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Mixing *O*-Containing and *N*-Containing Directing Groups for C−H Activation: A Strategy for the Synthesis of Highly Functionalized 2,2′-Biaryls

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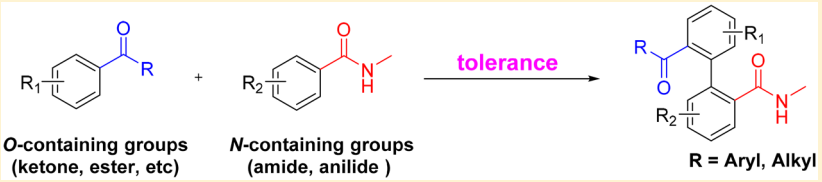
Supporting Information



ABSTRACT: A strategy combining *O*- and *N*-containing directing groups has been developed for the synthesis of 2,2′-biaryl via Pd-mediated C−H bond activation and oxidative coupling. This new transformation may proceed through a mechanism involving Pd(II) and Pd(IV) intermediates. We found the use of PTSA and HFIP to be critical for the reaction and suggest that these reagents could serve as efficient ligands for this C−C bond formation. This methodology provides broad functional group tolerance, excellent reactivity, and high yields.

INTRODUCTION

Transition-metal-catalyzed C−H activation has emerged as a powerful strategy for modern organic synthesis in the past decade.[1] In most studies, the use of coordinating moieties as directing groups, such as *N*-containing[2] or *O*-containing[3] functions, has emerged as a practical and essential strategy for site-selective functionalization. Directing groups (DGs) can position the transition metal to activate the proximate C−H bond with their coordinating ability, thus resulting in high levels of regioselective functionalization. Among DGs, *N*-containing groups (e.g., amide, anilide) and *O*-containing groups (e.g., ketone,[4] ester,[5] carbamate[6]) have been widely employed in the recent years, exhibiting unique efficiency in C−H functionalization.

Over the past few years, constructing a carbon−carbon bond directly from two simple C−H bonds has emerged as a powerful method for organic synthesis.[7] Typically, these studies employed an aryl substrate containing a DG and a coupling partner without such a group. Achieving high selectivity between two arene coupling partners remained challenging. For example, reactions between two substrates containing different DGs inevitably produced homocoupled biaryls as major products instead of the desired cross-coupled products under the current conditions. To date, very few examples employing two different DGs have been reported. Recently, the Shi group reported two examples using carboxylic acid containing reactants to couple with benzyl thioethers[8] or phenols,[9] which generated intramolecularly cyclized 2,2′-biaryl lactones (Scheme 1a). More recently, the Song group combined 8-aminoquinoline amide and 2-phenylpyridine to prepare difunctionalized biaryls with high regioselectivity[10] (Scheme 1b). Other *O*-containing groups (e.g., ketone, ester, carbamate, etc.) have also been employed as DGs, which provided additional synthetic routes for the synthesis of 2,2′-biaryls. However, these reactions were usually restricted to substrates containing weakly coordinating groups and had to be conducted under harsh conditions, such as using the strong acid TfOH as an additive[11] (Scheme 1c).

Inspired by the work of the Shi group using *O*-containing DGs and the study of Song and co-workers employing *N*-based DGs, we wondered whether a single reaction system could tolerate the *N*-containing DGs, such as amide and anilide, with *O*-containing DGs, such as ketones, esters, and carbamates, to afford cross-coupled 2,2′-biaryls (Scheme 1d). It is necessary to point out that these two types of directing groups were normally difficult to combine in one single reaction system because of their different reactivity. C−H functionalization directed by the *O*-containing DGs is generally incompatible with the majority of *N*-containing substrates because the strongly coordinating nitrogen atoms often outcompete other directing groups for catalyst binding, thus preventing activation of the C−H bonds proximate to *O*-containing DGs. For instance, to activate a C−H bond ortho to the amide or anilide groups, several equivalents of AcOH or TFA were sufficient to promote the reaction. On the other hand, strongly acidic TfOH

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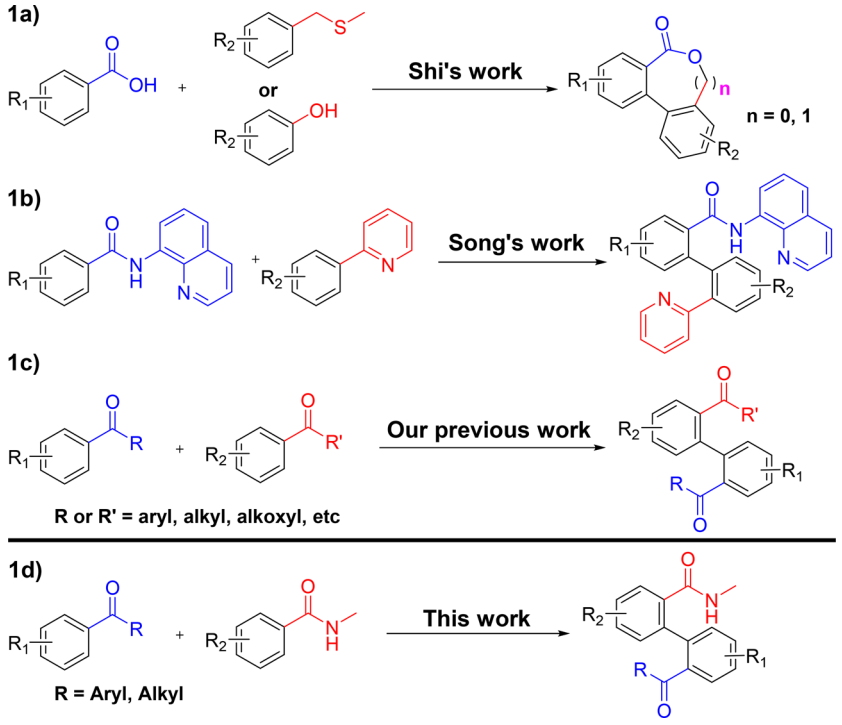
Scheme 1. Oxidative Coupling of Arenes Controlled by Two Different Directing Groups



had to be used as the additive to activate the proximate C−H bond of ketones or esters,. Thus, overcoming the mismatch of these two types of coordianting groups is a critical issue that needs to be addressed. Furthermore, this would provide a readily accessible route for the synthesis of variably functionalized 2,2′-biaryl scaffolds.

RESULTS AND DISCUSSION

Our goal was to find suitable conditions for combining *O*- and *N*-containing DGs in one single reaction system. As illustrated in Table 1, based on our previous results,[11] we first tested the combination of **1a**/**1b** in a 3:1 ratio. However, no desired product was obtained (entry 1). Next, we reversed the ratio of substrates to 1:3. To our delight, the target product was obtained in 8% yield, whereas the remaining **1a** was converted into the homocoupled product in this case (entry 2). Based on this result, we decided to test the mixed acid systems, which combined TfOH with other ligands, to see if the generally employed ligand combinations might be beneficial. Then various additives were screened. Upon addition of reagents bearing a hydroxyl group, such as EtOH and phenol, no desired product was detected (entries 3 and 4). We thus turned to some common carboxylic acids. Indeed, benzoic acid, AcOH, and PivOH as additives provided the desired products in low yields (entries 5−7). The efficiency of this cross-coupling protocol was improved by using TFA, which resulted in higher yields compared to the previously used carboxylic acids (23% yield) (entry 8). Addition of water improved the yield to 30% and resulted in higher selectivity (entry 9). Based on these results, we wondered if an acid additive containing a defined amount of water was helpful. Thus, we turned to PTSA ($TsOH{\cdot}H_2O$). Indeed, PTSA had a beneficial effect on the yield, which was improved to 40% (entry 10). Notably, almost no homocoupling of the aryl ketone was observed in this case, and the rest of the reactant could be recovered. The amount of PTSA also played an important role in promoting the cross-coupling process. To our delight, the yield could be significantly improved to 72% when 2 equiv of PTSA were added (entry 11). Further increasing the amount of PTSA to 3 equiv, however, reduced the yield of the desired product to 61% yield and resulted in inferior selectivity (entry 12). Moreover, no desired product was observed in the absence of oxidants, ligands, or the palladium catalyst, which implied that each of these components played a crucial role in this reaction system (entry 13).

On the basis of the above observations, a preliminary mechanistic experiment was set up to illustrate the definitive role of PTSA in the reaction. As shown in Scheme 2, the desired heterocoupled product **1c** was obtained in 72% yield when the ratio of **1a**/**1b** was 1:3, while the product of homocoupling of **1b** could only be isolated in 5% yield and 70% of **1b** was recovered (Scheme 2A). On the other hand, **1c** was only obtained in 6% yield when the ratio of **1a**/**1b** was 1:1 (Scheme 2B). When the ratio of **1a**/**1b** was 3:1, **1c** could not be obtained, but homocoupling of **1a** was isolated in 76% yield, only 12% of **1a** was recovered, and more than 90% of **1b** could be recovered (Scheme 2C). While we failed to isolate the cyclopalladated complex of **1b**, we obtained the complex of the reaction intermediate **2** and **2′** from the precursor **1a** using a stoichiometric amount of $Pd(OAc)_2$ successfully. As shown in Scheme 2D, when the reaction intermediate **2** and **1b** were employed as the reaction partners, **1c** could only be obtained in 8% yield. Interestingly, when we combined **2′** with **1b**, the yield of **1c** could be remarkably improved to 82% (Scheme 2E). These results could give some clues that **1a** might coordinate to the Pd(II) first. Furthermore, we could conclude that the homocoupling of ketone **1a** was the most preferred process, followed by the cross-coupling and finally by the homocoupling of benzamide **1b**. In addition, we suspected that PTSA might serve as a suitable ligand to stabilize the Pd(II) and Pd(IV) intermediates, which helped to promote the reaction process. Furthermore, when **1d** was used as the substrate, trace amounts

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Table 1. Optimization of Reaction Conditions[a]

1a 1b 1c

entry	conditions	yield[b] (%)
1	TfOH 2.0 equiv, **1a**/**1b** = 3:1 0.00 mmol of **1c**, 0.00 mmol of **1bb**, 0.11 mmol of **1aa** **1c**/**1bb**/**1aa** = **0:0:11**	not detected
2	TfOH 2.0 equiv, **1a**/**1b** = 1:3 0.0080 mmol of **1c**, 0.016 mmol of **1bb**, 0.036 mmol of **1aa** **1c**/**1bb**/**1aa** = **1:2:4.5**	8
3	TfOH 2.0 equiv, EtOH 2.0 equiv, **1a**/**1b** = 1:3 0.00 mmol of **1c**, 0.00 mmol of **1bb**, 0.00 mmol of **1aa** **1c**/**1bb**/**1aa** = **0:0:0**	NR
4	TfOH 2.0 equiv, phenol 2.0 equiv, **1a**/**1b** = 1:3 0.00 mmol of **1c**, 0.00 mmol of **1bb**, 0.00 mmol of **1aa** **1c:1bb:1aa** = **0:0:0**	NR
5	TfOH 2.0 equiv, benzoic acid 2.0 equiv, **1a**/**1b** = 1:3 0.00 mmol **1c**, 0.014 mmol **1bb**, 0.013 mmol **1aa** **1c:1bb:1aa** = **1:1.4:1.3**	10
6	TfOH 2.0 equiv, AcOH 2.0 equiv, **1a**/**1b** = 1:3 0.012 mmol of **1c**, 0.026 mmol **1bb**, 0.016 mmol **1aa** **1c:1bb:1aa** = **1:2.2:1.3**	12
7	TfOH 2.0 equiv, PivOH 2.0 equiv, **1a**/**1b** = 1:3 0.011 mmol of **1c**, 0.016 mmol of **1bb**, 0.019 mmol of **1aa** **1c**/**1bb**/**1aa** = **1:1.5:1.7**	11
8	TfOH 2.0 equiv, TFA 2.0 equiv, **1a**/**1b** = 1:3 0.023 mmol of **1c**, 0.050 mmol of **1bb**, 0.027 mmol of **1aa** **1c**/**1bb**/**1aa** = **1:2.2:1.2**	23
9	TfOH 2.0 equiv, H_2O 2.0 equiv, **1a**/**1b** = 1:3 0.030 mmol of **1c**, 0.020 mmol of **1bb**, 0.0080 mmol of **1aa** **1c**/**1bb**/**1aa** = **3.8:2.5:1**	30
10	PTSA 1.0 equiv, **1a**/**1b** = 1:3 0.040 mmol of **1c**, 0.0090 mmol of **1bb**, 0.0050 mmol of **1aa** **1c**/**1bb**/**1aa** = **8:1.8:1**	40
11	PTSA 2.0 equiv, **1a**/**1b** = 1:3 0.072 mmol of **1c**, 0.0075 mmol of **1bb**, 0.0020 mmol of **1aa** **1c**/**1bb**/**1aa** = **36:3.8:1**	72[c]
12	PTSA 3.0 equiv, **1a**/**1b** = 1:3 0.062 mmol **1c**, 0.012 mmol **1bb**, 0.0060 mmol **1aa** **1c**/**1bb**/**1aa** = **10:2:1**	61
13	no Pd(II), or no oxidants, or no additives 0.00 mmol of **1c**, 0.00 mmol of **1bb**, 0.00 mmol of **1aa** **1c**/**1bb**/**1aa** = **0:00**	NR

[a]Standard conditions: **1a** 0.1 mmol, $Pd(OAc)_2$ 0.10 equiv, $NaIO_4$ 1.6 equiv, $K_2S_2O_8$ 3.0 equiv, HFIP 1.5 mL, 70 °C. [b]NMR yield [c]Isolated yield. **1aa**, homocoupling of **1a**; **1bb**, homocoupling of **1b**.

of C−O bond formation product **1e** were observed (Scheme 2F), which implied that HFIP may serve as an effective ligand.

On the basis of these results, a possible mechanism for this reaction was suggested and is illustrated in Scheme 3. In the pathway A, step (i) involves the chelation of palladium to carbonyl oxygen atom from the ketone and the formation of adimeric Pd complex. In the second step (ii), Pd(II) can be oxidized into a possible Pd(IV) intermediate,[12] followed by ligand exchange with the benzamide during the third step (iii). The final step (iv) involves C−C bond-forming reductive elimination to afford the desirable product and turn Pd(IV) back into Pd(II). In another potential pathway B, the Pd(II) dimer may first go through a Pd(III) intermediate,[13] which is then further oxidized to Pd(IV). After reductive elimination, the desired 2,2′-difunctional biaryl product may be obtained.

With the optimal conditions in hand, we began to examine the reaction scope. As illustrated in Table 2, a broad range of highly diverse and complex 2,2′-difunctional biaryls (**2a**−**k**) were effectively constructed in good yields. We first tested the unsubstituted benzophenone as a starting material, from which the desired product **2a** could be obtained in satisfactory yields. For other benzophenones, electron-rich (**2b**) and electron-deficient (**2c**,**d**) functional groups were well tolerated. We could also obtain the desired compound in 51% yield using the sterically hindered *ortho*-substituted benzophenone (**2e**). Besides aromatic groups, alkyl groups including the adamantyl and *tert*-butyl groups (**2f**,**g**) were also compatible with the reaction conditions. Notably, ketones containing easily oxidizable *α*-proton could also be effectively transformed into the desired product (**2h**) with excellent chemoselectivity. When benzamides bearing electron-deficient groups, such as Cl, were tested, the cross-coupling products could be obtained in 65−70% yields (**2i**,**j**). Benzamides containing electron-rich groups, such as a methoxyl group, were cross-coupled equally efficiently (**2k**). Even the *o*-fluoro-substituted benzamide performed well in this reaction, which gave the desired product in 72% yield (**2l**). To our delight, the new reaction demonstrated compatibility with all these functional groups by generating the desired products in good yields.

We then tried to apply the developed conditions to further combinations merging *O*- and *N*-containing DGs. As illustrated in Table 3, in addition to benzamides, benzophenone also reacted with phenylacetamide (**3a**) as well as difluorobenzoyl-protected anilide (**3b**) to furnish the desired cross-coupling products. Carbamates also showed good compatibility with benzamide-, anilide-, as well as phenylacetamide-derivatized coupling partners (**3c**−**h**) in moderate to good yields. Furthermore, it was observed that this reaction system could also combine ester-containing aryls with anilide to afford, for example, compound **3i** in 60% yield (**3i**). In addition, another type of directing group, succinimide, also showed good compatibility with dichloro-substituted anilide to give **3j** in 61% yield. These 2,2′-difunctional biaryls can further serve as useful building blocks for constructing a variety of heterocycle scaffolds and related bioactive molecules.

CONCLUSION

In conclusion, we have developed a new strategy which can combine *O*- and *N*-containing DGs to provide diverse biaryl compounds. This transformation might proceed through a mechanism involving two different C−H activation steps involving distinct Pd(II) and Pd(IV) complexes. PTSA and HFIP facilitate the reaction and may serve as ligands in the mechanism. The developed method features broad functional group tolerance, excellent reactivity, and high product yields. Further synthetic applications of this reaction are in progress in our laboratory.

EXPERIMENTAL SECTION

I. Materials and Methods. All commercial materials (Alfa Aesar, Aladdin, and J&K Chemical, Ltd.) were used without further

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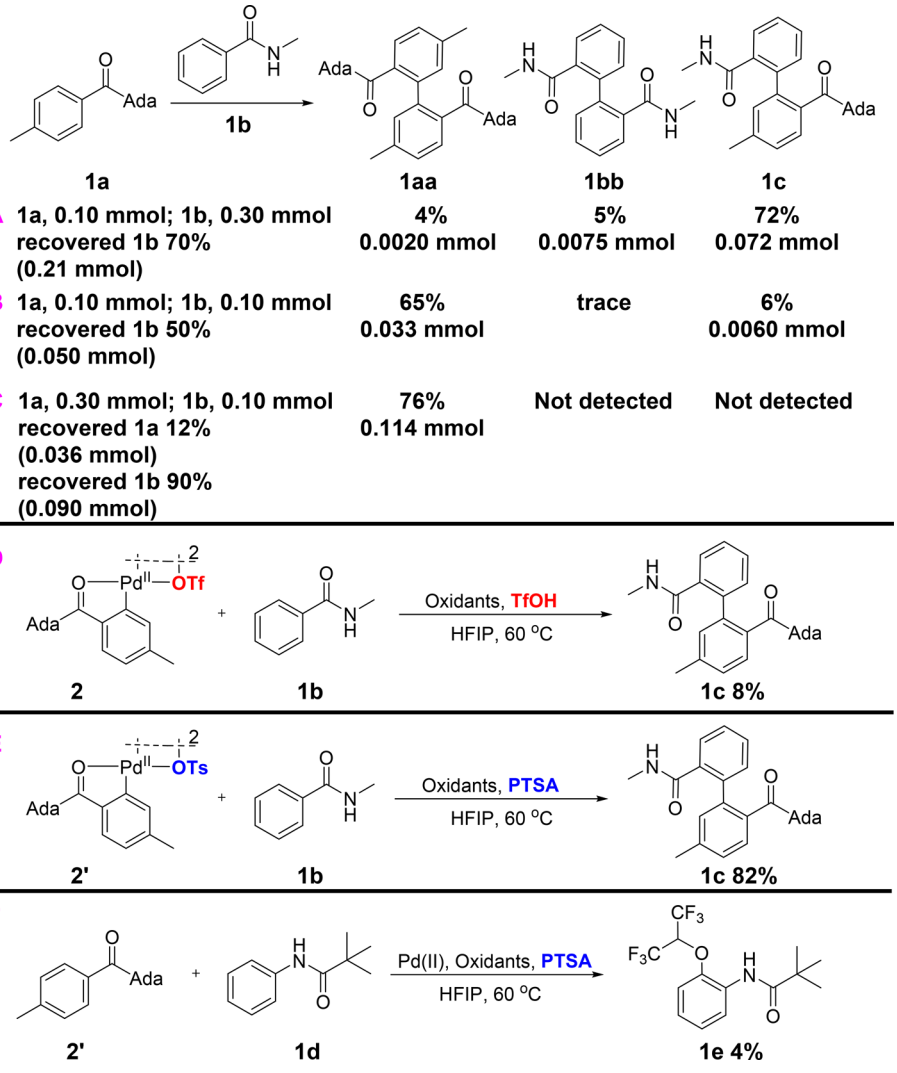
Scheme 2. Mechanism Investigation



Scheme 3. Proposed Mechanism

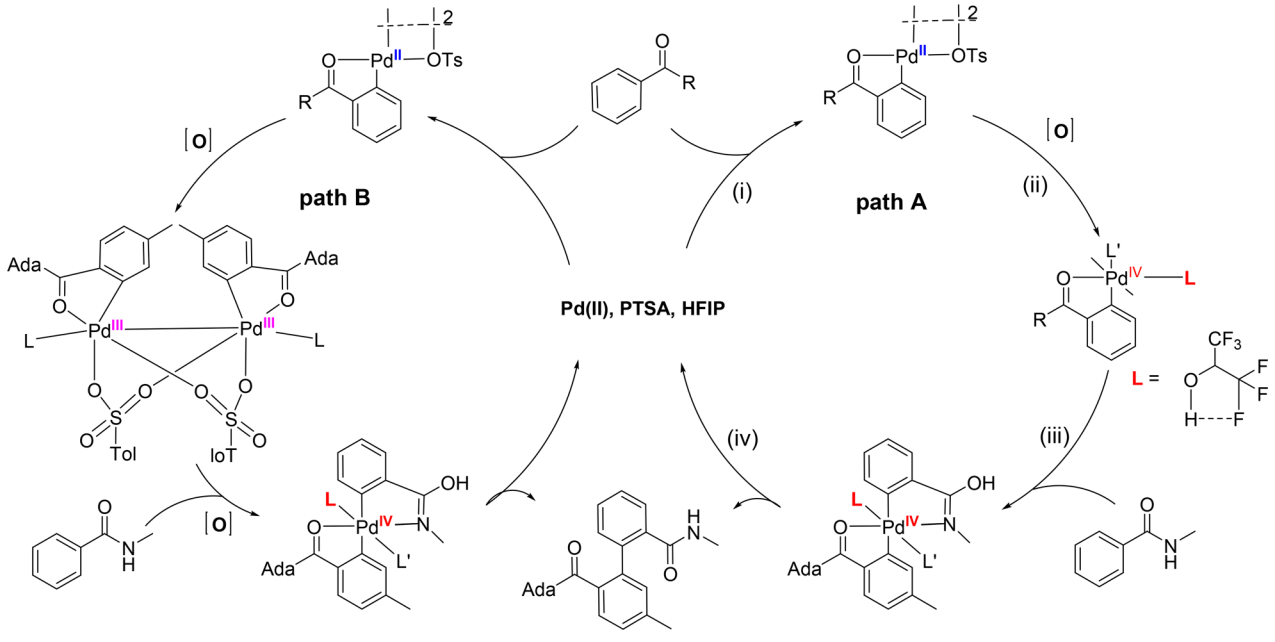


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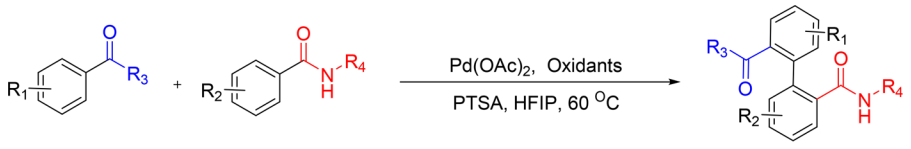
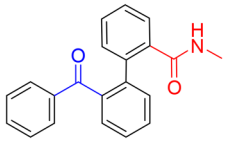
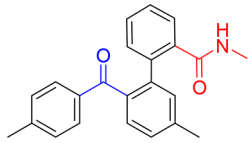
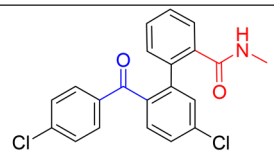
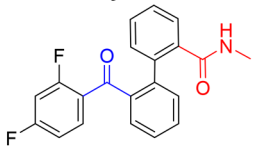
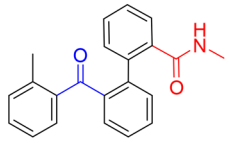
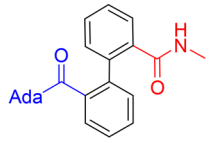
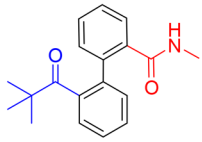
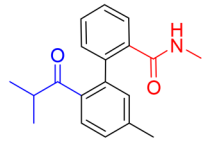
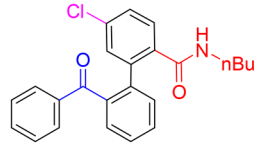
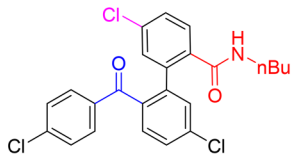
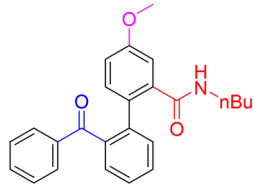
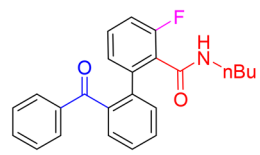
Table 2. Testing the Scope of the Reaction: Oxidative Coupling of Ketones with Benzamides[a]



		
2a 80%, 0.080 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 32:3:1**	**2b** 60%, 0.060 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 24:3:1**	**2c** 82%, 0.082 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 32.8:3:1**
		
2d 71%, 0.071 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 28.4:3:1**	**2e** 51%, 0.051 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 20.4:3:1**	**2f** 60%, 0.060 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 24:3:1**
		
2g 69%, 0.069 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 27.6:3:1**	**2h** 50%, 0.050 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 20:3:1**	**2i** 65%, 0.065 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 26:3:1**
		
2j 70%, 0.070 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 28:3:1**	**2k** 62%, 0.062 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 24.8:3:1**	**2l** 72%, 0.072 mmol Homo-coupling of ketone < 5% (0.0025 mmol) Homo-coupling of benzamide < 5% (0.0075 mmol) **Selectivity ratio > 28.8:3:1**

[a]Isolated yields are shown. Ketone 0.1 mmol, benzamide 3.0 equiv, $Pd(OAc)_2$ 0.10 equiv, $NaIO_4$ 1.6 equiv, $K_2S_2O_8$ 3.5 equiv, PTSA 4.0−6.0 equiv, HFIP 1.5 mL. Selectivity ratio = (cross-coupling product)/(homocoupling of benzamide)/(homocoupling of ketone).

purification. All solvents were analytical grade. The potassium persulfate was ground to a powder. The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE^{III} 400 MHz spectrometer in $CDCl_3$ using TMS or solvent peak as a standard. All ^{13}C NMR spectra were recorded with complete proton decoupling. Low-resolution mass spectral analyses were performed with a Waters AQUITY UPLC/MS. All reactions were carried out in sealed tube with Teflon cap. Analytical TLC was performed on Yantai Chemical Industry Research Institute silica gel 60 F254 plates, and flash column chromatography was performed on Qingdao Haiyang Chemical Co. Ltd. silica gel 60 (200−300mesh). The rotavapor was BUCHI's Rotavapor *R*$\bar{3}$.

II. General Procedure for the Synthesis of 2,2′-Biaryls. $Pd(OAc)_2$ (10% mmol), $NaIO_4$ (1.2−1.6 equiv), $K_2S_2O_8$ (3.0−4.0 equiv), and the starting material (substrate **1** (0.1 mmol), substrate **2** (3.0 equiv)) were dissolved in commercial hexafluoroisopropanol (HFIP) (1.5 mL) in a sealed tube. Following that, TfOH or TsOH·H_2O (3.6−4.4 equiv) was added into the reaction solution. The mixture was heated for 5−8 h at 35−60 °C. After completion of the reaction, the mixture was cooled to room temperature, and then saturated $NaHCO_3$ was added to quench the reaction. The reaction mixture was diluted with DCM and washed once with saturated aqueous $NaHCO_3$. The resulting mixture was concentrated in vacuo and then purified by column chromatography on 200−300 mesh silica gel to afford the desired products.

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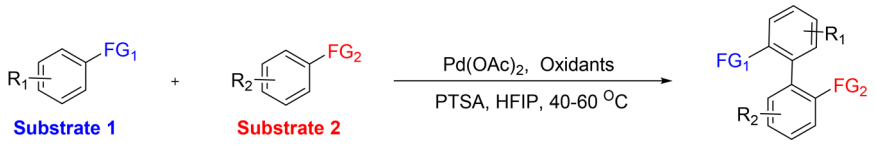
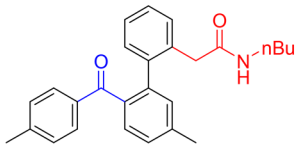
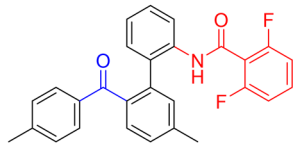
Table 3. Oxidative Coupling Controlled by Two Different Directing Groups[a]

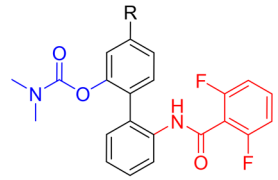




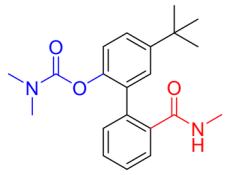
3a 66%, 0.066 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 26.4:3:1



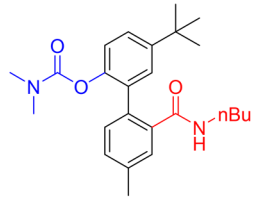
3b 70%, 0.070 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 28:3:1



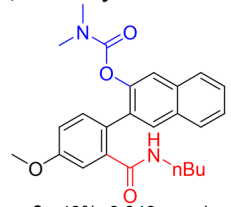
3c, **R= Me,** 73%, 0.073 mmol
3d, **R= OMe,** 60%, 0.060 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
3c, selectivity ratio > 28.4:3:1
3d, selectivity ratio > 28.4:3:1



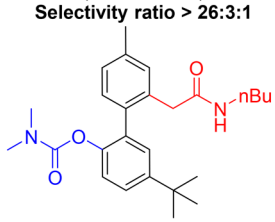
3e 65%, 0.065 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 26:3:1



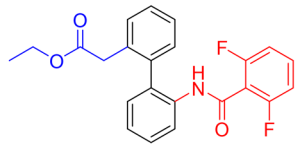
3f 72%, 0.072 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 28.8:3:1



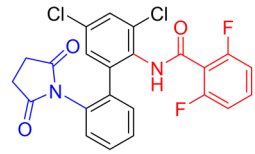
3g 43%, 0.043 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 17.2:3:1



3h 63%, 0.063 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 25.2:3:1



3i 60%, 0.060 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 24:3:1



3j 61%, 0.061 mmol
Homo-coupling of substrate 1 < 5% (0.0025 mmol)
Homo-coupling of substrate 2 < 5% (0.0075 mmol)
Selectivity ratio > 24.4:3:1

[a]Isolated yields are shown. Substrate 1 0.1 mmol, substrate 2 3.0 equiv, $Pd(OAc)_2$ 0.10 equiv, $NaIO_4$ 1.6 equiv, $K_2S_2O_8$ 3.5 equiv, PTSA 4.0 equiv, HFIP 1.5 mL. Selectivity ratio = (cross-coupling product)/(homocoupling of substrate 2)/(homocoupling of substrate 1).

III. Data of Products. *2′-((3r,5r,7r)-Adamantane-1-carbonyl)-N-methyl-[1,1′-biphenyl]-2-carboxamide (**1c**).* Following the general procedure, (3r,5r,7r)-adamantan-1-yl(*p*-tolyl)methanone (26 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (81 mg, 0.30 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (3.1 equiv, 60 mg) were used. The reaction mixture was stirred at 70 °C for 6 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.3). Finally, compound **1c** (27.9 mg, white solid) was isolated in 72% yield: mp 134.6−135.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.64 (dd, J = 7.6 Hz, J = 1.2 Hz, 1H), 7.54−7.50 (m, 1H), 7.38−7.29 (m, 3H), 7.15 (d, J = 7.6 Hz, 1H), 7.02 (s, 1H), 6.99 (dd, J = 7.2 Hz, J = 0.4 Hz, 1H), 2.54 (d, J = 5.2 Hz, 1H), 2.33 (s, 3H), 2.05 (s, 3H), 2.94−1.88 (m, 6H), 1.77−1.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.2, 170.1, 139.6, 139.5, 138.3, 137.7, 136.7, 131.4, 128.8, 128.7, 128.5, 128.0, 127.3, 125.2, 46.7, 39.5, 36.5, 28.2, 26.3, 21.4; IR (neat) ν_{max} 3314, 2904, 2851, 1656 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{30}NO_2$ $[M + H]^+$ 388.2277, found 388.2278.

*N-(2-((1,1,1,3,3,3-Hexafluoropropan-2-yl)oxy)phenyl)pivalamide (**1e**).* Following the general procedure, (3r,5r,7r)-adamantan-1-yl(*p*-tolyl)methanone (26 mg, 0.10 mmol), *N*-methylbenzamide (54 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (81 mg, 0.30 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (5.2 equiv, 100 mg) were used. The reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 4:1, R_f = 0.4). Finally, compound **1e** (4.2 mg, colorless syrup) was isolated in 4% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.47 (d, J = 8.0 Hz, 1H), 8.01 (br, 1H), 7.16 (t, J = 8.0 Hz, 1H), 7.08 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 4.93−4.88 (m, 1H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 176.9, 146.2, 129.6, 125.4, 124.0, 121.4, 114.0, 40.2, 27.5; ^{19}F NMR (400 MHz, $CDCl_3$) δ (ppm) −73.63; IR (neat) ν_{max} 3458, 2964, 1680, 1524 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{16}NO_2F_6$ $[M + H]^+$ 344.1085, found 344.1087.

*Preparation of Dimeric Pd Complex (**2**).* To a 15 mL sealed-tube were added adamantan-1-yl(4-methylphenyl)methanone **1a** (102 mg, 0.40 mmol), $Pd(OAc)_2$ (102 mg, 0.45 mmol), and 1 mL of DCE. The

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tube was sealed and stirred at 40 °C for 5 min. Then TfOH (45 mg, 0.3 mmol) was added. The vial was stirred at 40 °C for 2.5 min and then cooled to room temperature. The reaction mixture was filtered and washed with a 2 mL mixture of petroleum ether/DCE (1:1) to give the desired OTf's bridged palladacycle product **2** as yellow needles (189 mg, 93%) that could be characterized by NMR. This palladacycle compound was stable at room temperature in the dry solid state for about 1 week but sensitive to moisture: ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.14 (d, J = 8.4 Hz, 2H), 7.50 (s, 2H), 7.12 (d, J = 8.0 Hz, 2H), 2.34 (s, 6H), 2.14 (s, 12H), 2.09 (s, 6H), 1.84−1.74 (m, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 155.3, 146.7, 141.6, 133.10, 126.8, 120.7 (q, J_{C-F} = 320 Hz), 46.9, 35.6, 27.5, 22.2; ^{19}F NMR (400 MHz, DMSO-d_6) δ (ppm) −77.74. Spectral data are in agreement with literature values.[4d]

Preparation of Dimeric Pd Complex 2′. To a 15 mL sealed tube were added adamantan-1-yl(4-methylphenyl)methanone **1a** (102 mg, 0.40 mmol), $Pd(OAc)_2$ (102 mg, 0.45 mmol), and 1 mL of HFIP. The tube was sealed and stirred at 50 °C for 2.5 min. Then PTSA (90 mg, 0.46 mmol) was added. The vial was stirred at 50 °C for 15 min and then cooled to room temperature. The reaction mixture was filtered and washed with a 2 mL mixture of petroleum ether/DCE (1:1) to give the desired OTs's bridged palladacycle product **2′** as yellow needles (73 mg, 86%) that can be characterized by NMR. This palladacycle compound was stable at room temperature in the dry solid state for about 1 week but sensitive to moisture: ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.14 (d, J = 8.4 Hz, 2H), 7.50 (s, 2H), 7.47 (d, J = 8.0 Hz, 4H), 7.13−7.10 (m, 6H), 2.34 (s, 6H), 2.28 (s, 6H), 2.14 (s, 12H), 2.09 (s, 6H), 1.84−1.74 (m, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 155.3, 146.7, 145.8, 141.6, 137.6, 133.1, 128.0, 126.8, 125.5, 46.9, 35.6, 27.5, 22.2, 20.8.

*2′-Benzoyl-N-methyl--[1,1′-biphenyl]-2-carboxamide (**2a**).* Following the general procedure, benzophenone (19 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (100 mg, 0.37 mmol), HFIP 1.5 mL and $TsOH·H_2O$ (5.5 equiv, 100 mg) were used. The reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2a** (25.4 mg, white solid) was isolated in 80% yield: mp 111.4−112.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.91 (d, J = 7.6 Hz, 2H), 7.66−7.62 (m, 2H), 7.50 (d, J = 7.2 Hz, 3H), 7.45−7.41 (m, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.14 (br, 1H), 6.94 (d, J = 7.6 Hz, 1H), 2.58 (d, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 199.2, 170.3, 141.4, 138.1, 137.9, 137.4, 136.8, 134.1, 131.0, 130.8, 130.7, 129.4, 128.8, 128.7, 128.5, 128.3, 128.0, 126.9, 26.4; IR (neat) ν_{max} 3342, 3059, 2918, 1662 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{18}NO_2$ $[M + H]^+$ 316.1338, found 316.1332.

*N,5′-Dimethyl-2′-(4-methylbenzoyl)-[1,1′-biphenyl]-2-carboxamide (**2b**).* Following the general procedure, di-*p*-tolylmethanone (21 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (44 mg, 0.20 mmol), $K_2S_2O_8$ (81 mg, 0.30 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (5.0 equiv, 95 mg) were used. The reaction mixture was stirred at 60 °C for 6 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2b** (20.6 mg, colorless syrup) was isolated in 60% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.38−7.28 (m, 5H), 7.21−7.17 (m, 2H), 7.14 (s, 1H), 6.90 (d, J = 7.6 Hz, 1H), 2.59 (d, J = 4.7 Hz, 3H), 2.45 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 198.9, 170.4, 145.0, 141.6, 141.1, 138.4, 137.3, 135.3, 134.6, 131.6, 131.0, 129.5, 129.3, 128.8, 128.3, 127.9, 127.5, 126.9, 26.4, 21.9, 21.6; IR (neat) ν_{max} 3312, 2923, 1737, 1642, 1604 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{22}NO_2$ $[M + H]^+$ 344.1651, found 344.1649.

*5′-Chloro-2′-(4-chlorobenzoyl)-N-methyl-[1,1′-biphenyl]-2-carboxamide (**2c**).* Following the general procedure, bis(4-chlorophenyl)-methanone (26 mg, 0.10 mmol), *N*-butyl-4-chlorobenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (27 mg, 0.12 mmol), $K_2S_2O_8$ (86 mg, 0.30 mmol), HFIP (1.2 mL), and TfOH (3.5 equiv, 33 μL, in this case, PTSA was replaced by TfOH) were used. The reaction mixture was stirred at 65 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2c** (34 mg, yellow solid) was isolated in 82% yield: mp 128.6−129.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.81 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 7.6 Hz, 1H), 7.44 (m, 3H), 7.47−7.44 (m, 3H), 7.37−7.33 (d, J = 7.6 Hz, 1H), 6.93 (d, J = 7.2 Hz, 2H), 2.64 (d, J = 4.8 Hz 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.7, 143.2, 140.9, 137.0, 136.9, 136.8, 135.9, 135.0, 132.0, 131.1, 129.7, 129.2, 129.0, 128.5, 128.3, 127.3, 77.5, 77.2, 76.8, 26.5; IR (neat) ν_{max} 3417, 2921, 1655, 1646 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{16}Cl_2NO_2$ $[M + H]^+$ 384.0558, found 384.0556.

*2′-(2,4-Difluorobenzoyl)-N-methyl-[1,1′-biphenyl]-2-carboxamide (**2d**).* Following the general procedure, (2,4-difluorophenyl)-(phenyl)methanone (22 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (100 mg, 0.35 mmol), HFIP (1.5 mL), and TfOH (4.0 equiv, 37 μL) were used. The reaction mixture was stirred at 60 °C for 6 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2d** (24.7 mg, colorless syrup) was isolated in 71% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.79−7.74 (m, 1H), 7.64 (dd, J = 1.2 Hz, J = 7.6 Hz, 1H), 7.53−7.49 (m, 1H), 7.44−7.39 (m, 2H), 7.37−7.33 (m, 2H), 7.29−7.25 (m, 1H), 7.03 (d, J = 7.6 Hz, 1H), 7.01−6.96 (m, 1H), 6.91−6.85 (m, 1H), 6.81−6.81 (m, 1H), 2.60 (d, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 194.9, 170.2, 166.3 (dd, J_{C-F} = 256 Hz, J_{C-F} = 11.8 Hz), 162.7 (dd, J_{C-F} = 258 Hz, J_{C-F} = 12.7 Hz), 140.7, 139.1, 138.1, 137.2, 134.1 (dd, J_{C-F} = 10.5 Hz, J_{C-F} = 7.8 Hz), 131.4, 131.1, 129.6, 129.2, 128.3, 128.03, 128.00 (d, J_{C-F} = 2.2 Hz), 127.4, 122.6 (dd, J_{C-F} = 10.6 Hz, J_{C-F} = 3.5 Hz), 112.3 (dd, J_{C-F} = 21.5 Hz, J_{C-F} = 3.5 Hz), 105.3 (t, J_{C-F} = 25.5 Hz); IR (neat) ν_{max} 3327, 2920, 1649, 1607 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{16}F_2NO_2$ $[M + H]^+$ 352.1149, found 352.1140.

*N-Methyl-2′-(2-methylbenzoyl)-[1,1′-biphenyl]-2-carboxamide (**2e**).* Following the general procedure, phenyl(*o*-tolyl)methanone (20 mg, 0.10 mmol), *N*-butyl-4-chlorobenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.36 mmol), HFIP (1.2 mL), and $TsOH·H_2O$ (6.4 equiv, 125 mg) were used. The reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2e** (16.8 mg, colorless syrup) was isolated in 51% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.65 (dd, J = 0.4 Hz, J = 7.6 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.50 (dd, J = 1.6 Hz, J = 7.2 Hz, 1H), 7.47−7.43 (m, 1H), 7.39−7.32 (m, 4H), 7.30−7.24 (m, 3H), 7.05 (d, J = 6.8 Hz, 2H), 2.60 (d, J = 4.9 Hz, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 201.1, 170.3, 141.3, 140.4, 139.5, 138.5, 137.2, 136.7, 132.6, 132.5, 132.1, 131.1, 130.9, 129.4, 129.1, 128.8, 128.3, 128.0, 127.1, 125.6, 77.5, 77.2, 76.8, 26.4, 21.3; IR (neat) ν_{max} 3317, 2924, 1646 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{22}H_{20}NO_2$ $[M + H]^+$ 330.1494, found 330.1504.

*2′-(Adamantane-1-carbonyl)-N-methyl-[1,1′-biphenyl]-2-carboxamide (**2f**).* Following the general procedure, ((3r,5r,7r)-adamantan-1-yl)(phenyl)methanone (24 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (86 mg, 0.32 mmol), HFIP (1.3 mL), and $TsOH·H_2O$ (4.2 equiv, 80 mg) were used. The reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.30). Finally, compound **2f** (23 mg, white solid) was isolated in 60% yield: mp 174.5−175.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.64 (d, J = 7.2 Hz, 1H), 7.48−7.45 (m, 1H), 7.40−7.31 (m, 5H), 7.23−7.21 (m, 1H), 7.03 (d, J = 7.6 Hz, 1H), 2.53 (d, J = 4.8 Hz, 3H), 2.06 (s, 3H), 1.92 (d, J = 18.0 Hz, 6H), 1.77−1.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.3, 170.1, 139.5, 139.3, 138.1, 137.8, 130.1, 129.4, 128.9, 128.8, 128.5, 128.2, 126.7, 125.0, 77.5, 77.2, 76.8, 46.7, 39.5, 36.5, 28.1, 26.2;

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IR (neat) ν_{max} 3295, 2900, 2850, 1679, 1637 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{28}NO_2$ $[M + H]^+$ 374.2120, found 374.2129.

*N-Methyl-2′-pivaloyl-[1,1′-biphenyl]-2-carboxamide (**2g**).* Following the general procedure, 2,2-dimethyl-1-phenylpropan-1-one (17 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.3 mL) and $TsOH·H_2O$ (4.2 equiv, 80 mg) were used. The reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.30). Finally, compound **2g** (20 mg, white solid) was isolated in 69% yield: mp 103.4−104.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.64 (d, J = 7.2 Hz, 1H), 7.48−7.46 (m, 1H), 7.37−7.30 (m, 5H), 7.24−7.22 (m, 1H), 7.00 (d, J = 7.6 Hz, 1H), 2.54 (d, J = 4.8 Hz, 3H),1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.2, 170.1, 139.8, 139.3, 138.2, 137.7, 130.9, 129.6, 129.0, 128.5, 128.2, 126.8, 124.8, 77.5, 77.2, 76.8, 44.4, 28.3, 26.2; IR (neat) ν_{max} 3322, 2960, 2927, 1658 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{22}NO_2$ $[M + H]^+$ 296.1651, found 296.1647.

*2′-Isobutyryl-N,5′-dimethyl-[1,1′-biphenyl]-2-carboxamide (**2h**).* Following the general procedure, 2-methyl-1-(*p*-tolyl)propan-1-one (17 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (81 mg, 0.30 mmol), HFIP (1.3 mL), and $TsOH·H_2O$ (3.1 equiv, 60 mg) were used. The reaction mixture was stirred at 60 °C for 8 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.30). Finally, compound **2h** (15 mg, colorless syrup) was isolated in 50% yield: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.66 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.13 (s, 1H), 7.04 (s, 1H), 6.89 (d, J = 7.6 Hz, 1H), 3.39−3.33 (m, 1H), 2.56 (d, J = 4.8 Hz, 3H), 2.36 (s, 3H), 1.16−1.11 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.4, 141.6, 140.9, 139.0, 137.1, 135.8, 132.0, 128.5, 128.3, 127.8, 127.1, 77.5, 77.2, 76.8, 38.3, 29.8, 26.3, 21.5; IR (neat) ν_{max} 3316, 2970, 2930, 1654 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{19}H_{22}NO_2$ $[M + H]^+$ 296.1651, found 296.1652.

*2′-Benzoyl-N-butyl-5-chloro-[1,1′-biphenyl]-2-carboxamide (**2i**).* Following the general procedure, benzophenone (19 mg, 0.10 mmol), *N*-butyl-4-chlorobenzamide (70 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (100 mg, 0.40 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (6.5 equiv, 130 mg) were used. The reaction mixture was stirred at 70 °C for 10 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2i** (25 mg, colorless syrup) was isolated in 64% yield: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93−7.91 (m, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.61 (d, J = 8.2 Hz, 1H), 7.55−7.50 (m, 3H), 7.47−7.45 (m, 2H), 7.34−7.30 (m, 3H), 6.92 (d, J = 2.0 Hz, 1H), 3.26−3.21 (m, 1H), 2.95−2.92 (m, 1H), 1.00−0.85 (m, 4H), 0.70−0.67 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 198.9, 168.4, 140.3, 139.8, 137.7, 136.6, 136.1, 135.0, 134.3, 131.1, 130.9, 129.9, 128.9, 128.8, 128.6, 128.3, 127.4, 77.5, 77.2, 76.8, 39.4, 31.2, 19.9, 13.8; IR (neat) ν_{max} 3313, 2918, 1647 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{23}ClNO_2$ $[M + H]^+$ 392.1417, found 392.1414.

*N-Butyl-5,5′-dichloro-2′-(4-chlorobenzoyl)-[1,1′-biphenyl]-2-carboxamide (**2j**).* Following the general procedure, bis(4-chlorophenyl)-methanone (25 mg, 0.10 mmol), *N*-butyl-4-chlorobenzamide (68 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.5 mL), and TfOH (4.2 equiv, 39 μL) were used. The reaction mixture was stirred at 70 °C for 10 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2j** (32 mg, colorless syrup) was isolated in 70% yield: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.83 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.45 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.40−7.32 (m, 3H), 7.11 (t, J = 4.8 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 3.27 (q, J = 6.4 Hz, 1H), 2.97 (t, J = 6.0 Hz, 1H), 1.05−1.00 (m, 4H), 0.75−7.71 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 196.5, 167.9, 142.1, 141.2, 138.3, 137.5, 135.8, 135.7, 135.3, 134.7, 132.1, 131.2, 130.1, 129.9, 129.4, 128.8, 128.6, 127.7, 77.5, 77.2, 76.8, 39.4, 31.4, 20.0, 13.9; IR (neat) ν_{max} 3312, 2959, 2930, 1645 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{21}Cl_3NO_2$ $[M + H]^+$ 460.0638, found 460.0638.

*2′-Benzoyl-N-butyl-4-methoxy-[1,1′-biphenyl]-2-carboxamide (**2k**).* Following the general procedure, benzophenone (19 mg, 0.10 mmol), *N*-butyl-3-methoxybenzamide (63 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.13 mmol), $K_2S_2O_8$ (96 mg, 0.35 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (6.5 equiv, 130 mg) were used. The reaction mixture was stirred at 60 °C for 10 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2k** (24 mg, colorless syrup) was isolated in 62% yield: ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.53−7.46 (m, 3H), 7.41 (d, J = 4.4 Hz, 2H), 7.34 (d, J = 7.2 Hz, 1H), 7.30−7.28 (m, 1H), 7.19 (d, J = 2.8 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.72 (dd, J = 2.8 Hz, J = 8.4 Hz, 1H), 3.80 (s, 3H), 3.24 (s, 1H), 2.95 (s, 1H), 0.99−0.89 (m, 4H), 0.69 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 199.3, 169.3, 159.2, 141.2, 138.6, 138.3, 136.8, 134.1, 131.6, 130.8, 130.6, 130.3, 130.0, 128.8, 128.2, 126.7, 116.2, 112.5, 77.5, 77.2, 76.8, 55.5, 39.4, 31.2, 19.9, 13.9; IR (neat) ν_{max} 3314, 2958, 2931, 1648 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{26}NO_3$ $[M + H]^+$ 388.1913, found 388.1915.

*2′-Benzoyl-N-butyl-3-fluoro-[1,1′-biphenyl]-2-carboxamide (**2l**).* Following the general procedure, benzophenone (19 mg, 0.10 mmol), *N*-butyl-2-fluorobenzamide (60 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (96 mg, 0.35 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (6.5 equiv, 130 mg) were used. The reaction mixture was stirred at 65 °C for 12 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **2l** (27 mg, white solid) was isolated in 72% yield: mp 134.3−135.6 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.90−7.88 (m, 2H), 7.67−7.63 (m, 1H), 7.54−7.48 (m, 3H), 7.46−7.40 (m, 3H), 7.29−7.27 (m, 1H), 7.16−7.10 (m, 1H), 7.06−7.01 (m, 1H), 6.72 (d, J = 7.2 Hz, 1H), 3.23 (s, 1H), 2.96 (s, 1H), 0.95 (s,4H), 0.71−0.67 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 198.8, 164.7, 159.6 (d, J_{C-F} = 250 Hz), 140.2 (d, J_{C-F} = 3.7 Hz), 139.7 (d, J_{C-F} = 2.2 Hz), 138.1, 136.8, 134.1, 131.0, 130.8, 130.0 (d, J_{C-F} = 9.9 Hz), 128.8, 128.5, 127.2, 126.2 (d, J_{C-F} = 17.2 Hz), 124.2 (d, J_{C-F} = 3.1 Hz), 115.6, 115.4, 39.2, 31.2, 19.9, 13.8; IR (neat) ν_{max} 3256, 2957, 2930, 1667, 1647 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{24}H_{23}FNO_2$ $[M + H]^+$ 376.1713, found 376.1708.

*(E)-N-Butyl-2-(2′-((hydroxyimino)(p-tolyl)methyl)-5′-methyl-[1,1′-biphenyl]-2-yl)acetamide (**3a′**).* Following the general procedure, di-*p*-tolylmethanone (21 mg, 0.10 mmol), *N*-butyl-2-phenylacetamide (60 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.5 mL), and $TsOH·H_2O$ (4.2 equiv, 80 mg) were used. The reaction mixture was stirred at 60 °C for 16 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.25). Finally, compound **3a** was calculated in 66% yield (calculated based on the NMR with *p*-nitrobenzaldehyde as a standard). Then to a solution of **3a** in pyridine (1.5 mL) was added $NH_2OH·HCl$ (10.0 equiv) and the mixture refluxed for 8 h; after purification, we finally obtained **3a′**, and the structure of **3a′** confirmed the structure of **3a** (white solid): mp 132.1−133.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.14 (q, J = 7.2 Hz, 2H), 7.06−7.01 (m, 1H), 6.96 (d, J = 8.8 Hz, 5H), 6.99 (d, J = 7.2 Hz, 1H), 5.56 (t, J = 5.6 Hz, 1H), 3.26−3.17 (m, 2H), 3.14−2.97 (m, 2H), 2.37 (s, 3H), 2.27 (s, 3H), 1.34−1.14 (m,4H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) δ (ppm) 171.4, 158.0, 141.0, 140.5, 139.0, 138.8, 134.0, 133.2, 131.3, 130.5, 130.4, 129.9, 129.0, 128.4, 128.3, 127.7, 126.6, 77.5, 77.2, 76.8, 41.5, 39.5, 31.7, 21.5, 21.4, 20.1, 13.9; IR (neat) ν_{max} 3270, 2954, 2923, 1647, 1615 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_2O_2$ $[M + H]^+$ 415.2386, found 415.2386.

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*2,6-Difluoro-N-(5′-methyl-2′-(4-methylbenzoyl)-[1,1′-biphenyl]-2-yl)benzamide (**3b**).* Following the general procedure, 2,6-difluoro-*N*-phenylbenzamide (24 mg, 0.10 mmol), di-*p*-tolylmethanone (60 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.5 mL), and TfOH (3.2 equiv, 30 μL) were used. The reaction mixture was stirred at 60 °C for 5 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.30). Finally, compound **3b** (32 mg, colorless syrup) was isolated in 70% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.14 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.36−7.25 (m, 6H), 7.14 (d, J = 8.0 Hz, 1H), 7.05−7.03 (m, 2H), 6.89 (t, J = 8.0 Hz, 2H), 2.45 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 198.0, 170.1, 160.2 (dd, J_{C-F} = 251 Hz, J_{C-F} = 6 Hz), 158.7, 144.4, 140.9, 137.4, 136.7, 135.0, 134.8, 133.4, 131.8 (t, J_{C-F} = 10 Hz), 130.4, 130.0, 129.1, 128.7, 128.6, 128.2, 125.2, 124.0, 114.7 (t, J_{C-F} = 22 Hz), 112.2 (dd, J_{C-F} = 5.6 Hz, J_{C-F} = 1.9 Hz), 21.8, 21.5; IR (neat) ν_{max} 3310, 2922, 2852, 1655 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{28}H_{22}F_2NO_2$ $[M + H]^+$ 442.1619, found 442.1618.

*2′-(2,6-Difluorobenzamido)-4-methyl-[1,1′-biphenyl]-2-yl Dimethylcarbamate (**3c**).* Following the general procedure, *m*-tolyl dimethylcarbamate (18 mg, 0.10 mmol), 2,6-difluoro-*N*-phenylbenzamide (70 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.5 mL), and TfOH (3.2 equiv, 30 μL) were used. The reaction mixture was stirred at 45 °C for 10 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.40). Finally, compound **3c** (30 mg, colorless oil) was isolated in 73% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.28 (d, J = 8.2 Hz, 1H), 7.87 (s, 1H), 7.46−7.38 (m, 1H), 7.34−7.28 (m, 1H), 7.22−7.20 (m, 2H), 7.10 (d, J = 8.0 Hz, 1H), 7.01 (s, 1H), 6.89−6.86 (m, 2H), 2.75 (s, 5H), 2.73 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 160.1 (dd, J_{C-F} = 249 Hz, J_{C-F} = 6.0 Hz), 158.8, 155.1, 149.2, 140.0, 135.5, 131.8 (t, J_{C-F} = 10 Hz), 131.2, 130.8, 129.5, 128.6, 128.2, 126.9, 124.8, 123.6, 114.7 (t, J_{C-F} = 26 Hz), 112.2−111.9 (m), 36.6, 36.2, 21.3; IR (neat) ν_{max} 3396, 2918, 2850, 1705, 1691 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{21}F_2N_2O_3$ $[M + H]^+$ 411.1520, found 411.1521.

*2′-(2,6-Difluorobenzamido)-4-methoxy-[1,1′-biphenyl]-2-yldimethylcarbamate (**3d**).* Following the general procedure, 3-methoxyphenyl dimethylcarbamate (20 mg, 0.10 mmol), 2,6-difluoro-*N*-phenylbenzamide (75 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.5 mL), and TfOH (3.2 equiv, 30 μL) were used. The reaction mixture was stirred at 40 °C for 15 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.40). Finally, compound **3d** (26 mg, colorless oil) was isolated in 60% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.28 (d, J = 8.4 Hz, 1H), 7.82 (br, 1H), 7.43−7.39 (m, 1H), 7.33−7.28 (m, 1H), 7.21−7.19 (m, 3H), 6.90−6.84 (m, 3H), 6.75 (s, 1H), 3.83 (s, 1H), 2.75 (s, 3H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.0 (d, J_{C-F} = 255 Hz), 160.6, 154.8, 150.3, 135.7, 132.0, 131.8 (t, J_{C-F} = 10 Hz), 131.0, 129.3, 128.6, 124.8, 123.3, 122.9, 114.7 (t, J_{C-F} = 18 Hz), 112.2, 112.1 (t, J_{C-F} = 25 Hz), 55.7, 36.7, 36.3; IR (neat) ν_{max} 3253, 2924, 1706, 1687 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{21}F_2N_2O_4$ $[M + H]^+$ 427.1469, found 427.1472.

*5-tert-Butyl-2′-(methylcarbamoyl)-[1,1′-biphenyl]-2-yl Dimethylcarbamate (**3e**).* Following the general procedure, 4-*tert*-butylphenyl dimethylcarbamate (23 mg, 0.10 mmol), *N*-methylbenzamide (42 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.3 mL), and TsOH·H_2O (6.5 equiv, 130 mg) were used. The reaction mixture was stirred at 35 °C for 14 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.15). Finally, compound **3e** (23 mg, white solid) was isolated in 65% yield: mp 217.5−217.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (t, J = 4.4 Hz, 1H), 7.39−7.34 (m, 3H), 7.31−7.27 (m, 2H), 7.14 (d, J = 3.6 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 2.98 (s, 3H), 2.69 (s, 3H), 2.53 (d, J = 4.8 Hz, 3H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, CDCl3) δ (ppm) 170.2, 155.3, 149.3, 146.1, 137.7, 135.0, 133.4, 129.7, 129.3, 128.7, 128.6, 127.9, 125.8, 122.1, 77.5, 77.2, 76.8, 36.7, 36.4, 34.7, 31.6, 26.4; IR (neat) ν_{max} 3336, 2965, 2932, 1699, 1659 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{27}N_2O_3$ $[M + H]^+$ 355.2022, found 355.2021.

*5-tert-Butyl-2′-(butylcarbamoyl)-4′-methyl-[1,1′-biphenyl]-2-yl dimethylcarbamate (**3f**).* Following the general procedure, 4-*tert*-butylphenyl dimethylcarbamate (23 mg, 0.10 mmol), *N*-butyl-3-methylbenzamide (59 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (96 mg, 0.36 mmol), HFIP (1.5 mL), and TsOH·H_2O (5.2 equiv, 100 mg) were used. The reaction mixture was stirred at 35 °C for 14 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.15). Finally, compound **3f** (30 mg, white solid) was isolated in 72% yield: mp 156.2−156.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.54 (s, 1H), 7.34 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.27 (s, 1H), 7.16 (s, 3H), 7.05 (d, J = 8.4 Hz, 1H), 3.02−2.97 (m, 5H), 2.71 (s, 3H), 2.38 (s, 3H), 1.29 (s, 9H), 1.04 (s, 4H), 0.74 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.5, 155.2, 149.1, 146.3, 137.7, 137.6, 133.5, 132.2, 130.0, 129.7, 129.4, 128.9, 125.6, 122.0, 77.5, 77.2, 76.8, 39.8, 36.7, 36.4, 34.7, 31.6, 30.8, 21.2, 20.1, 13.9; IR (neat) ν_{max} 3301, 2958, 2870, 1707, 1652 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{35}N_2O_3$ $[M + H]^+$ 411.2648, found 411.2651.

*3-(2-(Butylcarbamoyl)-4-methoxyphenyl)naphthalen-2-yl Dimethylcarbamate (**3g**).* Following the general procedure, naphthalen-2-yl dimethylcarbamate (22 mg, 0.10 mmol), *N*-butyl-3-methoxybenzamide (64 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (90 mg, 0.32 mmol), HFIP (1.5 mL), and TsOH·H_2O (5.2 equiv, 100 mg) were used. The reaction mixture was stirred at 35 °C for 14 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.20). Finally, compound **3g** (19 mg, white solid) was isolated in 65% yield: mp 119.2−120.3 °C; ^{1}H NMR (400 MHz, CDCl3) δ (ppm) 7.80 (d, J = 8.8 Hz, 2H), 7.75 (s, 1H), 7.62 (s, 1H), 7.50−7.44 (m, 2H), 7.29−7.25 (m, 3H), 6.96 (dd, J = 2.8 Hz, J = 8.4 Hz, 1H), 3.89 (s, 3H), 3.23 (q, J = 6.4 Hz, 1H), 3.04 (s, 3H), 2.74 (s, 4H), 0.90−0.66 (m, 4H), 0.27 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) δ (ppm) 169.3, 159.2, 155.3, 147.1, 139.4, 133.3, 132.9, 131.8, 131.3, 130.9, 128.1, 127.2, 126.7, 126.6, 126.2, 119.9, 116.0, 113.1, 77.5, 77.2, 76.8, 55.6, 39.5, 36.8, 36.5, 30.9, 19.8, 13.4; IR (neat) ν_{max} 3320, 2955, 2925, 1703, 1647 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{29}N_2O_4$ $[M + H]^+$ 421.2127, found 421.2134.

*5-tert-Butyl-2′-(2-(butylamino)-2-oxoethyl)-4′-methyl-[1,1′-biphenyl]-2-yl Dimethylcarbamate (**3h**).* Following the general procedure, 4-*tert*-butylphenyl dimethylcarbamate (23 mg, 0.10 mmol), *N*-butyl-2-(m-tolyl)acetamide (60 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (30 mg, 0.14 mmol), $K_2S_2O_8$ (108 mg, 0.40 mmol), HFIP (1.5 mL), and TsOH·H_2O (5.2 equiv, 100 mg) were used. The reaction mixture was stirred at 45 °C for 14 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.20). Finally, compound **3h** (26.7 mg, white solid) was isolated in 63% yield: mp 100.1−100.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.30 (s, 1H), 7.14−7.04 (m, 4H), 6.29−6.26 (m, 1H), 3.45−3.35 (m, 2H), 3.12−3.06 (m, 2H), 2.82 (s, 3H), 2.71(s, 3H), 2.36 (s, 3H), 1.37−1.28 (m, 11H), 1.24−1.20 (m, 2H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.8, 155.1, 148.4, 146.7, 137.8, 134.7, 134.4, 133.2, 130.1, 130.0, 128.8, 126.9, 125.8, 122.2, 77.5, 77.2, 76.8, 41.3, 39.4, 36.6, 36.4, 31.7, 31.6, 21.3, 20.2, 13.9; IR (neat) ν_{max} 3296, 2955, 2934, 1711, 1642 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{37}N_2O_3$ $[M + H]^+$ 425.2804, found 425.2806.

*Ethyl 2-(2′-(2,6-Difluorobenzamido)-[1,1′-biphenyl]-2-yl)acetate (**3i**).* Following the general procedure, ethyl 2-phenylacetate (20 mg, 0.10 mmol), 2,6-difluoro-*N*-phenylbenzamide (69 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$

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(81 mg, 0.30 mmol), HFIP (1.5 mL), and TfOH (3.2 equiv, 30 μL) were used. The reaction mixture was stirred at 40 °C for 9 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 2:1, R_f = 0.20). Finally, compound **3i** (23.7 mg, colorless oil) was isolated in 60% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.49 (d, J = 8.4 Hz, 1H), 7.64 (br, 1H), 7.45−7.41 (m, 2H), 7.34−7.29 (m, 5H), 7.26−7.22 (m, 1H), 6.91 (t, J = 8.0 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.65 (s, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.4, 160.1 (dd, J_{C-F} = 251 Hz, J_{C-F} = 6.9 Hz), 158.6, 138.0, 135.2, 134.5, 132.5, 132.1, 132.0 (t, J_{C-F} = 10 Hz), 130.6, 130.4, 129.4, 129.1, 128.7, 128.2, 125.2, 114.7 (t, J_{C-F} = 20 Hz), 112.2 (d, J_{C-F} = 25 Hz), 61.1, 41.2, 14.3; IR (neat) ν_{max} 3308, 2985, 2931, 1732, 1676 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{20}F_2NO_3$ $[M + H]^+$ 396.1411, found 396.1417.

*N-(3,5-Dichloro-2′-(2,5-dioxopyrrolidin-1-yl)-[1,1′-biphenyl]-2-yl)-2,6-difluorobenzamide (**3j**).* Following the general procedure, *N*-(2,4-dichlorophenyl)-2,6-difluorobenzamide (30 mg, 0.10 mmol), 1-phenylpyrrolidine-2,5-dione (53 mg, 0.30 mmol), $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), $NaIO_4$ (35 mg, 0.16 mmol), $K_2S_2O_8$ (81 mg, 0.30 mmol), HFIP (1.5 mL), and TfOH (4.0 equiv, 37 μL) were used. The reaction mixture was stirred at 60 °C for 10 h. After completion of the reaction, the residue was purified by column chromatography on 200−300 mesh silica gel (petroleum ether/ethyl acetate = 1:1, R_f = 0.20). Finally, compound **3j** (29 mg, colorless syrup) was isolated in 61% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.76 (s, 1H), 7.56−7.46 (m, 4H), 7.35−7.28 (m, 1H), 7.23 (d, J = 7.6 Hz, 1H), 7.05 (s, 1H), 6.87 (t, J = 8.0 Hz, 2H), 2.87−2.79 (m, 1H), 2.73−2.65 (m, 2H), 2.53−2.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 177.2, 176.2, 160.2 (dd, J_{C-F} = 256 Hz, J_{C-F} = 6.7 Hz), 159.5, 139.8, 136.1, 135.4, 133.5, 132.1 (t, J_{C-F} = 10 Hz), 131.6, 130.2, 130.0, 129.9, 128.3, 127.6, 113.6 (t, J_{C-F} = 20 Hz), 112.2, 112.1 (dd, J_{C-F} = 20 Hz, J_{C-F} = 5.1 Hz), 28.5, 28.4; IR (neat) ν_{max} 3376, 2954, 2922, 1706, 1690 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{15}Cl_2F_2N_2O_3$ $[M + H]^+$ 475.0428, found 475.0425.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02863.

^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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