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N-Acylphthalimides: Efficient Acyl Coupling Reagents in Suzuki-Miyaura Cross-Coupling by N–C Cleavage Catalyzed by Pd-PEPPSI Precatalysts

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Abstract: We report a general, highly selective method for Suzuki-Miyaura cross-coupling of N-acylphthalimides via N–C(O) acyl cleavage catalyzed by Pd-PEPPSI type precatalysts. Of broad synthetic interest, the method introduces N-acylphthalimides as new, bench-stable, highly reactive, twist-controlled, amide-based precursors to acyl-metal intermediates. The reaction delivers functionalized biaryl ketones by acylative Suzuki-Miyaura cross-coupling with readily available boronic acids. Studies demonstrate that cheap, easily prepared and broadly applicable Pd-PEPPSI type precatalysts supported by a sterically-demanding IPr ancillary ligand provide high yields in this reaction. Preliminary selectivity studies and the effect of Pd-NHC complexes with allyl-type throw-away ligands are described. We expect that N-acylphthalimides will find significant use as amide-based acyl coupling reagents and cross-coupling precursors to acyl-metal intermediates.

Keywords: Suzuki cross-coupling; amide bond N–C cleavage; N–C activation; amide bond twist; acylation; ketones; acylative cross-coupling; palladium; N-heterocyclic carbene; Pd-PEPPSI

1. Introduction

The cross-coupling of amides by transition-metal-catalyzed N–C acyl cleavage has emerged as a powerful method for the construction of C–C and C–X bonds, enabling to utilize traditionally-inert amide derivatives in cross-coupling reactions of broad synthetic importance [1-8]. The amide bond cross-coupling manifold hinges upon the availability of amide bond precursors to achieve facile metal insertion into the N–C bond under operationally-simple and functional-group tolerant reaction conditions [9,10]. The ability to overcome amidic resonance ($n_N \rightarrow \pi^*_{C=O}$ conjugation, 15-20 kcal/mol in planar amides) [11] is supported by amide bond ground-state-destabilization and amide bond twist, which are well-known to facilitate oxidative addition of the amide N–C(O) bond [12].

To date, a wide range of amides and amide-based reagents, including the most reactive N-acyl-glutarimides [13] as well as anilides [14], N-Boc-carbamates [15], N-Ts-sulfonamides [16], N,N-di-Boc amides [17], N-acyl-saccharins [18,19], N-Ms-sulfonamides [20], N-acyl-pyrroles [21], N-Me-pyrimidines [22], N-acyl-succinimides [23-25] and N-Ac-amides [26] have been successfully engaged as electrophilic cross-coupling partners by N–C activation. In all examples described to date, the reactivity has been controlled by a ground-state-destabilization mechanism of the amide bond [12]. However, the widely-used as acylating reagents in organic synthesis N-acylphthalimides [27-29], relying on the versatile phthalimide ring typically associated with the classical Gabriel synthesis [30-32], are yet to be reported in the cross-coupling of amides by N–C(O) bond cleavage.

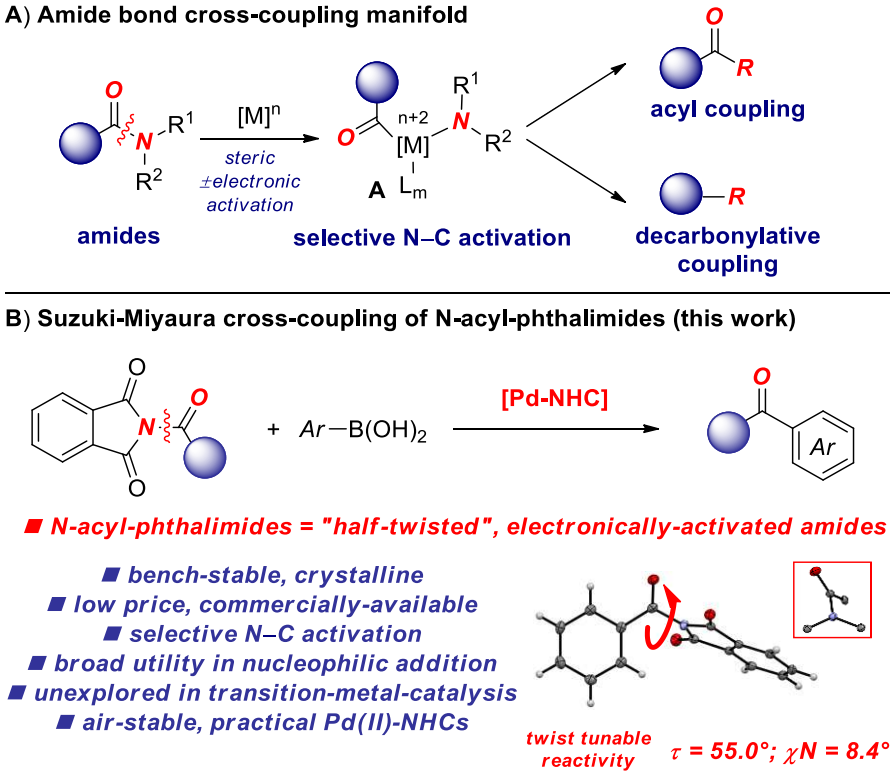
Structural studies showed high amide bond twist ($\tau = 55.0°$; $\chi_N = 8.4°$, Winkler-Dunitz distortion parameters) [33] and electronically-disconnected amide bond (ER < -1.0 kcal/mol, ER = resonance

energy, benzoyl phthalimide) [34], which are the controlling factors in N-acyl-glutarimides as the most reactive amide-based acyl-transfer reagents discovered to date. The major challenge in the N–C(O) metal insertion in N-acylphthalimides is the presence of benzylic carbonyls prone to unselective cleavage.

At the same time, the development of new catalyst systems has generated major advancements in the field of acyl cross-coupling of bench-stable electrophiles [1]. In particular, the advent of Pd-NHC catalysis (NHC = N-heterocyclic carbenes) [35,36], has revolutionized the field and enabled to employ previously unreactive precursors under mild and functional group tolerant conditions, owing to the strong σ-donating character of NHC ancillary ligands [37-40].

On the basis of our interest in amide bond cross-coupling and the development of new catalyst systems, we were intrigued to develop the cross-coupling of versatile N-acylphthalimides with high N–C(O) insertion selectivity.

In this *Special Issue on Suzuki-Miyaura Cross-Coupling*, we report a general, highly selective method for Suzuki-Miyaura cross-coupling of N-acylphthalimides via N–C(O) acyl cleavage catalyzed by Pd-PEPPSI type precatalysts (Scheme 1). The following features of our findings are notable: (1) Of broad synthetic interest, the method introduces N-acylphthalimides as new, bench-stable, highly reactive, twist-controlled, amide-based precursors to acyl metal intermediates. (2) The reaction delivers functionalized biaryl ketones by acylative Suzuki-Miyaura cross-coupling with readily available boronic acids. (3) Studies demonstrate that cheap, easily prepared and broadly applicable Pd-PEPPSI type precatalysts supported by a sterically-demanding IPr ancillary ligand provide high yields in this reaction. (4) Finally, preliminary selectivity studies and the effect of Pd-NHC complexes with allyl-type throw-away ligands are described. Collectively, we expect that N-acylphthalimides will find significant use as amide-based acyl coupling reagents and cross-coupling precursors en route to acyl-metal intermediates.



Scheme 1. (a) Context of this Work; (b) Cross-Coupling of N-Acyl-phthalimides by N–C Activation.

2. Results

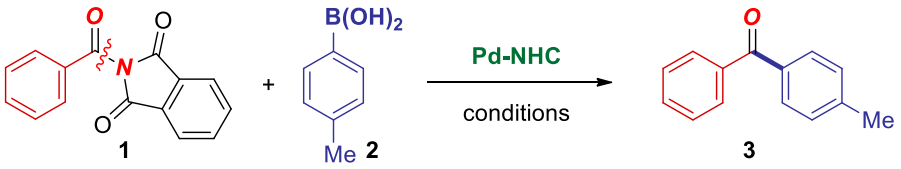
At the outset, the coupling of N-benzoylphthalimide with 4-tolylboronic acid was selected as the model system. Selected optimization results are shown in Table 1. N-Benzoylphthalimide is

unreactive under various Pd-phosphane conditions as well as in the more stringent Negishi cross-coupling [41]. From the start, we selected Pd-PEPPSI type precatalysts as our desired precatalysts for this coupling owing to the low price, ease of synthesis, versatility and the abundance of Pd-PEPPSI type precatalysts reported to date in diverse cross-couplings [42-44].

We were delighted to find that the desired cross-coupling proceeded in promising 27% yield using Pd-PEPPSI-IPr (3 mol%), 4-TolB(OH)$_2$ (2.0 equiv) and K_2CO_3 (3.0 equiv) in dioxane at 60 °C (entry 1). Increasing the reaction temperature had a major effect on the reaction efficiency, affording the product in 80% yield (entry 2). Our further attempts to improve the efficiency by changing the reaction stoichiometry were unsuccessful (entries 3-4). We found that by carefully optimizing reaction temperature, the cross-coupling could be achieved in 90% yield (entries 5-6), presumably by improving stability of the acyl-metal precursor. Interestingly, we found that the solvent choice had a major impact on the reaction (entry 7), while water [45] had a deleterious effect on the cross-coupling (entries 8-9).

Key insight was gained by evaluating several sterically- and electronically-differentiated Pd-NHC precatalysts (entries 10-12, Figure 1). The use of less sterically-demanding IMes ligand significantly decreased the reactivity (entry 10) [46]. Likewise, the extremely-sterically-bulky IPr* [47] ligand resulted in a considerable lower yield under the optimized conditions (entry 11). Furthermore, the use of a sterically-demanding aliphatic wingtip, as in IBu^t [48], resulted in virtually no conversion (entry 12). Generally, IPr is considered as a privileged NHC scaffold in the cross-coupling of aryl electrophiles [37-40]. The present study provides one of the first experimental observations into the ligand effect in the cross-coupling of acyl electrophiles by the Pd-NHC catalysis platform. While further studies are clearly needed to confirm these findings, it appears that at least in some amide cross-couplings IPr should be routinely selected as the first choice in examining the reactivity using Pd-NHC catalysts.

Table 1. Optimization of the Suzuki-Miyaura Cross-Coupling of N-Acyl-phthalimides.[1]



Entry	Catalyst	Ar-B(OH)$_2$ (equiv)	K_2CO_3 (equiv)	Solvent	*T* (°C)	Yield (%)
1	Pd-PEPPSI-IPr	2.0	3.0	dioxane	60	27
2	Pd-PEPPSI-IPr	2.0	3.0	dioxane	110	80
3[2]	Pd-PEPPSI-IPr	2.0	3.0	dioxane	110	80
4	Pd-PEPPSI-IPr	3.0	4.5	dioxane	110	50
5	Pd-PEPPSI-IPr	3.0	4.5	dioxane	80	90
6	Pd-PEPPSI-IPr	2.0	3.0	dioxane	80	89
7	Pd-PEPPSI-IPr	2.0	3.0	THF	80	27
8[3]	Pd-PEPPSI-IPr	2.0	3.0	THF	80	32
9[3]	Pd-PEPPSI-IPr	2.0	3.0	dioxane	80	<10
10	Pd-PEPPSI-IMes	2.0	3.0	dioxane	80	30
11	Pd-PEPPSI-IPr*	2.0	3.0	dioxane	80	24
12	Pd-PEPPSI-IBu^t	2.0	3.0	dioxane	80	<5

[1]Conditions: amide (1.0 equiv), 4-Tol-B(OH)$_2$, base, [Pd-NHC] (3 mol%), solvent (0.25 M), *T*, 15 h. [2][Pd-NHC] (6 mol%). [3]H_2O (5 equiv).

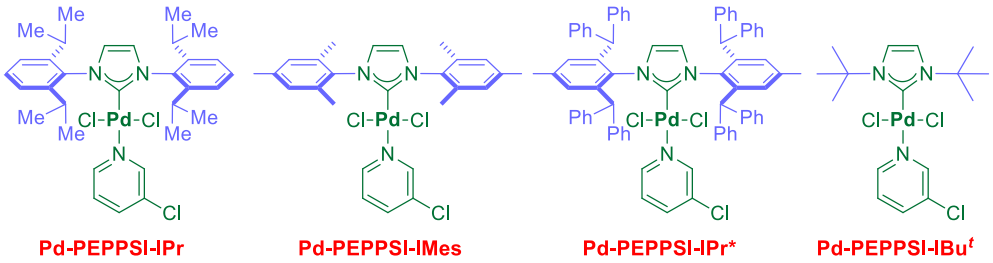
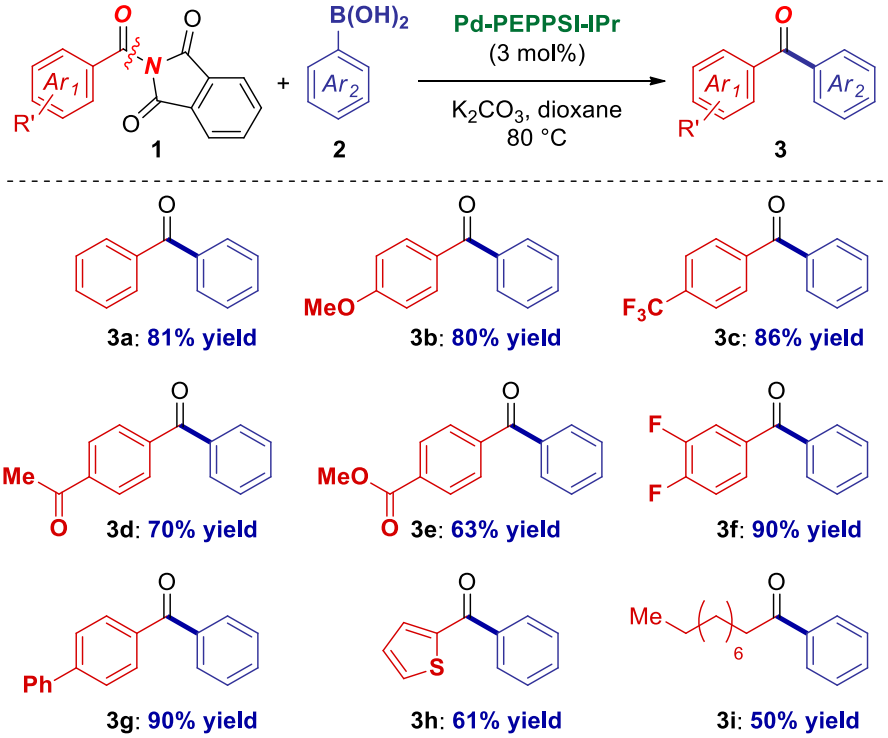


Figure 1. Structures of Air-Stable Pd-PEPPSI Catalysts in Cross-Coupling of N-Acyl-phthalimides.

With the catalyst system in hand, the scope of the reaction with respect to the N-acyl-phthalimide component was next investigated (Scheme 2). We were pleased to find that the reaction readily accommodates electronically-diverse substituents (**3a-3c**), including deactivating electron-donating groups (**3c**). Importantly, the reaction is compatible with electrophilic functional groups, such as ketones (**3d**) and esters (**3e**). It should be noted that these moieties would not be tolerated in the classic Weinreb amide synthesis [49]. Furthermore, polyfluorinated substrates (**3f**), biaryl amides (**3g**) as well as heterocycles important from the medicinal chemistry standpoint (**3h**) are competent substrates for the coupling. Finally, the reaction conditions are even compatible with the challenging alkyl amides (**3i**), which often require extensive optimization of the reaction parameters due to less facile metal insertion [1-8].

Scheme 2. Amide Scope in Pd-NHC-Catalyzed Cross-Coupling of N-Acyl-phthalimides.[1]

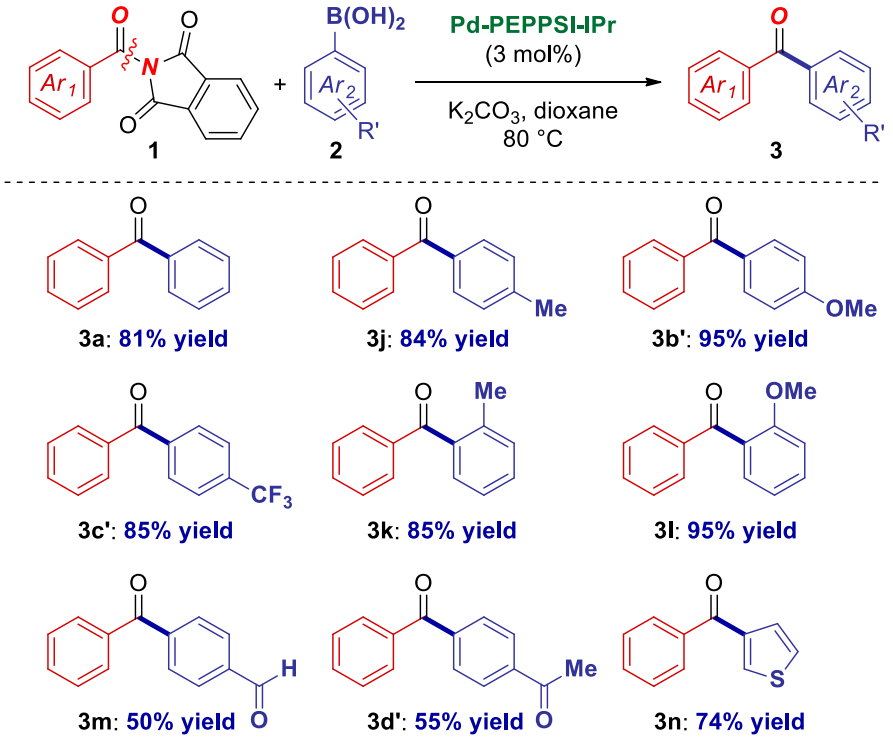


[1]Conditions: amide (1.0 equiv), $ArB(OH)_2$ (2.0 equiv), K_2CO_3 (3.0 equiv), Pd-PEPPSI-IPr (3 mol%), dioxane (0.25 M), 80 °C, 15 h. See SI for details.

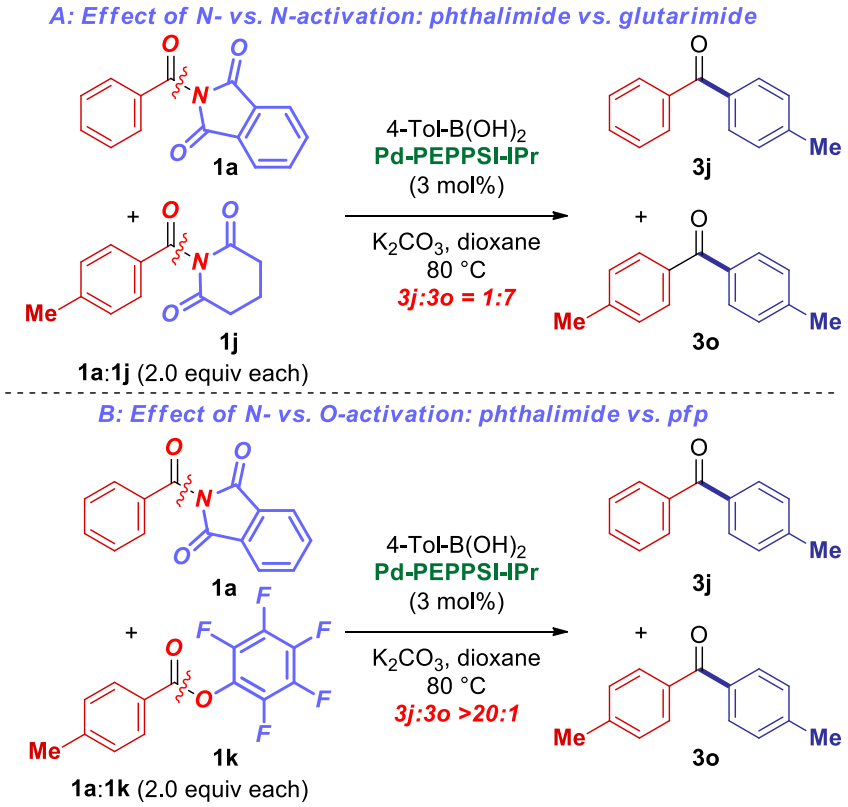
Next, the scope with respect to the boronic acid component was examined (Scheme 3). Pleasingly, the scope was also found to be broad, including a range of electron-donating (**3j-3b′**) and deactivated electron-withdrawing functional groups (**3c′**). Furthermore, steric hindrance was readily tolerated (**3k-3l**). As an important synthetic advantage, the reaction can be used to install electrophilic functional groups that would be problematic in stoichiometric nucleophilic additions,

such as aldehydes (**3m**) and ketones (**3d'**). Finally, we were pleased to find that heterocyclic boronic acids were also tolerated in this novel coupling (**3n**).

Scheme 3. Boronic Acid Scope in Pd-NHC-Catalyzed Cross-Coupling of N-Acyl-phthalimides.[1]

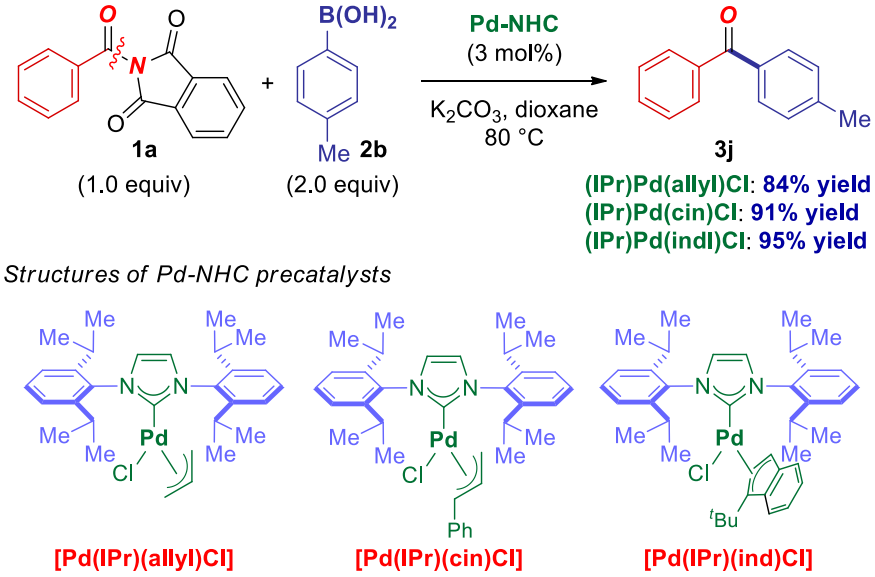


[1]Conditions: amide (1.0 equiv), $ArB(OH)_2$ (2.0 equiv), K_2CO_3 (3.0 equiv), Pd-PEPPSI-IPr (3 mol%), dioxane (0.25 M), 80 °C, 15 h. See SI for details.



Scheme 4. Competition Experiments.

Preliminary selectivity studies were conducted to gain insight into the reactivity of N-acylphthalimides in the N–C(O) cleavage reaction (Scheme 4). N-acylphthalimides represent "half-twisted", electronically-activated amides (τ = 55.0°) [33]. As expected, these reagents are more selective than "fully-perpendicular" (τ = 88.6°) N-acyl-glutarimides (Scheme 4A). Importantly, full selectivity in the cross-coupling of N-acylphthalimides in the presence of electronically-activated pfp esters (pfp = pentafluorophenyl) was observed (Scheme 4B) [50]. This further confirms the unique activation platform of the amide bond, wherein the selectivity is tuned by both sterics an electronics of N-substituents that for obvious reasons is not possible with other acyl electrophiles. Further mechanistic studies are ongoing.



Scheme 5. Suzuki-Miyaura Cross-Coupling of N-Acyl-phthalimides using Pd-NHC Catalysts with Allyl-Type Throw-Away Ligands.

Finally, although we were primarily interested in developing a cross-coupling method using readily-available Pd-PEPPSI type precatalysts, we considered it important to compare the reactivity of Pd-NHC precatalysts bearing pyridine throw-away ligands with allyl-type throw-away ligands (Scheme 5) [51]. As shown, we found that Pd-NHC precatalysts bearing allyl-type ligands, including (IPr)Pd(allyl)Cl [52], (IPr)Pd(cinnamyl)Cl [52] and (IPr)Pd(η^3-1-*t*-Bu-indenyl)Cl [53] all are able to accommodate the coupling, providing the desired product in high yields. Thus, as an important synthetic point, this cross-coupling is tolerant to the nature of the throw-away ligand. Future studies will focus on examination of the amide N–C cross-coupling directed to other throw-away ligands.

3. Discussion

In conclusion, using rational approach to amide bond ground-state-destabilization we have reported the first general method for the Suzuki-Miyaura cross-coupling of N-acylphthalimides. This study takes an important lesson from the recent breakthroughs in catalyst design for acyl cross-coupling reactions of amides, markedly accentuating the high efficiency and selectivity of Pd-NHC precatalysts to achieve cross-coupling of previously incompatible substrates. In a broader context, our report has introduced N-acylphthalimides as new, bench-stable, highly reactive, twist-controlled, amide-based precursors to acyl metal intermediates. Thus, N-acylphthalimides, classic reagents that rely on the versatile phthalimide ring typically associated with the Gabriel synthesis, are now available for amide bond cross-coupling reactions to afford acyl-metal intermediates. Equally importantly, the study has provided key insights into the structure-reactivity connection of Pd-NHC precatalysts in amide bond cross-coupling. We expect that these findings will offer a direct use of N-acylphthalimides in amide-based cross-coupling reactions in both acyl and decarbonylative manifolds that rely on a selective metal insertion into the N–C bond. Future studies

will involve application of the Pd-NHC cross-coupling platform of N-acylphthalimides to the synthesis of alkyl ketones using alkyl-9-BBN reagents and trialkylboranes [54,55].

4. Materials and Methods

General Information. General methods have been published.[13]

General Procedure for Cross-Coupling of N-Acylphthalimides. In a typical cross-coupling procedure, an oven-dried vial was charged with an amide substrate (neat, 1.0 equiv), boronic acid (typically, 2.0 equiv), potassium carbonate (typically, 3.0 equiv), Pd-PEPPSI-IPr (typically, 3 mol%), placed under a positive pressure of argon or nitrogen, and subjected to three evacuation/backfilling cycles under high vacuum. Dioxane (0.25 M) was added at room temperature, then the reaction mixture was placed in a preheated oil bath at 80 °C, and stirred at 80 °C. After the indicated time, the reaction was cooled down, diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography afforded the pure product. Unless previously reported, all new compounds have been characterized by ^{1}H NMR, ^{13}C NMR, HRMS and Mp if applicable.

Representative Procedure for Cross-Coupling of N-Acylphthalimides. An oven-dried vial was charged with 2-benzoylisoindoline-1,3-dione (neat, 281.3 mg, 1.0 mmol), 4-tolylboronic acid (272.0 mg, 2.0 mmol, 2.0 equiv), K_2CO_3 (414.6 mg, 3.0 mmol, 3.0 equiv), Pd-PEPPSI-IPr (3 mol%, 20.4 mg), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Dioxane (0.25 M) was added at room temperature, the reaction mixture was placed in a preheated oil bath at 80 °C, and stirred for 15 h at 80 °C. Next, the reaction mixture was cooled down, diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. A sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (hexanes/ethyl acetate) afforded the title product. Yield 84% (165.0 mg). White solid. Characterization data are included in the section below.

Characterization Data for Products 3a-3n (Schemes 2-3).

Benzophenone (3a). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 8.9 Hz, 4 H), 7.62 (t, *J* = 7.4 Hz, 2 H), 7.51 (t, *J* = 7.6 Hz, 4 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.8, 137.6, 132.4, 130.1, 128.3. **MS** = 182.1 (EI).

(4-Methoxyphenyl)(phenyl)methanone (3b). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.86 (d, *J* = 8.0 Hz, 2 H), 7.78 (d, *J* = 7.6 Hz, 2 H), 7.59 (t, *J* = 7.3 Hz, 1 H), 7.50 (t, *J* = 7.4 Hz, 2 H), 6.99 (d, *J* = 8.0 Hz, 2 H), 3.92 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 195.6, 163.2, 138.3, 132.6, 131.9, 130.2, 129.7, 128.2, 113.6, 55.5. **MS** = 212.1 (EI).

Phenyl(4-(trifluoromethyl)phenyl)methanone (3c). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.93 (d, *J* = 8.0 Hz, 2 H), 7.84 (d, *J* = 7.7 Hz, 2 H), 7.79 (d, *J* = 8.0 Hz, 2 H), 7.66 (t, *J* = 7.4 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 195.5, 140.7, 136.7, 133.7 (J^F = 32.5 Hz), 133.1, 130.1, 130.1, 128.5, 125.4 (J^F = 7.5 Hz), 123.7 (J^F = 273.0 Hz). **^{19}F NMR (471 MHz, $CDCl_3$)** δ -63.41. **MS** = 250.1 (EI).

1-(4-Benzoylphenyl)ethan-1-one (3d). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.09 (d, *J* = 8.2 Hz, 2 H), 7.89 (d, *J* = 8.2 Hz, 2 H), 7.83 (d, *J* = 7.5 Hz, 2 H), 7.65 (t, *J* = 7.4 Hz, 1 H), 7.53 (t, *J* = 7.7 Hz, 2 H), 2.70 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 197.5, 196.0, 139.6, 136.9, 133.0, 130.1, 130.1, 128.5, 128.2, 26.9. **MS** = 224.1 (EI).

Methyl 4-benzoylbenzoate (3e). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.17 (d, *J* = 8.2 Hz, 2 H), 7.87 (d, *J* = 8.2 Hz, 2 H), 7.83 (d, *J* = 7.5 Hz, 2 H), 7.64 (t, *J* = 7.4 Hz, 1 H), 7.53 (t, *J* = 7.6 Hz, 2 H), 3.99 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.0, 166.3, 141.3, 137.0, 133.2, 133.0, 130.1, 129.8, 129.5, 128.5, 52.5. **MS** = 240.1 (EI).

(3,4-Difluorophenyl)(phenyl)methanone (3f). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.76 (d, *J* = 7.7 Hz, 2 H), 7.68 (t, *J* = 9.0 Hz, 1 H), 7.60 (t, *J* = 13.0 Hz, 2 H), 7.50 (t, *J* = 7.7 Hz, 2 H), 7.27 (q, *J* = 8.3 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 194.2, 154.4 (dd, J^1 = 255.0, 12.5 Hz), 150.3 (dd, J^1 = 255.0, 12.5 Hz), 137.0, 134.6 (t, J^5 = 3.8 Hz), 132.9, 130.0, 128.6, 127.2 (q, J^5 = 3.8 Hz), 119.5 (dd, J^3 =17.5, 1.2 Hz), 117.4 (d, J^3 = 17.5 Hz). **^{19}F NMR (471 MHz, $CDCl_3$)** δ -130.59 (d, *J* = 21.4 Hz), -136.17 (d, *J* = 21.4 Hz). **MS** = 218.1 (EI).

[1,1'-Biphenyl]-4-yl(phenyl)methanone (3g). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.94-7.92 (d, *J* = 7.2 Hz, 2 H), 7.88-7.86 (d, *J* = 7.5 Hz, 2 H), 7.75-7.73 (d, *J* = 7.3 Hz, 2 H), 7.69-7.68 (d, *J* = 7.7 Hz, 2 H), 7.65-7.62 (t, *J* = 7.1 Hz, 1 H), 7.55-7.50 (m, 4 H), 7.45-7.42 (t, *J* = 6.7 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.4, 145.3, 140.0, 137.8, 136.3, 132.4, 130.8, 130.0, 129.0, 128.3, 128.2, 127.3, 127.0. **MS** = 258.1 (EI).

Phenyl(thiophen-2-yl)methanone (3h). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.90-7.89 (d, *J* = 8.2 Hz, 2 H), 7.76-7.75 (d, *J* = 4.9 Hz, 1 H), 7.68-7.67 (d, *J* = 3.7 Hz, 1 H), 7.64-7.61 (t, *J* = 7.5 Hz, 1 H), 7.54-7.51 (t, *J* = 7.7 Hz, 2 H), 7.20-7.19 (t, *J* = 4.8 Hz, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 188.3, 143.7, 138.2, 134.9, 134.2, 132.3, 129.2, 128.4, 128.0. **MS** = 188.1 (EI).

1-Phenyldecan-1-one (3i). Colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.99-7.98 (d, *J* = 8.2 Hz, 2 H), 7.59-7.56 (t, *J* = 7.6 Hz, 1 H), 7.50-7.47 (t, *J* = 7.7 Hz, 2 H), 3.00-2.97 (t, *J* = 7.6 Hz, 2 H), 1.79-1.73 (m, 2 H), 1.43-1.29 (m, 12 H), 0.92-0.89 (t, *J* = 6.1 Hz, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 200.7, 137.1, 132.9, 128.6, 128.1, 38.7, 31.9, 29.5, 29.5, 29.4, 29.3, 24.4, 22.7, 14.1. **MS** = 232.1 (EI).

Phenyl(*p*-tolyl)methanone (3j). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.81 (d, *J* = 7.7 Hz, 2 H), 7.75 (d, *J* = 7.5 Hz, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 7.50 (t, *J* = 7.2 Hz, 2 H), 7.31 (d, *J* = 7.7 Hz, 2 H), 2.47 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.5, 143.2, 138.0, 134.9, 132.1, 130.3, 129.9, 129.0, 128.2, 21.7. **MS** = 196.1 (EI).

Phenyl(*o*-tolyl)methanone (3k). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 7.7 Hz, 2 H), 7.60 (d, *J* = 6.9 Hz, 1 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 7.42 (t, *J* = 7.5 Hz, 1 H), 7.37-7.30 (m, 2 H), 7.30-7.27 (m, 1 H), 2.36 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 198.6, 138.6, 137.8, 136.8, 133.1, 131.0, 130.2, 130.1, 128.5, 128.5, 125.2, 20.0. **MS** = 196.1 (EI).

(2-Methoxyphenyl)(phenyl)methanone (3l). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.85-7.83 (d, *J* = 7.7 Hz, 2 H), 7.59-7.56 (t, *J* = 7.5 Hz, 1 H), 7.51-7.48 (t, *J* = 7.4 Hz, 1 H), 7.47-7.44 (t, *J* = 7.2 Hz, 2 H), 7.39-7.38 (d, *J* = 7.7 Hz, 1 H), 7.08-7.05 (t, *J* = 7.2 Hz, 1 H), 7.03-7.01 (d, *J* = 7.7 Hz, 1 H), 3.75 (s, 3 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 196.5, 157.4, 137.8, 132.9, 131.9, 129.9, 129.6, 128.9, 128.2, 120.5, 111.5, 55.6. **MS** = 212.1 (EI).

4-Benzoylbenzaldehyde (3m). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.16 (s, 1 H), 8.04-8.02 (d, *J* = 8.3 Hz, 2 H), 7.96-7.95 (d, *J* = 8.2 Hz, 2 H), 7.84-7.83 (d, *J* = 7.1 Hz, 2 H), 7.68-7.65 (t, *J* = 7.5 Hz, 1 H), 7.55-7.52 (t, *J* = 7.9 Hz, 2 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 195.9, 191.7, 142.6, 138.5, 136.8, 133.2, 130.4, 130.1, 129.5, 128.6. **MS** = 210.1 (EI).

Phenyl(thiophen-3-yl)methanone (3n). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.96 (s, 1 H), 7.88-7.87 (d, *J* = 8.1 Hz, 2 H), 7.64-7.60 (m, 2 H), 7.53-7.50 (t, *J* = 7.7 Hz, 2 H), 7.42-7.41 (m, 1 H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 190.0, 141.3, 138.7, 133.9, 132.3, 129.4, 128.6, 128.4, 126.2. **MS** = 188.1 (EI).

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