JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

# Iron-Catalyzed N-Alkylation of Azoles via Cleavage of an $sp^3$ C–H Bond Adjacent to a Nitrogen Atom

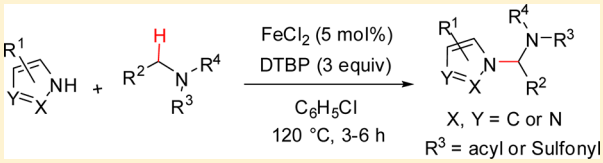
Qinqin Xia[†] and Wanzhi Chen*[,†,‡]

[†]Department of Chemistry, Zhejiang University, Xixi Campus, Hangzhou 310028, People's Republic of China

[‡]State Key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China

Supporting Information

**ABSTRACT:** Iron-catalyzed direct C–N bond formation between azoles and amides is described. The oxidative coupling reactions of $sp^3$ C–H bonds adjacent to a nitrogen atom in amides and sulfonamides with the N–H bond in azoles proceeded smoothly in the presence of $FeCl_2$ and di-*tert*-butyl peroxide (DTBP).

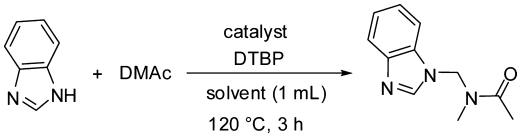



The formation of C–N bonds is one of the most important transformations in organic chemistry owing to the high prevalence of nitrogen-containing molecules of biological and pharmaceutical relevance.[1] Transition metal catalyzed cross-coupling reactions are among the most important methods for C–N bond formation. However, the need of preinstallation of reactive functional groups limits their further application. The direct C–N bond formation via C–H activation represents an extremely attractive and efficient route, because it is straightforward and has economic advantages over present procedures, which employ prefunctionalized substrates.[2] The catalytic $sp^3$ C–H bond activation is a challenging and powerful technology in organic synthesis.[3] Recently, catalytic oxidative functionalization of an $sp^3$ C–H bond adjacent to a heteroatom (nitrogen or oxygen) has attracted much interest.[4] Selective functionalization of C–H bonds adjacent to a nitrogen atom in simple amines and amides is of great importance for the synthesis of nitrogen-containing compounds. For example, Li and other groups have reported cross-dehydrogenative coupling (CDC) of C–H bonds adjacent to a nitrogen atom to give new C–C bonds.[4a−m] This reaction is more atom economical and environmentally friendly than traditional cross-coupling reactions. Recently, Shirakawa and co-workers have reported iron-catalyzed oxidative C–C coupling between alphatic amides and electron-rich arenes via direct $sp^3$ C–H bond activation adjacent to nitrogen atoms in amides.[5] However, construction of new C–N bonds via oxidative functionalization of an $sp^3$ C–H bond adjacent to a nitrogen atom is sparse.[2d,6] To the best of our knowledge, the direct conversion of an $sp^3$ C–H bond adjacent to a nitrogen atom into a C–N bond using azoles as the nitrogen sources has not been reported.

*N*-Alkylazoles are fundamental structural and functional units of many N-heterocyclic carbenes (NHC)[7] and ionic liquids.[8] Traditionally, *N*-alkylazoles are prepared by nucleophilic substitution of alkyl halides. Recently, we have reported direct C–N coupling of imidazoles and benzylic compounds for synthesis of imidazole derivatives.[9] Herein, we report iron-catalyzed N-alkylation of azoles via oxidative activation of C–H bond adjacent to a nitrogen atom.

Benzimidazole (**1a**) and *N*,*N*-dimethylacetamide (**2a**) were selected as the model substrates to establish optimized reaction conditions (Table 1). Various iron and copper salts were tested

**Table 1. Optimization of Reaction Conditions**[a]




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

| entry | catal. (mol %) | **2a** (equiv) | DTBP (equiv) | solvent | yield (%) |
|---|---|---|---|---|---|
| 1 | CuBr (10) | | 2 | DMAc | 66 |
| 2 | CuI (10) | | 2 | DMAc | 34 |
| 3 | $Cu(OTf)_2$ (10) | | 2 | DMAc | 41 |
| 4 | $FeSO_4 \cdot 7H_2O$ (10) | | 2 | DMAc | 19 |
| 5 | $FeCl_2$ (10) | | 2 | DMAc | 74 |
| 6 | $Fe(acac)_3$ (10) | | 2 | DMAc | 44 |
| 7 | $FeCl_2$ (10) | | 3 | DMAc | 97 |
| 8[b] | $FeCl_2$ (10) | | 3 | DMAc | 68 |
| 9 | $FeCl_2$ (10) | 8 | 3 | $C_6H_5Cl$ | 93 |
| 10 | $FeCl_2$ (10) | 6 | 3 | $C_6H_5Cl$ | 94 |
| 11 | $FeCl_2$ (10) | 4 | 3 | $C_6H_5Cl$ | 96 |
| 12 | $FeCl_2$ (10) | 2 | 3 | $C_6H_5Cl$ | 67 |
| **13** | **$FeCl_2$ (5)** | **4** | **3** | **$C_6H_5Cl$** | **96** |
| 14 | | 4 | 3 | $C_6H_5Cl$ | 17 |

[a]Reaction conditions: **1a** (0.5 mmol) under $N_2$. [b]100 °C

for the proposed reaction using di-*tert*-butyl peroxide (DTBP) as an oxidant in DMAc (Table 1, entries 1–6). Di-*tert*-butyl peroxide is a suitable oxidant,[5,10] and iron is an efficient catalyst in oxidative coupling reactions.[11] All the copper and iron salts are active regardless of their oxidation states. $FeCl_2$ showed relatively higher catalytic efficiency than other metal salts,

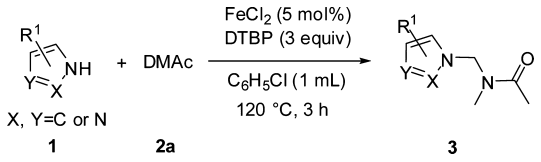
**Received:** July 24, 2012
**Published:** October 1, 2012

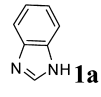
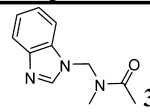
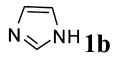
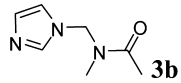
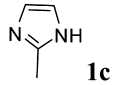
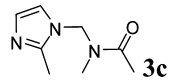
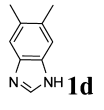
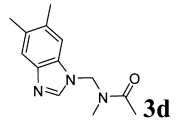
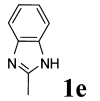
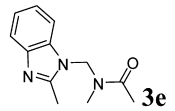
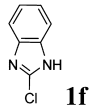
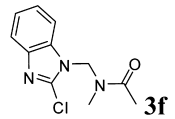
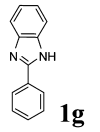
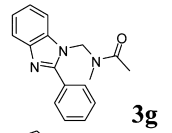
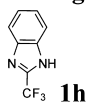
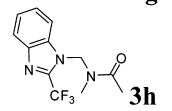
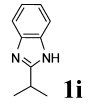
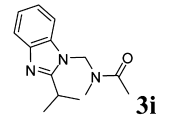
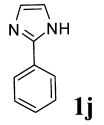
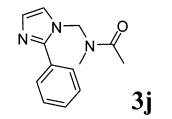
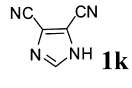
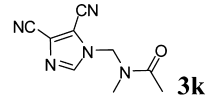
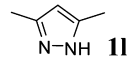
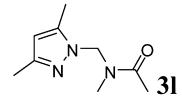
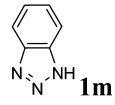
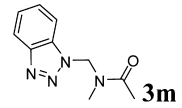




dx.doi.org/10.1021/jo301568e | *J. Org. Chem.* 2012, 77, 9366–9373

**Table 2. Reactions of Various Azoles with DMAc**[a]



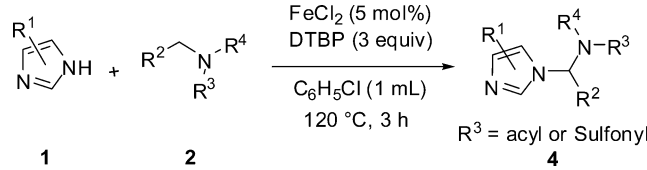

| entry | 1 | product | yield (%) |
|---|---|---|---|
| 1 |  **1a** |  **3a** | 96 |
| 2 |  **1b** |  **3b** | 72 |
| 3 |  **1c** |  **3c** | 44 |
| 4 |  **1d** |  **3d** | 52 |
| 5 |  **1e** |  **3e** | 83 |
| 6 |  **1f** |  **3f** | 75 |
| 7 |  **1g** |  **3g** | 80 |
| 8 |  **1h** |  **3h** | 87 |
| 9 |  **1i** |  **3i** | 84 |
| 10 |  **1j** |  **3j** | 81 |
| 11 |  **1k** |  **3k** | 75 |
| 12 |  **1l** |  **3l** | 76 |
| 13 |  **1m** |  **3m** | 69 |

[a]Reaction conditions: **1** (0.5 mmol), **2a** (2.0 mmol), $FeCl_2$ (0.025 mmol), DTBP (1.5 mmol), $C_6H_5Cl$ (1.0 mL), 120 °C, 3 h, under $N_2$.

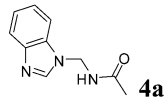
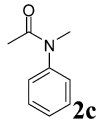
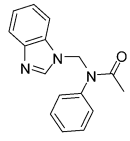
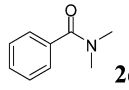
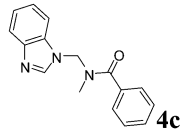
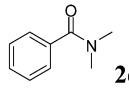
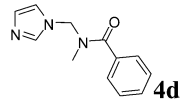
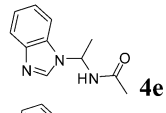
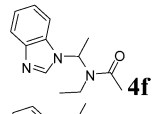
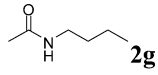
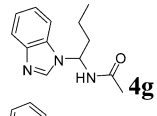
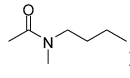
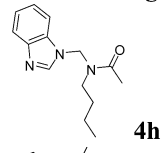
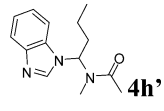
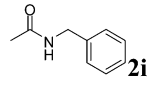
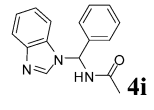
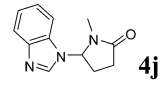
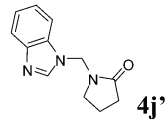
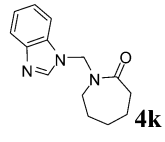
giving a yield of 74% in the presence of 2 equiv of DTBP at 120 °C, and thus was chosen as the catalyst for further optimization (entry 5). The compound **3a** was almost quantitatively obtained when the amount of DTBP was increased to 3 equiv (entry 7). When the reaction was carried out at 100 °C, the yield was decreased to 68% (entry 8). The reaction was also tested in $C_6H_5Cl$, and comparable yields could be obtained when 4−8 equiv of DMAc was used (entries 9−11). However, the yield of **3a** was decreased to 67% in the presence of 2 equiv of DMAc (entry 12). Furthermore, we found that the reaction


dx.doi.org/10.1021/jo301568e | J. Org. Chem. 2012, 77, 9366−9373

**Table 3. Reactions of Azoles with Various Amides and Sulfonamides**[a]

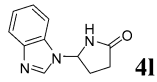
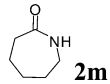
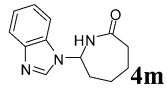
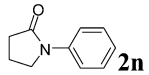
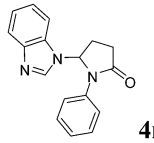
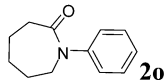
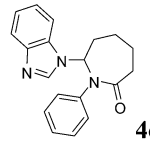
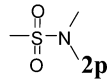
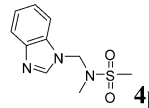
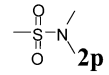
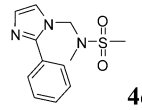



1 2 4

| entry | 1 | 2 | product | yield (%) |
|---|---|---|---|---|
| 1 | 1a |  2b |  4a | 75 |
| 2 | 1a |  2c |  4b | 44 |
| 3 | 1a |  2d |  4c | 95 |
| 4 | 1b |  2d |  4d | 96 |
| 5 | 1a |  2e |  4e | 55 |
| 6 | 1a |  2f |  4f | 75 |
| 7 | 1a |  2g |  4g | 47 |
| 8 | 1a |  2h |  4h  4h' | 82 (4h:4h' = 2.2:1) |
| 9 | 1a |  2i |  4i | 98 |
| 10 | 1a |  2j |  4j  4j' | 97 (4j:4j' = 3.1:1) |
| 11 | 1a |  2k |  4k | 79 |

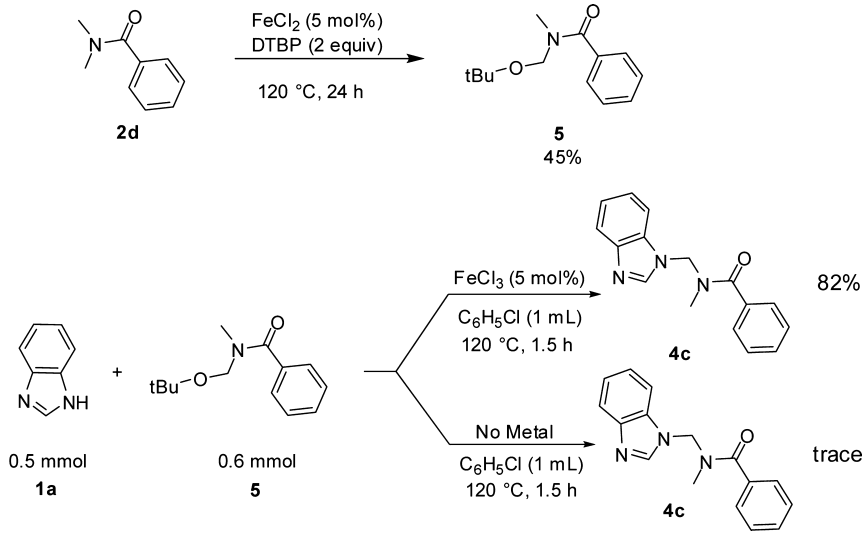

dx.doi.org/10.1021/jo301568e | J. Org. Chem. 2012, 77, 9366−9373

**Table 3. continued**

| entry | 1 | 2 | product | yield (%) |
|---|---|---|---|---|
| 12[b] | **1a** |  **2l** |  **4l** | 46 |
| 13[b] | **1a** |  **2m** |  **4m** | 53 |
| 14 | **1a** |  **2n** |  **4n** | 92 |
| 15 | **1a** |  **2o** |  **4o** | 42 |
| 16 | **1a** |  **2p** |  **4p** | 65 |
| 17 | **1j** |  **2p** |  **4q** | 68 |

[a]Reaction conditions: **1** (0.5 mmol), **2** (2.0 mmol), $FeCl_2$ (0.025 mmol), DTBP (1.5 mmol), $C_6H_5Cl$ (1.0 mL), 120 °C, 3 h, under $N_2$. [b]6 h.

**Scheme 1. An Investigation of Reaction Mechanism**



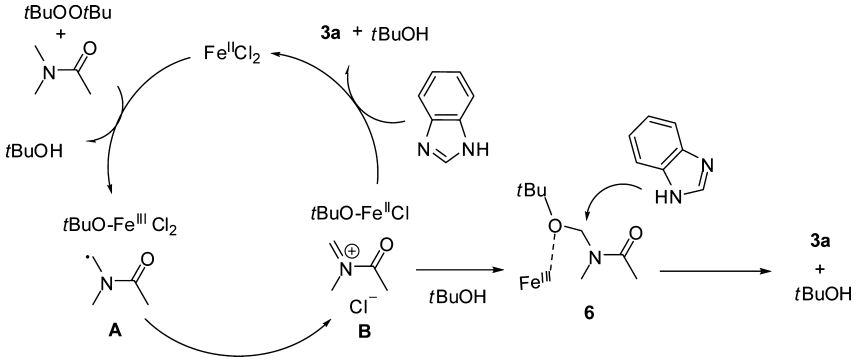

in the presence of 5 mol % of $FeCl_2$ gave identical result to those of 10 mol % of $FeCl_2$ (entry 13). Although the reaction could proceed without use of a metal catalyst, the yield is quite poor (entry 14).

The coupling of various azoles with DMAc **2a** was investigated under the optimized conditions, and the results were summarized in Table 2. The reaction of imidazole **1b** gave a slightly lower yield (Table 2, entry 2). A moderate yield was obtained when 2-methyl imidazole **1c** was applied (entry 3). Benzoimidazole **1d** having two methyl groups at its 5- and 6-positions showed relatively lower activity compared to **1a** (entry 4). 2-Substituted benzoimidazoles **1e**−**i** having either electron-withdrawing or electron-donating groups gave good yields (entries 5−9), indicating that the steric and electronic effect of groups at the 2-positions has little influence on the C−N coupling. 2-Phenyl imidazole **1j** showed higher reactivity than imidazole **1b** (entry 10). 4,5-Dicyanoimidazole **1k** bearing two strong electron-withdrawing substituents gave similar yield compared to imidazole **1b** (entry 11). Moreover, 3,5-dimethylpyrazole **1l** and benzotriazole **1m** afforded the corresponding products **3l** and **3m** in satisfactory yields (entries 12 and 13).

We next examined the coupling reactions of a series of amides and sulfonamides with imidazole (Table 3). The acyclic amides afforded the corresponding products with moderate to good yields (entries 1−9). A free N−H bond in *N*-methylacetamide **2b** can be tolerated but a lower yield was obtained compared to *N*,*N*-dimethylacetamide **2a** (entry 1). *N*-Methyl-*N*-phenylacetamide **2c** gave moderate yield probably due to the steric effect (entry 2). Reaction of *N*,*N*-


dx.doi.org/10.1021/jo301568e | J. Org. Chem. 2012, 77, 9366−9373

**Scheme 2. Possible Mechanism of Oxidative C−N Coupling**




dimethylbenzamide **2d** with benzoimidazole and imidazole yielded the desired products in excellent yields (entries 3 and 4). The methylene moieties of *N*-ethylacetamide, *N*,*N*-diethylacetamide, and *N*-butylacetamide are relatively more inert than methyl in *N*,*N*-dimethylacetamide (entries 5−7). The coupling reaction of *N*-butyl-*N*-methylacetamide **2h** with **1a** took place in the presence of $FeCl_2$ affording a mixture of **4h** and **4h′** in a ratio of 2.2:1 (entry 8). The results clearly demonstrate that C−H bonds of *N*-methyl are more active than those of *N*-methylene group. Benzyl C−H bond in *N*-benzylacetamide **2i** showed high reactivity giving **4i** in 98% yield (entry 9). Probably the benzyl group can stabilize the proposed acyliminium cation intermediate generated by oxidation.

The lactams also underwent the C−N coupling with benzoimidazole **1a** (entries 10−15). When 1-methylpyrrolidin-2-one **2j** was used, two products **4j** and **4j′** were formed in an overall yield of 97%. Unlike the chain amides described above, the functionalization of the $CH_2$ group adjacent to nitrogen atom in the ring is more facile than that of the N−Me group (entry 10). However, when 1-methylazepan-2-one **2k** was used, 1-((1*H*-benzo[d]imidazol-1-yl)methyl)azepan-2-one **4k** was isolated as the only product, and no functionalization product occurred at the ring was found (entry 11). Again, the free N−H bond can be tolerated, but **2l** and **2m** show lower activities than *N*-methyllactams (entries 12 and 13). Interestingly, reactions of 1-phenylpyrrolidin-2-one **2n** and 1-phenylazepan-2-one **2o** showed remarkable difference (entries 14 and 15). We speculate that the methylene C−H bonds of 5-membered lactams are more reactive than those of 7-membered lactams (entries 10, 11, 14 and 15). We further found that sulfonamides were also suitable for the direct C−N bond coupling (entries 16 and 17).

The mechanism of $FeCl_2$-catalyzed direct C−N coupling was briefly investigated. The oxidation of alkylamides with an oxygen-based oxidant to give $\alpha$-alkoxylamides has been known.[5,12] On the basis of this fact, the following control experiments were performed. As shown in Scheme 1, treatment of *N*,*N*-dimethylbenzamide **2d** with 2 equiv of DTBP gave *N*-(*tert*-butoxymethyl)-*N*-methylbenzamide **5** in 45% yield in the presence of $FeCl_2$. Further reaction of benzoimidazole **1a** with isolated **5** afforded **4c** in 82% yield when 5 mol % $FeCl_3$ was used. When the reaction was carried out under metal-free conditions, only a trace amount of **4c** was observed. Obviously, iron catalyst is crucial for the formation of both *N*-(*tert*-butoxymethyl)-*N*-methylbenzamide **5** and *N*-((1*H*-benzo[d]-imidazol-1-yl)methyl)-*N*-methylbenzamide **4c**.

Therefore, a possible mechanism is proposed in Scheme 2. The reaction is initiated by iron-assisted oxidation to form radical **A** from the H abstraction of DMAc. The radical **A** could be further oxidized to acyliminium ion **B** through a single-electron transfer process. The acyliminium ion **B** reacts with *t*-BuOH to give *tert*-butoxyamide **6**, and subsequent nucleophilic reaction of benzimidazole with *tert*-butoxyamide **6** assisted by Fe(III) ion would form the product **3a**. Another possibility is that benzimidazole directly reacts with acyliminium ion **B** to yield **3a**.

In summary, we have developed an efficient method for the synthesis of azole derivatives by an iron catalyzed direct C−N coupling of azoles and amides. The chemistry has several methodological advantages: (i) The catalyst−oxidant system is inexpensive and readily available. (ii) The C−N bonds can be formed directly from C−H bonds. (iii) A wide range of amides and sulfonamides can be used as substrate for N-alkylation of azoles.

## EXPERIMENTAL SECTION

**General Procedure for the Synthesis of Products 3 or 4.** An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with azole **1** (0.5 mmol), $FeCl_2$ (3.2 mg, 0.025 mmol), and amide **2** (2.0 mmol). The tube was evacuated and refilled with $N_2$, and this process was repeated three times. Then di-*tert*-butyl peroxide (220 mg, 1.5 mmol) in chlorobenzene (1.0 mL) was added. The resulting mixture was stirred at 120 °C for 3 h. After completion of the reaction, the resulting solution was cooled to room temperature. The reaction mixture was then filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (ethyl acetate/ethanol, 10:1) to afford the corresponding product.

***N*-((1*H*-Benzo[d]imidazol-1-yl)methyl)-*N*-methylacetamide (3a).**[13] Light yellow oil (97 mg, 96%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.89 (s, 1H), 7.71 (d, $J$ = 7.2 Hz, 1H), 7.50 (d, $J$ = 8.0 Hz, 1H), 7.21 (t, $J$ = 3.8 Hz, 2H), 5.63 (s, 2H), 2.91 (s, 3H), 2.03 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.4, 143.5, 143.4, 133.1, 123.5, 122.6, 120.1, 110.3, 55.0, 35.0, 21.7; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{11}H_{13}N_3O$ 203.1059, found 203.1061.

***N*-((1*H*-Imidazol-1-yl)methyl)-*N*-methylacetamide (3b).** Light yellow oil (55 mg, 72%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.59 (s, 1H), 6.99 (d, $J$ = 8.0 Hz, 2H), 5.38 (s, 2H), 2.97 (s, 3H), 2.05 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.5, 137.3, 129.3, 119.1, 57.1, 35.0, 21.6; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_7H_{11}N_3O$ 153.0902, found 153.0901.

***N*-Methyl-*N*-((2-methyl-1*H*-imidazol-1-yl)methyl)acetamide (3c).** Light yellow oil (37 mg, 44%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.97 (s, 1H), 6.90 (s, 1H), 5.44 (s, 2H), 2.99 (s, 3H), 2.44 (s, 3H), 2.14 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$171.1, 144.8, 127.3, 119.6, 55.8, 34.5, 21.7, 12.9; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_8H_{13}N_3O$ 167.1059, found 167.1061.


dx.doi.org/10.1021/jo301568e | J. Org. Chem. 2012, 77, 9366−9373

***N*-((5,6-Dimethyl-1*H*-benzo[d]imidazol-1-yl)methyl)-*N*-methylacetamide (3d).** Yellow oil (60 mg, 52%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.90 (s, 1H), 7.50 (s, 1H), 7.28 (s, 1H), 5.62 (s, 2H), 2.93 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H), 2.07 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.3, 142.7, 142.0, 132.7, 131.6, 131.5, 120.1, 110.3, 54.9, 34.8, 21.7, 20.5, 20.1; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1373.

***N*-Methyl-*N*-((2-methyl-1*H*-benzo[d]imidazol-1-yl)methyl)-acetamide (3e).** Yellow oil (90 mg, 83%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.59−7.57 (m, 1H), 7.36−7.34 (m, 1H), 7.15−7.13 (m, 2H), 5.62 (s, 2H), 2.77 (s, 3H), 2.55 (s, 3H), 2.04 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.0, 151.7, 142.2, 134.7, 122.6, 122.3, 118.9, 109.7, 53.1, 33.8, 21.8, 13.9; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{12}H_{15}N_3O$ 217.1215, found 217.1213.

***N*-((2-Chloro-1*H*-benzo[d]imidazol-1-yl)methyl)-*N*-methylacetamide (3f).** Yellow oil (89 mg, 75%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.70−7.63 (m, 2H), 7.31−7.29 (m, 2H), 5.87 (s, 2H), 2.98 (s, 3H), 2.16 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.4, 141.4, 140.2, 134.2, 123.9, 123.3, 119.2, 111.1, 53.7, 34.0, 21.8; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{11}H_{12}ClN_3O$ 237.0669, found 237.0674.

***N*-Methyl-*N*-((2-phenyl-1*H*-benzo[d]imidazol-1-yl)methyl)-acetamide (3g).** White solid (112 mg, 80%): mp 155−156 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.79 (d, $J$ = 7.2 Hz, 1H), 7.65−7.60 (m, 3H), 7.51 (s, 3H), 7.30−7.27 (m, 2H), 5.93 (s, 2H), 2.42 (s, 3H), 1.99 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.1, 154.3, 142.8, 134.3, 130.0, 129.8, 129.6, 128.9, 123.5, 123.0, 119.7, 111.4, 53.8, 33.1, 21.6; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{17}H_{17}N_3O$ 279.1372, found 279.1371.

***N*-Methyl-*N*-((2-(trifluoromethyl)-1*H*-benzo[d]imidazol-1-yl)-methyl)acetamide (3h).** Yellow oil (118 mg, 87%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 7.2 Hz, 1H), 7.59 (d, $J$ = 6.8 Hz, 1H), 7.37−7.31 (m, 2H), 5.91 (s, 2H), 2.81 (s, 3H), 2.13 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.4, 140.8, 140.5 (q, $J_{C-F}$ = 37.9 Hz), 134.5, 126.0, 124.1, 121.4, 118.9 (q, $J_{C-F}$ = 269.9 Hz), 111.9, 54.1, 33.1, 21.8; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{12}H_{12}F_3N_3O$ 271.0932, found 271.0931.

***N*-((2-Isopropyl-1*H*-benzo[d]imidazol-1-yl)methyl)-*N*-methylacetamide (3i).** White solid (103 mg, 84%): mp 121−122 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74−7.72 (m, 1H), 7.43−7.40 (m, 1H), 7.23−7.21 (m, 2H), 5.78 (s, 2H), 3.33−3.26 (m, 1H), 2.81 (s, 3H), 2.12 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.0, 160.4, 142.3, 134.6, 122.7, 122.4, 119.3, 109.5, 52.4, 33.4, 26.0, 21.8, 21.8; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{14}H_{19}N_3O$ 245.1528, found 245.1528.

***N*-Methyl-*N*-((2-phenyl-1*H*-imidazol-1-yl)methyl)acetamide (3j).** Light yellow oil (93 mg, 81%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47−7.38 (m, 5H), 7.10 (s, 1H), 7.04 (s, 1H), 5.51 (s, 2H), 2.56 (s, 3H), 1.98 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.4, 148.1, 130.1, 129.4, 129.1, 128.9, 128.7, 120.2, 56.5, 34.4, 21.6; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{13}H_{15}N_3O$ 229.1215, found 229.1213.

***N*-((4,5-Dicyano-1*H*-imidazol-1-yl)methyl)-*N*-methylacetamide (3k).** Light yellow oil (76 mg, 75%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (s, 1H), 5.56 (s, 2H), 3.24 (s, 3H), 2.13 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.6, 143.0, 122.7, 111.5, 111.4, 108.1, 58.6, 36.9, 21.5; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_9H_9N_5O$ 203.0807, found 203.0810.

***N*-((3,5-Dimethyl-1*H*-pyrazol-1-yl)methyl)-*N*-methylacetamide (3l).** Light yellow oil (69 mg, 76%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.74 (s, 1H), 5.48 (s, 2H), 3.00 (s, 3H), 2.22 (s, 3H), 2.13 (s, 3H), 2.03 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.7, 148.0, 139.9, 105.9, 58.0, 34.6, 21.8, 13.3, 10.8; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_9H_{15}N_3O$ 181.1215, found 181.1216.

***N*-((1*H*-Benzo[d][1,2,3]triazol-1-yl)methyl)-*N*-methylacetamide (3m).**[14] White solid (70 mg, 69%): mp 74−75 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.05 (d, $J$ = 8.0 Hz, 1H), 7.91 (d, $J$ = 8.4 Hz, 1H), 7.50 (t, $J$ = 7.8 Hz, 1H), 7.39 (t, $J$ = 7.6 Hz, 1H), 6.22 (s, 2H), 3.11 (s, 3H), 2.13 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.5, 146.0, 132.3, 127.8, 124.3, 119.5, 111.0, 57.4, 34.8, 21.6; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{10}H_{12}N_4O$ 204.1011, found 204.1008.

***N*-((1*H*-Benzo[d]imidazol-1-yl)methyl)acetamide (4a).** White solid (71 mg, 75%): mp 159−160 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.25 (br, 1H), 7.82 (s, 1H), 7.68 (t, $J$ = 4.2 Hz, 1H), 7.56 (t, $J$ = 4.6 Hz, 1H), 7.29−24 (m, 2H), 5.55 (d, $J$ = 6.8 Hz, 2H), 1.96 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.0, 143.2, 143.1, 132.8, 123.5, 122.7, 119.7, 110.2, 48.2, 22.8; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{10}H_{11}N_3O$ 189.0902, found 189.0905.

***N*-((1*H*-Benzo[d]imidazol-1-yl)methyl)-*N*-phenylacetamide (4b).** White solid (58 mg, 44%): mp 146−147 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (d, $J$ = 8.0 Hz, 1H), 7.70 (s, 1H), 7.38−7.20 (m, 6H), 6.85 (d, $J$ = 7.2 Hz, 2H), 6.00 (s, 2H), 1.85 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.0, 143.6, 143.5, 140.4, 132.9, 130.2, 129.0, 128.1, 123.3, 122.5, 120.1, 110.5, 56.0, 22.4; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{16}H_{15}N_3O$ 265.1215, found 265.1214.

***N*-((1*H*-Benzo[d]imidazol-1-yl)methyl)-*N*-methylbenzamide (4c).** Light yellow oil (126 mg, 95%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.18 (s,1H), 7.82 (d, $J$ = 6.4 Hz, 1H), 7.66 (s, 1H), 7.37−7.28 (m, 7H), 5.87 (s, 2H), 2.92 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.1, 143.6, 143.3, 134.5, 133.2, 130.4, 128.5, 127.0, 123.7, 122.8, 120.3, 110.2, 55.4, 36.2; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{16}H_{15}N_3O$ 265.1215, found 265.1212.

***N*-((1*H*-Imidazol-1-yl)methyl)-*N*-methylbenzamide (4d).** Light yellow oil (103 mg, 96%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.69 (s, 1H), 7.35 (s, 5H), 7.12 (s, 1H), 7.02 (s, 1H), 5.51 (s, 2H), 2.89 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.1, 137.6, 134.5, 130.4, 129.6, 128.5, 127.0, 119.4, 57.3, 36.2; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{12}H_{13}N_3O$ 215.1059, found 215.1058.

***N*-(1-(1*H*-Benzo[d]imidazol-1-yl)ethyl)acetamide (4e).** Yellow oil (56 mg, 55%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.51 (br, 1H), 7.80 (s, 1H), 7.72−7.63 (m, 2H), 7.32−7.25 (m, 2H), 6.55−6.48 (m, 1H), 1.95 (s, 3H), 1.82 (d, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.0, 143.1, 140.2, 132.6, 123.4, 122.7, 119.6, 111.1, 56.6, 22.8, 20.2; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{11}H_{13}N_3O$ 203.1059, found 203.1059.

***N*-(1-(1*H*-Benzo[d]imidazol-1-yl)ethyl)-*N*-ethylacetamide (4f).** White solid (87 mg, 75%): mp 135−136 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.15 (s, 1H), 7.79 (d, $J$ = 5.2 Hz, 1H), 7.48 (d, $J$ = 3.2 Hz, 1H), 7.31−7.26 (m, 3H), 3.17−3.10 (m, 2H), 2.16 (s, 3H), 1.90 (d, $J$ = 7.2 Hz, 3H), 0.74 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.6, 143.4, 139.8, 133.4, 123.6, 122.8, 120.2, 110.8, 58.8, 37.2, 21.6, 17.6, 15.3; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1371.

***N*-(1-(1*H*-Benzo[d]imidazol-1-yl)butyl)acetamide (4g).** Light yellow oil (54 mg, 47%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.82 (s, 1H), 7.70−7.68 (m, 1H), 7.58−7.56 (m, 1H), 7.39 (br, 1H), 7.25−7.21 (m, 2H), 6.30 (q, $J$ = 8.0 Hz, 1H), 2.11−2.03 (m, 2H), 1.91 (s, 3H), 1.39−1.26 (m, 2H), 0.90 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.0, 143.0, 140.6, 132.7, 123.4, 122.7, 119.8, 111.0, 60.0, 35.9, 22.9, 18.8, 13.3; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1368.

***N*-((1*H*-Benzo[d]imidazol-1-yl)methyl)-*N*-butylacetamide (4h).** Light yellow oil (69 mg, 56%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (s, 1H), 7.79 (d, $J$ = 8.4 Hz, 1H), 7.55 (d, $J$ = 7.2 Hz, 1H), 7.33−7.28 (m, 2H), 5.73 (s, 2H), 3.22 (t, $J$ = 7.8 Hz, 2H), 2.14 (s, 3H), 1.50−1.44 (m, 2H), 1.33−1.26 (m, 2H), 0.91 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.3, 143.5, 143.4, 133.2, 123.4, 122.4, 120.2, 110.0, 52.7, 47.1, 30.5, 21.3, 19.9, 13.5; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{14}H_{19}N_3O$ 245.1528, found 245.1530.

***N*-(1-(1*H*-Benzo[d]imidazol-1-yl)butyl)-*N*-methylacetamide (4h′).** Light yellow oil (32 mg, 26%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.13 (s, 1H), 7.82−7.79 (m, 1H), 7.58−7.56 (m, 1H), 7.32−7.30 (m, 2H), 7.14 (t, $J$ = 7.6 Hz, 1H), 2.69 (s, 3H), 2.45−2.21 (m, 2H), 2.14 (s, 3H), 1.52−1.46 (m, 2H), 1.07 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.1, 143.3, 140.1, 133.4, 123.5, 122.7, 120.0, 111.0, 61.9, 32.0, 28.7, 22.1, 18.5, 13.5; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{14}H_{19}N_3O$ 245.1528, found 245.1535.

***N*-((1*H*-Benzo[d]imidazol-1-yl)(phenyl)methyl)acetamide (4i).** White solid (130 mg, 98%): mp 173−175 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.72 (br, 1H), 7.55 (d, $J$ = 7.6 Hz, 1H), 7.44−7.40 (m, 2H), 7.26−7.10 (m, 8H), 1.93 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.0, 143.3, 141.6, 135.6, 132.7, 129.2, 129.0, 126.4, 123.4,


dx.doi.org/10.1021/jo301568e | J. Org. Chem. 2012, 77, 9366−9373

122.8, 119.9, 111.0, 62.2, 22.8; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{16}H_{15}N_3O$ 265.1215, found 265.1214.

**5-(1*H*-Benzo[d]imidazol-1-yl)-1-methylpyrrolidin-2-one (4j).** White solid (77 mg, 72%): mp 146−147 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.96 (s, 1H), 7.86−7.83 (m, 1H), 7.35−7.28 (m, 3H), 5.96−5.93 (m, 1H), 2.80−2.63 (m, 3H), 2.70(s, 3H), 2.37−2.29 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 173.8, 144.6, 141.1, 131.5, 123.8, 123.0, 121.0, 109.8, 71.9, 29.1, 27.3, 25.3; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{12}H_{13}N_3O$ 215.1059, found 215.1056.

**1-((1*H*-Benzo[d]imidazol-1-yl)methyl)pyrrolidin-2-one (4j′).** Light yellow oil (27 mg, 25%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.01 (s, 1H), 7.82−7.80 (m, 1H), 7.62−7.59 (m, 1H), 7.35−7.29 (m, 2H), 5.65 (s, 2H), 3.34 (t, $J$ = 7.0 Hz, 2H), 2.42 (t, $J$ = 8.0 Hz, 2H), 1.99 (quint, $J$ = 7.7 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.4, 143.6, 143.0, 133.0, 123.6, 122.7, 120.3, 110.1, 51.1, 45.7, 30.3, 17.4; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{12}H_{13}N_3O$ 215.1059, found 215.1058.

**1-((1*H*-Benzo[d]imidazol-1-yl)methyl)azepan-2-one (4k).** Light yellow oil (96 mg, 79%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.02 (s, 1H), 7.74−7.72 (m, 1H), 7.56−7.53 (m, 1H), 7.25−7.23 (m, 1H), 5.67 (s, 2H), 3.37−3.34 (m, 2H), 2.49−2.48 (m, 2H), 1.53−1.52 (m, 2H), 1.20 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.4, 143.5, 143.3, 133.0, 123.4, 122.5, 120.1, 110.5, 55.6, 48.5, 36.8, 29.4, 28.0, 22.9; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{14}H_{17}N_3O$ 243.1372, found 243.1372.

**5-(1*H*-Benzo[d]imidazol-1-yl)pyrrolidin-2-one (4l).** White solid (46 mg, 46%): mp 133−134 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.87 (s, 1H), 7.74−7.72 (m, 1H), 7.30−7.20 (m, 4H), 6.02−6.00 (m, 1H), 2.72−2.28 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 177.2, 144.3, 140.3, 131.6, 123.5, 122.9, 120.6, 109.9, 66.1, 28.7, 27.9; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{11}H_{11}N_3O$ 201.0902, found 201.0903.

**7-(1*H*-Benzo[d]imidazol-1-yl)azepan-2-one (4m).** White solid (61 mg, 53%): mp 173−174 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.96 (s, 1H), 7.81−7.78 (m, 1H), 7.47−7.45 (m, 1H), 7.47−7.43 (m, 1H), 7.36−7.29 (m, 2H), 6.41 (s, 1H), 5.83−5.79 (m, 1H), 2.66−2.44 (m, 3H), 2.34−2.31 (m, 1H), 2.18−2.15 (m, 1H), 2.01−1.98 (m, 1H), 1.87−1.69 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.3, 143.8, 140.2, 132.0, 123.6, 123.0, 120.7, 110.3, 65.8, 37.1, 35.3, 27.7, 22.5; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{13}H_{15}N_3O$ 229.1215, found 229.1213.

**5-(1*H*-Benzo[d]imidazol-1-yl)-1-phenylpyrrolidin-2-one (4n).** White solid (127 mg, 92%): mp 163−164 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.82 (s, 1H), 7.72−7.70 (m, 1H), 7.32−7.03 (m, 8H), 6.41−6.38 (m, 1H), 2.90−2.70 (m, 3H), 2.37−2.32 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 173.3, 144.4, 141.0, 135.7, 131.3, 129.3, 127.0, 123.7, 123.4, 122.9, 120.9, 109.9, 71.7, 29.9, 25.6; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{17}H_{15}N_3O$ 277.1215, found 277.1214.

**7-(1*H*-Benzo[d]imidazol-1-yl)-1-phenylazepan-2-one (4o).** White solid (62 mg, 42%): mp 170−171 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74 (d, $J$ = 8.0 Hz, 1H), 7.66 (s, 1H), 7.45−7.11 (m, 6H), 6.77 (d, $J$ = 7.2 Hz, 2H), 6.34 (d, $J$ = 9.2 Hz, 1H), 3.07−3.01 (m, 1H), 2.92−2.87 (m, 1H), 2.76−2.71 (m, 1H), 2.49−2.45 (m, 1H), 2.19−1.96 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 173.9, 143.1, 140.5, 138.3, 132.8, 129.2, 128.3, 127.8, 123.6, 122.9, 120.6, 109.7, 70.3, 36.7, 33.0, 26.0, 22.4; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{19}H_{19}N_3O$ 305.1528, found 305.1527.

***N*-((1*H*-Benzo[d]imidazol-1-yl)methyl)-*N*-methylmethanesulfonamide (4p).** Yellow oil (78 mg, 65%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (s, 1H), 7.82 (d, $J$ = 7.2 Hz, 1H), 7.67 (d, $J$ = 7.2 Hz, 1H), 7.39−7.31 (m, 2H), 5.62 (s, 2H), 2.98 (s, 3H), 2.71 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 143.6, 143.0, 133.2, 124.0, 123.0, 120.5, 110.0, 58.4, 38.4, 34.1; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{10}H_{13}N_3O_2S$ 239.0728, found 239.0724.

***N*-Methyl-*N*-((2-phenyl-1*H*-imidazol-1-yl)methyl)-methanesulfonamide (4q).** Yellow oil (90 mg, 68%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.53−7.51 (m, 2H), 7.47−7.44 (m, 3H), 7.25 (d, $J$ = 1.2 Hz, 1H), 7.15 (d, $J$ = 1.2 Hz, 1H), 5.45 (s, 2H), 2.67 (s, 3H), 2.51 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 148.2, 130.0, 129.4, 129.3, 129.2, 128.8, 120.5, 59.8, 38.6, 33.4; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{12}H_{15}N_3O_2S$ 265.0885, found 265.0885.

**General Procedure for the Synthesis of Products 5.** An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with $FeCl_2$ (25 mg, 0.2 mmol) and amide **2** (20 mmol). The tube was evacuated and refilled with $N_2$, and this process was repeated three times. Then di-*tert*-butyl peroxide (8.76 g, 60 mmol) was added. The resulting mixture was stirred at 120 °C for 3 h. After completion of the reaction, the resulting solution was cooled to room temperature. The reaction mixture was then filtered, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:3) to afford the corresponding product.

***N*-(*tert*-Butoxymethyl)-*N*-methylbenzamide (5).** Light yellow oil (2.0 g, 45%): Isolated as two rotamers of 3/1 ratio in $^1$H NMR; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.56 (d, $J$ = 7.2 Hz, 2H), 7.37−7.35 (m, 3H), 4.54/5.02 (s, 2H), 3.09/2.94 (s, 3H), 1.11/1.28 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.0, 171.1, 136.1, 135.5, 129.9, 129.6, 128.2, 128.0, 127.4, 126.8, 74.8, 74.2, 73.0, 70.7, 35.5, 32.8, 27.9, 27.6; HRMS (TOF MS EI$^+$) $m/z$ calcd for $C_{13}H_{19}NO_2$ 221.1416, found 221.1413.

## ■ ASSOCIATED CONTENT

### Supporting Information

Copies of $^1$H and $^{13}$C NMR spectra for **3a−m**, **4a−q** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION


### Corresponding Author

*E-mail: chenwzz@zju.edu.cn.


### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This project is supported by the Natural Science Foundation of China (No. 21072170).

## ■ REFERENCES


(1) (a) Halfen, J. A. *Curr. Org. Chem.* **2005**, *9*, 657. (b) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439.

(2) For reviews, see: (a) Collet, F.; Dodd, R. H.; Dauban, P. *Chem. Commun.* **2009**, 5061. (b) Zalatan, D. N.; Du Bois, J. *Top. Curr. Chem.* **2010**, *292*, 347. For examples, see: (c) Wang, Z.; Zhang, Y. M.; Fu, H.; Jiang, Y. Y.; Zhao, Y. F. *Org. Lett.* **2008**, *10*, 1863. (d) Liu, X. W.; Zhang, Y. M.; Wang, L.; Fu, H.; Jiang, Y. Y.; Zhao, Y. F. *J. Org. Chem.* **2008**, *73*, 6207. (e) Cundari, T. R.; Wiese, S.; Badiei, Y. M.; Gephart, R. T.; Mossin, S.; Varonka, M. S.; Melzer, M. M.; Meyer, K.; Warren, T. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 8850. (f) Froehr, T.; Sindlinger, C. P.; Kloeckner, U.; Finkbeiner, P.; Nachtsheim, B. J. *Org. Lett.* **2011**, *13*, 3754. (g) Wertz, S.; Kodama, S.; Studer, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 11511.

(3) For reviews on CDC reactions, see: (a) Li, C. J. *Acc. Chem. Res.* **2009**, *42*, 335. (b) Yoo, W. J.; Li, C. J. *Top. Curr. Chem.* **2010**, *292*, 281. (c) Scheuermann, C. J. *Chem.—Asian J.* **2010**, *5*, 436. (d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (e) Jones, K. M.; Klussmann, M. *Synlett* **2012**, *23*, 159.

(4) For papers on the functionalization of an sp$^3$ C−H bond adjacent to a nitrogen atom: (a) Li, Z. P.; Li, C. J. *J. Am. Chem. Soc.* **2004**, *126*, 11810. (b) Li, Z. P.; Li, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 3672. (c) Li, Z. P.; Li, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 6968. (d) Tsuchimoto, T.; Ozawa, Y.; Negoro, R.; Shirakawa, E.; Kawakami, Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 4231. (e) Angioni, S.; Ravelli, D.; Emma, D.; Dondi, D.; Fagnoni, M.; Albini, A. *Adv. Synth. Catal.* **2008**, *350*, 2209. (f) Tsuchikama, K.; Kasagawa, M.; Endo, K.; Shibata, T. *Org. Lett.* **2009**, *11*, 1821. (g) Shu, X. Z.; Xia, X. F.; Yang, Y. F.; Ji, K. G.; Liu, X. Y.; Liang, Y. M. *J. Org. Chem.* **2009**, *74*, 7464. (h) Xie, J.; Huang, Z. Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 10181. (i) Huang, L. H.; Niu, T. M.; Wu, J.; Zhang, Y. H. *J. Org. Chem.* **2011**, *76*, 1759. (j) Alagiri, K.;

Kumara, G. S.; Prabhu, K. R. *Chem. Commun.* **2011**, *47*, 11787. (k) Tang, R.-Y.; Xie, Y.-X.; Xie, Y.-L.; Xiang, J.-N.; Li, J.-H. *Chem. Commun.* **2011**, *47*, 1359. (l) Boess, E.; Sureshkumar, D.; Sud, A.; Wirtz, C.; Fares, C.; Klussmann, M. *J. Am. Chem. Soc.* **2011**, *133*, 8106. (m) Dai, C.; Meschini, F.; Narayanam, J. M.; Stephenson, C. R. *J. Org. Chem.* **2012**, *77*, 4425. For papers on the functionalization of an $sp^3$ C−H bond adjacent to an oxygen atom: (n) Zhang, Y. H.; Li, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 4242. (o) Pan, S. G.; Liu, J. H.; Li, H. R.; Wang, Z. Y.; Guo, X. W.; Li, Z. P. *Org. Lett.* **2010**, *12*, 1932. (p) Richter, H.; García Mancheño, O. *Eur. J. Org. Chem.* **2010**, *2010*, 4460. (q) He, T.; Yu, L.; Zhang, L.; Wang, L.; Wang, M. *Org. Lett.* **2011**, *13*, 5016.

(5) Shirakawa, E.; Uchiyama, N.; Hayashi, T. *J. Org. Chem.* **2011**, *76*, 25.

(6) (a) Zhang, Y. M.; Fu, H.; Jiang, Y. Y.; Zhao, Y. F. *Org. Lett.* **2007**, *9*, 3813. (b) Xuan, J.; Feng, Z.-J.; Duan, S.-W.; Xiao, W.-J. *RSC Adv.* **2012**, *2*, 4065. (c) Mao, X.; Wu, Y.; Jiang, X.; Liu, X.; Cheng, Y.; Zhu, C. *RSC Adv.* **2012**, *2*, 6733.

(7) (a) Diez-Gonzalez, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612. (b) Benhamou, L.; Chardon, E.; Lavigne, G.; Bellemin-Laponnaz, S.; Cesar, V. *Chem. Rev.* **2011**, *111*, 2705.

(8) (a) Pinkert, A.; Marsh, K. N.; Pang, S. S.; Staiger, M. P. *Chem. Rev.* **2009**, *109*, 6712. (b) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. *Chem. Rev.* **2008**, *108*, 2015.

(9) Xia, Q. Q.; Chen, W. Z.; Qiu, H. Y. *J. Org. Chem.* **2011**, *76*, 7577.

(10) (a) Li, Z. P.; Cao, L.; Li, C. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6505. (b) Guo, X.; Li, C. J. *Org. Lett.* **2011**, *13*, 4977.

(11) (a) Sarhan, A. A.; Bolm, C. *Chem. Soc. Rev.* **2009**, *38*, 2730. (b) Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Rev.* **2011**, *111*, 1293.

(12) (a) Murahashi, S.; Naota, T.; Kuwabara, T.; Saito, T.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1990**, *112*, 7820. (b) Naota, T.; Nakato, T.; Murahashi, S.-I. *Tetrahedron Lett.* **1990**, *31*, 7475. (c) Wang, D. H.; Hao, X. S.; Wu, D. F.; Yu, J. Q. *Org. Lett.* **2006**, *8*, 3387. (d) Wei, Y.; Ding, H.; Lin, S.; Liang, F. *Org. Lett.* **2011**, *13*, 1674.

(13) Johnson, F. E.; Cabasso, I. *Macromolecules* **2010**, *43*, 3634.

(14) Katritzky, A. R.; Yao, G.; Lan, X.; Zhao, X. *J. Org. Chem.* **1993**, *58*, 2086.