Direct Synthesis of Chalcones from Anilides with Phenyl Vinyl Ketones by Oxidative Coupling Through C–H Bond Activation

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ABSTRACT: A novel approach for synthesizing chalcones by Pd-catalyzed oxidative coupling is described. This is the first report of the efficient coupling reaction of acetanilides with phenyl vinyl ketones under mild conditions. Selective C–H activation occurred next to the acetamide group to afford 2-aminochalcone derivatives. The reaction proceeded under an O₂ atmosphere without any chemical co-oxidants.

INTRODUCTION

Chalcones are one of the most popular compounds in plants, such as vegetables, fruits, teas, and so on, and have various pharmacological activities, such as anti-inflammatory, antifungal, antimalarial, and antitumor activities. 1 Chalcone skeletons are not only used as privileged scaffolds in medicinal chemistry but also used for their fluorescent property. In addition, chalcone is the precursor of flavonoids in biosynthesis 2 as well as various heterocyclic compounds through chemical transformation. 3 Flavonoids are also important naturally occurring compound classified as polyphenols, and some flavonoids are known as colored compounds, anthocyanins. 4 Thus, chalcones are widely utilized in a variety of fields, and therefore, many methods of synthesizing chalcones have been reported. 1,4–6 Aldol condensation methods, including Claisen–Schmidt reactions and Wittig reactions, are classic representative methods for synthesizing chalcone skeletons (Scheme 1). However, some functionalized chalcones are difficult to synthesize and require several steps.

We are interested in the reaction of hypervalent iodine reagents with chalcones and have studied the transformation of the acetals obtained from the rearrangement of N-protected aminoaldehydes into heterocyclic compounds such as indoles and quinolines. 4 However, in these syntheses, the synthesis of N-protected aminoaldehydes is problematic. The synthesis of 2-aminobenzaldehydes, the precursors of 2-aminochalcone in Claisen–Schmidt or Wittig reactions, is challenging in terms of the number of steps, selectivity of reaction, and yields. For example, we attempted to synthesize 2-amino-4-methoxybenzaldehyde derivatives from inexpensive 3-methoxyaniline derivative by the introduction of formyl groups with the Friedel–Crafts reaction or direct formylation, resulting in poor selectivity. Then, we chose rather expensive 2-nitro-3-methoxybenzaldehyde as a starting material. However, a similar problem such as selectivity in the synthesis or less commercial availability should occur in syntheses of other derivatives. We then explored a more convenient approach for synthesizing 2-aminochalcones without using 2-aminobenzaldehydes as a starting material. Cross-coupling reactions are powerful tools for the synthesis of various biaryl and related compounds. 5 Direct arylation or allylation of the nonfunctionalized position using a directing group is a convenient method for making such compounds in few steps. Many methods for the synthesis of biaryls by direct arylation using a directing group have been reported. 5,6 Direct arylation of aniline derivatives has also been reported, 6a but most studies have employed acrylates as a coupling partner; few have used vinyl

Scheme 1. General Method for the Synthesis of Chalcones

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ketones such as phenyl vinyl ketone, the precursor of chalcones.7

**RESULTS AND DISCUSSION**

We first examined the oxidative coupling reaction of 3-methoxyacetanilide 1a with 4-methoxyphenyl vinyl ketone 2a using Pd(OAc)_2 and K_2S_2O_8 as co-oxidants under an O_2 atmosphere with reference to Youn’s method.7a The reaction proceeded but the yield of the corresponding chalcone 3a was 24% (Table 1, entry 1). The desired coupling reaction proceeded by employing Cu(OAc)_2 as a co-oxidant, resulting in 3a at a 32% yield (entry 3). Using Pd(OCOCF_3)_2 instead of Pd(OAc)_2 as a catalyst, 3a was obtained at 41% yield without using CF_3COOH as a solvent (entry 4). Increasing the amount of Pd(OCOCF_3)_2 to 20 mol % yielded the compound at 82% yield (entry 5).

Next, we reacted nonsubstituted acetanilide 1b under the above conditions (Table 2), and 3b was obtained at only 16% yield even at 50 °C (entry 2). We reexamined the reaction conditions and observed that the use of CF_3COOH as a co-solvent enhanced the reaction even at room temperature (entries 8–12), and a 9:1 ratio of (CH_2Cl)_2−CF_3COOH and higher concentration gave the best yield (57%) (entry 11). Surprisingly, in the absence of Cu(OAc)_2, the reaction proceeded at a yield (55%) similar to that in the presence of Cu(OAc)_2 (57%) under the O_2 atmosphere (entries 12 and 11).8

Next, we explored the substrate scope of direct coupling reactions between acetanilides and 4-methoxyphenyl vinyl ketone for the synthesis of chalcones (Table 3). 3-methoxyacetanilide 1a yielded the corresponding chalcone 3a, but the yield was 42% under these conditions (entry 2). On the basis of thin-layer chromatography (TLC) analyses, 4-methoxyphenyl vinyl ketone 2a was consumed rapidly and acetanilide 1a remained after the consumption of 2a. Then, we applied the slow addition of 2a using a syringe pump and the yield improved up to 85% over 8 h and the by-product generated from 2a was decreased (entry 3); this process was employed for further investigation. 3,4-Dimethoxyacetanilide 1c was reacted with 4-methoxyphenyl vinyl ketone 2a under the conditions above, according the corresponding 2-aminochalcone 3c at high yield (94%) (entry 4). However, other electron-rich acetanilides, 4-methoxyacetanilide 1d and 2-methoxyacetanilide 1e, resulted in moderate-to-low yields (49 and 18%, respectively) (entries 5 and 6). It should be noted that the acetanilide 1f bearing Cl atom on the aromatic ring proceeded the desired coupling reaction according 3f in 82% yield without any cross-coupling reaction product at the position of Cl atom (entry 7). On the other hand, 3-methylacetanilide 1g gave the corresponding 2-aminochalcone 3g at good yield (68%) (entry 8). These results indicate that the electron-donating effect on the ortho position of the acetamide group is important for this reaction. 3-Chloroacetanilide 1h underwent the coupling reaction but the yield was 25% (entry 9). In the case of 3-nitroacetanilide 1i,

| Table 1. Coupling Reaction of 3-Methoxyacetanilide and 4-Methoxyphenyl Vinyl Ketone |
|---|
| entry | catalyst (mol %) | co-oxidant (eq) | solvent | time (h) | yield (%) |
| 1 | Pd(OAc)_2 (10) | K_2S_2O_8 (1.0) | CH_2Cl_2−CF_3COOH | 1.5 | 24 |
| 2 | Pd(OAc)_2 (10) | oxone (1.0) | CH_2Cl_2−CF_3COOH | 24 | 24 |
| 3 | Pd(OAc)_2 (10) | Cu(OAc)_2 (0.1) | CH_2Cl_2−CF_3COOH | 24 | 32 |
| 4 | Pd(OCOCF_3)_2 (10) | Cu(OAc)_2 (0.1) | (CH_2Cl)_2 | 24 | 41 |
| 5 | Pd(OCOCF_3)_2 (20) | Cu(OAc)_2 (0.2) | (CH_2Cl)_2 | 24 | 82 |

| Table 2. Re-Optimization of the Coupling Reaction |
|---|
| entry | solvent | yield (%) |
| 1 | (CH_2Cl)_2 | 7 |
| 2 | (CH_2Cl)_2 | 16 |
| 3 | CH_2CN | 5 |
| 4 | AcOH | 3 |
| 5 | toluene | 11 |
| 6 | THF | N.R. |
| 7 | DMF | N.R. |
| 8 | (CH_2Cl)_2−CF_3COOH (1:1) | 18 |
| 9 | (CH_2Cl)_2−CF_3COOH (4:1) | 39 |
| 10 | (CH_2Cl)_2−CF_3COOH (9:1) | 47 |
| 11 | (CH_2Cl)_2−CF_3COOH (9:1) | 57 |
| 12 | (CH_2Cl)_2−CF_3COOH (9:1) | 55 |

"The reaction was conducted at room temperature. "No reaction. "The reaction was conducted at a concentration of 2.0 M. "Without Cu(OAc)_2."
corresponding chalcone 3i was obtained even at 50 °C owing to its strong electron-withdrawing property (entry 10).

Next, we examined the scope of phenyl vinyl ketones employing the same conditions used in Table 3 (Table 4). The coupling reaction of 3-methoxyphenyl vinyl ketone 2b with 1a afforded the corresponding chalcone 3j at 51% yield (entry 2). In the case of 2-methoxyphenyl vinyl ketone 2c, a better result was obtained using the optimized conditions shown in Table 1 [Pd(OCOCF₃)₂ and Cu(OAc)₂ in (CH₂Cl)₂], affording the corresponding chalcone 3k at 60% yield and the poor result was obtained under the conditions used in Table 3 (entry 3). Next, the nonsubstituted phenyl vinyl ketone 2d was reacted with 1a to give 3l in 44% yield but afforded at good yield (74%) using the conditions shown in Table 1 (entry 4). The reaction of 4-tolyl vinyl ketone 2e with 1a proceeded at moderate yield (58%) (entry 5). As an electron-withdrawing group, the reaction with 4-chlorophenyl vinyl ketone 2f afforded 3n at 73% yield (entry 6). The more electron-deficient 4-nitrophenyl vinyl ketone 2g also underwent the coupling reaction at 49% yield (entry 7). Methyl vinyl ketone 2h was also reacted to give the corresponding coupling product 3p in 51% yield, which was improved to 79% yield employing the conditions indicated in Table 1 (entry 8).

Pd-catalyzed coupling reactions of acetanilide and phenyl vinyl ketone should proceed via a C–H activation mechanism, and a plausible reaction mechanism is illustrated in Scheme 2. First, Pd(II) was inserted into the C–H bond of the ortho position of the acetamide group, producing the monomeric or dimeric cyclopalladation species coordinated by the oxygen of acetamide. Then, coordination of the olefin followed by β-Hydride elimination took place to afford the aminochalcone.

**Table 3. Pd-Catalyzed Coupling Reaction of Various Acetanilides with 4-Methoxyphenyl Vinyl Ketone**

| Entry | Acetanilide (1) | Chalcone (3) | Yield (%) |
|-------|-----------------|-------------|-----------|
| 1     | 1a              | 3a          | 85        |
| 2     | 1b              | 3b          | 55        |
| 3     | 1c              | 3c          | 42        |
| 4     | 1d              | 3d          | 94        |
| 5     | 1e              | 3e          | 49        |
| 6     | 1f              | 3f          | 18        |
| 7     | 1g              | 3g          | 68        |
| 8     | 1h              | 3h          | 25        |
| 9     | N.R.            | N.R.        | N.R.      |

*A solution of 2a in (CH₂Cl)₂ was added for 8 h via a syringe pump to the solution of acetanilide 1 in (CH₂Cl)₂−CF₃COOH. No reaction.*

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derivative, where the generated Pd(0) was reoxidized under an O2 atmosphere to give Pd(II). An alternative pathway involving the Pd(II)/Pd(IV) cycle cannot be ruled out.9 Although it is not clear why no chemical oxidant is needed for the reaction, the combination of substrates may affect the oxidation of Pd(0).

CONCLUSIONS

In conclusion, we developed a new convenient method of synthesizing 2-aminochalcones. This is the first report of the Pd-catalyzed direct cross-coupling reaction of acetanilides and phenyl vinyl ketones. A variety of acetanilides, except for those with a strong electron-withdrawing substituent, were susceptible to this reaction, as well as various vinyl ketones. It is noteworthy that no chemical co-oxidant was necessary in this reaction, and atmospheric O2 was a sufficient co-oxidant. We believe that our method offers a new and easy way to synthesize aminochalcones.

EXPERIMENTAL SECTION

General Information. 1H NMR and 13C NMR spectra were recorded on a 400 MHz spectrometer in CDCl3 or DMSO-d6 with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet,
brs = broad singlet), coupling constant (Hz), and integration. High-resolution mass spectra (HRMS) were recorded on a double-focusing mass spectrometer using electrospray ionization (ESI). Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification. Each regiosomer exhibited similar \( R_t \) values on TLC plates run with various solvents. Some could not be separated from the primary reaction product and remained as a mixture. In mixed samples, the ratio of regiosomer was determined by \( ^1H \) NMR; pure data were obtained for those regiosomers that could be isolated.

**General Procedure for Conducting Pd-Catalyzed Coupling Reactions of Acetanilides and 4-Methoxyphenyl vinyl ketone (Table 3).** Typical Procedure from 1a and 2a to 3a (Method A) (Table 3, Entry 3). Pd(OOCF\(_2\)\(_3\))\(_3\) (33 mg, 0.1 mmol) and CF\(_2\)COOH (0.025 mL) were added to a solution of acetanilide 1a (83 mg, 0.5 mmol) in (CH\(_2\)Cl\(_2\) (0.225 mL) and then, the inside of the reaction flask was replaced with O\(_2\). A solution of phenyl vinyl ketone 2a (122 mg, 0.75 mmol) in (CH\(_2\)Cl\(_2\) (0.5 mL) was added to a syringe pump over 8 h. The resulting solution was stirred at room temperature under the O\(_2\) atmosphere (O\(_2\) balloon) for an additional 16 h (total 24 h). Saturated aqueous NaHCO\(_3\) was added to the resultant solution, and the mixture was extracted with CH\(_2\)Cl\(_2\). The organic layer was dried over Na\(_2\)SO\(_4\) and evaporated in vacuo. The residue was purified by column chromatography on a silica gel (CH\(_2\)Cl\(_2\)/AcOEt = 5/1) to give 3a (138 mg, 85%).

**Typical Procedure from 1a and 2c to 3k (Method B) (Table 4, Entry 3).** A solution of Pd(OOCF\(_2\)\(_3\))\(_3\) (33 mg, 0.1 mmol), Cu(OAc)\(_2\) (18 mg, 0.1 mmol), and 2c (122 mg, 0.75 mmol) in (CH\(_2\)Cl\(_2\) (0.5 mL) was added to a solution of vinyl phenyl ketone 1a (83 mg, 0.5 mmol) in (CH\(_2\)Cl\(_2\) (0.5 mL)), and then, the inside of the reaction flask was replaced with O\(_2\). The resulting solution was stirred for 24 h and evaporated in vacuo. The residue was purified by column chromatography on a silica gel (CH\(_2\)Cl\(_2\)/AcOEt = 5/1) to give 3k (98 mg, 60%).

**N-[5-Methoxy-2-[3-(4-methoxyphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3a).** Yellow solid; 138 mg, 85%. mp 170–172 °C; \(^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.01 (d, 2H, \( J = 8.8 \) Hz), 7.92 (d, 1H, \( J = 15.2 \) Hz), 7.63 (d, 1H, \( J = 7.8 \) Hz), 7.56 (s, 1H), 7.42 (d, 1H, \( J = 15.2 \) Hz), 6.97 (d, 2H, \( J = 8.8 \) Hz), 6.76 (d, 1H, \( J = 7.8 \) Hz), 3.98 (s, 3H), 3.85 (s, 3H), 2.26 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \( \delta \) 193.1, 163.2, 168.8, 187.6; HRMS (ESI): [M + Na]\(^+\) calcd for C\(_{19}\)H\(_{18}\)ClO\(_3\)NNa, 348.1207; found, 348.1197.

**N-[5-Chloro-2-[3-(4-methoxyphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3c).** Yellow solid; 61 mg, 25%. mp 189–190 °C; \(^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.04 (d, 2H, \( J = 8.8 \) Hz), 7.91 (d, 1H, \( J = 15.4 \) Hz), 7.40 (d, 1H, \( J = 15.4 \) Hz), 7.38 (s, 1H), 7.14 (s, 1H), 7.00 (d, 2H, \( J = 8.8 \) Hz), 3.95 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 2.25 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \( \delta \) 23.1, 55.5, 55.6, 56.0, 109.0, 110.3, 114.0, 120.2, 121.9, 130.8, 130.9, 132.2, 139.0, 147.0, 151.0, 163.1, 169.0, 187.5; HRMS (ESI): [M – H]\(^+\) calcd for C\(_{18}\)H\(_{16}\)NO\(_3\), 356.1498; found, 356.1468.

**N-[4-Chloro-2-[3-(4-methoxyphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3d).** Yellow solid; 80 mg, 49%. mp 138–140 °C; \(^1H\) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.01 (d, 2H, \( J = 8.8 \) Hz), 7.88 (d, 1H, \( J = 15.4 \) Hz), 7.56 (d, 1H, \( J = 8.8 \) Hz), 7.45 (d, 1H, \( J = 15.4 \) Hz), 7.40 (s, 1H), 7.17 (d, 1H, \( J = 8.8 \) Hz), 6.97 (d, 2H, \( J = 8.8 \) Hz), 3.89 (s, 3H), 3.84 (s, 3H), 2.12 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \( \delta \) 23.0, 55.6, 55.6, 110.9, 114.0, 117.0, 122.9, 128.5, 130.4, 130.8, 130.9, 131.0, 138.9, 157.1, 163.3, 168.8, 187.5; HRMS (ESI): [M + Na]\(^+\) calcd for C\(_{18}\)H\(_{16}\)NO\(_3\)Na, 348.1212; found, 348.1185.

**N-[4-Methoxy-2-[3-(4-methoxyphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3e).** Yellow solid; 29 mg, 18%. mp 138–140 °C; \(^1H\) NMR (400 MHz, DMSO-d\(_6\)): \( \delta \) 9.40 (s, 1H), 8.14 (d, 2H, \( J = 8.6 \) Hz), 7.82 (d, 1H, \( J = 16.4 \) Hz), 7.70–7.67 (m, 2H), 7.33 (t, 1H, \( J = 8.2 \) Hz), 7.14 (d, 1H, \( J = 8.2 \) Hz), 7.09 (d, 2H, \( J = 8.6 \) Hz), 3.87 (s, 3H), 3.80 (s, 3H), 2.06 (s, 3H); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \( \delta \) 22.7, 55.6, 55.8, 113.2, 114.0, 118.5, 122.8, 126.6, 127.4, 130.4, 130.9, 133.2, 139.5, 155.0, 163.2, 168.8, 187.6; HRMS (ESI): [M + Na]\(^+\) calcd for C\(_{18}\)H\(_{16}\)NO\(_3\)Na, 348.1212; found, 348.1185.
N-[5-Methoxy-2-[(2-methoxyphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3K). Yellow solid; 98 mg, 60%–202 °C. 1H NMR (400 MHz, CDCl3): δ 7.78 (d, 1H, J = 15.4 Hz), 7.64 (d, 1H, J = 7.8 Hz), 7.58–7.46 (m, 3H), 7.29 (d, 1H, J = 15.4 Hz), 7.05–6.98 (m, 2H), 6.74 (d, 1H, J = 7.8 Hz), 3.90 (s, 3H), 3.84 (s, 3H), 2.23 (s, 3H). 13C NMR (100 MHz, DMSO-d6): δ 23.2, 55.4, 55.8, 111.4, 112.3, 120.5, 121.6, 125.1, 128.2, 129.2, 129.5, 132.8, 138.5, 139.2, 157.7, 161.2, 168.8, 192.0; HRMS (ESI): [M + Na]+ calcd for C19H19O4NNa, 348.1212; found, 348.1186.

N-[5-Methoxy-2-[3-(2-methoxyphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3L). Yellow solid; 110 mg, 74% mp 155–157 °C. 1H NMR (400 MHz, CDCl3): δ 7.99 (d, 2H, J = 6.8 Hz), 7.95 (d, 1H, J = 15.6 Hz), 7.90 (d, 2H, J = 8.4 Hz), 7.63 (d, 1H, J = 8.0 Hz), 7.54 (s, 1H), 7.41 (d, 1H, J = 15.6 Hz), 7.28 (d, 2H, J = 8.4 Hz), 6.76 (d, 1H, J = 8.0 Hz), 3.84 (s, 3H), 2.43 (s, 3H), 2.25 (s, 3H). 13C NMR (100 MHz, DMSO-d6): δ 23.4, 55.4, 111.1, 112.1, 120.1, 121.4, 128.4, 128.7, 128.8, 132.9, 137.9, 139.5, 139.8, 161.4, 168.9, 189.2; HRMS (FAB): [M + Na]+ calcd for C13H17O3N, 295.1208; found, 295.1210.

N-[5-Methoxy-2-[3-(4-methylphenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3M). Yellow solid; 90 mg, 58%. mp 170–172 °C. 1H NMR (400 MHz, CDCl3): δ 7.93 (d, 2H, J = 15.6 Hz), 7.90 (d, 2H, J = 8.4 Hz), 7.63 (d, 1H, J = 8.0 Hz), 7.54 (s, 1H), 7.41 (d, 1H, J = 15.6 Hz), 7.28 (d, 2H, J = 8.4 Hz), 6.76 (d, 1H, J = 8.0 Hz), 3.85 (s, 3H), 2.26 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 24.3, 55.6, 109.8, 112.8, 120.1, 120.3, 128.2, 129.9, 133.6, 138.7, 139.3, 139.8, 162.2, 169.5, 189.8; HRMS (ESI): [M + Na]+ calcd for C13H17O3N, 332.1263; found, 332.1252.

N-[5-Methoxy-2-[3-(4-chlorophenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3N). Yellow solid; 121 mg, 73%. mp 176–178 °C. 1H NMR (400 MHz, CDCl3): δ 7.92–7.96 (m, 3H), 7.65 (d, 1H, J = 8.6 Hz), 7.51 (s, 1H), 7.47 (d, 2H, J = 8 Hz), 7.37 (d, 1H, J = 15.2 Hz), 6.78 (d, 1H, J = 8.6 Hz), 3.85 (s, 3H), 2.26 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 24.3, 55.6, 109.8, 112.8, 120.1, 120.3, 128.2, 129.9, 133.6, 138.7, 139.3, 139.8, 162.2, 169.5, 189.8; HRMS (ESI): [M + Na]+ calcd for C13H17O3N, 352.0716; found, 352.0690.

N-[5-Methoxy-2-[3-(4-nitrophenyl)-3-oxo-1-propen-1-yl]phenyl]acetamide (3O). Yellow solid; 84 mg, 49%. mp 190–192 °C. 1H NMR (400 MHz, CDCl3): δ 8.34 (d, 2H, J = 8.6 Hz), 8.14 (d, 2H, J = 8.6 Hz), 7.97 (d, 1H, J = 15.4 Hz), 7.69 (d, 1H, J = 7.6 Hz), 7.46–7.43 (m, 1H), 7.37 (d, 1H, J = 15.4 Hz), 6.80 (d, 1H, J = 7.6 Hz), 3.86 (s, 3H), 2.26 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 24.6, 55.8, 109.6, 113.2, 120.4, 124.0, 128.6, 129.5, 138.8, 140.7, 143.2, 150.2, 162.8, 188.6; HRMS (ESI): [M + Na]+ calcd for C13H17O3N, 363.0957; found, 363.0946.

N-[5-Methoxy-2-[3-(3-oxo-1-buten-1-yl)phenyl]acetamide (3P). Yellow solid; 92 mg, 79%. mp 174–176 °C. 1H NMR (400 MHz, CDCl3): δ 7.61 (d, 1H, J = 16.0 Hz), 7.51 (d, 1H, J = 8.6 Hz), 7.38 (s, 1H), 6.75 (d, 1H, J = 8.6 Hz), 6.61 (d, 1H, J = 16.0 Hz), 3.83 (s, 3H), 2.33 (s, 3H), 2.24 (s, 3H); 13C NMR (100 MHz, DMSO-d6): δ 23.4, 27.4, 55.4, 110.9, 111.8, 120.6, 125.5, 128.0, 138.5, 138.9, 161.1, 168.8, 197.8; HRMS (ESI): [M + Na]+ calcd for C13H17O3N, 256.0950; found, 256.0938.
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