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Unsymmetrical Biaryls by Palladium-Catalyzed Coupling of Aryl Halides with Internal Reduction

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Aryl bromides containing a (1,4,5,6-tetrahydro-6-oxopyridin-3-yl)methyl substituent can be coupled with aryl halides yielding unsummetrical biaryls. In the course of this process, the cyclic enamide is oxidized to the 2(1*H*)-pyridinone. The reaction proceeds by a six-membered palladacycle resulting from allylic C–H bond activation of the cyclic enamide, leading to a six-membered palladacycle. A subsequent transmetalation reaction with an aryl-Pd-X intermediate eventually leads to mixed biaryls by reductive elimination and β-hydride elimination. The best yields were obtained with 2 equiv. of aryl halide. The required substrates were prepared from bromoiodobenzenes by a sequence consisting of a Heck reaction with allyl alcohol, enamine formation, Michael addition to ethyl acrylate, and heterocycle formation with benzylamine.

Introduction

Biaryl compounds are important in many fields of chemistry.[1] For example, chiral biaryls function as efficient ligands in asymmetric synthesis.[2] Furthermore, the biaryl subunit can be found in many natural products such as alkaloids or certain unusual peptide-based natural products.[3] Finally, biaryl compounds are very common in material science.[4,5] Classical methods for aryl–aryl bond formation include reductive methods such as the Ullmann coupling, which employs an aryl halide and copper.[1] In addition, catalytic cross-coupling reactions belong to the standard repertoire in biaryl synthesis.[1,6] A useful variation in this regard is the decarboxylative biaryl coupling.[7] Newer methods for the formation of such bonds are based on direct arylation. In this case, an arylmetal species reacts selectively with the C–H bond of another arene.[8,9]

From a practical point of view, the unsymmetrical coupling of two aryl halides would also be very useful. In fact, some processes are known in which two different aryl halides are coupled in the presence of a palladium catalyst. In these methods, regeneration of Pd^0 is achieved by adding an organic reducing agent, like formate, 2-propanol, or an amine. For example, 4-nitrobiphenyl was produced in 32% from iodobenzene and 4-nitrobromobenzene (4 equiv.) in the presence of $Pd(OAc)_2$, nBu_4NBr, and iPr_2NEt.[10] In addition, some homocoupling of iodobenzene (21%) was observed. We reasoned that a more efficient process might be possible if the reducing agent were contained in one of the aryl halide substrates. This concept is illustrated in Figure 1. Thus, if a Y–H bond were in proximity to the halide, then the initial C–X insertion of Pd^0 might be followed by activation of the neighboring Y–H bond, leading to palladacycle **C**. This would allow for the formation of palladacycle **D**, which then would react with the second aryl halide **E**, leading to palladacycle **F**. A reductive elimination would form the desired biaryl bond, generating a Heck-type intermediate **G**. A final β-elimination should then regenerate the

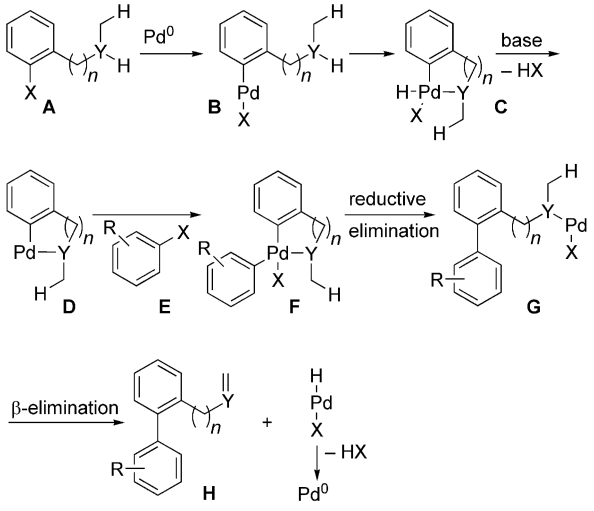

Figure 1. Novel strategy for achieving unsymmetrical biaryl coupling from two different aryl halides. Ligands are omitted for simplicity. Y = C or heteroatom, n = 1–3 (to achieve palladacycles of ring size 5–7).

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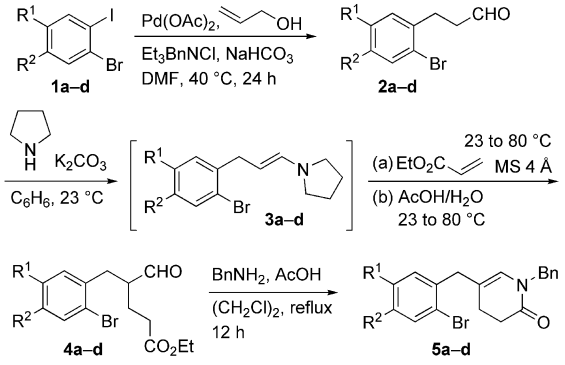
Pd^0. However, this plan would collapse if the palladium would leave palladacycle **C**, as is often the case.[11] In this paper, we demonstrate the realization of this novel concept with piperidin-2-one-substituted aryl bromides.

Results and Discussion

The required substrates were prepared from bromoiodobenzenes[12–14] **1a–d** (Scheme 1 and Table 1) by a Jeffery–Heck coupling[15] with allyl alcohol, yielding 3-(2-bromo)-phenylpropanals **2a–d**. Aldehydes **2a–d** were then converted into the corresponding enamines with pyrrolidine in the presence of K_2CO_3. Treatment of the crude enamines with ethyl acrylate followed by acidic work-up furnished 4-formyl esters **4a–d**.[16] As shown in previous work,[17] the 4-formyl esters provide piperidinones by reductive amination with benzylamine and sodium cyanoborohydride. If the reducing agent was omitted and the formyl esters were simply reacted with benzylamine in refluxing dichloroethane, cyclic enamides **5a–d** were the sole products. The yields for the individual steps of the sequence shown in Scheme 1 are listed in Table 1.



Scheme 1. Synthesis of cyclic enamides **5a–d** by Heck coupling, Michael addition of the enamines **3a–d** to ethyl acrylate, and cyclization of 4-formyl esters **4a–d** with benzylamine.

Table 1. Yields for the transformations leading to piperidinones **5a–d**.

Entry	R^1	R^2	Coupling step (%)	Michael addition (%)	Cyclization to the enamide (%)
1	H	H	**2a** (80)	**4a** (75)	**5a** (85)
2	H	Me	**2b** (70)	**4b** (72)	**5b** (78)
3	OMe	H	**2c** (70)	**4c** (73)	**5c** (83)
4	H	OMe	**2d** (74)	**4d** (64)	**5d** (89)

In related work, we recently discovered that 5-(2-bromobenzyl)-substituted piperidin-2-ones form the corresponding homobiaryls in the presence of $Pd(OAc)_2$, Ph_3P, and Cs_2CO_3 at elevated temperatures.[18] As an example, the transformation of **5a** to biaryl **8a** is shown in Figure 2. Besides the desired biaryl compound, we also observed the formation of debromo derivative **6a** and pyridinone **7a**. As shown in Figure 2, one of the 3,4-dihydro-2(1*H*)-pyridinones was oxidized to the fully unsaturated ring system during this process. The formation of biaryl **8a** can only be explained by C–H bond activation of the initial aryl-palladium species, leading to a palladacycle such as **D** (Figure 1). This intermediate must then react with a second aryl bromide to form the biaryl bond.

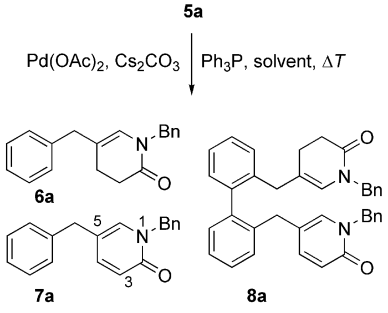


Figure 2. Formation of homobiaryl **8a** from cyclic enamide **5a**.

We became interested in seeing whether or not unsymmetrical biaryls would form between 5-(2-bromobenzyl)-substituted 3,4-dihydro-2(1*H*)-pyridinones **5** and an added aryl halide by a palladium-catalyzed C–H activation/aryl-aryl-bond-forming domino process,[19] as indicated in Figure 3. Initially, the parent dihydro-2(1*H*)-pyridinone **5a** was treated with varying amounts of a phenyl halide. We used the same reaction conditions [$Pd(OAc)_2$ (10 mol-%), Ph_3P (20 mol-%), Cs_2CO_3 (4 equiv.), DMF, 120 °C] as used previously for the formation of biaryl compounds like **8a**.[18] We needed to determine how many equiv. of phenyl halide would give the best yield of the corresponding unsymmetrical biaryl compound **9a**. These results are shown in Table 2.

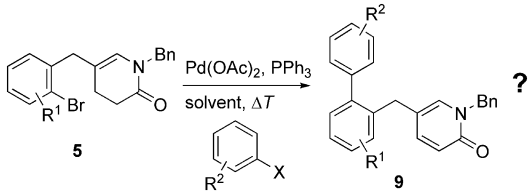


Figure 3. Possible formation of unsymmetrical biaryls from cyclic enamides **5** and an added aryl halide.

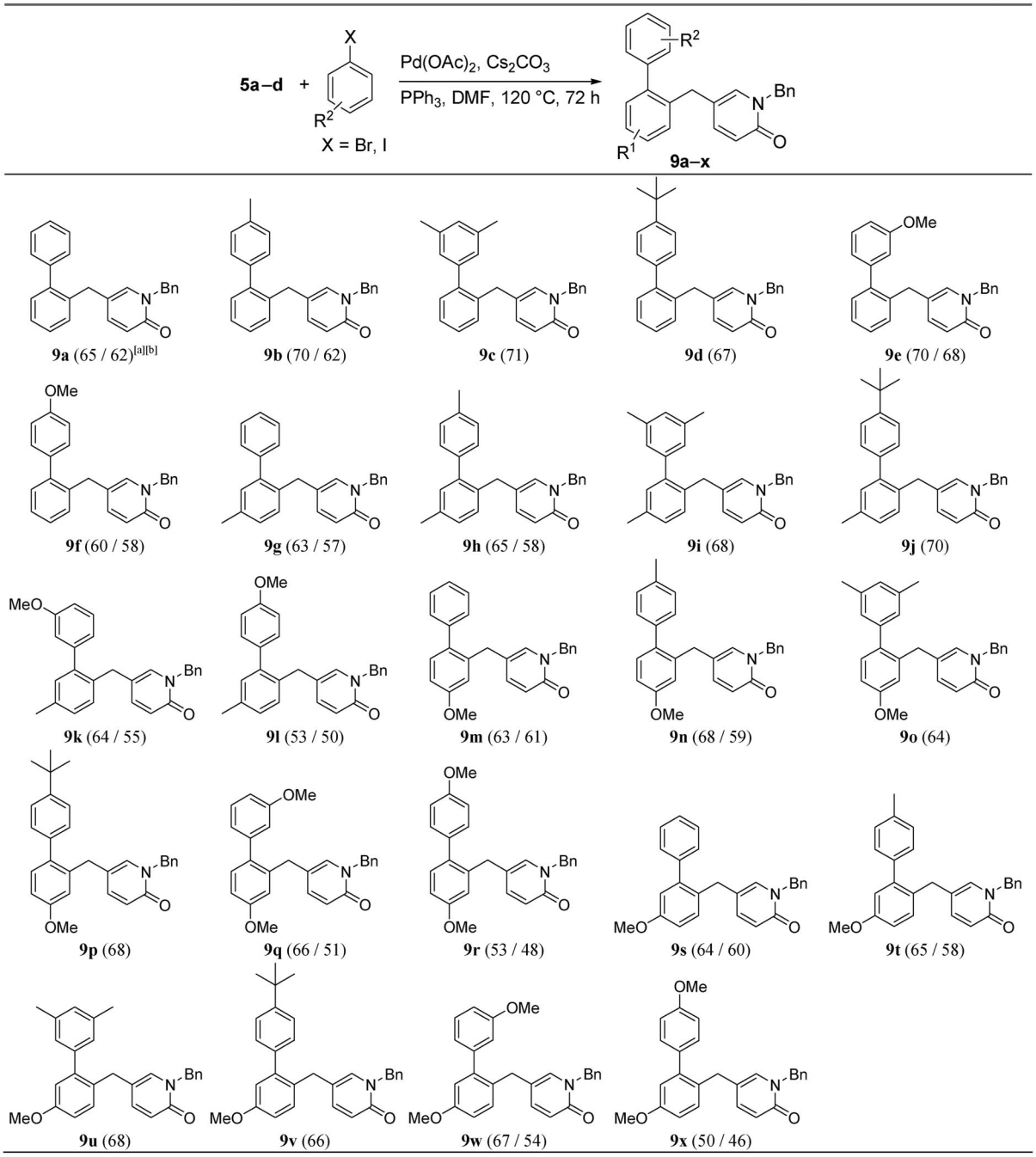
Table 2. Reaction of piperidinone **5a** with various halobenzenes and in various amounts in the presence of $Pd(OAc)_2$, base, and Ph_3P.[a]

Entry	X in aryl halide	Equiv. of aryl halide	% Yield of **6a**	% Yield of **9a**[b]
1	I	1.1[c]	8	32
2	I	5	–	41
3	I	3	–	53
4	I	2	8	62
5	Br	2	7	65
6	Cl	2	–	trace[d]

[a] All reactions were carried out with $Pd(OAc)_2$ (0.1 equiv.), Ph_3P (0.2 equiv.), and Cs_2CO_3 (4 equiv.) at 120 °C for 72 h. [b] Isolated yields of **9a**. [c] Under these conditions, **7a** (16%) and **8a** (30%) were also isolated. [d] **8a** (43%), **7a** (18%), and **6a** (12%) were isolated.

If a slight excess (1.1 equiv.) of iodobenzene was used, biaryl **9a** was formed in 32% yield (Table 2, Entry 1). However, debrominated **6a** (8%), pyridinone **7a** (16%), and a substantial amount of homo coupling product **8a** (30%) were also observed. Accordingly, the amount of the halide was increased. Indeed, 5 equiv. of iodobenzene led to a 41% yield of biaryl **9a**. Under these conditions, the formation of the other possible products could be suppressed. Using 3 equiv. of iodobenzene produced 53% of **9a** (Table 2, Entry 3). It seems that too much halobenzene interferes with the efficiency of the catalytic cycle. In fact, with 2 equiv. of iodobenzene, the yield of **9a** improved to 62% (Table 2, Entry 4). Now small amounts of debrominated piperidinone **6a** (8%) were also formed. Replacing iodobenzene with bromobenzene (2 equiv.) turned out to be optimal with regard to the yield of **9a** (65%) (Table 2, Entry 5). On the other hand, with chlorobenzene, only a trace of biaryl **9a** could be detected. Instead, some of dimer **8a** (43%), **7a** (18%),

Table 3. Reaction of 3,4-dihydro-2(1*H*)-pyridinones **5a**–**d** with various halobenzenes in the presence of $Pd(OAc)_2$, base, and Ph_3P.

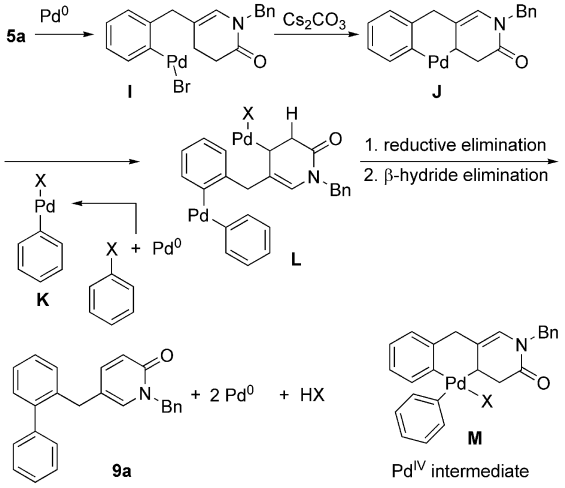


[a] The first number is the yield with the aryl bromide, and the second number is the yield with the corresponding iodide. [b] In all the reactions, 5–8% of debrominated **6** were also observed.

and **6a** (12%) were isolated. Ultimately, the conditions found in Entry 5 of Table 2 provided the best yield of biaryl **9a**.

Therefore, these conditions were applied to the other enamides **5b–d** from Scheme 1. The enamides were reacted in the presence of $Pd(OAc)_2$ (0.1 equiv.), Ph_3P (0.2 equiv.), and Cs_2CO_3 (4 equiv.) in DMF at 120 °C for 72 h with several bromo- or iodobenzenes. As shown in Table 3, biaryl derivatives **9** were formed in yields ranging from 46–70%. In every case where both the bromide and the iodide were studied, slightly higher yields were obtained with the bromobenzene derivative. However, the reason for this difference can not be given at the moment. The newly formed pyridinone part of biaryl derivatives **9** shows a characteristic doublet (H-3, J = 9.4 Hz), doublet of doublets (H-4, J = 9.4 and 2.5 Hz), and doublet (H-6, J = 2.5 Hz) at around 6.5, 6.9, and 6.5 ppm, respectively. Initial attempts at the cross-coupling of alkyl bromides (e.g. 1-bromohexane) were not successful.

In this domino process, the formation of pyridin-2(1*H*)-one **7a** and the biphenyl-substituted pyridinone **9a** can only be explained by allylic C–H bond activation by base-induced cyclopalladation of aryl-palladium species **I**, resulting in palladacycle **J** (Scheme 2).[20] This palladacycle most likely undergoes a transmetalation-type exchange of aryl ligands[21] to give bis-organopalladium species **L**. From there, a β-hydride elimination and a reductive elimination will lead to biaryl **9a**. The formation of 2(1*H*)-pyridinone **7a** can be explained as well by β-hydride elimination and reductive elimination from palladacycle **J**. The transmetalation process (**K** + **J** → **L**) avoids the intermediacy of Pd^{IV} intermediates[22] such as **M**, which seem like less probable structures.



Scheme 2. Proposed mechanism explaining the formation of **9a**. For simplicity, phosphane ligands are omitted.

The mechanism suggested in Scheme 2 is somewhat reminiscent of the classical Catellani process, where an initial aryl-palladium species inserts norbornene, which allows a subsequent formal C–H insertion to produce a five-membered palladacycle (Pd^{II}) that is ready for further coupling reactions.[23–27]

Conclusions

In summary, we demonstrated the facile synthesis of 5-substituted 3,4-dihydro-1*H*-pyridin-2-ones from easily accessible 4-formyl esters with a 2-bromophenyl group at the terminus. These enamides entered into a novel domino reaction pathway in the presence of a palladium catalyst. Thus, with the 2-bromobenzyl substituent, the aryl-palladium species underwent a C–H bond activation to form a palladium intermediate, which reacted with another aryl bromide to form unsymmetrical biaryl compounds such as **9a**. These transformations are unprecedented and further illustrate the power of transition-metal-catalyzed transformations.

Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded at 295 K in $CDCl_3$ with a Bruker Avance 400 spectrometer. Chemical shifts are calibrated to the residual proton and carbon resonance of the solvent, $CDCl_3$ (δ_H = 7.25 and δ_C = 77.0 ppm). HRMS (FT-ICR) was performed with a Bruker Daltonic APEX 2 spectrometer with electron spray ionization (ESI). Analytical LC-MS was performed with an HP 1100 Series system connected with an Agilent G1946C ESI MS detector operating in the positive mode with a fragmenter voltage of 40 eV; column: Nucleosil 100–5, C-18 HD, 5 μm, 70 × 3 mm, Macherey–Nagel; eluent: 5 mM NaCl/acetonitrile, gradient: 0–10–15–17–20 min with 20–80–80–99–99% acetonitrile, flowrate of 0.5 mL min^{-1}. Flash chromatography was performed on J. T. Baker silica gel (43–60 μm). Thin-layer chromatography was performed on Machery–Nagel Polygram Sil G/UV_{254} plates. Solvents were distilled prior to use. Petroleum ether with a boiling range of 40–60 °C was used. Reactions were generally run under nitrogen atmosphere.

Typical Procedure. 1-Benzyl-5-(1,1′-biphenyl-2-ylmethyl)pyridin-2(1*H*)-one (9a): In an oven-dried Schlenk tube fitted with a rubber septum, to a solution of bromoenamide **5a** (100 mg, 0.28 mmol) and bromobenzene (88.2 mg, 0.56 mmol) in anhydrous DMF (2 mL) were added together Ph_3P (14.7 mg, 20 mol-%), Cs_2CO_3 (366 mg, 1.12 mmol), and $Pd(OAc)_2$ (6.3 mg, 10 mol-%) at room temperature in a purging nitrogen atmosphere. The magnetically stirred reaction mixture was then heated in an oil bath at 120 °C for 72 h. The reaction was cooled to room temperature and washed with aqueous HCl (3 N). After separation of the layers, the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and filtered. Concentration of the filtrate and purification of the crude material by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9a** (64 mg, 65%) as a brown viscous oil. IR (neat): $\tilde{\nu}$ = 3059, 3030, 2924, 1668, 1597, 1538, 1496, 1477, 1454, 1352, 1260, 1141, 1073, 1030, 836, 751, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.05 (m, 14 H, Ar-H), 6.96 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.50 (d, J = 2.5 Hz, 1 H, H-6), 6.46 (d, J = 9.4 Hz, 1 H, H-3), 4.96 (s, 2 H, NCH_2Ph), 3.62 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (OC=O), 142.2 (C-2′), 141.2 (C-1′′), 140.9 (C-6), 136.6 (C), 136.5 (C), 135.1 (C-4), 130.3 (CH), 129.7 (CH), 128.9 (2 C, CH), 128.7 (2 C, CH), 128.1 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 127.6 (C, CH), 127.0 (CH), 126.7 (CH), 120.7 (C-3), 118.7 (C-5), 51.6 (NCH_2Ph), 35.3 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{25}H_{22}NO$ $[M + H]^+$ 352.1696; found 352.1696.

1-Benzyl-5-[(4′-methyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9b): The reaction was performed with enamide **5a** (100 mg, 0.27 mmol) and 4-bromotoluene (96 mg, 0.56 mmol) in anhydrous DMF (2 mL) with Ph_3P (14.7 mg, 20 mol-%), Cs_2CO_3 (366 mg, 1.12 mmol), and $Pd(OAc)_2$ (6.3 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9b** (72 mg, 70%) as a brown viscous oil. R_f = 0.45 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3025, 2922, 1666, 1598, 1537, 1496, 1481, 1445, 1388, 1352, 1263, 1141, 1074, 1030, 826, 761, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.10 (m, 9 H, Ar-H), 7.12 (d, 2 H) and 7.02 (d, J = 7.9 Hz, 2 H, Ar-H), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.54 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.62 (s, 2 H, CH_2Ar), 2.38 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 142.2 (C-2′), 141.1 (C-6), 138.3 (C-1′′), 136.7 (2 C, C), 136.5 (C), 135.2 (C-4), 130.4 (CH), 129.7 (CH), 128.9 (2 C, CH), 128.8 (2 C, CH), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 127.5 (CH), 126.7 (CH), 120.7 (C-3), 119.0 (C-5), 51.7 (NCH_2Ph), 35.3 (CH_2Ar), 21.1 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{26}H_{24}NO$ $[M + H]^+$ 366.1852; found 366.1852.

1-Benzyl-5-[(3′,5′-dimethyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9c): The reaction was performed with enamide **5a** (100 mg, 0.28 mmol) and bromoxylene (104 mg, 0.56 mmol) in anhydrous DMF (2 mL) with Ph_3P (14.7 mg, 20 mol-%), Cs_2CO_3 (366 mg, 1.12 mmol), and $Pd(OAc)_2$ (6.3 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 1:1) furnished the biarylpyridinone **9c** (76 mg, 71%) as a brown viscous oil. R_f = 0.48 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2918, 1667, 1601, 1536, 1495, 1453, 1352, 1260, 1140, 1074, 1030, 852, 834, 762, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.10 (m, 9 H, Ar-H), 6.98 (s, 1 H, H-4′′), 6.97 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.77 (s, 2 H, H-2′′, H-6′′), 6.58 (d, J = 2.5 Hz, 1 H, H-6), 6.49 (d, J = 9.4 Hz, 1 H, H-3), 4.99 (s, 2 H, NCH_2Ph), 3.62 (s, 2 H, CH_2Ar), 2.30 (s, 6 H, 2 $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 142.4 (C-2′), 141.2 (2 C, C-1′′, C-6), 137.6 (2 C, C), 136.6 (C), 136.5 (C), 135.2 (C-4), 130.2 (CH), 129.6 (CH), 128.7 (2 C, CH), 128.5 (CH), 127.9 (2 C, CH), 127.8 (CH), 127.4 (CH), 126.8 (2 C, CH), 126.6 (CH), 120.6 (C-3), 119.1 (C-5), 51.6 (NCH_2Ph), 35.3 (CH_2Ar), 21.2 (2 C, 2 $ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO$ $[M + H]^+$ 380.2009; found 380.2008.

1-Benzyl-5-[(4′-*tert*-butyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9d): The reaction was performed with enamide **5a** (100 mg, 0.28 mmol) and 4-*tert*-butylbromobenzene (119.7 mg, 0.56 mmol) in anhydrous DMF (2 mL) with Ph_3P (14.7 mg, 20 mol-%), Cs_2CO_3 (366 mg, 1.12 mmol), and $Pd(OAc)_2$ (6.3 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 1:1) furnished biarylpyridinone **9d** (77 mg, 67%) as a brown viscous oil. R_f = 0.5 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3027, 2962, 2867, 1668, 1599, 1537, 1496, 1482, 1454, 1397, 1362, 1266, 1141, 1029, 1005, 836, 766, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, 2 H) and 7.10 (d, J = 8.1 Hz, 2 H, Ar-H), 7.38–7.10 (m, 9 H, Ar-H), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.61 (d, J = 2.5 Hz, 1 H, H-6), 6.49 (d, J = 9.4 Hz, 1 H, H-3), 4.99 (s, 2 H, NCH_2Ph), 3.65 (s, 2 H, CH_2Ar), 1.36 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 149.9 (C-4′′), 142.1 (C-2′), 141.2 (C-6), 138.2 (C-1′′), 136.8 (C), 136.4 (C), 135.2 (C-4), 130.4 (CH), 129.6 (CH), 128.7 (4 C, CH), 127.8 (CH), 127.7 (2 C, CH), 127.4 (CH), 126.7 (CH), 125.0 (2 C, CH), 120.7 (C-3), 119.0 (C-5), 51.7 (NCH_2Ph), 35.2 (CH_2Ar), 34.5 (C), 31.4 [$C(CH_3)$] ppm. HRMS (ESI): calcd. for $C_{29}H_{30}NO$ $[M + H]^+$ 408.2322; found 408.2321.

1-Benzyl-5-[(3′-methoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9e): The reaction was performed with enamide **5a** (100 mg, 0.28 mmol) and 3-bromoanisole (105 mg, 0.56 mmol) in anhydrous DMF (2 mL) with Ph_3P (14.7 mg, 20 mol-%), Cs_2CO_3 (366 mg, 1.12 mmol), and $Pd(OAc)_2$ (6.3 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) furnished biarylpyridinone **9e** (75 mg, 70%) as a brown viscous oil. R_f = 0.35 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3061, 2935, 1667, 1598, 1537, 1495, 1476, 1454, 1352, 1263, 1220, 1176, 1043, 1020, 834, 761, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.12 (m, 10 H, Ar-H), 6.97 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.86 (dd, J = 8.1, 1.8 Hz, 1 H, H-4′′), 6.71 (d, J = 8.1 Hz, 1 H, H-6′′), 6.70 (d, J = 1.8 Hz, 1 H, H-2′′), 6.57 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.74 (s, 3 H, OCH_3), 3.62 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 159.3 (C-3′′), 142.6 (C-2′), 142.1 (C-1′′), 141.0 (C-6), 136.6 (C), 136.5 (C), 135.2 (C-4), 130.1 (CH), 129.7 (CH), 129.1 (CH), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 127.7 (CH), 126.7 (CH), 121.4 (CH), 120.7 (C-3), 118.8 (C-5), 114.5 (CH), 112.6 (CH), 55.1 (OCH_3), 51.6 (NCH_2Ph), 35.3 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{26}H_{24}NO_2$ $[M + H]^+$ 382.1802; found 382.1803.

1-Benzyl-5-[(4′-methoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9f): The reaction was performed with enamide **5a** (100 mg, 0.28 mmol) and 4-bromoanisole (105 mg, 0.56 mmol) in anhydrous DMF (2 mL) with Ph_3P (14.7 mg, 20 mol-%), Cs_2CO_3 (366 mg, 1.12 mmol), and $Pd(OAc)_2$ (6.3 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) furnished biarylpyridinone **9f** (64 mg, 60%) as a brown viscous oil. R_f = 0.35 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3061, 3029, 2934, 2836, 1667, 1598, 1537, 1496, 1454, 1353, 1295, 1244, 1177, 1141, 1106, 1074, 1035, 1002, 834, 765, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.23 (m, 5 H, Ar-H), 7.23–7.12 (m, 4 H, Ar-H), 7.04 (d, 2 H) and 6.84 (d, J = 8.7 Hz, 2 H, Ar-H], 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.54 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.83 (s, 3 H, OCH_3), 3.61 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 158.7 (C-4′′), 141.9 (C-2′), 141.0 (C-6), 136.8 (C), 136.5 (C), 135.1 (C-4), 133.6 (C-1′′), 130.5 (CH), 130.1 (2 C, CH), 129.7 (CH), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 127.4 (CH), 126.7 (CH), 120.7 (C-3), 118.9 (C-5), 113.5 (2 C, CH), 55.2 (OCH_3), 51.6 (NCH_2Ph), 35.4 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{26}H_{24}NO_2$ $[M + H]^+$ 382.1802; found 382.1801.

1-Benzyl-5-[(5-methyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9g): The reaction was performed with enamide **5b** (100 mg, 0.27 mmol) and bromobenzene (85 mg, 0.55 mmol) in anhydrous DMF (2 mL) with Ph_3P (14 mg, 20 mol-%), Cs_2CO_3 (352 mg, 1.1 mmol), and $Pd(OAc)_2$ (6 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9g** (62 mg, 63%) as a brown viscous oil. R_f = 0.45 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2923, 2853, 1667, 1600, 1496, 1487, 1454, 1443, 1388, 1352, 1260, 1142, 1073, 1029, 825, 757, 734, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.22 (m, 6 H, Ar-H), 7.22–7.05 (m, 6 H, Ar-H), 7.02 (s, 1 H, H-6′), 6.97

(dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.49 (d, J = 2.5 Hz, 1 H, H-6), 6.45 (d, J = 9.4 Hz, 1 H, H-3), 4.95 (s, 2 H, NCH_2Ph), 3.57 (s, 2 H, CH_2Ar), 2.35 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 142.1 (C-2′), 141.4 (C-1′′), 141.0 (C-6), 136.5 (C), 136.4 (C), 135.0 (C-4), 133.6 (C), 131.1 (CH), 129.7 (CH), 129.0 (2 C, CH), 128.7 (2 C, CH), 128.3 (CH), 128.1 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 126.9 (CH), 120.7 (C-3), 119.0 (C-5), 51.7 (NCH_2Ph), 35.0 (CH_2Ar), 20.9 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{26}H_{24}NO$ $[M + H]^+$ 366.1852; found 366.1854.

1-Benzyl-5-[(4′,5-dimethyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9h): The reaction was performed with enamide **5b** (100 mg, 0.27 mmol) and 4-bromotoluene (92.4 mg, 0.54 mmol) in anhydrous DMF (2 mL) with Ph_3P (14 mg, 20 mol-%), Cs_2CO_3 (352 mg, 1.1 mmol), and $Pd(OAc)_2$ (6 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9h** (67 mg, 65%) as a brown viscous oil. R_f = 0.45 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2921, 1667, 1599, 1537, 1515, 1495, 1454, 1352, 1262, 1176, 1142, 1074, 1030, 908, 824, 736, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–6.95 (m, 12 H, Ar-H), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.54 (d, J = 2.5 Hz, 1 H, H-6), 6.49 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.58 (s, 2 H, CH_2Ar), 2.38 (s, 3 H) and 2.34 (s, 3 H, 2 $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 142.0 (C-2′), 141.1 (C-6), 138.5 (C-1′′), 136.5 (2 C, C), 136.3 (C), 135.1 (C-4), 133.6 (C), 131.1 (CH), 129.6 (CH), 128.9 (2 C, CH), 128.8 (2 C, CH), 128.7 (2 C, CH), 128.2 (CH), 127.9 (2 C, CH), 127.8 (CH), 120.7 (C-3), 119.2 (C-5), 51.7 (NCH_2Ph), 34.9 (CH_2Ar), 21.1 (CH_3) and 20.9 (CH_3, 2 $ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO$ $[M + H]^+$ 380.2009; found 380.2011.

1-Benzyl-5-[(3′,5,5′-trimethyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9i): The reaction was performed with enamide **5b** (100 mg, 0.27 mmol) and bromoxylene (100 mg, 0.54 mmol) in anhydrous DMF (2 mL) with Ph_3P (14 mg, 20 mol-%), Cs_2CO_3 (352 mg, 1.1 mmol), and $Pd(OAc)_2$ (6 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 1:1) furnished biarylpyridinone **9i** (73 mg, 68%) as a brown viscous oil. R_f = 0.48 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2918, 1668, 1597, 1537, 1496, 1454, 1351, 1258, 1140, 1073, 1031, 852, 825, 795, 736, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.15 (m, 5 H, Ar-H), 7.09 (1 H, H-4′) and 7.05 (2 d, J = 7.9 Hz, 1 H, H-3′), 7.03 (s, 1 H, H-6′), 6.97 (s, 1 H, H-4′′), 6.97 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.77 (s, 2 H, H-2′′, H-6′′), 6.58 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.58 (s, 2 H, CH_2Ar), 2.35 (s, 3 H) and 2.30 (s, 6 H, 3 $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 142.3 (C-2′), 141.4 (C-1′′), 141.2 (C-6), 137.5 (2 C, C), 136.5 (C), 136.2 (C), 135.1 (C-4), 133.6 (C), 130.9 (CH), 129.5 (CH), 128.7 (2 C, CH), 128.4 (CH), 128.1 (CH), 127.9 (2 C, CH), 127.8 (CH), 126.8 (2 C, CH), 120.6 (C-3), 119.3 (C-5), 51.6 (NCH_2Ph), 34.9 (CH_2Ar), 21.2 (2 C) and 20.9 (C, 3 $ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{28}H_{28}NO$ $[M + H]^+$ 394.2165; found 394.2166.

1-Benzyl-5-[(4′-*tert*-butyl-5-methyl-1,1′-biphenyl-2-yl)methyl]-pyridin-2(1*H*)-one (9j): The reaction was performed with enamide **5b** (100 mg, 0.27 mmol) and 4-*tert*-butyl-bromobenzene (113 mg, 0.54 mmol) in anhydrous DMF (2 mL) with Ph_3P (14 mg, 20 mol-%), Cs_2CO_3 (352 mg, 1.1 mmol), and $Pd(OAc)_2$ (6 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 1:1) furnished biarylpyridinone **9j** (80 mg, 70%) as a brown viscous oil. R_f = 0.5 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2961, 1668, 1601, 1537, 1495, 1454, 1392, 1362, 1260, 1142, 1074, 1030, 836, 729, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, 2 H) and 7.09 (d, J = 8.1 Hz, 2 H, Ar-H), 7.38–7.12 (m, 5 H, Ar-H), 7.14–7.05 (m, 2 H, Ar-H), 7.05 (s, 1 H, H-6′), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.61 (d, J = 2.5 Hz, 1 H, H-6), 6.49 (d, J = 9.4 Hz, 1 H, H-3), 4.99 (s, 2 H, NCH_2Ph), 3.61 (s, 2 H, CH_2Ar), 2.35 (s, 3 H, $ArCH_3$), 1.35 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 149.9 (C-4′′), 142.0 (C-2′), 141.2 (C-6), 138.3 (C-1′′), 136.5 (C), 136.2 (C), 135.1 (C-4), 133.7 (C), 131.2 (CH), 129.5 (CH), 128.7 (4 C, CH), 128.1 (CH), 127.7 (3 C, CH), 125.0 (2 C, CH), 120.7 (C-3), 119.3 (C-5), 51.8 (NCH_2Ph), 34.8 (CH_2Ar), 34.5 (C), 31.4 [3 C, $C(CH_3)_3$], 20.9 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{30}H_{32}NO$ $[M + H]^+$ 422.2480; found 422.2478.

1-Benzyl-5-[(3′-methoxy-5-methyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9k): The reaction was performed with enamide **5b** (100 mg, 0.27 mmol) and 3-bromoanisole (101 mg, 0.54 mmol) in anhydrous DMF (2 mL) with Ph_3P (14 mg, 20 mol-%), Cs_2CO_3 (352 mg, 1.1 mmol), and $Pd(OAc)_2$ (6 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) furnished biarylpyridinone **9k** (69 mg, 64%) as a brown viscous oil. R_f = 0.35 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3030, 2924, 1667, 1599, 1536, 1481, 1454, 1352, 1262, 1223, 1165, 1036, 822, 792, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.15 (m, 6 H, Ar-H), 7.11 (1 H, H-4′) and 7.07 (2d, J = 7.9 Hz, 1 H, H-3′), 7.04 (s, 1 H, H-6′), 6.97 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.86 (dd, J = 8.1, 1.8 Hz, 1 H, H-4′′), 6.71 (d, J = 8.1 Hz, 1 H, H-6′′), 6.69 (d, J = 1.8 Hz, 1 H, H-2′′), 6.56 (d, J = 2.5 Hz, 1 H, H-6), 6.47 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.74 (s, 3 H, OCH_3), 3.58 (s, 2 H, CH_2Ar), 2.35 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 159.3 (C-3′′), 142.8 (C-2′), 141.9 (C-1′′), 141.1 (C-6), 136.5 (C), 136.3 (C), 135.1 (C-4), 133.5 (C), 130.9 (CH), 129.6 (CH), 129.1 (CH), 128.7 (2 C, CH), 128.4 (CH), 127.9 (2 C, CH), 127.8 (CH), 121.4 (CH), 120.7 (C-3), 119.2 (C-5), 114.5 (CH), 112.5 (CH), 55.2 (OCH_3), 51.7 (NCH_2Ph), 34.9 (CH_2Ar), 20.9 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_2$ $[M + H]^+$ 396.1958; found 396.1959.

1-Benzyl-5-[(4′-methoxy-5-methyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9l): The reaction was performed with enamide **5b** (100 mg, 0.27 mmol) and 4-bromoanisole (101 mg, 0.54 mmol) in anhydrous DMF (2 mL) with Ph_3P (14 mg, 20 mol-%), Cs_2CO_3 (352 mg, 1.1 mmol), and $Pd(OAc)_2$ (6 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) furnished biarylpyridinone **9l** (57 mg, 53%) as a brown viscous oil. R_f = 0.35 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3031, 2930, 1667, 1600, 1537, 1495, 1454, 1292, 1245, 1176, 1073, 1029, 834, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.22 (m, 3 H, Ar-H), 7.19 (d, J = 7.9 Hz, 2 H, Ar-H), 7.09 (1 H, H-4′) and 7.06 (2d, J = 7.9 Hz, 1 H, H-3′), 7.04 (d, 2 H) and 6.84 (d, J = 8.7 Hz, 2 H, Ar-H), 7.01 (s, 1 H, H-6′), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.54 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.82 (s, 3 H, OCH_3), 3.58 (s, 2 H, CH_2Ar), 2.34 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.6 (C-4′′), 141.7 (C-2′), 141.1 (C-6), 136.5 (C), 136.3 (C), 135.0 (C-4), 133.8 (2 C, C), 131.3 (CH), 130.0 (2 C, CH), 129.6 (CH), 128.7 (2 C, CH), 128.1 (CH), 127.9 (2 C, CH), 127.8 (CH), 120.7 (C-3), 119.2 (C-5), 113.5 (2 C, CH), 55.2 (OCH_3), 51.6 (NCH_2Ph),

34.9 (CH_2Ar), 20.9 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_2$ $[M + H]^+$ 396.1958; found 396.1958.

1-Benzyl-5-[(4-methoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9m): The reaction was performed with enamide **5c** (100 mg, 0.26 mmol) and bromobenzene (81 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9m** (62 mg, 63%) as a brown viscous oil. R_f = 0.38 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2924, 1666, 1599, 1537, 1483, 1443, 1234, 1157, 1049, 832, 766, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.23 (m, 6 H, Ar-H), 7.23–7.06 (m, 4 H, Ar-H), 7.13 (d, J = 8.4 Hz, 1 H, H-6′), 6.98 (dd, J = 9.4, 2.54 Hz, 1 H, H-4), 6.83 (dd, J = 8.4, 2.8 Hz, 1 H, H-5′), 6.70 (d, J = 2.8 Hz, 1 H, H-3′), 6.53 (d, J = 2.5 Hz, 1 H, H-6), 6.47 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.79 (s, 3 H, OCH_3), 3.59 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.9 (C-4′), 141.0 (2 C, C and CH, C-6), 138.0 (C), 136.5 (C), 135.1 (C-4), 134.8 (C), 131.4 (CH), 129.3 (2 C, CH), 128.7 (2 C, CH), 128.1 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 126.8 (CH), 120.8 (C-3), 118.6 (C-5), 115.4 (CH), 111.7 (CH), 55.2 (OCH_3), 51.6 (NCH_2Ph), 35.5 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{26}H_{24}NO_2$ $[M + H]^+$ 382.1802; found 382.1802.

1-Benzyl-5-[(4-methoxy-4′-methyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9n): The reaction was performed with enamide **5c** (100 mg, 0.26 mmol) and 4-bromotoluene (88.6 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9n** (70 mg, 68%) as a brown viscous oil. R_f = 0.38 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2924, 1667, 1601, 1537, 1491, 1454, 1352, 1266, 1234, 1158, 1111, 1049, 1004, 830, 728, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.15 (m, 5 H, Ar-H), 7.12 (d, J = 8.4 Hz, 1 H, H-6′), 7.10 (d, 2 H) and 7.00 (d, J = 7.9 Hz, 2 H, Ar-H), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.81 (dd, J = 8.4, 2.5 Hz, 1 H, H-5′), 6.70 (d, J = 2.5 Hz, 1 H, H-3′), 6.56 (d, J = 2.5 Hz, 1 H, H-6), 6.50 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.78 (s, 3 H, OCH_3), 3.59 (s, 2 H, CH_2Ar), 2.37 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.8 (C-4′), 141.1 (C-6), 138.0 (2 C, C), 136.5 (C), 136.4 (C), 135.2 (C-4), 134.8 (C), 131.4 (CH), 129.2 (2 C, CH), 128.8 (4 C, CH), 127.9 (2 C, CH), 127.8 (CH), 120.8 (C-3), 118.9 (C-5), 115.3 (CH), 111.7 (CH), 55.2 (OCH_3), 51.7 (NCH_2Ph), 35.5 (CH_2Ar), 21.1 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_2$ $[M + H]^+$ 396.1958; found 396.1957.

1-Benzyl-5-[(4-methoxy-3′,5′-dimethyl-1,1′-biphenyl-2-yl)methyl]-pyridin-2(1*H*)-one (9o): The reaction was performed with enamide **5c** (100 mg, 0.26 mmol) and bromoxylene (96 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9o** (68 mg, 64%) as a brown viscous oil. R_f = 0.42 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2915, 1667, 1602, 1537, 1497, 1454, 1352, 1295, 1234, 1157, 1077, 1038, 854, 832, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.16 (m, 5 H, Ar-H), 7.13 (d, J = 8.4 Hz, 1 H, H-6′), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.95 (s, 1 H, H-4′′), 6.81 (dd, J = 8.4, 2.5 Hz, 1 H, H-5′), 6.76 (s, 2 H, H-2′′, H-6′′), 6.69 (d, J = 2.5 Hz, 1 H, H-3′), 6.62 (d, J = 2.5 Hz, 1 H, H-6), 6.51 (d, J = 9.4 Hz, 1 H, H-3), 5.00 (s, 2 H, NCH_2Ph), 3.78 (s, 3 H, OCH_3), 3.59 (s, 2 H, CH_2Ar), 2.29 (s, 6 H, 2 $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.8 (C-4′), 141.2 (C-6), 140.9 (C), 138.0 (C), 137.6 (2 C, C), 136.5 (C), 135.2 (CH, C-4), 135.0 (C), 131.2 (CH), 128.7 (2 C, CH), 128.3 (CH), 127.9 (2 C, CH), 127.8 (CH), 127.1 (2 C, CH), 120.7 (C-3), 119.0 (C-5), 115.2 (CH), 111.6 (CH), 55.2 (OCH_3), 51.6 (NCH_2Ph), 35.5 (CH_2Ar), 21.2 (2 C, 2 $ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{28}H_{28}NO_2$ $[M + H]^+$ 410.2115; found 410.2111.

1-Benzyl-5-[(4′-*tert*-butyl-4-methoxy-1,1′-biphenyl-2-yl)methyl]-pyridin-2(1*H*)-one (9p): The reaction was performed with enamide **5c** (100 mg, 0.26 mmol) and 4-*tert*-butyl-bromobenzene (110 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9p** (77 mg, 68%) as a brown viscous oil. R_f = 0.45 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2868, 1667, 1604, 1537, 1492, 1462, 1454, 1362, 1268, 1235, 1158, 1115, 1050, 1003, 834, 779, 733, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, 2 H) and 7.07 (d, J = 8.5 Hz, 2 H, Ar-H), 7.38–7.13 (m, 5 H, Ar-H), 7.14 (d, J = 8.4 Hz, 1 H, H-6′), 7.00 (dd, J = 9.4, 2.8 Hz, 1 H, H-4), 6.82 (dd, J = 8.4, 2.5 Hz, 1 H, H-5′), 6.69 (d, J = 2.5 Hz, 1 H, H-3′), 6.63 (d, J = 2.5 Hz, 1 H, H-6), 6.50 (d, J = 9.4 Hz, 1 H, H-3), 4.99 (s, 2 H, NCH_2Ph), 3.78 (s, 3 H, OCH_3), 3.61 (s, 2 H, CH_2Ar), 1.34 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.8 (C-4′), 149.7 (C-4′′), 141.2 (C-6), 138.1 (C), 137.9 (C), 136.5 (C), 135.3 (C-4), 134.7 (C), 131.4 (CH), 129.0 (2 C, CH), 128.7 (2 C, CH), 127.8 (3 C, CH), 125.0 (2 C, CH), 120.8 (C-3), 118.9 (C-5), 115.2 (CH), 111.7 (CH), 55.2 (OCH_3), 51.7 (NCH_2Ph), 35.4 (CH_2Ar), 34.5 (C), 31.4 [3 C, $C(CH_3)_3$] ppm. HRMS (ESI): calcd. for $C_{30}H_{32}NO_2$ $[M + H]^+$ 438.2428; found 438.2427.

1-Benzyl-5-[(3′,4-dimethoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9q): The reaction was performed with enamide **5c** (100 mg, 0.26 mmol) and 3-bromoanisole (97 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) first furnished biarylpyridinone **9q** (70 mg, 66%) as a brown viscous oil. R_f = 0.32 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2935, 1667, 1599, 1537, 1505, 1496, 1479, 1454, 1389, 1352, 1317, 1292, 1235, 1222, 1159, 1115, 1075, 1052, 1017, 832, 731, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.14 (m, 6 H, Ar-H), 7.14 (d, J = 8.4 Hz, 1 H, H-6′), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.85 (dd, J = 8.4, 1.8 Hz, 1 H, H-4′′), 6.82 (dd, J = 8.4, 2.5 Hz, 1 H, H-5′), 6.70 (d, J = 2.5 Hz, 1 H, H-3′), 6.69 (d, J = 8.4 Hz, 1 H, H-6′′), 6.68 (d, J = 1.8 Hz, 1 H, H-2′), 6.60 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.78 (s, 3 H) and 3.74 (s, 3 H, 2 OCH_3), 3.59 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 159.3 (C-3′′), 159.0 (C-4′), 142.4 (C), 141.0 (C-6), 138.0 (C), 136.5 (C), 135.2 (C-4), 134.6 (C), 131.2 (CH), 129.1 (CH), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 121.8 (CH), 120.8 (C-3), 118.7 (C-5), 115.4 (CH), 114.9 (CH), 112.3 (CH), 111.7 (CH), 55.2, 55.1 (2 OCH_3), 51.6 (NCH_2Ph), 35.5 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_3$ $[M + H]^+$ 412.1907; found 412.1907.

1-Benzyl-5-[(4,4′-dimethoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9r): The reaction was performed with enamide **5c** (100 mg, 0.26 mmol) and 4-bromoanisole (97 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) first furnished biarylpyridinone **9r** (56 mg, 53%) as a brown viscous oil. R_f = 0.32 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2936, 2834, 1666, 1605, 1537, 1490, 1454, 1352, 1244, 1177, 1107, 1049, 1000, 834, 731, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.14 (m, 5 H, Ar-H), 7.11 (d, J = 8.4 Hz, 1 H, H-6′), 7.02 (d, 2 H) and 6.83 (d, J = 8.7 Hz, 2 H, Ar-H), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.81 (dd, J = 8.4, 2.5 Hz, 1 H, H-5′), 6.70 (d, J = 2.5 Hz, 1 H, H-3′), 6.56 (d, J = 2.5 Hz, 1 H, H-6), 6.47 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.82 (s, 3 H) and 3.78 (s, 3 H, 2 OCH_3), 3.58 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 158.8 (C-4′), 158.5 (C-4′′), 141.0 (C-6), 138.2 (C), 136.5 (C), 135.1 (C-4), 134.4 (C), 133.3 (C), 131.5 (CH), 130.4 (2 C, CH), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 120.8 (C-3), 118.7 (C-5), 115.4 (CH), 113.5 (2 C, CH), 111.7 (CH), 55.2 (2 OCH_3), 51.6 (NCH_2Ph), 35.6 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_3$ [M + H]$^+$ 412.1907; found 412.1909.

1-Benzyl-5-[(5-methoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9s): The reaction was performed with enamide **5d** (100 mg, 0.26 mmol) and bromobenzene (81 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9s** (63 mg, 64%) as a brown viscous oil. R_f = 0.38 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2935, 1667, 1601, 1537, 1485, 1443, 1352, 1297, 1264, 1220, 1175, 1143, 1073, 1037, 876, 757, 735, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.23 (m, 6 H, Ar-H), 7.23–7.06 (m, 5 H, Ar-H), 6.95 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.83 (dd, J = 8.4, 2.8 Hz, 1 H, H-4′), 6.75 (d, J = 2.8 Hz, 1 H, H-6′), 6.48 (d, J = 2.5 Hz, 1 H, H-6), 6.46 (d, J = 9.4 Hz, 1 H, H-3), 4.95 (s, 2 H, NCH_2Ph), 3.80 (s, 3 H, OCH_3), 3.54 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.2 (C-5′), 143.4 (C-1′), 141.3 (C-1′′), 141.0 (C-6), 136.5 (C), 134.9 (C-4), 130.8 (CH), 128.9 (2 C, CH), 128.8 (C-2′), 128.7 (2 C, CH), 128.1 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 127.1 (CH), 120.7 (C-3), 119.3 (C-5), 115.6 (CH), 113.2 (CH), 55.3 (OCH_3), 51.7 (NCH_2Ph), 34.6 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{26}H_{24}NO_2$ [M + H]$^+$ 382.1802; found 382.1803.

1-Benzyl-5-[(5-methoxy-4′-methyl-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9t): The reaction was performed with enamide **5d** (100 mg, 0.26 mmol) and 4-bromotoluene (88.6 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9t** (67 mg, 65%) as a brown viscous oil. R_f = 0.38 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2936, 1667, 1603, 1537, 1495, 1454, 1443, 1352, 1297, 1221, 1175, 1142, 1073, 1039, 877, 825, 736, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.14 (m, 5 H, Ar-H), 7.11 (d, 2 H) and 7.02 (d, J = 7.9 Hz, 2 H, Ar-H), 7.09 (d, J = 8.4 Hz, 1 H, H-3′), 6.99 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.83 (dd, J = 8.4, 2.5 Hz, 1 H, H-4′), 6.75 (d, J = 2.5 Hz, 1 H, H-6′), 6.52 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.79 (s, 3 H, OCH_3), 3.54 (s, 2 H, CH_2Ar), 2.38 (s, 3 H, $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.1 (C-5′), 143.3 (C-1′), 141.1 (C-6), 138.3 (C), 136.7 (C), 136.5 (C), 135.0 (C-4), 130.7 (CH), 128.8 (5 C, C-2′, 4 CH), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 120.7 (C-3), 119.5 (C-5), 115.6 (CH), 113.1 (CH), 55.2 (OCH_3), 51.7 (NCH_2Ph), 34.5 (CH_2Ar), 21.1 ($ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_2$ [M + H]$^+$ 396.1958; found 396.1958.

1-Benzyl-5-[(5-methoxy-3′,5′-dimethyl-1,1′-biphenyl-2-yl)methyl]-pyridin-2(1*H*)-one (9u): The reaction was performed with enamide **5d** (100 mg, 0.26 mmol) and bromoxylene (96 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9u** (72 mg, 68%) as a brown viscous oil. R_f = 0.42 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3028, 2917, 2834, 1667, 1601, 1537, 1495, 1454, 1443, 1351, 1281, 1238, 1196, 1171, 1141, 1072, 1038, 852, 836, 796, 773, 735, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.16 (m, 5 H, Ar-H), 7.07 (d, J = 8.4 Hz, 1 H, H-3′), 6.97 (s, 1 H, H-4′′), 6.96 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.82 (dd, J = 8.4, 2.5 Hz, 1 H, H-4′), 6.77 (s, 2 H, H-2′′, H-6′′), 6.76 (d, J = 2.5 Hz, 1 H, H-6′), 6.56 (d, J = 2.5 Hz, 1 H, H-6), 6.49 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.79 (s, 3 H, OCH_3), 3.54 (s, 2 H, CH_2Ar), 2.29 (s, 6 H, 2 $ArCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.0 (C-5′), 143.5 (C-1′), 141.2 (2 C, C-1 and CH, C-6), 137.6 (2 C, C), 136.5 (C), 135.0 (C-4), 130.6 (CH), 128.7 (3 C, C-2 and 2 CH), 128.6 (CH), 127.9 (2 C, CH), 127.8 (CH), 126.7 (2 C, CH), 120.6 (C-3), 119.6 (C-5), 115.4 (CH), 113.1 (CH), 55.2 (OCH_3), 51.7 (NCH_2Ph), 34.5 (CH_2Ar), 21.2 (2 C, 2 $ArCH_3$) ppm. HRMS (ESI): calcd. for $C_{28}H_{28}NO_2$ [M + H]$^+$ 410.2115; found 410.2113.

1-Benzyl-5-[(4′-*tert*-butyl-5-methoxy-1,1′-biphenyl-2-yl)methyl]-pyridin-2(1*H*)-one (9v): The reaction was performed with enamide **5d** (100 mg, 0.26 mmol) and 4-*tert*-butyl-bromobenzene (110 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 3:2) furnished biarylpyridinone **9v** (75 mg, 66%) as a brown viscous oil. R_f = 0.45 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2962, 2867, 1667, 1602, 1537, 1494, 1454, 1393, 1362, 1298, 1267, 1176, 1140, 1107, 1093, 1039, 1013, 836, 731, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, 2 H) and 7.08 (d, J = 8.4 Hz, 2 H, Ar-H), 7.38–7.12 (m, 5 H, Ar-H), 7.07 (d, J = 8.4 Hz, 1 H, H-3′), 6.99 (dd, J = 9.4, 2.8 Hz, 1 H, H-4), 6.83 (dd, J = 8.4, 2.5 Hz, 1 H, H-4′), 6.77 (d, J = 2.8 Hz, 1 H, H-6′), 6.58 (d, J = 2.5 Hz, 1 H, H-6), 6.48 (d, J = 9.4 Hz, 1 H, H-3), 4.98 (s, 2 H, NCH_2Ph), 3.79 (s, 3 H, OCH_3), 3.56 (s, 2 H, CH_2Ar), 1.34 [s, 9 H, $C(CH_3)_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.1 (C-5′), 150.1 (C-4′′), 143.3 (C-1′), 141.2 (C-6), 138.2 (C), 136.5 (C), 135.1 (C-4), 130.7 (CH), 128.9 (C-2′), 128.7 (2 C, CH), 128.6 (2 C, CH), 127.8 (3 C, CH), 125.0 (2 C, CH), 120.7 (C-3), 119.6 (C-5), 115.6 (CH), 113.2 (CH), 55.3 (OCH_3), 51.8 (NCH_2Ph), 34.5 (C), 34.4 (CH_2Ar), 31.4 [3 C, $C(CH_3)_3$] ppm. HRMS (ESI): calcd. for $C_{30}H_{32}NO_2$ [M + H]$^+$ 438.2428; found 438.2426.

1-Benzyl-5-[(3′,5-dimethoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9w): The reaction was performed with enamide **5d** (100 mg, 0.26 mmol) and 3-bromoanisole (97 mg, 0.52 mmol) in

anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) furnished biarylpyridinone **9w** (72 mg, 67%) as a brown viscous oil. R_f = 0.32 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3029, 2936, 2834, 1667, 1600, 1537, 1496, 1482, 1454, 1352, 1266, 1235, 1205, 1170, 1141, 1074, 1030, 821, 735, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.14 (m, 6 H, Ar-H), 7.09 (d, J = 8.4 Hz, 1 H, H-3′), 6.98 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.87 (dd, J = 8.4, 1.8 Hz, 1 H, H-4′′), 6.84 (dd, J = 8.4, 2.5 Hz, 1 H, H-4′), 6.77 (d, J = 2.5 Hz, 1 H, H-6′), 6.70 (d, J = 8.4 Hz, 1 H, H-6′′), 6.69 (d, J = 1.8 Hz, 1 H, H-2′′), 6.55 (d, J = 2.5 Hz, 1 H, H-6), 6.46 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.79 (s, 3 H) and 3.74 (s, 3 H, 2 OCH_3), 3.55 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (C=O), 159.3 (C-3′′), 158.1 (C-6′), 143.2 (C-1′), 142.6 (C-1′′), 141.0 (C-6), 136.5 (C), 135.0 (C-4), 130.8 (CH), 129.1 (CH), 128.7 (3 C, C-2′ and 2 CH), 127.9 (2 C, CH), 127.8 (CH), 121.3 (CH), 120.7 (C-3), 119.3 (C-5), 115.4 (CH), 114.4 (CH), 113.3 (CH), 112.7 (CH), 55.3, 55.2 (2 OCH_3), 51.7 (NCH_2Ph), 34.5 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_3$ $[M + H]^+$ 412.1907; found 412.1908.

1-Benzyl-5-[(4′,5-dimethoxy-1,1′-biphenyl-2-yl)methyl]pyridin-2(1*H*)-one (9x): The reaction was performed with enamide **5d** (100 mg, 0.26 mmol) and 4-bromoanisole (97 mg, 0.52 mmol) in anhydrous DMF (2 mL) with Ph_3P (13.6 mg, 20 mol-%), Cs_2CO_3 (337.7 mg, 1.0 mmol), and $Pd(OAc)_2$ (5.8 mg, 10 mol-%). After combining the reagents at room temperature, the mixture was heated to 120 °C, as described for **5a**. Purification of the crude product by flash chromatography (ethyl acetate/hexane, 1:4 to 7:3) furnished biarylpyridinone **9x** (53 mg, 50%) as a brown viscous oil. R_f = 0.32 (ethyl acetate/hexane, 4:1). IR (neat): $\tilde{\nu}$ = 3030, 2934, 2835, 1667, 1603, 1537, 1494, 1454, 1441, 1352, 1292, 1246, 1220, 1175, 1142, 1108, 1073, 1039, 1024, 877, 834, 776, 734, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.23 (m, 3 H, Ar-H), 7.18 (d, J = 7.9 Hz, 2 H, Ar-H), 7.08 (d, J = 8.4 Hz, 1 H, H-3′), 7.04 (d, 2 H) and 6.83 (d, J = 8.7 Hz, 2 H, Ar-H), 6.98 (dd, J = 9.4, 2.5 Hz, 1 H, H-4), 6.82 (dd, J = 8.4, 2.5 Hz, 1 H, H-4′), 6.74 (d, J = 2.5 Hz, 1 H, H-6′), 6.52 (d, J = 2.5 Hz, 1 H, H-6), 6.46 (d, J = 9.4 Hz, 1 H, H-3), 4.97 (s, 2 H, NCH_2Ph), 3.82 (s, 3 H) and 3.79 (s, 3 H, 2 OCH_3), 3.54 (s, 2 H, CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (C=O), 158.7 (C-4′′), 158.1 (C-5′), 143.0 (C), 141.0 (C-6), 136.5 (C), 134.9 (C-4), 133.6 (C), 130.8 (CH), 130.0 (2 C, CH), 129.0 (C-2′), 128.7 (2 C, CH), 127.9 (2 C, CH), 127.8 (CH), 120.7 (C-3), 119.4 (C-5), 115.8 (CH), 113.5 (2 C, CH), 113.0 (CH), 55.3 (2 OCH_3), 51.6 (NCH_2Ph), 34.5 (CH_2Ar) ppm. HRMS (ESI): calcd. for $C_{27}H_{26}NO_3$ $[M + H]^+$ 412.1907; found 412.1908.

Supporting Information (see also the footnote on the first page of this article): Copies of NMR spectra for all new compounds.

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[1] J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359–1469.
[2] J. M. Brunel, *Chem. Rev.* **2005**, *105*, 857–897.
[3] L. Feliu, M. Planas, *Int. J. Pept. Res. Ther.* **2005**, *11*, 53–97.
[4] S. Laschat, A. Baro, N. Steinke, F. Giesselmann, C. Hägele, G. Scalia, R. Judele, E. Kapatsina, S. Sauer, A. Schreivogel, M. Tosoni, *Angew. Chem.* **2007**, *119*, 4916–4973; *Angew. Chem. Int. Ed.* **2007**, *46*, 4832–4887.
[5] R. Kandre, K. Feldman, H. E. H. Meijer, P. Smith, A. D. Schlüter, *Angew. Chem.* **2007**, *119*, 5044–5047; *Angew. Chem. Int. Ed.* **2007**, *46*, 4956–4959, and references cited therein.
[6] S. P. Stanforth, *Tetrahedron* **1998**, *54*, 263–303.
[7] O. Baudoin, *Angew. Chem.* **2007**, *119*, 1395–1397; *Angew. Chem. Int. Ed.* **2007**, *46*, 1373–1375.
[8] For some reviews, see: a) K. Godula, D. Sames, *Science* **2006**, *312*, 67–72; b) L.-C. Campeau, K. Fagnou, *Chem. Commun.* **2006**, 1253–1264; c) O. Daugulis, V. G. Zaitsev, D. Shabashov, Q.-N. Pham, A. Lazareva, *Synlett* **2006**, 3382–3388; d) I. J. S. Fairlamb, *Annu. Rep. Prog. Chem. Sect. B: Org. Chem.* **2007**, *103*, 68–89; e) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174–238.
[9] For recent examples, see: a) G. Cuny, M. Bois-Choussy, J. Zhu, *Angew. Chem.* **2003**, *115*, 4922–4925; *Angew. Chem. Int. Ed.* **2003**, *42*, 4774–4777; b) G. Cuny, M. Bois-Choussy, J. Zhu, *J. Am. Chem. Soc.* **2004**, *126*, 14475–14484; c) S. Hernández, R. SanMartin, I. Tellitu, E. Domínguez, *Org. Lett.* **2003**, *5*, 1095–1098.
[10] J. Hassan, C. Hathroubi, C. Gozzi, M. Lemaire, *Tetrahedron* **2001**, *57*, 7845–7855.
[11] For some reviews, see: a) J. F. Hartwig, *Angew. Chem.* **1998**, *110*, 2154–2177; *Angew. Chem. Int. Ed.* **1998**, *37*, 2046–2067; b) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644–4680; c) C. Mauger, G. A. Mignani, *Aldrichimica Acta* **2006**, *39*, 17–24.
[12] Compound **1b**: a) R. R. Bard, J. F. Bunnett, R. P. Traber, *J. Org. Chem.* **1979**, *44*, 4918–4924; b) G. P. M. van Klink, H. J. R. de Boer, G. Schat, O. S. Akkerman, F. Bickelhaupt, A. L. Spek, *Organometallics* **2002**, *21*, 2119–2135.
[13] Compound **1c**: S.-i. Kuwabe, K. E. Torraca, S. L. Buchwald, *J. Am. Chem. Soc.* **2001**, *123*, 12202–12206.
[14] Compound **1d**: K. Orito, T. Hatakeyama, M. Takeo, H. Suginome, *Synthesis* **1995**, 1273–1277.
[15] a) T. Jeffery, *Tetrahedron Lett.* **1991**, *32*, 2121–2124; b) J. P. Wolfe, R. A. Rennels, S. L. Buchwald, *Tetrahedron* **1996**, *52*, 7525–7546; c) L. F. Tietze, K. Kahle, T. Raschke, *Chem. Eur. J.* **2002**, *8*, 401–407; d) D. Bruyère, D. Bouyssi, G. Balme, *Tetrahedron* **2004**, *60*, 4007–4017.
[16] A. Padwa, M. A. Brodney, J. P. Marino Jr., S. M. Sheehan, *J. Org. Chem.* **1997**, *62*, 78–87.
[17] G. Satyanarayana, M. E. Maier, *Tetrahedron* **2008**, *64*, 356–363.
[18] G. Satyanarayana, M. E. Maier, *Org. Lett.* **2008**, *10*, 2361–2364.
[19] For some reviews of domino processes, see: a) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; b) G. Poli, G. Giambastiani, A. Heumann, *Tetrahedron* **2000**, *56*, 5959–5989; c) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem.* **2006**, *118*, 7292–7344; *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186.
[20] For reviews of the chemistry of palladacycles, see: a) G. Dyker, *Chem. Ber./Recueil* **1997**, *130*, 1567–1578; b) G. Dyker, *Angew. Chem.* **1999**, *111*, 1808–1822; *Angew. Chem. Int. Ed.* **1999**, *38*, 1699–1712.
[21] D. J. Cardenas, B. Martin-Matute, A. M. Echavarren, *J. Am. Chem. Soc.* **2006**, *128*, 5033–5040.
[22] For the chemistry of Pd^{IV} complexes, see: a) A. J. Canty, *Acc. Chem. Res.* **1992**, *25*, 83–90; b) A. J. Canty, J. L. Hoare, N. W. Davies, P. R. Traill, *Organometallics* **1998**, *17*, 2046–2051.
[23] a) M. Catellani, F. Frignani, A. Rangoni, *Angew. Chem.* **1997**, *109*, 142–145; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 119–122; b) M. Catellani, F. Cugini, *Tetrahedron* **1999**, *55*, 6595–6602; c) M. Catellani, E. Motti, M. Minari, *Chem. Commun.* **2000**, 157–158; d) F. Faccini, E. Motti, M. Catellani, *J. Am. Chem. Soc.* **2004**, *126*, 78–79.
[24] For reviews, see: a) M. Catellani, *Synlett* **2003**, 298–313; b) M. Catellani, E. Motti, N. Della Ca, R. Ferraccioli, *Eur. J. Org.*

Chem. **2007**, 4153–4165; c) J. B. Johnson, T. Rovis, *Angew. Chem.* **2008**, *120*, 852–884; *Angew. Chem. Int. Ed.* **2008**, *47*, 840–871.

[25] a) C. Bressy, D. Alberico, M. Lautens, *J. Am. Chem. Soc.* **2005**, *127*, 13148–13149; b) B. Mariampillai, D. Alberico, V. Bidau, M. Lautens, *J. Am. Chem. Soc.* **2006**, *128*, 14436–14437; c) P. Thansandote, M. Raemy, A. Rudolph, M. Lautens, *Org. Lett.* **2007**, *9*, 5255–5258; d) A. Rudolph, N. Rackelmann, M. Lautens, *Angew. Chem.* **2007**, *119*, 1507–1510; *Angew. Chem. Int. Ed.* **2007**, *46*, 1485–1488.

[26] G. Karig, M.-T. Moon, N. Thasana, T. Gallagher, *Org. Lett.* **2002**, *4*, 3115–3118.

[27] For further illustrative examples, see: a) G. Dyker, *Angew. Chem.* **1992**, *104*, 1079–1081; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1023–1025; b) G. Dyker, *Angew. Chem.* **1994**, *106*, 117–119; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 103–105; c) O. Baudoin, A. Herrbach, F. Gueritte, *Angew. Chem.* **2003**, *115*, 5914–5918; *Angew. Chem. Int. Ed.* **2003**, *42*, 5736–5740; d) J. Hitce, P. Retailleau, O. Baudoin, *Chem. Eur. J.* **2007**, *13*, 792–799; e) J. Hitce, O. Baudoin, *Adv. Synth. Catal.* **2007**, *349*, 2054–2060.

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