JOC The Journal of Organic Chemistry

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Palladium-Catalyzed Direct *ortho*-Acylation through an Oxidative Coupling of Acetanilides with Toluene Derivatives

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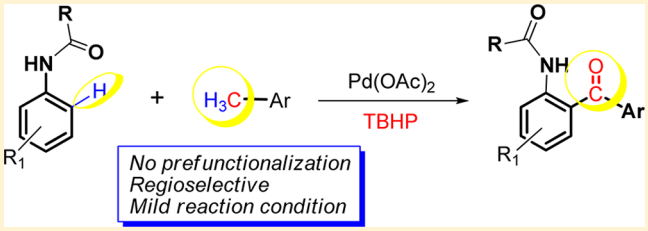
Supporting Information

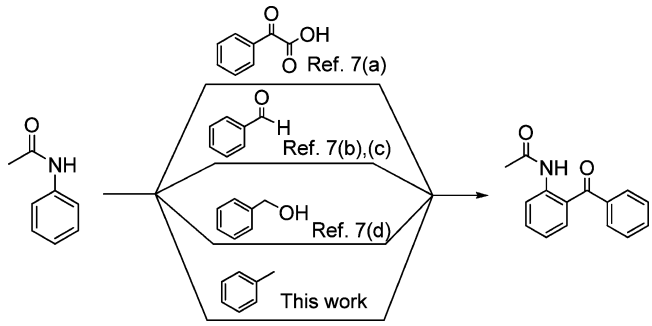
ABSTRACT: A facile *ortho*-acylation of acetanilides by a Pd-catalyzed oxidative C−H activation was developed in which low toxic, stable, and commercially available toluene derivatives were first used as acylation reagents by a tandem reaction to form *o*-acylacetanilides with moderate to good yields. Inexpensive, safe, and environmentally benign TBHP was proved to be an effective oxidant for these transformations.



In the past decade, transition-metal-catalyzed C−H bond functionalization protocols have emerged as a valuable and atom-economical alternative to traditional cross-couplings in the construction of carbon−carbon and carbon−heteroatom bonds and thus have profoundly changed the landscape of organic synthesis.[1] In this strategy, directing groups commonly play a key role by assisting the chelation of substrate to catalyst to activate C−H bond and subsequently achieve the functionalization. In numerous strongly or weakly coordinating directing groups, acylamino group was noticeable. Using acylamino as a directing group, the *ortho* C−H bond of acetanilide could be highly regioselectively functionalized. Some pioneering works such as alkylation,[2] arylation,[3] halogenation,[4] olefination,[5] alkoxylation,[6] and acylation[7] were reported in succession. Further studies on the acylamino group directed C−H bond functionalization would be desirable to construct polyfunctional acetanilide derivatives.

o-Acylacetanilides are important structural motifs and resourceful intermediates for preparing many useful compounds such as natural products, dyes, and pharmaceuticals.[8] For the synthesis of this kind of compounds, except traditional methods such as Friedel−Crafts acylation and oxidation of the corresponding secondary alcohols by various oxidants,[9] the palladium-catalyzed directed acylations were developed in recent years (Scheme 1). Ge and co-workers developed a Pd-catalyzed decarboxylative *ortho*-acylation of acetanilides with *α*-oxocarboxylic acids;[7a] using arylaldehydes as coupling partners, Wang and Li reported *ortho*-acylation of acetanilides, respectively;[7b,c] considering benzylic alcohols can be oxidized to be benzaldehydes, Yuan using benzylic alcohols as starting materials, TBHP as the oxidant, successfully developed the acylation reaction of acetanilides via oxidative cross-coupling.[7d] Even so, in all of these procedures, relatively expensive and unstable prefunctionalized reagents should be employed as the acyl sources. Our continuous interest in metal-catalyzed C−H bond activation prompted us to explore the reaction of Pd-catalyzed *ortho*-directed multiple C−H bond activation using substrates without prefunctionalization. It is well-known that toluene derivatives are low toxic, stable, commercially available, and easy to handle and thus may be potentially used as ideal acylation reagents to achieve aryl ketones. Herein, we present a facile palladium-catalyzed regioselective acylation reaction of acetanilides with no prefunctionalized toluene derivatives as acylation reagents to afford *o*-acylacetanilides.

Scheme 1. Strategies toward Syntheses of *o*-Acylacetanilides

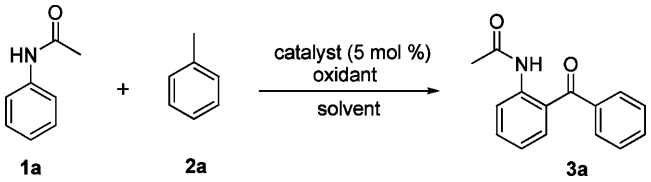


We initially used acetanilide (**1a**) and toluene (**2a**) as the substrates to optimize the reaction conditions. The results of this transition-metal-catalyzed oxidative coupling reaction were summarized in Table 1. $Pd(OAc)_2$ was first chosen as a catalyst for this transformation, and toluene was used as both reactant and solvent. The presence of an oxidant was requisite for this reaction. Therefore, the oxidant screening was investigated.

Received: September 29, 2012
Published: November 26, 2012

dx.doi.org/10.1021/jo302125h | J. Org. Chem. 2012, 77, 11339−11344

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

entry	catalyst	oxidant (eq)	solvent	yield[b] (%)
1	$Pd(OAc)_2$	TBHP (4)	toluene	78
2	$Pd(OAc)_2$	TBHP (5)	toluene	77
3	$Pd(OAc)_2$	TBHP (3)	toluene	65
4	$Pd(OAc)_2$	TBHP (4)	dioxane	70
5	$Pd(OAc)_2$	TBHP (4)	DMF	76
6	$Pd(OAc)_2$	TBHP (4)	DCE	64
7	$Pd(OAc)_2$	TBHP (4)	DMSO	81 (80, 62)[c]
8	$Pd(OAc)_2$	TBHP (4)	H_2O	62
9	$Pd(OAc)_2$	H_2O_2 (4)	toluene	0
10	$Pd(OAc)_2$	DTBP (4)	toluene	trace
11	$Pd(OAc)_2$	BPO (4)	toluene	0
12	$Pd(OAc)_2$	$K_2S_2O_8$ (4)	toluene	0
13	$Pd(OAc)_2$	O_2 (1 atm)	toluene	0
14	$Pd(OAc)_2$	TBHP (4)	DMSO	47[d]
15	$PdCl_2$	TBHP (4)	DMSO	57
16	$PdCl_2(PPh_3)_2$	TBHP (4)	DMSO	24
17	$RuCl_3$	TBHP (4)	DMSO	0
18	$Ru[Cp(PPh_3)_2Cl]$	TBHP (4)	DMSO	0

[a]Unless otherwise specified, all reactions were carried out with acetanilide (**1a**, 0.5 mmol), toluene (**2a**, 1.0 mmol), catalyst (5 mol %), and oxidant (2.0 mmol) in 1.0 mL of solvent under air atmosphere at 100 °C for 20 h. [b]Isolated yields. [c]At 110 and 80 °C, respectively. [d]The mole ratio of **1a** and **2a** was 1:1.

Some generally used oxidants, such as H_2O_2, TBHP, DTBP, BPO, O_2, and $K_2S_2O_8$, were tested, in which TBHP was found to be the best one, while others showed little effect (entries 9−13). To gain the ideal yield, the amount of TBHP was also examined and it turned out that 4 equiv of TBHP could bring the highest yield of 78%. Increasing the amount of TBHP to 5 equiv could not raise the yield evidently, while decreasing that to 3 equiv led to a reduction of the yield (entries 1−3). Considering the requirement for enlarging the applicability of this reaction, it was essential to select a suitable solvent. It was found that the reaction could proceed in a solvent such as dioxane, DMF, DCE, DMSO, and even H_2O (entries 4−8). DMSO gave the highest yield, which would be significant when other toluene derivatives, except toluene, were employed as acylation regents. Thus, DMSO was chosen as the general solvent for this acylation reaction. Furthermore, different transition-metal catalysts were also tested, in which $Pd(OAc)_2$ was proved to have the highest catalytic activity for this transformation, and the appropriate amount of $Pd(OAc)_2$ was 5 mol %, but $PdCl_2$ and $PdCl_2(PPh_3)_2$ were less effective (entries 15 and 16). Some Ru catalysts such as $RuCl_3$ and $Ru[Cp(PPh_3)_2Cl]$ revealed no catalytic activity to this reaction (entries 17 and 18). Besides, when the mole ratio of **1a** and **2a** was changed from 1/2 to 1/1, the yield decreased obviously to 47% (entry 14). At 100 °C, the reaction proceeded smoothly and finished in 20 h with the highest yield of 81%. Increasing the temperature to 110 °C did not lead to the obvious rise of the yield. At a temperature of 80 °C, the yield decreased sharply (entry 7).

Under the optimized reaction conditions, the substrate scope was studied. As summarized in Table 2, a number of toluene derivatives were employed as acylation regents to react with acetanilide (**1a**) to generate the desired *ortho* C−H bond acylation products. In general, the reactions of acetanilide with the toluene derivatives with electron-donating groups (such as CH_3, OCH_3) or weakly electron-withdrawing groups (such as Cl, Br) on the aromatic ring gave moderate to good yields. But the presence of strongly electron-withdrawing group such as nitro and acetyl restrained the reaction. It is worth noting that to the toluene derivatives with more than one methyl group such as xylene, mesitylene, and 1,2,4,5-tetramethylbenzene, the reaction only took place on one methyl group and the others remained (**3ab−af**). This result was attributable to that one of the methyl groups on the aromatic ring was preoxidized to carbonyl group and its electron-withdrawing property was unfavorable to the subsequent oxidation. α-Methylnaphthalene and β-methylnaphthalene also could be employed as acylation reagents to react with acetanilide giving moderate yields (**3ao**, **3ap**). Furthermore, a halo group (e.g., Br, Cl) on aromatic rings could remain in the products (**3ag−al**). The tolerance of the reaction to these functional groups in substrates provided the possibility for the further useful transformation of the products.

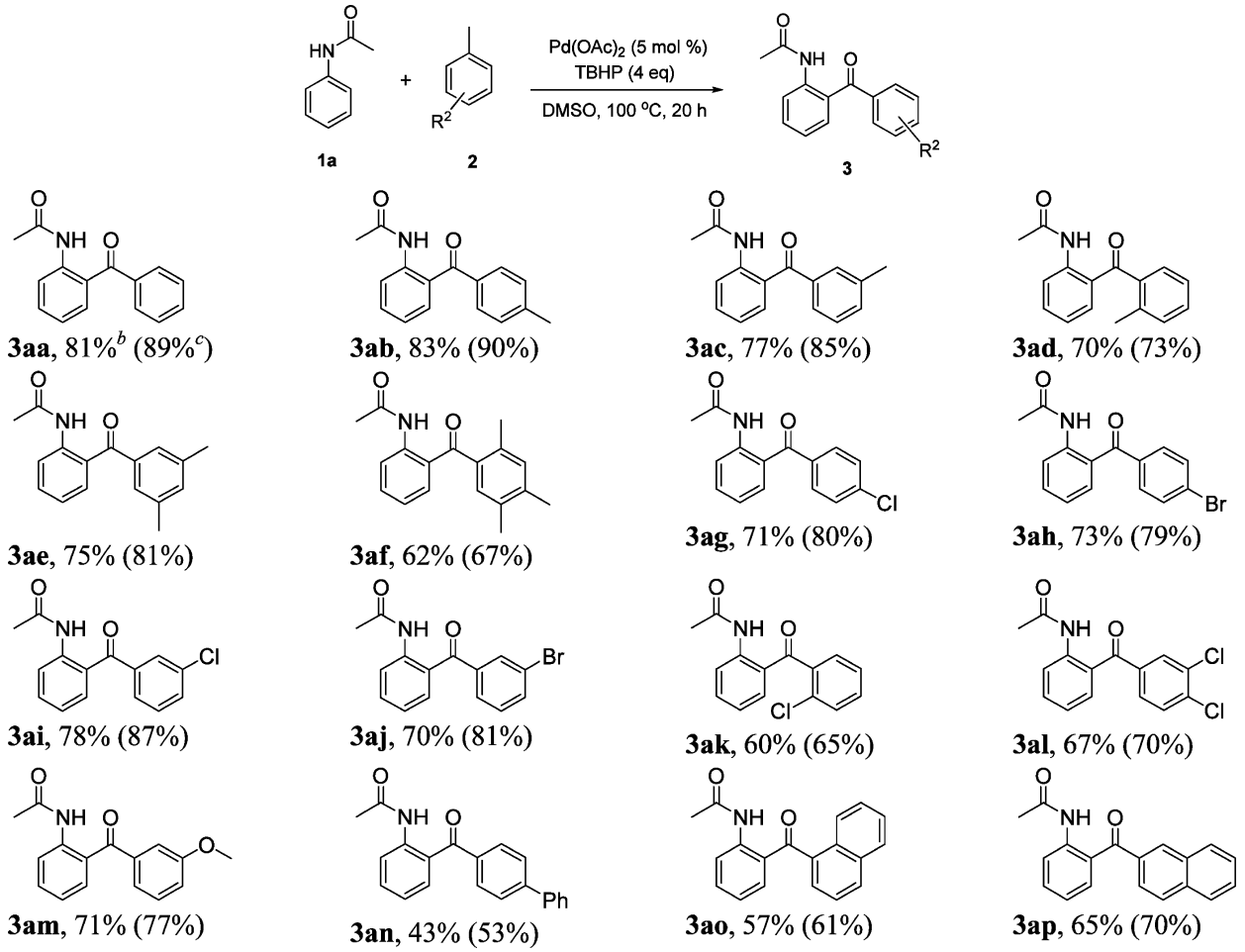
The *ortho*-acylation of a series of substituted acetanilides under the optimized reaction conditions was performed as well, and the results are shown in Table 3. For most substrates used, the reaction gave moderate to good yields. The reaction of acetanilides with a methyl group at the *meta*- or *para*-position of the amido group gave *ortho*-acylation yields comparable to those of unsubstituted acetanilides (**3ba**, **3ca**). An interesting regioselectivity could be found that when a *meta*-substituent existed at acetanilide, in which only acylation at the *para*-position of this substituent took placed because of the steric hindrance (**3ca**, **3ea**, **3ha**). Unfortunately, to *ortho*-substituted acetanilide, only a trace of desired product was detected (**3ia**), which could also be attributed to the steric effect.[10] It seems that this method was not favorable to the acetanilides with strongly electron-withdrawing groups. For example, when a nitro group existed, almost no *ortho*-acylation product was obtained (**3ja**), and some hydrolyzed product of acetanilide was found in the reaction mixture. Furthermore, the *ortho*-acylations of *N*-phenylpropionamide, *N*-phenylisobutyramide, and *N*-phenylbenzamide also gave good yields (**3ka−ma**).

Based on the above results and previous research, a plausible reaction pathway was suggested (Scheme 2). Our experiment showed that the presence of ascorbic acid (radical scavenger) could inhibit this reaction, which suggested that a radical was generated in this procedure. Furthermore, without acetanilide, the toluene was oxidized to benzaldehyde by TBHP with a low yield regardless of palladium catalyst. Thus, the possible mechanism of this acylation reaction may be as follows. First, the palladium catalyst reacted with acetanilide by chelation-directed C−H activation to form a cyclopalladated intermediate (**A**), which was confirmed by many previous reports.[7] Second, the palladacycle (**A**) reacted with the acyl radical which was in situ formed from benzaldehyde (by the oxidation of toluene) to generate either reactive Pd(IV)[11] or the dimeric Pd(III)[12] species **B**. Finally, the intermediate **B** underwent reductive elimination to afford the acylation product **C**, at the same time, the Pd (II) was regenerated for the next catalytic cycle.

In summary, we have developed an efficient method for the direct *ortho*-acylation of acetanilides via a Pd-catalyzed directed sp^2 C−H bond activation. Low toxic, stable, and commercially

dx.doi.org/10.1021/jo302125h | J. Org. Chem. 2012, 77, 11339−11344

Table 2. *Ortho*-Acylation of Toluene Derivatives to Acetanilide[a]



[a]All of the reactions were carried out using acetanilide (**1a**, 0.50 mmol), toluene derivatives (**2**, 1.0 mmol), $Pd(OAc)_2$ (5 mol %), TBHP (2.0 mmol), and DMSO (1.0 mL) at 100 °C in air atmosphere for 20 h. [b]Isolated yields. [c]Conversions.

available toluene derivatives were used as acyl sources, and inexpensive, safe, and environmentally benign TBHP was employed to be an effective oxidant in these transformations. The reaction exhibited good functional group tolerance. The mild reaction conditions provide future opportunities to apply this methodology in the synthesis of natural products and other useful compounds.

EXPERIMENTAL SECTION

General Methods. All reactions were run in a sealed tube with a Teflon-lined cap under air atmosphere. All reagents were commercially available and were used without purification. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ [using $(CH_3)_4Si$ (for ^1H, $\delta = 0.00$; for ^{13}C, $\delta = 77.00$) as internal standard]. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Melting points are uncorrected. For the HRMS measurements, Q-TOF was used.

General Experimental Procedures and Characterizations. Acetanilide (0.5 mmol), toluene derivative (1.0 mmol), $Pd(OAc)_2$ (0.025 mmol), TBHP (2.0 mmol, 70% aq), and DMSO (1.0 mL) were added in a 25 mL sealed tube with a Teflon-lined cap. The mixture was heated at 100 °C (oil bath temperature) for 20 h. After being cooled to room temperature, the volatiles were removed under reduced pressure, and the residue was purified by a flash column chromatography on silica gel using hexane/ethyl acetate as eluent to give the corresponding product.

*N-(2-Benzoylphenyl)acetamide (**3aa**).*[7a] Yield: 81% (97 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 10.83 (s, 1H), 8.64 (d, J = 8.3 Hz, 1H), 7.71 (t, J = 4.2 Hz, 2H), 7.62–7.56 (m, 3H), 7.52–7.48 (m, 2H), 7.10 (s, 1H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.8, 169.2, 140.5, 138.6, 134.3, 133.5, 132.5, 129.9, 128.3, 123.3, 122.1, 121.5, 25.3. ESI-MS $[M - H]^-$: 237.7.

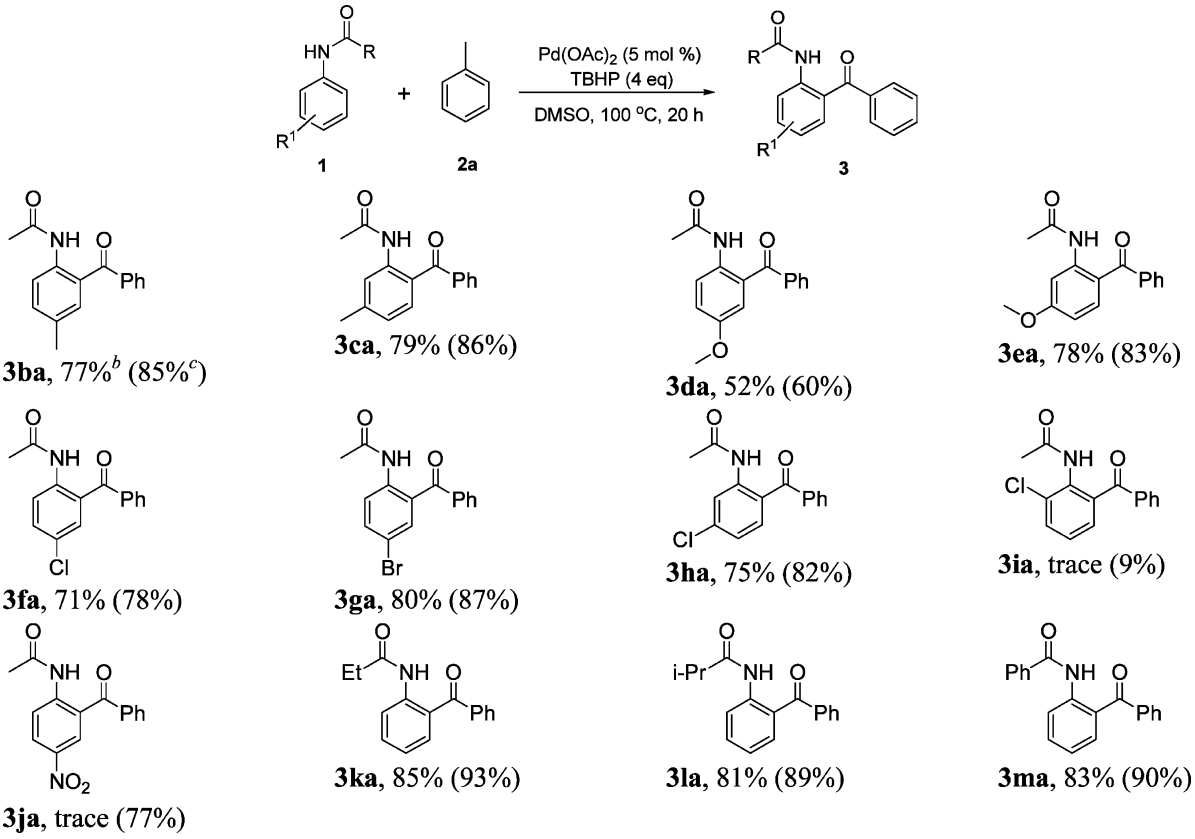
*N-(2-(4-Methylbenzoyl)phenyl)acetamide (**3ab**).*[7a] Yield: 83% (105 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 10.74 (s, 1H), 8.60 (d, J = 8.6 Hz, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.59–7.55 (m, 2H), 7.31–7.25 (m, 2H), 7.11–7.07 (m, 1H), 2.46 (s, 3H), 2.23(s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.3, 169.1, 143.5, 140.2, 135.8, 133.9, 133.3, 130.2, 129.0, 123.7, 122.0, 121.6, 25.2, 21.7. ESI-MS $[M - H]^-$: 251.7.

*N-(2-(3-Methylbenzoyl)phenyl)acetamide (**3ac**).*[7b] Yield: 77% (97 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 10.82 (s, 1H), 8.63 (d, J = 8.2 Hz, 1H), 7.60–7.54 (m, 3H), 7.49 (d, J = 7.4 Hz, 1H), 7.44–7.36 (m, 2H), 7.12–7.08 (m, 1H), 2.44 (s, 3H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.0, 169.2, 140.4, 138.7, 138.3, 134.2, 133.5, 133.3, 130.3, 128.1, 127.2, 123.4, 122.0, 121.5, 25.3, 21.3. ESI-MS $[M - H]^-$: 251.7.

*N-(2-(2-Methylbenzoyl)phenyl)acetamide (**3ad**).*[7a] Yield: 70% (88 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 11.57 (s, 1H), 8.77 (d, J = 8.4 Hz, 1H), 7.60–7.56 (m, 1H), 7.40 (d, J = 7.8 Hz, 2H), 7.32–7.24 (m, 3H), 7.04–6.99 (m, 1H), 2.31 (s, 3H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.9, 169.6, 141.6, 139.3, 135.9, 135.3, 134.5, 130.9, 130.2, 127.9, 125.4, 122.5, 122.2, 120.8, 25.6, 19.7. ESI-MS $[M - H]^-$: 251.7.

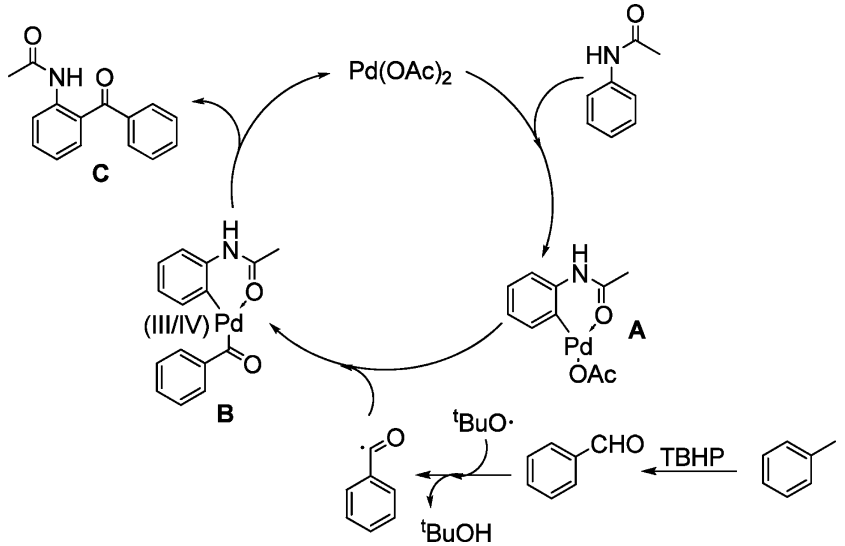
dx.doi.org/10.1021/jo302125h | J. Org. Chem. 2012, 77, 11339–11344

Table 3. *Ortho*-Acylation of Toluene to Acetanilides[a]



[a]All the reactions were carried out using acetanilide (**1**, 0.50 mmol), toluene (**2a**, 1.0 mmol), $Pd(OAc)_2$ (5 mol %), TBHP (2.0 mmol), DMSO (1.0 mL) at 100 °C in air atmosphere for 20 h. [b]Isolated yields. [c]Conversions.

Scheme 2. Proposed Mechanism for the Pd-Catalyzed *Ortho*-Acylation Reaction



N-(2-(3,5-Dimethylbenzoyl)phenyl)acetamide (***3ae***). Yield: 75% (100 mg). Pale yellow solid. Mp: 83−85 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.81 (s, 1H), 8.62 (d, J = 8.6 Hz, 1H), 7.58 (t, J = 7.4 Hz, 2H), 7.31 (s, 2H), 7.24 (s, 1H), 7.12−7.08 (m, 1H), 2.39 (s, 6H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.2, 169.2, 140.3, 138.7, 138.1, 134.2, 134.1, 133.5, 127.6, 123.6, 122.1, 121.5, 25.3, 21.2. HRMS (ESI): calcd for $C_{17}H_{17}NO_2$[Na] 290.1157, found 290.1154.

N-(2-(2,4,5-Trimethylbenzoyl)phenyl)acetamide (***3af***). Yield: 62% (87 mg). Pale yellow solid. Mp: 76−78 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.49 (s, 1H), 8.73 (d, J = 8.4 Hz, 1H), 7.59−7.54 (m, 1H), 7.45−7.43 (m, 1H), 7.07 (s, 1H), 7.05−7.00 (m, 2H), 2.31 (s, 3H), 2.29 (s, 3H), 2.25(s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.9, 169.5, 141.2, 139.3, 136.8, 134.9, 134.4, 133.6, 133.5, 132.3, 129.5, 123.1, 122.1, 120.8, 25.5, 19.7, 19.3, 19.2. HRMS (ESI): calcd for $C_{18}H_{19}NO_2$[Na] 304.1313, found 304.1332.

N-(2-(4-Chlorobenzoyl)phenyl)acetamide (***3ag***).[7a] Yield: 71% (97 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.72 (s, 1H), 8.63 (d, J = 8.4 Hz, 1H), 7.68−7.66 (m, 2H), 7.60 (s, 1H), 7.53−7.48 (m, 3H), 7.12 (t, J = 4.0 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ

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198.3, 169.2, 140.5, 139.1, 136.9, 134.5, 133.2, 131.3, 128.7, 123.0, 122.2, 121.7, 25.3. ESI-MS [M − H]$^-$: 271.6.

N-(2-(4-Bromobenzoyl)phenyl)acetamide (**3ah**).[7a] Yield: 73% (116 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.73 (s, 1H), 8.63 (d, J = 8.3 Hz, 1H), 7.66−7.64 (m, 2H), 7.61−7.58 (t, J = 7.7 Hz, 3H), 7.53−7.51 (m, 1H), 7.12−7.09 (m, 1H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 169.2, 140.5, 137.3, 134.5, 133.2, 131.7, 131.4, 127.6, 122.9, 122.2, 121.7, 25.3. ESI-MS [M − H]$^-$: 315.4.

N-(2-(3-Chlorobenzoyl)phenyl)acetamide (**3ai**).[7b] Yield: 78% (107 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.77 (s, 1H), 8.65 (d, J = 8.4 Hz, 1H), 7.70 (t, J = 1.8 Hz, 1H), 7.61−7.52 (m, 4H), 7.45 (d, J = 7.8 Hz, 1H), 7.12 (s, 1H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.2, 169.2, 140.7, 140.3, 134.7, 134.6, 133.4, 132.4, 129.7, 129.6, 127.9, 122.7, 122.2, 121.7, 25.3. ESI-MS [M − H]$^-$: 272.8.

N-(2-(3-Bromobenzoyl)phenyl)acetamide (**3aj**).[7b] Yield: 70% (111 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.77 (s, 1H), 8.65 (d, J = 8.4 Hz, 1H), 7.85 (t, J = 1.6 Hz, 1H), 7.73 (t, J = 4.4 Hz, 1H), 7.62 (t, J = 3.9 Hz, 2H), 7.40−7.36 (t, J = 8.4 Hz, 1H), 7.12 (s, 1H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.1, 169.2, 140.7, 140.5, 135.3, 134.8, 133.4, 132.6, 129.9, 128.4, 122.6, 122.2, 121.27 121.7, 25.3. ESI-MS [M − H]$^-$: 315.4.

N-(2-(2-Chlorobenzoyl)phenyl)acetamide (**3ak**).[7a] Yield: 60% (82 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.56 (s, 1H), 8.81 (d, J = 8.4 Hz, 1H), 7.61 (s, 1H), 7.49−7.47 (m, 2H), 7.40−7.33 (m, 3H), 7.03 (s, 1H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.3, 169.6, 141.9, 138.8, 135.9, 134.6, 131.2, 130.9, 130.1, 128.7, 126.7, 122.3, 121.3, 120.7, 25.6. ESI-MS [M − H]$^-$: 271.6.

N-(2-(3,4-Dichlorobenzoyl)phenyl)acetamide (**3al**). Yield: 67% (104 mg). Pale yellow solid. Mp: 108−110 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.66 (s, 1H), 8.61 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 1.8 Hz, 1H), 7.61−7.47 (m, 4H), 7.13 (d, J = 8.0 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 196.9, 169.2, 140.5, 138.2, 134.9, 133.1, 133.0, 131.6, 130.5, 130.5, 128.9, 126.0, 122.4, 25.3. HRMS (ESI): calcd for $C_{15}H_{11}NO_2Cl_2$[Na] 330.0065, found 330.0059.

N-(2-(3-Methoxybenzoyl)phenyl)acetamide (**3am**).[7d] Yield: 71% (96 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.80 (s, 1H), 8.63 (d, J = 8.7 Hz, 1H), 7.60−7.57 (m, 2H), 7.39 (d, J = 8.2 Hz, 1H), 7.28−7.25 (m, 2H), 7.15 (s, 1H), 7.10 (s, 1H), 3.87 (s, 3H), 2.25 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.5, 169.2, 159.5, 140.5, 139.9, 134.3, 133.5, 129.3, 123.3, 122.6, 122.1, 121.5, 118.9, 114.3, 55.5, 25.3. ESI-MS [M − H]$^-$: 267.6.

N-(2-(4-Phenylbenzoyl)phenyl)acetamide (**3an**). Yield: 43% (68 mg). White solid. Mp: 130−131 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.79 (s, 1H), 8.65 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.74 (t, J = 4.2 Hz, 2H), 7.69−7.63 (m, 4H), 7.53−7.44 (m, 3H), 7.14(s, 1H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.2, 169.2, 145.4, 140.4, 139.8, 137.2, 134.2, 133.4, 130.6, 129.0, 128.3, 127.3, 127.0, 123.5, 122.1, 121.6, 25.3. HRMS (ESI): calcd for $C_{21}H_{17}NO_2$[Na] 338.1157, found 338.1187.

N-(2-(2-Naphthoyl)phenyl)acetamide (**3ap**).[7a] Yield: 65% (94 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.79 (s, 1H), 8.66 (d, J = 8.3 Hz, 1H), 8.20 (s, 1H), 7.99−7.93 (m, 3H), 7.86−7.84 (m, 1H), 7.65−7.59 (m, 4H), 7.13(s, 1H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.6, 169.2, 140.4, 135.8, 135.2, 134.2, 133.5, 132.1, 131.8, 129.4, 128.5, 128.4, 127.8, 127.0, 125.6, 123.7, 122.2, 121.7, 25.3. ESI-MS [M − H]$^-$: 287.7.

N-(2-(1-Naphthoyl)phenyl)acetamide (**3ao**).[7a] Yield: 57% (83 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.60 (s, 1H), 8.80 (d, J = 7.8 Hz, 1H), 8.03 (d, J = 9.3 Hz, 1H), 7.97−7.94 (m, 2H), 7.60−7.51 (m, 5H), 7.45−7.43 (m, 1H), 6.97 (s, 1H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.2, 169.6, 141.6, 137.0, 135.4, 134.8, 133.6, 131.2, 130.6, 128.5, 127.4, 127.2, 126.6, 125.3, 124.4, 123.2, 122.2, 120.9, 25.6. ESI-MS [M − H]$^-$: 287.7.

N-(2-Benzoyl-4-methylphenyl)acetamide (**3ba**).[7a] Yield: 77% (98 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.65 (s, 1H), 8.50 (d, J = 8.5 Hz, 1H), 7.71 (t, J = 4.2 Hz, 2H), 7.64−7.61 (m, 1H), 7.53−7.49 (t, J = 7.6 Hz, 2H), 7.39 (d, J = 8.1 Hz, 1H), 7.35 (s, 1H), 2.31 (s, 3H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.7, 169.1, 138.7, 138.0, 134.9, 133.5, 132.5, 131.7, 129.9, 128.3, 121.6, 25.2, 20.8. ESI-MS [M − H]$^-$: 251.7.

N-(2-Benzoyl-5-methylphenyl)acetamide (**3ca**).[7a] Yield: 79% (100 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.03 (s, 1H), 8.51 (s, 1H), 7.67 (t, J = 4.2 Hz, 2H), 7.62−7.58 (m, 1H), 7.51−7.45 (m, 3H), 6.89 (d, J = 8.0 Hz, 1H), 2.44 (s, 3H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.7, 169.3, 145.9, 140.8, 139.0, 133.9, 132.2, 129.7, 128.3, 122.9, 121.7, 120.5, 25.4, 22.2. ESI-MS [M − H]$^-$: 251.5.

N-(2-Benzoyl-4-methoxyphenyl)acetamide (**3da**).[7d] Yield: 52% (70 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.33 (s, 1H), 8.49 (d, J = 9.1 Hz, 1H), 7.75 (t, J = 4.3 Hz, 2H), 7.64−7.61 (m, 1H), 7.53−7.49 (t, J = 7.6 Hz, 2H), 7.15 (d, J = 9.1 Hz, 1H), 7.06 (d, J = 3.0 Hz, 1H), 3.77 (s, 3H), 2.21 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.1, 168.8, 154.2, 138.3, 133.5, 132.7, 130.0, 128.4, 125.1, 123.5, 119.3, 118.2, 55.7, 25.0. ESI-MS [M − H]$^-$: 267.7.

N-(2-Benzoyl-5-methoxyphenyl)acetamide (**3ea**).[7d] Yield: 78% (105 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.57 (s, 1H), 8.38 (d, J = 2.6 Hz, 1H), 7.59 (t, J = 4.2 Hz, 2H), 7.57−7.51 (m, 1H), 7.49−7.44 (m, 3H), 6.53 (d, J = 8.9 Hz, 1H), 3.88 (s, 3H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.9, 169.6, 164.6, 143.8, 139.5, 136.3, 131.7, 129.3, 128.2, 115.5, 108.9, 104.8, 55.6, 25.5. ESI-MS [M − H]$^-$: 267.7.

N-(2-Benzoyl-4-chlorophenyl)acetamide (**3fa**).[7d] Yield: 71% (97 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.63 (s, 1H), 8.60 (d, J = 8.6 Hz, 1H), 7.70 (t, J = 4.2 Hz, 2H), 7.66−7.62 (m, 1H), 7.54−7.51 (m, 4H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.4, 169.1, 138.9, 137.8, 133.9, 133.0, 132.6, 129.9, 128.6, 127.2, 124.6, 123.1, 25.2. ESI-MS [M − H]$^-$: 271.5.

N-(2-Benzoyl-4-bromophenyl)acetamide (**3ga**).[13] Yield: 80% (127 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.63 (s, 1H), 8.55 (d, J = 9.6 Hz, 1H), 7.72−7.68 (m, 2H), 7.67−7.63 (m, 3H), 7.53 (t, J = 7.6 Hz, 2H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.3, 169.1, 139.4, 137.8, 136.8, 135.5, 133.0, 129.9, 128.6, 124.9, 123.3, 114.6, 25.3. ESI-MS [M − H]$^-$: 315.5.

N-(2-Benzoyl-5-chlorophenyl)acetamide (**3ha**).[7a] Yield: 75% (103 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.97 (s, 1H), 8.74 (d, J = 1.9 Hz, 1H), 7.67−7.59 (m, 3H), 7.52−7.47 (m, 3H), 7.05 (d, J = 8.5 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.0, 169.4, 141.6, 140.7, 138.4, 134.7, 132.7, 129.7, 128.5, 122.3, 121.3, 121.1, 25.8. ESI-MS [M − H]$^-$: 271.5.

N-(2-Benzoylphenyl)propionamide (**3ka**).[14] Yield: 85% (108 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.88 (s, 1H), 8.65 (d, J = 8.1 Hz, 1H), 7.67 (t, J = 4.2 Hz, 2H), 7.62−7.56 (m, 3H), 7.57−7.52 (m, 3H), 7.46 (t, J = 7.6 Hz, 2H), 7.07−7.03 (m, 1H), 2.44 (q, J = 7.6 Hz, 2H) 1.26 (t, J = 7.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.7, 173.0, 140.6, 138.7, 134.3, 133.6, 132.4, 129.9, 128.3, 123.1, 121.9, 121.5, 31.4, 9.6. ESI-MS [M − H]$^-$: 251.7.

N-(2-Benzoylphenyl)isobutyramide (**3la**).[7a] Yield: 81% (108 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.99 (s, 1H), 8.69 (d, J = 7.8 Hz, 1H), 7.68 (t, J = 4.1 Hz, 2H), 7.58−7.54 (m, 3H), 7.49−7.45 (m, 2H), 7.04 (d, J = 7.6 Hz, 1H), 2.63−2.58 (m, 1H), 1.28 (d, J = 7.0 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.8, 176.3, 140.9, 138.7, 134.4, 133.7, 132.4, 129.8, 128.3, 123.1, 121.9, 121.4, 37.3, 19.5. ESI-MS [M − H]$^-$: 265.7.

N-(2-Benzoylphenyl)benzamide (**3ma**).[7d] Yield: 83% (125 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.00 (s, 1H), 8.92 (d, J = 8.2 Hz, 1H), 8.11−8.08 (m, 2H), 7.74 (t, J = 4.3 Hz, 2H), 7.66−7.59 (m, 3H), 7.56−7.49 (m, 5H), 7.14 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.4, 165.9, 141.2, 138.8, 134.7, 134.6, 134.1, 132.4, 132.1, 129.8, 128.9, 128.4, 127.4, 123.1, 122.2, 121.5. ESI-MS [M − H]$^-$: 299.6.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (Project 21272117 and 20972068) and the Priority Academic Program Development of Jiangsu Higher Education Institutions.

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