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Original article

# An efficient synthesis of substituted 1,4-diazepines by a Pd catalyzed amination and sequential hydrogenation condensation

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ABSTRACT

An efficient synthesis of substituted 1,4-diazepines is developed. The accessible intermediates have been obtained *via* Pd-catalyzed amination. The subsequent hydrogenation and intramolecular condensation sequences could be conducted successively in one pot without special operation. The mild and general strategy enables the synthesis of various substituted 1,4-diazepines in high yields.


## 1. Introduction

Substituted 1,4-diazepines are an important class of pharmacologically active heterocyclic structure moieties which exist in natural products [1] and clinical drugs, such as olanzapine [2] and clozapine [3]. Most previously reported methods for the assembly of 1,4-diazepine derivatives required multistep syntheses, which suffer from difficulties in the preparation of intermediates, such as amide or lactam, and introducing additional groups to the heterocyclic scaffold to yield diverse molecules [4–7]. The harsh conditions, purification after each step and low total yields make it difficult to obtain such derivatives.

More recently, Tsvelikhovsky and Buchwald developed a novel and general method to provide access to 1,4-diazepine derivatives that involve two steps of palladium-catalyzed, cross-coupling reactions and subsequent intramolecular condensation [8]. This method avoided almost all of the difficulties previously encountered in 1,4-diazepine synthesis. However, Buchwald's method still has some limitations in the availability of starting materials. *o*-Bromochlorobenzene is commercially available, but others with different substituents are rare, or difficult to prepare. The second cross-coupling requires only one chloro-substituent in the intermediate. Other halo substituents in the intermediate molecules may cause selectivity problem. Obviously, additional carbonyl or ester substituted materials were also not tolerated in the second amination–cyclization step.

In recent years, metal-catalyzed amination methodology has become an efficient tool to synthesize complex heterocycles [9,10]. During studies on heterocyclic syntheses and palladium catalyzed amination [11–14], we envisioned a change from the starting dihalobenzenes to *o*-bromonitrobenzenes according to our retrosynthetic analysis, the limitation could be overcome and diverse target molecules can be achieved. Herein, we report an efficient and mild method for the synthesis of 1,4-diazepine derivatives.

## 2. Experimental

*Typical procedure for the preparation of* ***3a***: A mixture of $PdCl_2(PPh_3)_2$, 2-bromonitrobenzene (**1a**) (1.3 mmol), 2-aminobenzophenone (**2a**) (1 mmol) and $Cs_2CO_3$ (5 mmol) in toluene (10 mL) was stirred at 110 °C for 18 h under an argon atmosphere. After removal of the solvent in vacuo, the residue was partitioned between ethyl acetate and water. The product **3a** was isolated as an orange solid in 95% yield by silica gel chromatography (PE/EA = 32/1).

*Typical procedure for the preparation of* ***5a***: 32 mg of 10% Pd/C was added into a solution of **3a** (1 mmol) in MeOH (5 mL). The mixture was stirred under $H_2$ at r.t. for 30 min and filtered. *p*-TSA (5 mol %) was added to the filtrate and stirred for 5 min. The mixture was concentrated and purified by silica gel chromatography (PE/EA = 16/1) to give product **5a** as a yellow solid in 93% yield.

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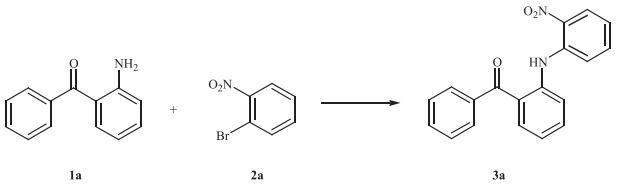
**Table 1**
Pd-catalyzed amination of 2-bromo nitrobenzenes and 2-aminobenzophenone under different reaction conditions[a].

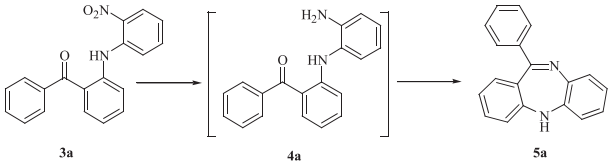


**1a** **2a** **3a**

| Entry | Catalyst | Ligand | Solvent | Temp. (°C) | Yield[b] (%) |
|---|---|---|---|---|---|
| 1 | $PdCl_2(PPh_3)_2$ | – | DMF | 120 | 50 |
| 2 | $Pd(dba)_3$ | dppf | Toluene | 120 | 43 |
| 3 | $Pd(OAc)_2$ | dppf | Toluene | 110 | 32 |
| 4 | $PdCl_2$ | dppf | Toluene | 120 | 55 |
| 5 | $PdCl_2(PPh_3)_2$ | – | Toluene | 110 | 95 |
| 6 | $PdCl_2(PPh_3)_2$ | – | 1,4-Dioxane | 110 | 84 |
| 7 | $PdCl_2(PPh_3)_2$ | – | *N*-Methyl pyrrolidinone | 120 | 77 |

[a] Reaction conditions: **1a** (2.5 mmol), **2a** (3 mmol), Pd catalyst (0.25 mmol), ligand (0.3 mmol), $Cs_2CO_3$ (7 mmol), solvent (10 mL), 110–120 °C, 18 h.
[b] Isolated yields.

**Table 2**
The hydrogenation and intramolecular condensation conditions.

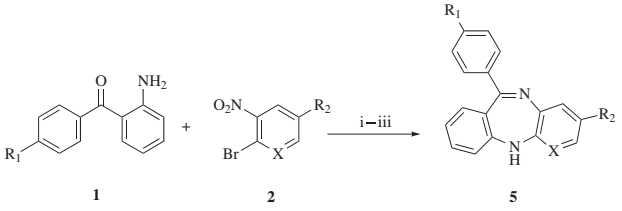


**3a** **4a** **5a**

| Entry | Hydrogenation | Intramolecular condensation | Yield[c] (%) |
|---|---|---|---|
| 1[a] | Pd/C (10 g %) hydrogenation in methanol, r.t. for 30 min | Dioxane, 4 Å MS, reflux for 4 h | 25 |
| 2[b] | | Dioxane, *p*-TSA, reflux for 1 h | 80 |
| 3 | | Filtrate, *p*-TSA, r.t. 5 min | 93 |

[a] 4 Å MS 200 mg.
[b] *p*-TSA 5 mol%.
[c] Isolated yields.

**Table 3**
The preparation of various 1,4-diazepine derivatives.[a]



**1** **2** **5**

| Entry | $R_1$ | $R_2$ | X | **5** | Yield[b] (%) |
|---|---|---|---|---|---|
| 1 | H | F | CH | **b** | 90.3 |
| 2 | H | $OCH_3$ | CH | **c** | 92.2 |
| 3 | H | $CF_3$ | CH | **d** | 92.3 |
| 4[c] | H | H | N | **e** | 95.1 |
| 5 | H | Cl | CH | **f** | 85.3 |
| 6 | H | $COOCH_3$ | CH | **g** | 82.1 |
| 7 | $-CH_3$ | H | CH | **h** | 93.1 |
| 8 | $-CH_3$ | F | CH | **i** | 91.3 |
| 9 | $-CH_3$ | $OCH_3$ | CH | **j** | 94.2 |
| 10 | $-CH_3$ | $CF_3$ | CH | **k** | 93.3 |
| 11 | $-CH_3$ | H | N | **l** | 95.2 |

[a] Reagents and conditions: (i) **1** (2.5 mmol), **2** (3.0 mmol), $PdCl_2(PPh_3)_2$ (0.25 mmol), $Cs_2CO_3$ (7 mmol), toluene (10 mL), 110–120 °C, 18 h. (ii) 10% Pd/C methanol, r.t., 30 min. (iii) *p*-TSA (5 mol %), r.t. 5 min.
[b] Isolated total yield after column chromatography of the products.
[c] Reaction was carried out with 25 mmol of **1**.

## 3. Results and discussion

We initially conducted the reaction using 2-aminobenzophenone **1a** and 2-bromonitrobenzenes **2a** as substrate in the presence of $PdCl_2(PPh_3)_2$, $Cs_2CO_3$ at 120 °C in DMF under an argon atmosphere. However, a complicated mixture was observed, which contained the desired product **3a** in only 50% yield (Table 1, entry 1). Different catalysts, ligands and solvents were then screened for the cross-coupling of 2-bromonitrobenzene and 2-aminodibenzophenone. Reactions conducted utilizing $Pd_2(dba)_3$, $Pd(OAc)_2$ and $PdCl_2$ with ligand 1,1′-bis(diphenylphosphino)ferrocene (dppf) gave **3a** in low yields (Table 1, entries 2–4). The best result was obtained using $PdCl_2(PPh_3)_2$ as catalyst, and toluene as solvent, which gave product **3a** in 95% yield (Table 1, entry 5), whereas the same reaction in 1,4-dioxane gave **3a** in 84% yield, and in *N*-methylpyrrolidone gave 77% yield (Table 1, entries 6 and 7, respectively).

These results indicated the coupling reaction proceeded smoothly and consistently within the planned reaction sequence. After the optimized reaction conditions were established, subsequent hydrogenation generated the corresponding amine compound which is difficult to isolate due to its unstable properties. We have investigated the intramolecular condensation conditions without purification of compound **4a**. To our delight, **5a** could be obtained in 93% yield after 5 min at r.t. by adding catalytic amounts of *p*-TSA to the filtrate, where 10% Pd/C had been removed (Table 2 entry 3).

With optimized reaction conditions established, we examined the scope of the method for the assembly of 1,4-diazepine derivatives. A variety of substitutions on the *o*-bromonitroaromatic ring was tolerated, including electron-withdrawing (Table 3, entries 3, 6, and 10) and electron-donating groups (Table 3, entries 2 and 9), as well as with fluoro substitution on the aromatic ring (Table 3, entries 1 and 8) and with 2-bromo-3-nitropyridine (Table 3, entries 4 and 11). It is noteworthy that the chloro substituent and the carboxylic ester group remained intact in the reactions and gave products in high yields (Table 3, entries 5 and 6). The two step sequence to substituted 1,4-diazepines gave yields ranging from 82% to 95%, which corresponds to a yield of 90% to 98% over each step of the sequence. Furthermore, the reaction could be scaled up to gram amounts without any problem [15].

## 4. Conclusion

In conclusion, we have developed an efficient and convenient synthesis of 1,4-diazepine derivatives *via* Pd-catalyzed amination, hydrogenation and intramolecular condensation sequences. The conditions of the coupling and cyclization have been fully investigated. The efficiency and substituent tolerance of these procedures have been demonstrated by synthesizing a number of functionalized 1,4-diazepine derivatives. Considering the short steps and mild conditions for the synthesis, together with the inexpensive starting material and catalytic system, this method provides an expansion on the substrate scope of Buchward's strategy, as well as an alternative route for the synthesis of 1,4-diazepine derivatives.

## Acknowledgment

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## References

[1] R.D. Charan, G. Schlingmann, J. Janso, et al., Diazepinomicin, a new antimicrobial alkaloid from a marine *Micromonospora* sp., J. Nat. Prod. 67 (2004) 1431–1433.
[2] B. Fulton, K.L. Goa, Olanzapine. A review of its pharmacological properties and therapeutic efficacy in the management of schizophrenia and related psychoses, Drugs 53 (1997) 281–298.
[3] A. Fitton, R.C. Heel, Clozapine. A review of its pharmacological properties, and therapeutic use in schizophrenia, Drugs 40 (1990) 722–747.
[4] A.W.H. Wardrop, G.L. Sainsbury, J.M. Harrison, T.D. Inch, Preparation of some dibenz[b,f][1,4]oxazepines and dibenz[b,e]azepines, J. Chem. Soc., Perkin Trans. 1 (1976) 1279–1285.
[5] X. Xu, S. Guo, Q. Dang, J. Chen, X. Bai, A new strategy toward fused-pyridine heterocyclic scaffolds: Bischler–Napieralski-type cyclization, followed by sulfoxide extrusion reaction, J. Comb. Chem. 9 (2007) 773–782.
[6] Y. Liao, B.J. Venhuis, N. Rodenhuis, et al., New (sulfonyloxy)piperazinyldibenzazepines as potential atypical antipsychotics: chemistry and pharmacological evaluation, J. Med. Chem. 42 (1999) 2235–2244.
[7] R.A. Smits, H.D. Lim, B. Stegink, et al., Characterization of the histamine H4 receptor binding site. Part 1. Synthesis and pharmacological evaluation of dibenzodiazepine derivatives, J. Med. Chem. 49 (2006) 4512–4516.
[8] D. Tsvelikhovsky, S.L. Buchwald, Concise palladium-catalyzed synthesis of dibenzodiazepines and structural analogues, J. Am. Chem. Soc. 133 (2011) 14228–14231.
[9] J.F. Hartwig, Transition metal catalyzed synthesis of arylamines and aryl ethers from aryl halides and triflates: scope and mechanism, Angew. Chem. Int. Ed. 37 (1998) 2046–2067.
[10] D.S. Surry, S.L. Buchwald, Biaryl phosphane ligands in palladium-catalyzed amination, Angew. Chem. Int. Ed. 47 (2008) 6338–6361.
[11] K. Liu, D. Yin, Efficient method for the synthesis of 2,3-unsubstituted nitro containing indoles from *o*-fluoronitrobenzenes, Org. Lett. 11 (2009) 637–639.
[12] G. Zhang, H. Zhang, X. Wang, et al., Synthesis of new riminophenazines with pyrimidine and pyrazine substitution at the 2-N position, Molecules 16 (2011) 6985–6991.
[13] G. Li, Q. Xiao, C. Li, X. Wang, D. Yin, A facile preparation of tetralins from arene-1,4-diones using titanium(IV) chloride and triethylsilane, Tetrahedron Lett. 52 (2011) 6827–6830.
[14] G. Zhang, X. Wang, C. Li, D. Yin, Palladium-catalyzed cross-coupling of electron-deficient heteroaromatic amines with heteroaryl halides, Synth. Commun. 43 (2012) 456–463.
[15] Compound **5a**: $^1$H NMR (300 MHz, $CD_3Cl$): $\delta$ 7.710 (d, 2H, $J$ = 5.4 Hz), 7.404 (m, 3H), 7.323 (m, 2H), 7.014 (m, 3H), 6.918 (m, 1H), 6.779 (m, 1H), 6.704 (m, 1H), 4.975 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 169.49, 154.45, 142.60, 141.32, 140.85, 132.19, 131.94, 129.93, 128.67, 127.96, 127.56, 126.81, 124.17, 122.42, 119.70. HRMS (*m/z*) (M+H): Calcd. for $C_{19}H_{14}N_2$: 271.123, found: 271.1233. Mp 129–131 °C. IR (KBr): 3350, 1609, 1571, 1445, 1283, 960. Compound **5b**: $^1$H NMR (300 MHz, $CD_3Cl$): $\delta$ 7.69 (d, 1H, $J$ = 6.6 Hz), 7.44 (m, 3H), 7.38 (td, 1H, $J$ = 7.8 Hz, $J$ = 1.5 Hz), 7.01 (m, 2H), 6.93 (m, 2H), 6.77 (d, 1H, $J$ = 4.5 Hz), 6.72 (dd, 1H, $J$ = 7.8 Hz, $J$ = 2.7 Hz), 6.63 (m, 1H), 4.97 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.58, 160.97, 158.58, 154.50, 142.05 ($J$ = 9 Hz), 140.90, 138.64, 132.15 ($J$ = 6 Hz), 130.26, 129.64, 128.01, 127.45, 122.60, 120.08 ($J$ = 9 Hz), 119.69, 114.58 ($J$ = 23 Hz), 112.88 ($J$ = 23 Hz). HRMS (*m/z*) (M+H): Calcd. for $C_{19}H_{13}FN_2$: 289.1136, found: 289.1142. Mp 103–105 °C. IR (KBr): 3352, 1613, 1466, 1216, 1107, 866. Compound **5c**: $^1$H NMR (300 MHz, $CD_3Cl$): $\delta$ 7.70 (d, 2H, $J$ = 7.8 Hz), 7.43 (m, 3H), 7.37 (m, 1H), 6.99 (d, 1H, $J$ = 7.5 Hz), 6.89 (m, 2H), 6.74 (d, 1H, $J$ = 7.5 Hz), 6.60 (s, 2H), 3.77 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.00, 156.61, 155.03, 141.67, 141.29, 135.77, 132.15, 131.94, 129.97, 129.58, 127.94, 127.44, 122.28, 120.24, 119.51, 113.13, 112.55, 55.59. HRMS (*m/z*) (M+H): Calcd. for $C_{20}H_{16}N_2O$: 301.1335, found: 301.1339. Mp 149–152 °C. IR (KBr): 3349, 2400, 1666, 1501, 1328, 1243, 1117, 960. Compound **5d**: $^1$H NMR (300 MHz, $CD_3Cl$): $\delta$ 7.70 (d, 2H, $J$ = 6.9 Hz), 7.56 (s, 1H), 7.41 (m, 3H), 7.27 (m, 2H), 6.97 (m, 2H), 6.74 (t, 2H, $J$ = 7.5 Hz), 5.12 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.85, 153.40, 145.85, 140.77, 140.72, 132.38, 132.36, 130.41, 129.62, 128.07, 127.50, 126.01, 125.98, 123.51, 123.47, 122.93, 119.99, 119.85. HRMS (*m/z*) (M+H): Calcd. for $C_{20}H_{13}F_3N_2$: 339.1104, found: 339.1105. Mp 129–131 °C. IR (KBr): 3267, 2400, 1607, 1445, 1325, 1123, 1074, 960, 751. Compound **5e**: $^1$H NMR (300 MHz, $CD_3Cl$): $\delta$ 7.95 (d, 1H, $J$ = 4.8 Hz), 7.68 (d, 2H, $J$ = 7.5 Hz), 7.56 (d, 1H, $J$ = 7.8 Hz), 7.38 (m, 3H), 7.29 (t, 1H, $J$ = 7.5 Hz), 7.01 (m, 2H), 6.92 (m, 1H), 6.83 (d, 1H, $J$ = 5.1 Hz Hz), 6.19 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.06, 153.39, 152.01, 145.05, 140.80, 136.52, 135.24, 132.51, 132.30, 130.27, 129.64, 128.01, 127.13, 122.32, 120.40, 119.98. HRMS (*m/z*) (M+H): Calcd. for $C_{18}H_{13}N_3$: 272.1182, found: 272.1187. Mp 183–186 °C. IR (KBr): 3277, 2380, 1703, 1454, 1227, 1021, 960. Compound **5f**: $^1$H NMR (300 MHz, $CD_3Cl$): $\delta$ 7.67 (d, 2H, $J$ = 6.9 Hz), 7.42 (m, 3H), 7.30 (m, 2H), 6.95 (m, 3H), 6.76 (d, 1H, $J$ = 8.1 Hz), 6.61 (d, 1H, $J$ = 8.1 Hz). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.78, 154.18, 119.84, 141.75, 141.40, 140.71, 132.30, 130.39, 129.67, 129.09, 128.13, 128.04, 127.34, 126.40, 122.71, 120.58. HRMS (*m/z*) (M+H): Calcd. for $C_{19}H_{14}ClN_2$: 305.0840, found: 305.0845. Mp 191–193 °C. IR (KBr): 3274, 2336, 1601, 1423, 1255, 1064, 960. Compound **5g**: $^1$H NMR (400 MHz, $CD_3Cl$): $\delta$ 7.98 (s, 1H), 7,60 (m, 3H), 7.42–7.52 (m, 3H), 7,35 (t, 1H, $J$ = 5.4 Hz), 7.03 (m, 1H), 7.01 (m, 1H), 6.79 (d, 1H, $J$ = 7.6 Hz), 6.73 (d, 1H, $J$ = 7.6 Hz), 5.21 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 166.552, 153.289, 147.334, 140.777, 132.660, 132.477, 132.344, 130.495, 130.320, 130.045, 129.641, 128.398, 128.036, 127.399, 126.095, 122.809, 120.019, 119.592, 51.968. HRMS (*m/z*) (M+H): Calcd. for $C_{21}H_{17}O_2N_2$, 329.1284, found 329.1286. Mp 159–162 °C. IR (KBr): 3285, 1238, 1078, 1054, 975, 730. Compound **5h**: $^1$H NMR (400 MHz, $CD_3Cl$): $\delta$ 7.60 (d, 2H, $J$ = 8 Hz), 7.29 (m, 2H), 7.19 (m, 2H), 7.02 (m, 3H), 6.91 (t, 1H, $J$ = 7.2 Hz), 6.77 (d, 1H, $J$ = 8 Hz), 6.69 (d, 1H, $J$ = 6.8 Hz), 4.97 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 169.36, 154.39, 142.62, 140.95, 140.12, 138.49, 132.18, 131.82, 129.54, 128.64, 127.59, 126.57, 124.10, 122.32, 119.67, 119.66, 21.38. HRMS (*m/z*) (M+H): Calcd. for $C_{20}H_{16}N_2$:

285.1386, found: 285.1386. Mp 168–170 °C. IR (KBr): 3347, 1577, 1466, 1238, 876. Compound **5i**: $^1$H NMR (400 MHz, $CD_3Cl$): $\delta$ 7.59 (d, 2H, $J$ = 7.6 Hz), 7.29 (m, 1H), 7.20 (m, 2H), 7.03 (m, 2H), 6.94 (m, 1H), 6.78 (d, 1H, $J$ = 8 Hz), 6.71 (m, 1H), 6.62 (m, 1H), 4.92 (s, 1H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.43, 160.92, 158.53, 154.43, 142.14, 140.53, 138.66, 138.06, 132.01 ($J$ = 17 Hz), 129.62, 128.69, 127.46, 122.49, 120.11, 119.65, 114.40 ($J$ = 24 Hz), 112.61 ($J$ = 23 Hz), 21.36. HRMS ($m/z$) (M+H): Calcd. for $C_{20}H_{15}FN_2$: 303.1292, found: 303.1296. Mp 145–148 °C. IR (KBr): 3345, 1620, 1487, 1220, 1113, 960. Compound **5j**: $^1$H NMR (400 MHz, $CD_3Cl$): $\delta$ 7.60 (d, 2H, $J$ = 7.6 Hz), 7.31 (m, 1H), 7.19 (d, 2H, $J$ = 7.6 Hz), 7.02 (m, 1H), 6.91 (t, 1H, $J$ = 7.6 Hz), 6.88 (s, 1H), 6.77 (d, 1H, $J$ = 8 Hz), 6.65 (m, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 169.87, 156.60, 154.98, 141.80, 140.20, 138.47, 135.80, 132.19, 131.83, 129.59, 128.65, 127.51, 122.23, 120.18, 119.48, 112.93, 112.44, 55.59, 21.38. HRMS ($m/z$) (M+H): Calcd. for $C_{21}H_{18}N_2O$: 315.1492, found 315.1495. Mp 178–180 °C. IR (KBr): 3300, 1567, 1433, 1203, 1103, 982. Compound **5k**: $^1$H NMR (400 MHz, $CD_3Cl$): $\delta$ 7.60 (d, 2H, $J$ = 8 Hz), 7.55 (m, 1H), 7.31 (m, 1H), 7.21 (m, 5H), 7.05 (m, 1H), 6.95 (m, 1H), 6.75 (m, 2H), 5.11 (s, 1H), 2.41 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.67, 153.36, 145.84, 140.91, 140.75, 137.91, 132.41, 132.24, 129.64, 128.87, 127.58, 125.90, 125.87, 123.27, 123.24, 122.87, 119.94, 119.78, 21.42. HRMS ($m/z$) (M+H): Calcd. for $C_{21}H_{15}F_3N_2$: 353.1260, found: 353.1264. Mp 180–183 °C. IR (KBr): 3309, 2740, 1637, 1325, 1076, 960, 751. Compound **5l**: $^1$H NMR (400 MHz, $CD_3Cl$): $\delta$ 7.93 (d, 1H, $J$ = 4 Hz), 7.55 (m, 3H), 7.31 (t, 1H, $J$ = 7.6 Hz), 7.21 (d, 2H, $J$ = 7.6 Hz), 6.98 (m, 2H), 6.91 (m, 1H), 6.84 (m, 1H), 5.91 (s, 1H), 2.41 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 170.93, 153.31, 151.96, 144.88, 140.62, 138.00, 136.36, 135.32, 132.42, 132.35, 129.68, 128.74, 127.17, 122.31, 120.37, 120.02, 21.42. HRMS ($m/z$) (M+H): Calcd. for $C_{19}H_{15}N_3$: 286.1339, found: 286.1347. Mp 175–177 °C. IR (KBr): 3223, 2246, 1667, 1411, 1227, 1021, 960.