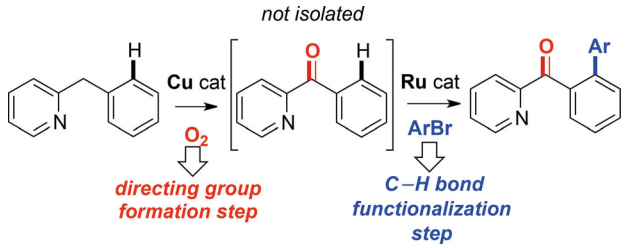


Figure 1. One-pot catalysis involving directing group formation and transition metal-catalyzed C–H bond functionalization. FG = functional group, DG = directing group, E = coupling partner. Non-isolated intermediates are indicated in brackets.

nium(II) catalysts where isomerization or dehydrogenation transformations are followed by C(sp^2)–H and C(sp^3)–H bond activation reactions.[7] Surprisingly, the one-pot utilization of two different transition metal catalysts for each step (directing group formation and C–H bond activation) has received no attention as yet [Eq. (3), Figure 1].[8] Overcoming such a challenge clearly offers exponential possibilities towards chemical diversity since multiple catalysts compatible with C–H bond activation could be employed for different chemical transformations in a one-pot fashion. Herein, we present such an approach by means of a one-pot chemical transformation comprising two metal-catalyzed steps without the isolation of intermediates. It involves (i) a copper(I)-catalyzed oxidation to form a directing group followed by (ii) a ruthenium(II)-catalyzed C(sp^2)–H bond functionalization [Eq. (3), Figure 1).



Scheme 1. One-pot directing group formation and C(sp^2)–H bond functionalization involving two distinct transition metal catalysts.

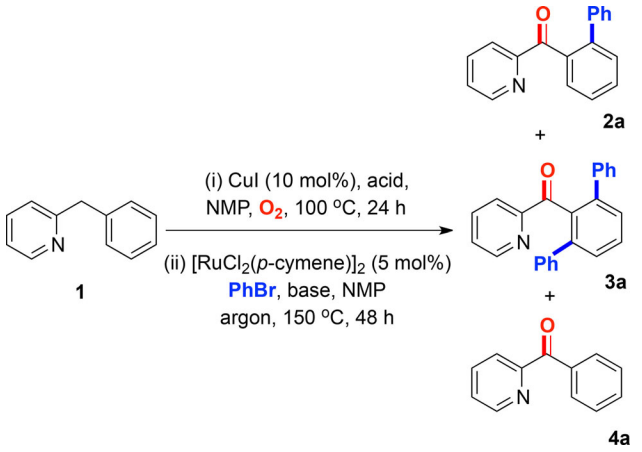
For this study, we turned our attention to the reactivity of rather flexible 2-benzylpyridine derivatives (Scheme 1), which are known not to follow C(sp^2)–H bond activation reactions.[9a] On the other hand, more rigid 2-benzoylpyridine derivatives[9a] have been recently found to participate in ruthenium(II)-catalyzed C(sp^2)–H bond functionalization reactions *via* six-membered ruthenacycles.[9] Unfortunately, the introduction of the 2-pyridyl ketone directing group requires the utilization of over-stoichiometric amounts of elemental sulfur (S_8) during their synthesis, which makes this strategy not suitable from an atom-economy point of view.[10] Recently, the groups of Maes and Kappe have independently reported very efficient methods for the oxidation of a large variety of nitrogen-containing derivatives with copper(I) catalysts in the presence of carboxylic acids and environmentally friendly molecular oxygen.[11] Since copper salts and carboxylic acids are in some cases necessary, thus compatible, for metal-catalyzed C–H bond functionalization reactions,[12] we anticipated that two reactions involving two different transition metal catalysts (copper and ruthenium) could be coupled in a one-pot fashion without the isolation of 2-benzoylpyridine intermediates (Scheme 1). This approach would represent a sustainable synthesis of highly functionalized 2-benzoylpyridine derivatives, which are key motifs relevant for biological applications[13] as well as for the design of metal-coordinating ligands.[14] It is relevant to mention that a few reverse reaction sequences involving first C(sp^2)–H bond activation catalyzed by ruthenium(II) have been described.[15]

Results and Discussion

Initially, we focused on the search for the optimal reaction conditions to obtain **2a** from **1** (Table 1). Although the copper-catalyzed oxidation of 2-benzylpyridines (**1**) was reported to take place in DMSO (dimethyl sulfoxide) as solvent,[11] this solvent was found inappropriate for the ruthenium-catalyzed C–H bond functionalization step (0% formation of **2a**; Table 1, entry 1). Interestingly, we found that the oxidation step successfully took place (almost full conversion of **1** was observed in all cases; Table 1, entries 2–10) with NMP (*N*-methyl-2-pyrrolidone) as solvent at a high concentration of 1 M (*versus* the previously reported 0.5 M).[11] This finding is relevant since the best results so far obtained for the C–H bond functionalization of 2-benzoylpyridine derivatives (such as **4a**) required the exclusive use of NMP as solvent.[9a] The influence of the carboxylic acid in the first step was first evaluated keeping the same reaction conditions in the second step (see reaction conditions in Table 1). When acetic acid was employed, only 7% of the targeted **2a** was obtained (Table 1, entry 2); whereas 18% of **2a** was formed using 2-mesitylcarboxylic acid ($MesCO_2H$), however, 16% of **1** remained unreacted (Table 1, entry 3). A similar result was obtained with 1-$AdCO_2H$ which provided **2a** in a low 20% yield (Table 1, entry 4). Benzoic acid was the most suitable carboxylic acid leading to full conversion of **1** and 69% of isolated **2a** after column chromatography (Table 1, entry 5). The base employed in the second step had an important impact (Table 1, entries 5–9) and among the different bases, the best results were found employing K_2CO_3 (Table 1, entry 5).

As such, the best conditions found for the one-pot directing group formation/C–H bond functionalization of **1** required an atmosphere of O_2, 10 mol% of CuI, benzoic acid (1 equivalent) and NMP as solvent at 100 °C for 24 h in the first step. The second step (C–H bond functionalization) was carried out at 150 °C for 48 h under an inert atmosphere after adding to the reaction mixture 5 mol% of $[RuCl_2(p\text{-cymene})]_2$, K_2CO_3 (4 equivalents), phenyl bromide (1.5 equivalents) and NMP (which was introduced to dilute the reaction mixture at 0.25 M). Under these optimized reaction conditions, full conversion of **1** was reached and **2a** was isolated in 69% yield in a one-pot fashion (Table 1, entry 5). Longer reaction

Table 1. Optimization of the one-pot directing group formation/C–H bond functionalization of **1**.[a]



Entry	Acid	Base	Conversion[b]	**2a**:**3a**:**4a** [%][c]
1[d]	$PhCO_2H$	K_2CO_3	>99	0:0:100
2	AcOH	K_2CO_3	98	7:0:91
3	$MesCO_2H$	K_2CO_3	84	18:0:66
4	1-$AdCO_2H$	K_2CO_3	>99	20:0:80
5	$PhCO_2H$	K_2CO_3	>99	72:8:20 (69)
6	$PhCO_2H$	Na_2CO_3	>99	33:0:67
7	$PhCO_2H$	Cs_2CO_3	>99	3:0:97
8	$PhCO_2H$	$KHCO_3$	>99	41:5:54
9	$PhCO_2H$	$NaHCO_3$	>99	33:1:66
10[e]	$PhCO_2H$	K_2CO_3	>99	0:0:100
11[f]	$PhCO_2H$	K_2CO_3	<5[g]	0:0:0
12[h]	$PhCO_2H$	K_2CO_3	92	13:0:79

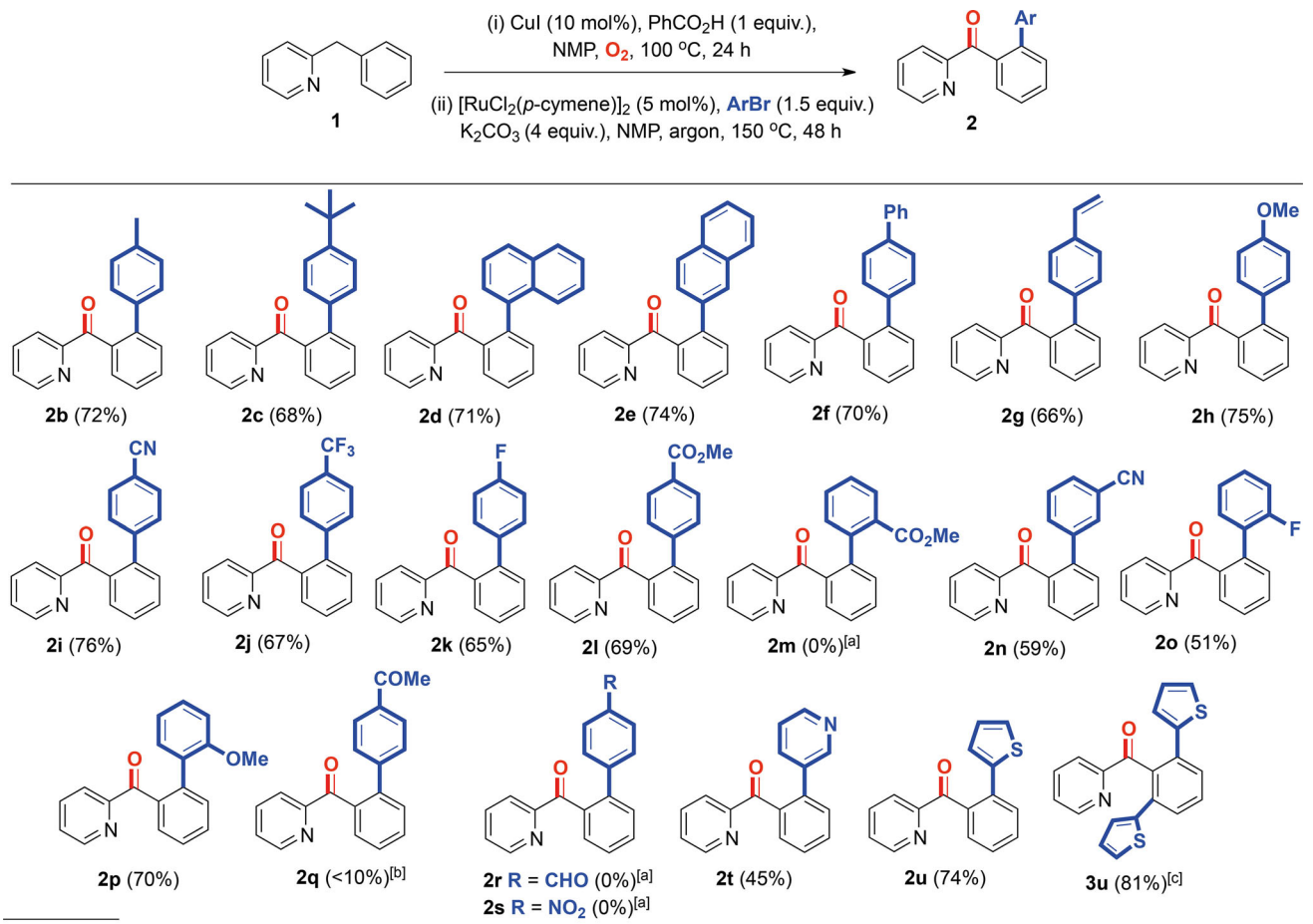
[a] *Reaction conditions:* (i) **1** (0.5 mmol), CuI (0.05 mmol), acid (0.5 mmol), NMP (0.5 mL), O_2, 100 °C, 24 h; (ii) base (2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol), PhBr (0.75 mmol), NMP (1.5 mL), argon, 150 °C, 48 h.
[b] Conversion determined by GC-MS analysis and ^{1}H NMR spectroscopy.
[c] In parenthesis, isolated yield of **2a**.
[d] DMSO was used instead of NMP.
[e] Second step was performed under an oxygen atmosphere.
[f] First step was performed under an argon atmosphere.
[g] Arylation of **1** was observed in traces amounts.
[h] DMA was used instead of NMP.

times, temperature variation and changing the number of equivalents of acid and base in each step did not provide significant variations of the overall conversion and selectivity. Additional control experiments performing both steps simultaneously under oxygen conditions revealed the exclusive formation of **4a** (Table 1, entry 10); and under argon conditions <5% arylation of **1** was observed (Table 1, entry 11). Other polar solvents such as DMA (*N*,*N*-dimethylacetamide) led to low reactivity in the second step (13% of **2a**, Table 1, entry 12).

With the optimized conditions in hand, different aryl bromides were reacted with benzylpyridine **1** following the one-pot directing group formation/C–H bond functionalization transformation (Figure 2). 4-Alkyl- and 4-aryl-substituted compounds **2b**–**2g** were obtained in good isolated yields around 70%. The one-pot transformation is also compatible with 4-OMe (**2h**), 4-CN (**2i**), 4-CF_3 (**2j**), 4-F (**2k**) and 4-CO_2Me (**2l**) groups. Unfortunately, 2-CO_2Me-substituted **2m** was not formed. In this case, dehalogenation of the corresponding aryl bromide was observed by GC-MS analysis and ^{1}H NMR spectroscopy. On the other hand, 3-CN groups were also well tolerated (**2n**). 2-F-substituted **2o** was obtained with a poor 51% yield, whereas 2-OMe-substituted **2p** gave a higher yield (70%). This protocol unfortunately gave poor yields in the case of ketones (**2q**); and it was not compatible with aldehyde (**2r**) and nitro (**2s**) functional groups (decomposition of the aryl bromide employed in the second step was observed by GC-MS analysis). Interestingly, heteroaromatic derivatives were also synthesized by the one-pot procedure. For example, 3-pyridyl-substituted **2t** and 2-thiophene-substituted **2u** were isolated in 45% and 74% yield, respectively. Additionally, if more than two equivalents of 2-bromothiophene were employed in the second step, a high yield of the corresponding difunctionalized compound **3u** (81%) was obtained. The molecular structures of **2a**, **2k** and **2u** were further confirmed by X-ray diffraction studies (Figure 3).

Next, the one-pot directing group formation/C–H bond functionalization of various substituted benzylpyridines (**5a**–**5e**) was attempted to demonstrate the feasibility of the one-pot approach (Figure 4).[11b,16] In all cases full conversions were observed, and the efficiency of the methodology was governed by the second step, that is, the C–H bond functionalization step. As such, the sterically demanding 2-Me-substituted **5a** was readily oxidized in the first step, however the C–H bond functionalization did not proceed so well (30% yield), in line with previous findings.[9a] The 4-substituted benzylpyridines **5b**–**5d** efficiently gave rise to the corresponding mono-arylated benzoylpyridines **6b**, **6c** and **6d** in 71%, 55% and 67% isolated yields, respectively. The 3-CN-susbstituted benzylpyridine **5e** also reacted to form **6e** in 60% yield. When 2.5 equivalents were employed in the second step, benzylpyridine derivatives **5c** and **5d** provided the corresponding diphenylated benzoylpyridines **7c** and **7d** in 84% and 78% yields, respectively.

Finally, in order to further show the potential of this unique protocol, we explored a one-pot three-step oxidation/C–H bond functionalization/hydrogenation transformation. Inspired by the ability of some ruthenium catalysts to promote hydrogenation reactions after olefin metathesis,[17] we envisaged that a similar stepwise procedure might be possible in our case. As such, we performed in a one-pot fashion (i) the copper-catalyzed oxidation followed by (ii)



[a] ArBr decomposition.
[b] Not isolated, yield estimated by GC-MS analysis and ^{1}H NMR spectroscopy.
[c] 2.5 equivalents of aryl bromide were employed in the second step.

Figure 2. Substrate scope and limitations of the one-pot directing group formation/C–H bond functionalization. In parenthesis, isolated yields are displayed.

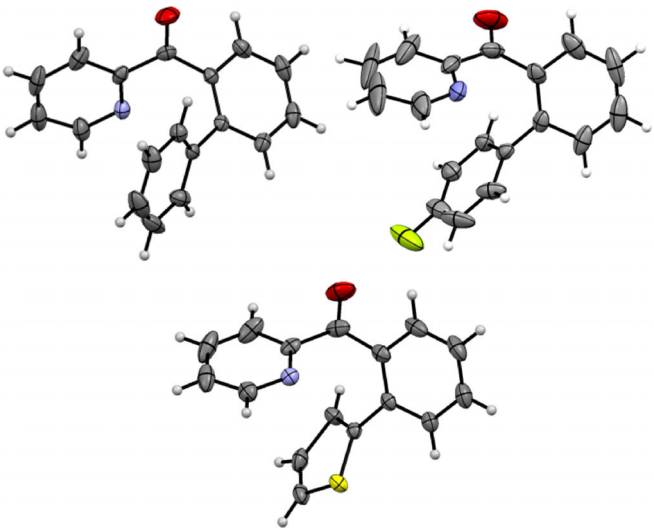
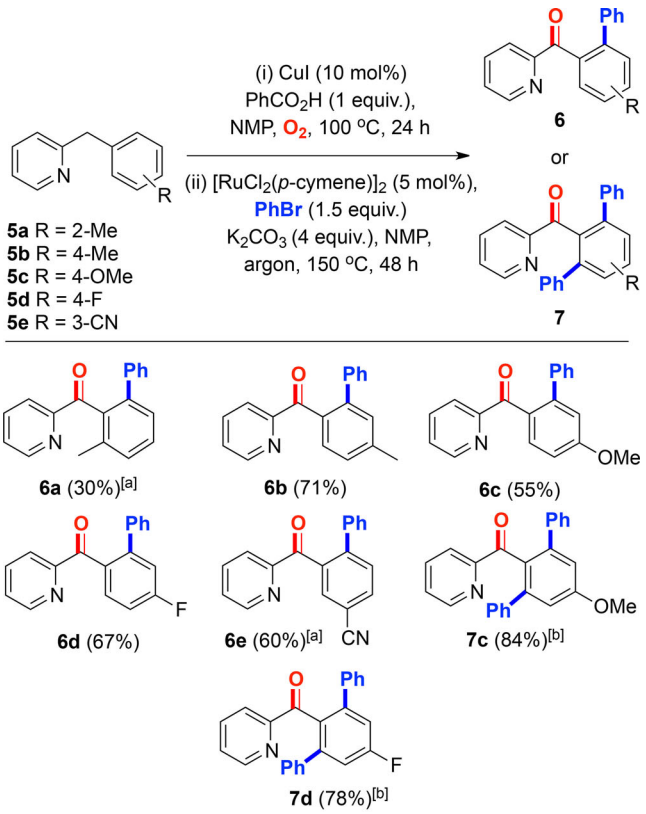


Figure 3. X-ray molecular structures of **2a** (*top, left*), **2k** (*top, right*) and **2u** (*bottom*).

a ruthenium-catalyzed C–H bond functionalization and (iii) a final hydrogenation step utilizing molecular hydrogen and the remaining metal catalysts (Scheme 2). In this manner, **8** was isolated in 64% yield starting from 2-benzylpyridine **1**, showing that up to three distinct catalysts {CuI for oxidation, $[RuCl_2(p\text{-cymene})]_2$ for C–H bond functionalization to introduce a *p*-styrene moiety and [Ru-H] species for alkene hydrogenation} can be coupled in a one-pot fashion. Under these conditions (1 bar of H_2 in the third step), the remaining ruthenium species arising from the second step selectively hydrogenated the alkene double bond in the third step, leaving the (2-pyridyl) ketone directing group intact. Alternatively, when the hydrogenation step was performed at higher pressure (40 bar of H_2), hydrogenation of the ketone occurred, as exemplified in the synthesis of **9** in an isolated yield of 55% (Scheme 2). These two examples show that, in a one-pot fashion, post-functionalization is doable either in the coupling partner introduced at the C–H bond functionalization step (**8**) or



[a] Not isolated, yield estimated by GC-MS analysis and ^{1}H NMR spectroscopy.

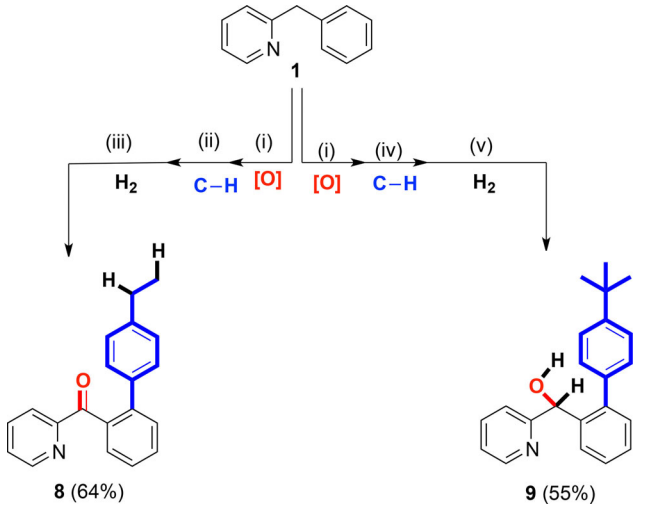
[b] 2.5 equivalents of bromobenzene were employed in the second step.

Figure 4. One-pot directing group formation/C–H bond functionalization from substituted 2-benzylpyridines **5a**–**5e**. In parenthesis, isolated yields are displayed.

within the directing group introduced in the first step (**9**). It is worth noting that compounds bearing the (2-pyridin-2-yl)methanol fragment – as it is the case in **9** – are key molecules for medicinal applications[18] and the presented methodology enables their synthesis in a more sustainable and versatile manner.

Conclusions

In summary, we have successfully developed a one-pot procedure involving two transition metal-catalyzed reactions in which one of them comprises a sensitive C–H bond activation step. In this case, a copper(I)-catalyzed oxidation forms a 2-pyridyl ketone directing group that is stepwise followed by a ruthenium(II)-catalyzed C–H bond functionalization step. As such, new C=O and C–C bonds are efficiently formed in a one-pot fashion employing 2-benzylpyridine derivatives as substrates. The potential of this approach relies on the ability to employ multiple transition metal catalysts compatible with C–H bond functionalization reactions without isolation of intermediates and reducing the costs devoted to work-up operations. This was ultimately exemplified with one-pot three-step transition metal-catalyzed transformations leading to highly functionalized molecules with formation of up to four new bonds in a straightforward manner. Complex catalytic systems inspired from the presented one-pot approach are expected to provide new tools to pave the way towards more sustainable transformations involving transition metal-catalyzed C–H bond functionalization.



Scheme 2. One-pot directing group formation/C–H bond functionalization/hydrogenation employing three distinct transition metal catalysts. In parenthesis, isolated yields are displayed (no work-up was performed between each step). *Reaction conditions:* (i) **1** (0.5 mmol), CuI (0.05 mmol), benzoic acid (0.5 mmol), NMP (0.5 mL), O_2, 100 °C, 24 h; (ii) K_2CO_3 (2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol), 4-bromostyrene (0.75 mmol), NMP (1.5 mL), argon, 150 °C, 48 h; (iii) H_2 (1 bar), 150 °C, 12 h; (iv) K_2CO_3 (2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol), 1-bromo-4-*tert*-butylbenzene (0.75 mmol), NMP (1.5 mL), argon, 150 °C, 48 h; (v) H_2 (40 bar), 150 °C, 12 h.

Experimental Section

General Methods

All reagents were obtained from commercial sources and used as supplied. NMP was distilled under reduced pressure and stored over molecular sieves under an argon atmosphere. 2-Benzylpyridines **5a–5e** were prepared according to literature procedures.[11b,16] Technical grade petroleum ether (40–60 °C) and ethyl acetate were used for column chromatography. $CDCl_3$ was stored under nitrogen over molecular sieves. NMR spectra were recorded on an AVANCE III 400 spectrometer. ^{1}H NMR spectra were referenced to residual protiated solvent ($\delta = 7.26$ ppm for $CDCl_3$) and ^{13}C chemical shifts are reported relative to deuterated solvents ($\delta =$ 77.2 ppm for $CDCl_3$). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet,

and br. for broad. GC-MS analyses were performed with a GCMS-QP2010S (Shimadzu) instrument with a GC-2010 equipped with a 30 m capillary column (Supelco, SLBTM-5 ms, fused silica capillary column, 30 m × 0.25 mm × 0.25 mm film thickness), which was used with helium as the vector gas. The following GC conditions were used: initial temperature 80 °C for 2 min, then rate 20 °C min^{-1} until 280 °C and 280 °C for 28 min. Melting points were performed on a LEICA VMHB Kofler system. HR-MS were recorded on a Waters Q-Tof 2 mass spectrometer at the corresponding facilities of the CRMPO, Centre Régional de Mesures Physiques de l'Ouest, Université de Rennes 1.

General Procedure for the One-Pot Directing Group Formation and C–H Bond Functionalization of 2-Benzylpyridines 1 and 5a–5e

CuI (0.05 mmol, 0.0095 g, 0.1 equiv.), benzoic acid (0.5 mmol, 0.061 g, 1 equiv.), 2-benzylpyridine derivatives (0.5 mmol, 1 equiv.) and NMP (0.5 mL) were introduced in a dry Schlenk tube and flushed with O_2 for 1 min. The Schlenk tube was connected to a balloon filled with O_2. The reaction mixture was stirred at 100 °C during 24 h. Then, the reaction mixture was cooled down to room temperature and flushed with vacuum/argon over 3–5 cycles. Under an argon atmosphere, K_2CO_3 (2 mmol, 0.276 g, 4 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol, 0.015 g, 0.05 equiv.), aryl bromide (0.75 mmol, 1.5 equiv.) and NMP (1.5 mL) were introduced. The reaction mixture was stirred at 150 °C for 48 h. The reaction mixture was diluted with dichloromethane and filtered over a pad of Celite. After solvent evaporation under vacuum, the desired product **2** (or **6**) was purified by silica gel column chromatography with a mixture of petroleum ether and ethyl acetate as the eluent.

2-Biphenyl 2-pyridyl ketone (2a): Colourless solid, yield: 89 mg (69%); mp 108–110 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.44 (d, 1H, J = 4.5 Hz), 7.82 (d, 1H, J = 8.1 Hz), 7.70–7.59 (m, 3H), 7.54–7.48 (m, 2H), 7.28–7.11 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.4, 154.6, 148.7, 141.9, 140.7, 138.4, 136.3, 130.9, 129.8, 129.3, 129.1, 128.0, 127.1, 127.0, 125.9, 123.7; GC: t_R = 13.1 min; MS (EI): m/z = 259 (M^+, 40), 230 (90), 181 (85), 152 (100), 78 (20), 51 (25); HR-MS (ESI): m/z = 282.0889, calcd. for $[M+Na]^+$ $C_{18}H_{13}NONa$: 282.08893 (0 ppm). Crystals suitable for single crystal X-ray diffraction studies were grown by slow diffusion of *n*-hexane into a concentrated solution of **2a** in ethyl acetate at room temperature.[19]

2-(*p*-Tolyl)phenyl 2-pyridyl ketone (2b): Colourless solid, yield: 98 mg (72%); mp 109–111 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.45 (d, 1H, J = 4.3 Hz), 7.81 (d, 1H, J = 7.7 Hz), 7.67–7.62 (m, 2H), 7.59–7.55 (m, 1H), 7.48–7.44 (m, 2H), 7.424–7.21 (m, 1H), 7.13 (d, 2H, J = 8.0 Hz), 6.96 (d, 2H, J = 7.7 Hz), 2.22 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.7, 154.8, 149.0, 142.1, 138.5, 138.0, 137.0, 136.5, 131.0, 130.0, 129.5, 129.1, 128.9, 127.0, 126.1, 124.0, 21.2; GC: t_R = 13.7 min; MS (EI): m/z = 273 (M^+, 60), 244 (100), 195 (88), 165 (55), 152 (75), 78 (20), 51 (20); HR-MS (ESI): m/z = 296.1051, calcd. for $[M+Na]^+$ $C_{19}H_{15}NONa$: 296.10513 (0 ppm).

2-(*p*-*tert*-Butylphenyl)phenyl 2-pyridyl ketone (2c): Colourless solid, yield: 107 mg (68%); mp 112–114 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.39 (d, 1H, J = 3.8 Hz), 7.73 (d, 1H, J = 7.7 Hz), 7.68 (d, 1H, J = 7.4 Hz), 7.59 (t, 2H, J = 7.4 Hz), 7.48 (t, 2H, 7.4 Hz), 7.14–7.16 (m, 5H), 1.20 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.8, 155.1, 150.1, 148.9, 142.2, 138.6, 137.9, 136.3, 131.1, 129.8, 129.5, 129.1, 127.1, 125.8, 125.0, 123.9, 34.5, 31.3; GC: t_R = 15.1 min; MS (EI): m/z = 315 (M^+, 60), 286 (80), 181 (45), 106 (45), 78 (100), 57 (80): HR-MS (ESI): m/z = 338.1524, calcd, for $[M+Na]^+$ $C_{22}H_{21}NONa$: 338.15208 (1 ppm).

2-(1-Naphthyl)phenyl 2-pyridyl ketone (2d): Colourless solid, yield: 110 mg (71%); mp 97–99 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.06 (d, 1H, J = 4.6 Hz), 7.83 (dd, 1H, J = 7.5 Hz, J = 1.3 Hz), 7.66–7.69 (m, 1H), 7.64 (dd, 1H, J = 7.3 Hz, J = 1.6 Hz), 7.60 (dd, 1H, J = 7.5 Hz, J = 1.4 Hz), 7.56–7.58 (m, 1H), 7.51 (dd, 1H, J = 7.4 Hz, J = 1.1 Hz), 7.37–7.40 (m, 2H), 7.34–7.36 (m, 2H), 7.18–7.25 (m, 2H), 6.90–6.93 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.1, 154.7, 148.0, 140.1, 139.8, 138.3, 135.8, 133.2, 131.6, 131.1, 130.6, 129.5, 128.0, 127.7, 127.5, 126.6, 125.8, 125.6, 125.1, 124.7, 122.7; GC: t_R = 16.5 min; MS (EI): m/z = 309 (M^+, 90), 280 (100), 231 (97), 202 (98), 101 (35), 78 (20), 51 (20); HR-MS (ESI): m/z = 332.1046, calcd. for $[M+Na]^+$ $C_{22}H_{15}NONa$: 332.10458 (0 ppm), m/z = 292.1119, calcd. for $[M-H_2O+H]^+$ $C_{22}H_{14}N$: 292.11207 (1 ppm).

2-(2-Naphthyl)phenyl 2-pyridyl ketone (2e): Colourless solid, yield: 114 mg (74%); mp 98–100 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.35 (d, 1H, J = 4.0 Hz), 7.77 (d, 1H, J = 8.0 Hz), 7.46–7.73 (m, 9H), 7.39–7.42 (m, 3H), 7.06 (ddd, 1H, J = 7.5 Hz, J = 4.8 Hz, J = 1.0 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.4, 154.6, 148.6, 141.8, 138.5, 138.2, 136.2, 132.8, 132.1, 130.9, 130.0, 129.5, 128.3, 127.9, 127.7, 127.4, 127.2, 127.1, 126.1, 125.9, 125.8, 123.5; GC: t_R = 17.6 min; MS (EI): m/z = 309 (M^+, 90), 280 (100), 231 (97), 202 (98), 101 (35), 78 (20), 51 (20); HR-MS (ESI): m/z = 332.1048, calcd. for $[M+Na]^+$ $C_{22}H_{15}NONa$: 332.10513 (1 ppm).

2-(*p*-Terphenyl 2-pyridyl ketone (2f): Colourless solid, yield: 117 mg (70%); mp 113–115 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.44 (d, 1H, J = 4.1 Hz), 7.83 (d, 1H, J = 7.8 Hz), 7.69 (d, 1H, J = 7.7 Hz), 7.59–7.65 (m, 2H), 7.52 (d, 2H, J = 7.2 Hz), 7.48–7.50 (m, 2H), 7.38–7.42 (m, 4H), 7.30–7.34 (m, 3H), 6.59 (ddd, 1H, J = 7.7 Hz, J = 4.6 Hz, J = 0.9 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.3, 154.6, 148.7, 141.5, 140.5, 139.7, 139.7, 138.3, 136.3, 130.9, 129.7, 129.5, 129.4, 128.7, 127.2, 127.1, 126.8, 126.7, 125.9, 123.7; GC: t_R = 21.5 min; MS (EI): m/z = 335 (M^+, 90), 306 (100), 257 (90), 228 (60), 152 (20), 78 (20), 51 (20); HR-MS (ESI): m/z = 358.1202, calcd. for $[M+Na]^+$ $C_{24}H_{17}NONa$: 358.12023 (0 ppm).

2-(*p*-Styryl)phenyl 2-pyridyl ketone (2g): Colourless solid, yield: 94 mg (66%); mp 108–110 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.43 (d, 1H, J = 4.7 Hz), 7.83 (d, 1H, J = 7.8 Hz), 7.64–7.67 (m, 2H), 7.59 (td, 1H, J = 7.6 Hz, J = 1.2 Hz), 7.45–7.50 (m, 2H), 7.22–7.24 (m, 1H), 7.20 (s, 4H), 6.59 (dd, 1H, J = 17.6 Hz, J = 10.9 Hz), 5.65 (d, 1H, J = 17.6 Hz), 5.18 (d, 1H, J = 10.9 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.3, 154.5, 148.8, 141.5, 140.2, 138.3, 136.4, 136.3, 136.3, 130.9, 129.7, 129.3, 129.2, 127.1, 126.0, 125.9, 123.8, 113.9 ppm. GC: t_R = 14.4 min. MS (EI): m/z = 285 (M^+, 80), 256 (100), 178 (75), 152 (35), 127 (20), 78 (20), 51 (20); HR-MS (ESI): m/z = 308.1051, calcd. for $[M+Na]^+$ $C_{20}H_{15}NONa$: 308.10458 (2 ppm); m/z = 268.1124, calcd. for $[M-H_2O+H]^+$ $C_{20}H_{14}N$: 268.11207 (1 ppm).

2-(*p*-Anisyl)phenyl 2-pyridyl ketone (2h): Colourless solid, yield: 108 mg (75%); mp 101–103 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.43 (d, 1H, J = 4.2 Hz), 7.79 (d, 1H, J = 7.7 Hz), 7.62–7.66 (m, 2H), 7.56 (td, 1H, J = 7.6 Hz, J = 1.2 Hz), 7.42–7.47 (m, 2H), 7.19–7.23 (m, 1H), 7.15 (d, 2H, J = 8.6 Hz), 6.68 (d, 2H, J = 8.6 Hz), 3.70 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.6, 158.7, 154.6, 148.7, 141.4, 138.2, 136.3, 133.1, 130.8, 130.2, 129.7, 129.2, 126.7, 125.9, 123.7, 113.5, 55.1; GC: t_R = 14.7 min; MS (EI): m/z = 289 (M^+, 90), 274 (5), 260 (80), 246 (10), 231 (100), 196 (10), 183 (15), 168 (50), 139 (70), 109 (30), 78 (20); HR-MS (ESI): m/z = 290.1198, calcd. for $[M+Na]^+$ $C_{19}H_{15}NO_2Na$: 290.11810 (6 ppm).

2-(*p*-Cyanophenyl)phenyl 2-pyridyl ketone (2i): Colourless solid, yield: 108 mg (76%); mp 109–111 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.44 (d, 1H, J = 4.5 Hz), 7.90 (d, 1H, J = 7.9 Hz), 7.73 (td, 1H, J = 7.7 Hz, J = 1.6 Hz), 7.67 (d, 1H, J = 7.6 Hz), 7.63 (td, 1H, J = 7.6 Hz, J = 1.1 Hz), 7.54 (td, 1H, J = 7.5 Hz, J = 0.8 Hz), 7.47 (d, 2H, J = 8.1 Hz), 7.43 (d, 1H, J = 7.9 Hz), 7.36 (d, 2H, J = 8.2 Hz), 7.29–7.32 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 197.4, 154.1, 148.8, 145.7, 140.1, 138.2, 136.7, 131.8, 131.1, 129.8, 129.7, 129.6, 128.1, 126.5, 123.8, 118.6, 110.8; GC: t_R = 15.0 min; MS (EI): m/z = 284 (M^+, 25), 255 (100), 206 (60), 178 (30), 151 (50), 114 (10), 78 (15), 51 (10); HR-MS (ESI): m/z = 307.0844, calcd. for $[M+Na]^+$ $C_{19}H_{12}N_2ONa$: 307.08418 (1 ppm).

2-(*p*-Trifluoromethylphenyl)phenyl 2-pyridyl ketone (2j): Colourless solid, yield: 110 mg (67%); mp 86–88 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.44 (d, 1H, J = 4.3 Hz), 7.86 (d, 1H, J = 7.7 Hz), 7.69 (td, 1H, J = 7.7 Hz, J = 1.7 Hz), 7.67 (dd, 1H, J = 7.7 Hz, J = 1.2 Hz), 7.62 (td, 1H, J = 7.6 Hz, J = 1.4 Hz), 7.53 (td, 1H, J = 7.5 Hz, J = 1.2 Hz), 7.45 (dd, 1H, J = 8.0 Hz, J = 0.6 Hz), 7.42 (d, 2H, J = 8.2 Hz), 7.36 (d, 2H, J = 8.2 Hz), 7.24–7.28 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 197.7, 154.3, 148.8, 144.4, 140.5, 138.3, 136.6, 131.0, 129.8, 129.6, 129.3, 129.1 (q, $J_{C,F}$ = 31.8 Hz), 127.8, 126.3, 124.9 (q, $J_{C,F}$ = 3.4 Hz), 124.0 (q, $J_{C,F}$ = 270.9 Hz), 123.8; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ = −62.7; GC: t_R = 12.5 min; MS (EI): m/z = 327 (M^+, 30), 298 (100), 249 (80), 201 (65), 152 (55), 78 (25), 51 (25); HR-MS (ESI): m/z = 350.07687, calcd. for $[M+Na]^+$ $C_{19}H_{12}NOF_3Na$: 350.0772 (1 ppm); m/z = 328.0950, calcd. for $[M+H]^+$ $C_{19}H_{13}NOF_3$: 328.09492 (0 ppm); m/z = 308.0880, calcd. for $[M-HF+H]^+$ $C_{19}H_{12}NOF_2$: 308.0887 (2 ppm).

2-(*p*-Fluorophenyl)phenyl 2-pyridyl ketone (2k): Colourless solid, yield: 90 mg (65%); mp 131–133 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.46 (d, 1H, J = 4.5 Hz), 7.83 (d, 1H, J = 7.7 Hz), 7.74–7.70 (m, 2H), 7.59 (td, 1H, J = 7.5 Hz, J = 1.2 Hz), 7.49 (td, 1H, J = 7.5 Hz, J = 0.7 Hz), 7.42 (d, 1H, J = 7.6 Hz), 7.23–7.25 (m, 1H), 7.18–7.21 (m, 2H), 6.84 (t, 2H, J = 8.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.3, 162.0 (d, $J_{C,F}$ = 245.0 Hz), 154.5, 148.8, 140.8, 138.4, 136.8 (d, $J_{C,F}$ = 3.2 Hz), 136.5, 130.9, 130.6 (d, $J_{C,F}$ = 8.3 Hz), 129.8, 129.3, 127.2, 126.1, 123.7, 114.9 (d, $J_{C,F}$ = 21.4 Hz); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ = −115.4; GC: t_R = 12.9 min; MS (EI): m/z = 277 (M^+, 60), 248 (100), 199 (85), 170 (80), 151 (20), 78 (20), 51 (22); HR-MS (ESI): m/z = 300.0802, calcd. for $[M+Na]^+$ $C_{18}H_{12}NOFNa$: 300.08006 (0 ppm). Crystals suitable for single crystal X-ray diffraction studies were grown by slow evaporation of a concentrated solution of **2e** in chloroform at room temperature.

2-(*p*-Methyl benzoate)phenyl 2-pyridyl ketone (2l): Colourless solid, yield: 109 mg (69%); mp 118–120 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.41 (d, 1H, J = 4.6 Hz), 7.86 (d, 1H, J = 7.5 Hz), 7.83 (d, 2H, J = 8.2 Hz), 7.65–7.69 (m, 2H), 7.61 (td, 1H, J = 7.4 Hz, J = 1.1 Hz), 7.53 (td, 1H, J = 7.4 Hz, J = 0.6 Hz), 7.47 (d, 1H, J = 7.6 Hz), 7.32 (d, 2H, J = 8.2 Hz), 7.22–7.25(m, 1H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 197.9, 166.8, 154.3, 148.8, 145.5, 140.9, 138.3, 136.5, 131.0, 129.7, 129.6, 129.3, 129.1, 127.8, 126.3, 126.2, 123.7, 52.0; GC: t_R = 16.3 min; MS (EI): m/z = 317 (M^+, 35), 306 (100), 257 (90), 228 (60), 152 (20), 78 (20), 51 (20); HR-MS (ESI): m/z = 340.0945, calcd. for $[M+Na]^+$ $C_{20}H_{15}NO_3Na$: 340.09441 (0 ppm).

2-(*m*-Cyanophenyl)phenyl 2-pyridyl ketone (2n): Colourless solid, yield: 84 mg (59%); mp 94–96 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.46 (d, 1H, J = 4.4 Hz), 7.91 (d, 1H, J = 7.8 Hz), 7.73 (td, 1H, J = 7.8 Hz, J = 1.7 Hz), 7.68 (dd, 1H, J = 7.5 Hz, J = 0.8 Hz), 7.61–7.65 (m, 1H), 7.53–7.57 (m, 2H), 7.48 (d, 1H, J = 7.8 Hz), 7.42 (d, 2H, J = 7.7 Hz), 7.28–7.31 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 197.4, 154.2, 148.9, 142.2, 139.6, 138.2, 136.7, 133.4, 132.4, 131.2, 130.6, 129.8, 129.8, 128.8, 128.0, 126.5, 123.8, 118.5, 112.2; GC: t_R = 15.0 min; MS (EI): m/z = 284 (M^+, 25), 255 (100), 206 (60), 178 (30), 151 (50), 114 (10), 78 (15), 51 (10); HR-MS (ESI): m/z = 307.0844, calcd. for $[M+Na]^+$ $C_{19}H_{12}N_2ONa$: 307.08418, (1 ppm).

2-(*o*-Fluorophenyl)phenyl 2-pyridyl ketone (2o): Colourless solid, yield: 71 mg (51%); mp 129–131 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.50 (d, 1H, J = 4.3 Hz), 7.87 (d, 1H, J = 7.8 Hz), 7.73 (dd, 1H, J = 7.6 Hz, J = 1.0 Hz), 7.69 (td, 1H, J = 7.8 Hz, J = 1.6 Hz), 7.61 (td, 1H, J = 7.6 Hz, J = 1.3 Hz), 7.51 (td, 1H, J = 7.6 Hz, J = 1.2 Hz), 7.47 (t, 1H, J = 7.6 Hz), 7.24–7.28 (m, 1H), 7.23 (td, 1H, J = 7.6 Hz, J = 1.7 Hz), 7.09–7.15 (m, 1H), 7.00 (td, 1H, J = 7.5 Hz, J = 1.1 Hz), 6.83–6.88 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 196.7, 159.0 (d, $J_{C,F}$ = 244.9 Hz), 154.4, 148.7, 138.2, 136.4, 135.7, 131.5 (d, $J_{C,F}$ = 3.1 Hz), 131.0, 130.8, 129.8, 129.3 (d, $J_{C,F}$ = 8.4 Hz), 128.4 (d, $J_{C,F}$ = 15.5 Hz), 127.6, 126.0, 123.9 (d, $J_{C,F}$ = 3.2 Hz), 123.8, 115.2 (d, $J_{C,F}$ = 22.4 Hz); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ = −115.8; GC: t_R = 13.1 min; MS (EI): m/z = 277 (M^+, 30), 248 (97), 230 (35), 199 (100), 170 (95), 151 (25), 129 (30), 78 (25), 51 (27); HR-MS (ESI): m/z = 300.0795, calcd. for $[M+Na]^+$ $C_{18}H_{12}NOFNa$: 300.07951 (0 ppm).

2-(*o*-Anisyl)phenyl 2-pyridyl ketone (2p): Colourless solid, yield: 101 mg (70%); mp 102–104 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 8.51 (d, 1H, J = 4.3 Hz), 7.84 (d, 1H, J = 7.8 Hz), 7.65–7.69 (m, 2H), 7.57 (td, 1H, J = 7.6 Hz, J = 1.2 Hz), 7.41–7.45 (m, 2H), 7.23–7.26 (m, 2H), 7.11 (td, 1H, J = 7.9 Hz, J = 1.6 Hz), 6.89 (td, 1H, J = 7.4 Hz, J = 0.8 Hz), 6.59 (d, 1H, J = 8.2 Hz), 3.41 (s. 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 196.0, 155.1, 154.5, 148.6, 138.0, 138.0, 136.2, 131.0, 131.0, 130.9, 129.6, 129.2, 128.9, 126.8, 125.7, 123.7, 120.7, 110.0, 54.4; GC: t_R = 14.1 min; MS (EI): m/z = 289 (M^+, 90), 274 (5), 260 (80), 246 (10), 231 (100), 196 (10), 183 (15), 168 (50), 139 (70), 109 (30), 78 (20); HR-MS (ESI): m/z = 312.0997, calcd. for $[M+Na]^+$ $C_{19}H_{15}NO_2Na$: 312.0995 (1 ppm); m/z = 272.1071, calcd. for $[M-H_2O+H]^+$ $C_{19}H_{14}NO$: 272.10699 (0 ppm); m/z = 290.1178, calcd. for $[M+H]^+$ $C_{19}H_{16}NO_2$: 290.11755 (1 ppm).

2-(*m*-Pyridyl)phenyl 2-pyridyl ketone (2t): Pale yellow solid, yield: 59 mg (45%); mp 126–128 °C; ^{1}H NMR

(400.1 MHz, $CDCl_3$): δ = 8.51 (br s, 1H), 8.44 (d, 1H, J = 4.7 Hz), 8.37 (br s, 1H), 7.90 (d, 1H, J = 7.7 Hz), 7.75 (d, 1H, J = 7.5 Hz), 7.70 (d, 1H, J = 7.5 Hz), 7.64 (t, 1H, J = 7.3 Hz), 7.56 (d, 1H, J = 7.5 Hz), 7.40–7.49 (m, 2H), 7.25–7.28 (m, 1H), 7.09 (dd, 1H, J = 7.7 Hz, J = 5.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 197.6, 154.2, 149.5, 148.9, 148.1, 138.4, 138.2, 136.7, 136.2, 131.1, 130.0, 128.5, 127.9, 126.8, 126.4, 123.8, 122.7; GC: t_R = 13.8 min; MS (EI): m/z = 260 (M^+, 10), 231 (100), 182 (45), 154 (10), 127 (40), 102 (10), 77 (10), 51 (10); HR-MS (ESI): m/z = 260.1022, calcd. for $[M+H]^+$ $C_{17}H_{13}N_2O$: 261.10224 (0 ppm).

2-(*o*-Thiophenyl)phenyl 2-pyridyl ketone (2u): Pale red solid, yield: 98 mg (74%); mp 123–125 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.46 (d, 1H, J = 4.6 Hz), 7.88 (d, 1H, J = 7.8 Hz), 7.69 (td, 1H, J = 7.7 Hz, J = 1.6 Hz), 7.61 (d, 1H, J = 7.4 Hz), 7.52–7.56 (m, 2H), 7.46–7.50 (m, 1H), 7.24–7.27 (m, 1H), 7.10 (dd, 1H, J = 5.0 Hz, J = 0.7 Hz), 6.80 (dd, 1H, J = 3.5 Hz, J = 0.8 Hz), 6.74 (dd, 1H, J = 4.9 Hz, J = 3.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.2, 154.3, 149.0, 142.1, 138.7, 136.4, 133.8, 130.7, 130.0, 129.0, 127.7, 127.7, 127.2, 126.2, 126.1, 123.6; GC: t_R = 13.3 min; MS (EI): m/z = 265 (M^+, 55), 236 (60), 187 (55), 159 (10), 115 (100), 78 (10), 51 (10); HR-MS (ESI): m/z = 288.0455, calcd. for $[M+Na]^+$ $C_{16}H_{11}NOSNa$: 288.04536 (0 ppm). Crystals suitable for single crystal X-ray diffraction studies were grown by slow diffusion of *n*-hexane into a concentrated solution of **2u** in ethyl acetate at room temperature.

2,6-Bis(*o*-thiophenyl)phenyl 2-pyridyl ketone (3u): Pale red solid, yield: 173 mg (81%); mp 135–137 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.51 (d, 1H, J = 4.4 Hz), 7.81 (d, 1H, J = 7.8 Hz), 7.66 (td, 1H, J = 7.7 Hz, J = 1.6 Hz), 7.49–7.55 (m, 3H), 7.24–7.27 (m, 1H), 7.15 (dd, 2H, J = 5.0 Hz, J = 0.7 Hz), 6.88 (dd, 2H, J = 3.4 Hz, J = 0.9 Hz), 6.82 (dd, 2H, J = 5.0 Hz, J = 3.7 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.9, 154.4, 149.2, 141.1, 139.0, 136.4, 133.1, 130.0, 129.1, 127.8, 127.1, 126.4, 126.2, 122.9; GC: t_R = 18.6 min; MS (EI): m/z = 347 (M^+, 70), 318 (100), 269 (80), 240 (35), 208 (35), 157 (20), 78 (15), 51 (10); HR-MS (ESI): m/z = 370.0332, calcd. for $[M+Na]^+$ $C_{20}H_{13}NOS_2Na$: 370.03308 (0 ppm).

2-Phenyl-6-methylphenyl 2-pyridyl ketone (6a): 30% purity according to ^1H NMR spectroscopy and GC/MS analysis. This compound could not be separated from the corresponding non-phenylated benzoylpyridine derivative **10a**.[20] As such, only selected data are provided for **6a**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.50 (d, 1H, J = 4.4 Hz), 7.76 (d, 1H, J = 7.8 Hz), 7.864 (td, 1H, J = 7.6 Hz, J = 1.5 Hz), 7.09–7.48 (m, 9H), 2.30 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.1, 154.7, 140.7, 140.4, 138.7, 136.4, 135.5, 129.3, 129.2, 129.1, 127.8, 127.1, 126.9, 126.2, 123.0, 19.8; GC: t_R = 13.1 min; MS (EI): m/z = 272 (M^+, 35), 244 (100), 195 (40), 165 (45), 152 (50), 129 (20), 80 (25), 51 (10).

2-Phenyl-4-methylphenyl 2-pyridyl ketone (6b): Colourless solid, yield: 97 mg (71%); mp 99–101 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.41 (d, 1H, J = 4.3 Hz), 7.78 (d, 1H, J = 7.8 Hz), 7.61 (td, 1H, J = 7.8 Hz, J = 1.5 Hz), 759 (d, 1H, J = 7.6 Hz), 7.27–7.31 (m, 2H), 7.06–7.23 (m, 6H), 7.24–2.47 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.3, 154.9, 148.6, 142.1, 141.3, 140.8, 136.2, 135.5, 130.6, 129.7, 129.0, 127.9, 127.8, 126.9, 125.7, 123.7, 21.54; GC: t_R = 13.7 min; MS (EI): m/z = 273 (M^+, 45), 244 (100), 195 (95), 165 (65), 152 (85), 115 (25), 78 (25), 51 (30); HR-MS (ESI): m/z = 296.1046, calcd. for $[M+Na]^+$ $C_{19}H_{15}NONa$: 296.10458 (0 ppm).

2-Phenyl-4-methoxyphenyl 2-pyridyl ketone (6c): Colourless solid, yield: 80 mg (55%); mp 95–97 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.40 (d, 1H, J = 4.4 Hz), 7.75 (d, 1H, J = 7.8 Hz), 7.70 (d, 1H, J = 8.6 Hz), 7.61 (td, 1H, J = 7.6 Hz, J = 0.6 Hz), 7.23 (d, 1H, J = 7.4 Hz), 7.09–7.19 (m, 4H), 7.00 (dd, 1H, J = 8.4 Hz, J = 2.3 Hz), 6.95 (d, 1H, J = 2.3 Hz), 3.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 197.2, 161.6, 155.2, 148.5, 144.6, 140.8, 136.6, 132.1, 130.6, 129.0, 128.0, 127.1, 125.6, 123.8, 115.4, 112.6, 55.5; GC: t_R = 15.0 min; MS (EI): m/z = 289 (M^+, 20), 260 (50), 211 (100), 168 (20), 139 (35), 78 (10), 51 (10); HR-MS (ESI): m/z = 312.0995, calcd. for $[M+Na]^+$ $C_{19}H_{15}NO_2Na$: 312.0995 (0 ppm).

2-Phenyl-4-fluorophenyl 2-pyridyl ketone (6d): Colourless solid, yield: 93 mg (67%); mp 126–128 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.39 (d, 1H, J = 4.6 Hz), 7.81 (d, 1H, J = 7.9 Hz), 7.62–7.70 (m, 2H), 7.11–7.23 (m, 8H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 197.2, 163.9 (d, $J_{C,F}$ = 250.7 Hz), 154.5, 148.7, 144.9 (d, $J_{C,F}$ = 8.5 Hz), 139.7, 136.4, 134.5 (d, $J_{C,F}$ = 2.6 Hz), 131.9 (d, $J_{C,F}$ = 9.2 Hz), 128.9, 128.2, 127.6, 126.1, 123.7, 116.8 (d, $J_{C,F}$ = 22.2 Hz), 114.2 (d, $J_{C,F}$ = 21.8 Hz); $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$): δ = −109.0; GC: t_R = 12.8 min; MS (EI): m/z = 277 (M^+, 40), 248 (95), 199 (100), 170 (75), 151 (15), 78 (10), 51 (15); HR-MS (ESI): m/z = 300.0794, calcd. for $[M+Na]^+$ $C_{18}H_{12}NOFNa$: 300.07951 (0 ppm).

2-Phenyl-3-cyanophenyl 2-pyridyl ketone (6e): 60% purity according to ^1H NMR spectroscopy and GC-MS analysis. This compound could not be separated from the corresponding bis-phenylated derivative **7e** [GC: t_R = 20.9 min; MS (EI): m/z = 360 (M^+, 40), 331 (100), 282 (70), 253 (30), 226 (20), 207 (50), 151 (10), 78 (20) 51 (10)]. As such, only selected data are provided for **6e**: ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.40 (d, 1H, J = 4.5 Hz), 7.84 (dd, 1H, J = 8.0 Hz, J = 1.6 Hz,), 7.70 (td, 1H, J = 7.7 Hz, J = 1.5 Hz), 7.58 (d, 1H, J = 8.0 Hz), 7.27–7.29 (m, 1H), 7.18–7.23 (m, 7H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 196.3, 153.4, 148.8, 146.1, 139.5, 139.0, 136.7, 133.7, 132.8, 130.6, 128.8, 128.3, 128.2, 126.7, 123.6, 118.2, 111.2; GC: t_R = 15.1 min; MS (EI): m/z = 284 (M^+, 30), 255 (100), 206 (40), 177 (25), 151 (45), 114 (10), 78 (15), 51 (15).

2,6-Diphenyl-4-methoxyphenyl 2-pyridyl ketone (7c): Colourless solid, yield: 153 mg (84%); mp 134–136 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.44 (d, 1H, J = 4.8 Hz), 7.56 (d, 1H, J = 7.8 Hz), 7.50 (td, 1H, J = 7.7 Hz, J = 1.5 Hz), 7.27–7.30 (m, 4H), 7.12–7.20 (m, 7H), 6.96 (s, 2H), 3.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 199.2, 159.7, 155.7, 148.6, 143.0, 140.6, 136.1, 131.3, 129.0, 127.9, 127.1, 125.7, 123.0, 114.6, 55.4; GC: t_R = 20.4 min; MS (EI): m/z = 365 (M^+, 25), 336 (50), 287 (100), 272 (10), 244 (10), 215 (30), 78 (10); HR-MS (ESI): m/z = 388.1306, calcd. for $[M+Na]^+$ $C_{25}H_{19}NO_2Na$: 388.1308 (0 ppm).

2,6-Diphenyl-4-fluorophenyl 2-pyridyl ketone (7d): Colourless solid, yield: 137 mg (78%); mp 125–127 °C; ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.45 (d, 1H, J = 4.8 Hz), 7.58 (d, 1H, J = 7.8 Hz), 7.52 (td, 1H, J = 7.6 Hz, J = 1.3 Hz), 7.25–7.27 (m, 4H), 7.13–7.20 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.7, 162.2 (d, $J_{C,F}$ = 250.7 Hz), 155.1, 148.7, 143.5 (d, $J_{C,F}$ = 8.4 Hz), 139.5, 136.2, 134.7 (d, $J_{C,F}$ = 2.7 Hz), 128.9, 128.0, 127.5, 126.0, 122.9, 115.8 (d, $J_{C,F}$ = 21.9 Hz);

$^{19}C\{^1H\}$ NMR (376 MHz, $CDCl_3$): $\delta = -111.8$; GC: $t_R =$ 16.5 min; MS (EI): $m/z = 353$ (M^+, 20), 324 (70), 275 (100), 246 (20), 226 (25), 78 (10), 51 (10); HR-MS (ESI): $m/z =$ 376.1109, calcd. for $[M+Na]^+$ $C_{24}H_{16}NOFNa$: 376.11081 (0 ppm); $m/z = 336.1184$, calcd. for $[M-H_2O+H]^+$ $C_{24}H_{15}NF$: 336.1183 (0 ppm).

Synthesis and Characterization of 2-(*p*-Ethylphenyl)-phenyl 2-Pyridyl Ketone (8)

CuI (0.05 mmol, 0.0095 g, 0.1 equiv.), benzoic acid (0.5 mmol, 0.061 g, 1 equiv.), 2-benzylpyridine derivative **1** (0.5 mmol, 1 equiv.) and NMP (0.5 mL) were introduced in a dry Schlenk tube and flushed with O_2 for 1 min. The Schlenk tube was connected to a balloon filled with O_2. The reaction mixture was stirred at 100 °C during 24 h. Then, the reaction mixture was cooled down to room temperature and flushed with vacuum/argon over 3–5 cycles. Under an argon atmosphere, K_2CO_3 (2 mmol, 0.276 g, 4 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol, 0.015 g, 0.05 equiv.), 4-bromostyrene (0.75 mmol, 1.5 equiv.) and NMP (1.5 mL) were introduced. The reaction mixture was stirred at 150 °C for 48 h. Then, the Schlenk tube was capped with balloon filled with H_2 and the reaction mixture was stirred at 150 °C for 12 h. Back down to room temperature, the pressure was slowly released and the reaction mixture was diluted with dichloromethane prior to being filtered over a pad of Celite. After solvent evaporation under vacuum, the desired product **8** was purified by silica gel column chromatography with a mixture of petroleum ether and ethyl acetate as the eluent and obtained as a colourless solid; yield: 92 mg (64%); mp 102–104 °C. ^1H NMR (400.1 MHz, $CDCl_3$): $\delta = 8.42$ (d, 1H, $J =$ 4.2 Hz), 7.78 (d, 1H, $J = 7.8$ Hz), 7.56–7.66 (m, 3H), 7.47 (t, 2H, $J = 7.4$ Hz), 7.18–7.21 (m, 1H), 7.14 (d, 2H, $J = 8.0$ Hz), 6.97 (d, 2H, $J = 8.0$ Hz), 2.51 (q, 2H, $J = 7.6$ Hz), 1.12 (t, 3H, $J = 7.6$ Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta = 198.5$, 154.8, 148.7, 143.1, 142.0, 138.3, 138.0, 136.2, 130.9, 129.8, 129.3, 129.1, 127.5, 126.9, 125.8, 123.8, 28.4, 15.5; GC: $t_R =$ 14.2 min; MS (EI): $m/z = 287$ (M^+, 50), 258 (100), 209 (15), 181 (55), 152 (30), 122 (10), 78 (15), 51 (10); HR-MS (ESI): $m/z = 310.1203$, calcd. for $[M+Na]^+$ $C_{20}H_{17}NONa$: 310.12023 (0 ppm); $m/z = 270.1275$, calcd. for $[M-H_2O+H]^+$ $C_{20}H_{16}N$: 270.12772 (1 ppm).

Synthesis and Characterization of (4′-*tert*-Butyl-[1,1′-biphenyl]-2-yl)(pyridin-2-yl)methanol (9)

In a 10-mL autoclave, CuI (0.05 mmol, 0.0095 g, 0.1 equiv.), benzoic acid (0.5 mmol, 0.061 g, 1 equiv.), 2-benzylpyridine derivative **1** (0.5 mmol, 1 equiv.) and NMP (0.5 mL) were charged and flushed with O_2 for 1 min. The autoclave was pressurized with O_2 (*ca.* 1 bar) and the reaction mixture was stirred at 100 °C during 24 h. Then, the reaction mixture was cooled down to room temperature and the pressure was slowly released followed by argon flushing over 5 min. Under an argon atmosphere, K_2CO_3 (2 mmol, 0.276 g, 4 equiv-), $[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol, 0.015 g, 0.05 equiv-), 1-bromo-4-*tert*-butylbenzene (0.75 mmol, 1.5 equiv-) and NMP (1.5 mL) were introduced. The autoclave was then pressurized with argon (*ca.* 1 bar) and the reaction mixture was stirred at 150 °C for 48 h. Then, the reaction mixture was cooled down to room temperature and the pressure was slowly released followed by H_2 flushing over 5 min. Then, the autoclave was pressurized with H_2 (40 bar) and the reaction mixture was stirred at 150 °C for 12 h. Back down at room temperature, the pressure was slowly released and the reaction mixture was diluted with dichloromethane prior to being filtered over a pad of Celite. After solvent evaporation under vacuum, the desired product **9** was purified by silica gel column chromatography with a mixture of petroleum ether and ethyl acetate as the eluent and obtained as a colourless solid; yield: 87 mg (55%); mp 108–110 °C. ^1H NMR (400.1 MHz, $CDCl_3$): $\delta = 8.53$ (d, 1H, $J =$ 4.7 Hz), 7.54 (td, 1H, $J = 7.7$ Hz, $J = 1.4$ Hz), 7.41–7.46 (m, 4H), 7.27–7.32 (m, 3H), 7.20–7.22 (m, 1H), 7.13–7.17 (m, 1H), 6.84 (d, 1H, $J = 7.9$ Hz), 5.93 (s, 1H), 5.39 (br s, 1H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): $\delta = 161.3$, 150.0, 147.3, 142.0, 140.6, 137.8, 136.7, 130.1, 129.3, 128.2, 127.8, 127.6, 125.2, 122.2, 121.8, 70.7, 34.6, 31.4; GC: $t_R =$ 15.2 min; MS (EI): $m/z = 317$ (M^+, 70), 284 (15), 243 (45), 165 (20), 108 (30), 80 (100), 57 (50), 52 (15); HR-MS (ESI): $m/z = 340.1671$, calcd. for $[M+Na]^+$ $C_{22}H_{23}NONa$: 340.16718 (0 ppm).

CCDC 1471276 (**2a**), CCDC 1471277 (**2k**), and CCDC 1471278 (**2u**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

Dr. T. Roisnel is acknowledged for performing X-ray diffractions studies. The authors wish to thank CNRS and Université de Rennes 1 for financial support, and the contribution of the COST Action CA15106 (C–H Activation in Organic Synthesis, CHAOS).

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