JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

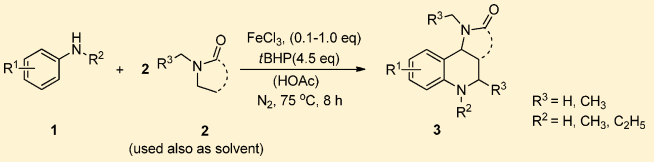
$FeCl_3$-Catalyzed Cascade Cyclization in One Pot: Synthesis of Ring-Fused Tetrahydroquinoline Derivatives from Arylamines and *N*-Substituted Lactams

Manman Sun, Tianshui Zhang, and Weiliang Bao*

Department of Chemistry, Zhejiang University (Xixi Campus), Hangzhou 310028, People's Republic of China

Supporting Information

ABSTRACT: Multiple cross-dehydrogenative-coupling reactions catalyzed by $FeCl_3$ in one pot were developed. Arylamines and *N*-substituted lactams were reacted, and ring-fused tetrahydroquinoline derivatives were formed by two C−C bonds and one C−N bond formation as well as one C−N bond cleavage. The lactams were also used as solvent.



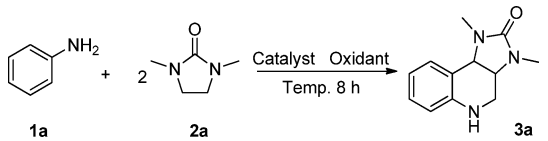
Formation of new C−X (X = C, O, N) bonds by direct and selective cross-dehydrogenative-coupling (CDC) reactions is one of the most challenging research areas in organic chemistry.[1] Most of the reported CDC reactions only formed one C−X bond. CDC reactions concerning two or more C−X bonds formation in one pot are rare, probably owing to the limit of regioselectivity.[2] Multicomponent reactions constitute a large group of transformations with growing relevance in organic chemistry as they display many features of the ideal synthesis.[3] Therefore, one-pot multicomponent CDC reactions, especially catalyzed by readily available, cheap, and low-toxic copper or iron salts, should be a promising way to synthesize structurally complex and diverse compounds.

The activation of an sp^3 C−H bond α to a nitrogen atom presents a direct and efficient method to synthesize or modify the nitrogen-containing molecules which are widespread structural motifs in biologically active compounds.[4] In recent years, a number of excellent results of this powerful approach were obtained, such as couplings with sp^3 C−H bonds,[5] sp^2 C−H bonds,[6] sp C−H bonds,[7] and X−H bonds (X = O, N).[8] Among them, couplings with sp^3 C−H bonds were restricted to the pronuleophilic sp^3 C−H bonds activated by carbonyl group or nitro group.[5] Little with unactivated sp^3 C−H bond was reported.[9] Double activation of the same methyl or methylene group α to a nitrogen atom can provide a nonconventional method to synthesize methylene-bridged or methine-bridged bis-substituted compounds.[10] In this paper, we report not only a methylene-bridge formation with two different substituents, but also another C−C bond formation via double C−H bond activation of two different molecules to form a heterocycle.

Tetrahydroquinoline rings are found in numerous biologically active natural products and pharmacologically relevant therapeutic agents.[11] Conventional synthesis of the tetrahydroquinoline ring motif, including hydrogenation of quinolines,[12] cyclization and transformation of relevant molecules,[13] and multimolecule condensation approaches,[14] often require tedious synthetic procedures or harsh conditions. Inspired by successful multicomponent synthesis of other heterocyclic compounds by C−H bond activation,[2a,15] we report a new one-pot synthesis of tricyclic tetrahydroquinolines (**3**) via multiple CDC reactions from arylamines (**1**) and lactams (**2**).

As the combination of iron salt and peroxide oxidant was proved to be a very nice oxidative agent for activation of sp^3 C−H bond α to a nitrogen atom,[6a,c,e,7d] we first applied $FeCl_3$/*t*-BHP to the reaction of aniline **1a** with 1,3-dimethylimidazolidin-2-one **2a**. The desired product **3a** was isolated in 64% yield after 8 h at 75 °C (Table 1, entry 1). Then several iron,

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	oxidant	temp (°C)	yield (%)
1	$FeCl_3$	*t*-BuOOH	75	64
2	$FeBr_3$	*t*-BuOOH	75	40
3	$FeCl_3.6H_2O$	*t*-BuOOH	75	46
4	$FeCl_2.4H_2O$	*t*-BuOOH	75	41
5	$FeSO_4$	*t*-BuOOH	75	54
6	CuI	*t*-BuOOH	75	38
7	$Cu(OTf)_2$	*t*-BuOOH	75	30
8	$ZrCl_4$	*t*-BuOOH	75	29
9	$FeCl_3$	$(t\text{-BuO})_2$	75	8
10	$FeCl_3$	30% H_2O_2	75	trace
11	$FeCl_3$	O_2	75	trace
12	$FeCl_3$	*t*-BuOOH	60	39
13	$FeCl_3$	*t*-BuOOH	100	58
14[b]	$FeCl_3$	*t*-BuOOH	75	30

[a]Reaction conditions: catalyst (0.05 mmol), oxidant (2.25 mmol), and substrate **1a** (0.5 mmol) in **2a** (2.0 mL) for 8 h under the nitrogen atmosphere. [b]Under air atmosphere.

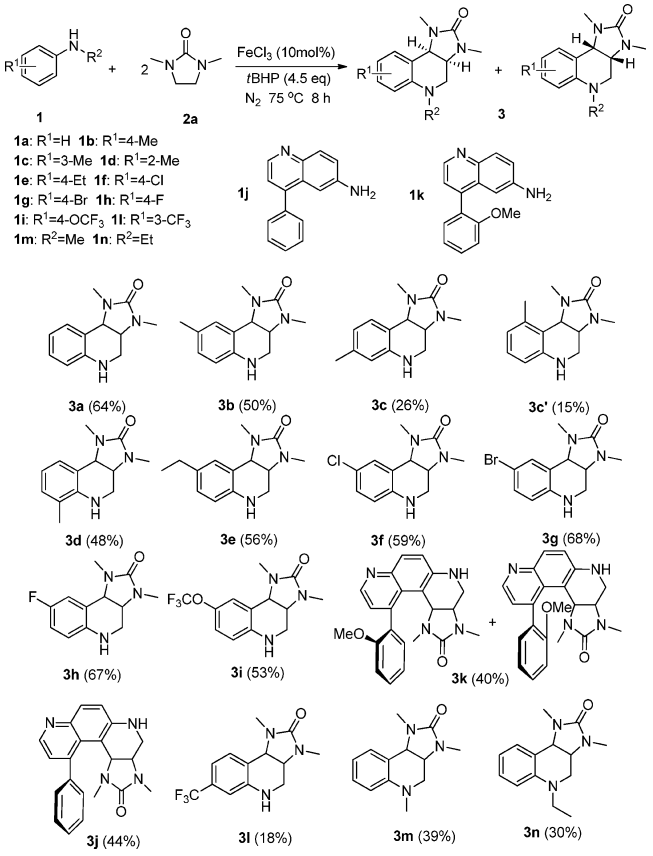
Received: May 12, 2013
Published: July 2, 2013

   dx.doi.org/10.1021/jo400979h | J. Org. Chem. 2013, 78, 8155−8160

copper, or zirconium salts and other oxidants were screened to enhance the yield (Table 1, entries 2−11). Unfortunately, no system was better than $FeCl_3$/*t*-BHP. Elevated or lowered temperatures also did not result in higher yields (Table 1, entries 12 and 13). When the reaction was conducted under air, the yield was sharply declined. This means the reaction involved radical step(s), and as a radical scavenger, the O_2 in air blocked the reaction (Table 1, entry 14). Therefore, the reaction was carried out best at 75 °C under nitrogen atmosphere using the $FeCl_3$/*t*-BHP as the oxidative agent.

To explore the scope and the generality of the reaction, a variety of substituted arylamines **1** reacted with **2a** under the optimized reaction conditions (Scheme 1). Both moderate

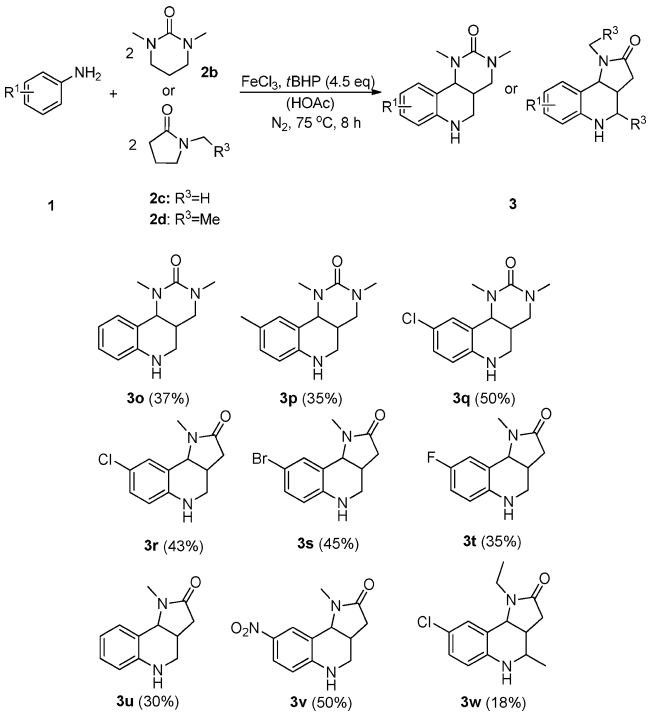
Scheme 1. One-Pot Reaction of Arylamines 1 with 2a



electron-donating and electron-withdrawing arylamines worked comparatively well (Scheme 1, **3a**−**k**). A strong electron-withdrawing group resulted in comparatively low yield (Scheme 1, **3l**). With regard to arylamines which may produce region-selective isomers, the product structure was mainly determined by electronic effects. The reaction of **1c** with **2a** generated two isomers **3c** and **3c**′, which could be separated. Obviously the electron density of the two reaction sites in **1c** was different. However, only one region-selective isomer was obtained in the incorporation of **1j**, **1k**, or **1l** with **2a**, although the products **3k** and **3l** should be very steric hindered. This means the difference of electron density between the two possible sites in **1j**, **1k** and **1l** is significant. Additionally, nonfree rotation resulted in two conformational isomers (**3k**, see NMR spectra). N-Substituted anilines **1m** and **1n** were also used to react with **2a**. To our surprise, the desired products **3m** and **3n** were obtained as the major products, although minor N-dealkylated product **3a** was isolated in 11% and 20% yields. The molecular structure of **3m** was unambiguously elucidated by X-ray crystallography (see the Supporting Information). It can be seen from NMR spectra and X-ray crystallography that quinoline and imidazo rings were syn-fused and only one pair of chiral isomers were formed.

Subsequently, the scope of lactams were also examined (Scheme 2). Substrates **2b**, **2c**, and **2d** all reacted with different

Scheme 2. One-Pot Reaction Involving a Coupling of a Methylene *α* to Nitrogen Atom with an Unactivated Methylene

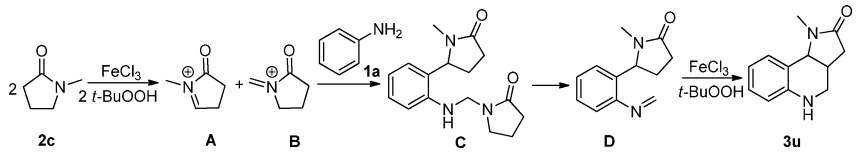


anilines. It should be pointed out that a coupling on an unactivated methylene must be involved in these reactions. When 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one **2b** was examined, the corresponding products **3o**, **3p**, and **3q** were obtained in moderate yields. 1-Methylpyrrolidin-2-one **2c** was also used to react with 4-chloroaniline **1f**. No product was obtained under the optimized reaction conditions. Fortunately, the cyclized product **3r** was isolated in 43% yield when stoichiometric $FeCl_3$ and 1 equiv of acetic acid were employed. Substituted anilines, such as **1g** and **1h**, also generated the corresponding products **3s** and **3t** in 45% and 35% yields when reacted with **2c**. Aniline **1a** is easily oxidized. Product **3u** could be obtained in low yield when the aniline was slowly added to the reaction mixture at 75 °C. 4-Nitroaniline **1o** is not easily oxidized. Product **3v** was obtained in high yield after the temperature was raised to 100 °C. Interestingly, 1-ethylpyrrolidin-2-one **2d** could also incorporate with 4-chloroaniline **1f**. Product **3w** was obtained in 18% yield after **1f** and **2d** were treated with 1.0 equiv of $FeCl_3$, 1.0 equiv of HOAc, and 6.0 equiv of *t*-BHP at 95 °C.

According to all the above results, a plausible mechanism was proposed as shown in Scheme 3. The sp^3 C−H bond *α* to the nitrogen atom in **2c** was activated to generate iminium ions **A** and **B** through single-electron-transfer processes under the action of $FeCl_3$ and *t*-BHP.[6c,e] When **1a** was added to the

dx.doi.org/10.1021/jo400979h | J. Org. Chem. 2013, 78, 8155−8160

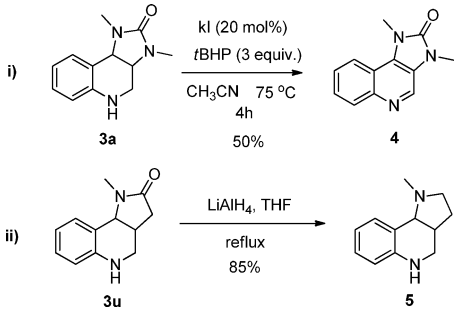
Scheme 3. Plausible Mechanism



mixture, the iminium ion **A** reacted with **1a** via Friedel−Crafts-type reaction giving a new C−C bond, and the iminium ions **B** reacted with **1a** via nucleophilic addition reaction giving a new C−N bond, and the intermediate **C** was generated (no matter which step was taken place first). Then an elimination reaction was taken place and a C−N bond was cleaved.[10] Further SET oxidative process of intermediate **D** resulted in the generation of product **3u**.

Quinoline-3,4-diamines are important intermediates to synthesize nonxanthine adenosine antagonists.[16] Pyrroloquinolines constitute the nucleus of the martinellines possessing antibacterial activity as well as affinity for adrenergic, muscarinic, and bradykinin receptors.[17] Selective oxidation or reduction of the ring-fused tetrahydroquinolines **3** provides rapid access to the structural motifs **4** or **5** (Scheme 4).

Scheme 4. Two Important Applications of 3



Therefore, the highly efficient synthesis of quinoline derivatives and unusual pyrroloquinolines is realized using two steps from simple starting materials, in contrary to the tedious synthetic procedures in classic methods.

But the drawback of our reaction is that the yields are not satisfactory. Several factors affect the yields. Arylamines with electron-donating groups were easily oxidized. Arylamines with electron-withdrawing groups may reserve in some percents because of low reactivity. For **2b**, **2c**, and **2d**, the step from **D** (see mechanism scheme) to final products was not easy. Also two side products were detected in few yields. One is the coupling product of NH in arylamine with methyl group in lactam, which can not further cyclize. The other is the dehydrogenation product 4.

In summary, we have introduced a simple and efficient one-pot protocol to synthesize the ring-fused tetrahydroquinoline derivatives through multiple cross-dehydrogenative-coupling (CDC) reactions from arylamines and lactams catalyzed by $FeCl_3$. The course of the reaction included two C−C bonds and one C−N bond formation as well as one C−N bond cleavage. Product **3** could be selectively oxidized or reduced to provide a rapid access to quinoline derivatives or pyrroloquinolines, which are important synthetic intermediates to biologically active compounds.

EXPERIMENTAL SECTION

General Remarks. All reactions were carried out in oven-dried Schlenk tubes. All the reagents were commercially available. The catalyst $FeCl_3$ was anhydrous (≥98%) from Sinopharm Chemical Reagent Co., Ltd. Merck 60 silica gel was used for chromatography, and Whatman silica gel plates with fluorescence F254 were used for thin-layer chromatography (TLC) analysis. All products were confirmed by ^{1}H NMR, ^{13}C NMR, HRMS, and IR. Melting points were uncorrected.

General Procedure. To a mixture of $FeCl_3$ and **2** (2 mL), **1** (0.5 mmol) was added. Then *t*-BHP (5−6 M in water) was added dropwise into the mixture under nitrogen at room temperature. The resulting mixture was stirred at 75 °C for 8 h. Then the cooled reaction mixture was dissolved in water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with water, dried with anhydrous $MgSO_4$. After evaporating the solvent under reduced pressure, the residue was purified by silica gel column chromatography with ethyl acetate to give the pure product **3**. It should be mentioned that products **3a**−**q** were obtained with $FeCl_3$ (0.05 mmol, 8 mg) and *t*-BHP (2.25 mmol, 408 μL), **3r**−**3v** were obtained with $FeCl_3$ (0.5 mmol, 81 mg), HOAc (0.5 mmol, 30 mg), and *t*-BHP (2.25 mmol, 408 μL), **3w** was obtained with $FeCl_3$ (0.5 mmol, 81 mg), HOAc (0.5 mmol, 30 mg), and *t*-BHP (3.0 mmol, 544 μL).

(±)-(*R*,*S*)-1,3-Dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3a): gray solid; yield 64% (69 mg); mp 117−119 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.17−7.11 (m, 2H), 6.77 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 4.33 (d, J = 8.4 Hz, 1H), 3.85−3.80 (m, 1H), 3.28 (dd, J_1 = 3.6 Hz, J_2 = 11.2 Hz, 1H), 3.18 (dd, J_1 = 3.6 Hz, J_2 = 11.6 Hz, 1H), 2.88 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.4, 146.1,, 1501, 131.0, 128.9, 118.1, 117.9, 115.5, 55.2, 54.6, 41.5, 29.1, 28.4; IR (neat) ν = 3318, 2872, 1683, 1608, 1450, 1396, 1336, 1288, 1123, 1015; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{15}N_3O$ 217.1215, found 217.1213.

(±)-(*R*,*S*)-1,3,8-Trimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo-[4,5-*c*]quinolin-2(9b*H*)-one (3b): gray solid; yield 50% (58 mg); mp 145−146 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 6.97−6.94 (m, 2H), 6.58 (d, J = 8.0 Hz, 1H), 4.29 (d, J = 8.0 Hz, 1H), 3.81 (br, 1H), 3.84−3.79 (m, 1H), 3.25 (dd, J_1 = 4.0 Hz, J_2 = 11.2 Hz, 1H), 3.17 (dd, J_1 = 6.8 Hz, J_2 = 11.2 Hz, 1H), 2.88 (s, 3H), 2.78 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.4, 143.7, 131.3, 129.6, 127.4, 118.1, 115.6, 55.2, 54.8, 41.7, 29.2, 28.5, 20.5; IR (neat) ν = 3312, 2917, 1679, 1620, 1513, 1441, 1395, 1367, 1321, 1274, 1158, 1050, 1015, 820, 785, 759, 731, 698; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1372.

(±)-(*R*,*S*)-1,3,7-Trimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo-[4,5-*c*]quinolin-2(9b*H*)-one (3c): gray solid; yield 26% (30 mg); mp 191−194 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.05 (d, J = 7.6 Hz, 1H), 6.59 (d, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H), 6.48 (s, 1H), 4.29 (d, J = 8.0 Hz, 1H), 3.80 (br, 1H), 3.82−3.77 (m, 1H), 3.27 (dd, J_1 = 4.0 Hz, J_2 = 11.2 Hz, 1H), 3.15 (dd, J_1 = 7.6 Hz, J_2 = 11.6 Hz, 1H), 2.87 (s, 3H), 2.77 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.5, 145.9, 138.9, 131.0, 119.1, 116.0, 115.1, 55.0, 54.5, 41.4, 29.1, 28.5, 21.1; IR (neat) ν = 3319, 2947, 1681, 1619, 1584, 1498, 1442, 1404, 1367, 1333, 1290, 1135, 1016, 966, 863; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1375.

(±)-(*R*,*S*)-1,3,9-Trimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo-[4,5-*c*]quinolin-2(9b*H*)-one (3c′): brown solid; yield 15% (17 mg); mp 186−188 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.03 (t, J = 8.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.54 (d, J = 7.6 Hz, 1H), 4.84 (d, J = 9.2 Hz, 1H), 3.96−3.91 (m, 1H), 3.61 (br, 1H), 3.29 (dd, J_1 = 3.2 Hz, J_2 =

dx.doi.org/10.1021/jo400979h | J. Org. Chem. 2013, 78, 8155−8160

12.0 Hz, 1H), 2.96 (dd, J_1 = 3.6 Hz, J_2 = 11.6 Hz, 1H), 2.88 (s, 3H), 2.59 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.3, 148.1, 138.4, 128.4, 121.3, 118.0, 113.9, 57.0, 51.2, 42.8, 28.4, 28.3, 19.0; IR (neat) ν = 3292, 2915, 1676, 1593, 1498, 1444, 1402, 1366, 1318, 1260, 1192, 1119, 1086, 1038, 1001, 861, 794, 751, 728, 683, 622; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1370.

(±)-(*R*,*S*)-1,3,6-Trimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo-[4,5-*c*]quinolin-2(9b*H*)-one (3d): gray solid; yield 48% (55 mg); mp 164−165 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.07−7.04 (m, 2H), 6.71 (t, J = 7.6 Hz, 1H), 4.34 (d, J = 8.0 Hz, 1H), 3.85 (br, 1H), 3.85−3.80 (m, 1H), 3.34 (dd, J_1 = 4.0 Hz, J_2 = 11.6 Hz, 1H), 3.21 (dd, J_1 = 7.2 Hz, J_2 = 11.2 Hz, 1H), 2.89 (s, 3H), 2.77 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.5, 144.2, 130.0, 129.0, 122.5, 117.4, 117.3, 55.4, 54.5, 41.4, 29.2, 28.5, 17.0; IR (neat) ν = 3362, 2860, 1686, 1601, 1499, 1441, 1393, 1329, 1268, 1125, 1073, 1017; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1371.

(±)-(*R*,*S*)-8-Ethyl-1,3-dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3e): gray solid; yield 56% (69 mg); mp 75−77 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.00 (s, 1H), 6.98 (d, J = 6.4 Hz, 1H), 6.61 (d, J = 9.2 Hz, 1H), 4.30 (d, J = 8.4 Hz, 1H), 3.84−3.9 (m, 1H), 3.26 (dd, J_1 = 4.4 Hz, J_2 = 11.2 Hz, 1H), 3.17 (dd, J_1 = 7.2 Hz, J_2 = 11.2 Hz, 1H), 2.87 (s, 3H), 2.78 (s, 3H), 2.57 (q, J = 7.6 Hz, 2H), 1.20 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.4, 143.9, 134.1, 130.2, 128.4, 118.0, 115.6, 55.3, 54.8, 41.7, 29.2, 28.5, 27.9, 15.9; IR (neat): ν = 3317, 2959, 1680, 1619, 1512, 1442, 1395, 1368, 1327, 1274, 1158, 1051, 1014, 898, 825, 784, 758, 732, 699, 622; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{14}H_{19}N_3O$ 245.1528, found 245.1532.

(±)-(*R*,*S*)-8-Chloro-1,3-dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3f): gray solid; yield 59% (74 mg); mp 206−208 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.12 (d, J = 2.4 Hz, 1H), 7.09 (dd, J_1 = 2.4 Hz, J_2 = 8.4 Hz, 1H), 6.60 (d, J = 8.4 Hz, 1H), 4.28 (d, J = 8.0 Hz, 1H), 3.85−3.80 (m, 1H), 3.27 (dd, J_1 = 4.0 Hz, J_2 = 11.6 Hz, 1H), 3.18 (dd, J_1 = 6.8 Hz, J_2 = 11.6 Hz, 1H), 2.87 (s, 3H), 2.79 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.2, 144.8, 130.4, 128.8, 122.5, 119.4, 116.7, 54.9, 54.4, 41.5, 29.2, 28.5; IR (neat) ν = 3311, 2949, 2873, 1681, 1607, 1499, 1442, 1396, 1366, 1291, 1182, 1133, 1089, 1015, 896, 822, 758, 733, 698, 629; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{14}ClN_3O$ 251.0825, found 251.0827.

(±)-(*R*,*S*)-8-Bromo-1,3-dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3g): brown solid; yield 68% (100 mg); mp 164−166 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.26 (d, J = 2.4 Hz, 1H), 7.21 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 4.28 (d, J = 8.0 Hz, 1H), 3.84−3.80 (m, 1H), 3.27 (dd, J_1 = 4.0 Hz, J_2 = 11.6 Hz, 1H), 3.17 (dd, J_1 = 6.8 Hz, J_2 = 11.2 Hz, 1H), 2.87 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.2, 145.2, 133.3, 131.6, 120.0, 117.1, 109.4, 54.9, 54.3, 41.3, 29.2, 28.4; IR (neat) ν = 3310, 2867, 1680, 1601, 1494, 1442, 1405, 1365, 1279, 1179, 1133, 1077, 1014, 895, 819, 782, 758, 733, 698; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{14}BrN_3O$ 295.0320, found 295.0317.

(±)-(*R*,*S*)-8-Fluoro-1,3-dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3h): yellow solid; yield 67% (79 mg); mp 137−139 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 6.91−6.85 (m, 2H), 6.62 (dd, J_1 = 4.8 Hz, J_2 = 8.8 Hz, 1H), 4.31 (d, J = 8.4 Hz, 1H), 3.87−3.82 (m, 1H), 3.24 (dd, J_1 = 4.0 Hz, J_2 = 11.6 Hz, 1H), 3.19 (dd, J_1 = 6.4 Hz, J_2 = 11.6 Hz, 1H), 2.88 (s, 3H), 2.79 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.2, 155.5 (d, J_{C-F} =235.4 Hz), 142.5, 119.3 (d, J_{C-F} =6.3 Hz), 116.8 (d, J_{C-F} =21.9 Hz), 116.5 (d, J_{C-F} =6.9 Hz), 115.7 (d, J_{C-F} =22.5 Hz), 55.1, 54.7, 41.9, 29.2, 28.4; IR (neat) ν = 3314, 2874, 1679, 1504, 1444, 1397, 1367, 1321, 1248, 1212, 1147, 1051, 1016, 964, 934, 876, 823, 784; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{14}FN_3O$ 235.1121, found 235.1123.

(±)-(*R*,*S*)-1,3-Dimethyl-8-(trifluoromethoxy)-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3i): white solid; yield 53% (80 mg); mp 72−73 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.03−6.90 (m, 2H), 6.64 (d, J = 8.8 Hz, 1H), 4.32 (d, J = 8.0 Hz, 1H), 4.02 (br, 1H), 3.87−3.82 (m, 1H), 3.29 (dd, J_1 = 4.0 Hz, J_2 = 11.2 Hz, 1H), 3.20 (dd, J_1 = 6.8 Hz, J_2 = 11.2 Hz, 1H), 2.88 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 161.0, 145.9, 141.1, 124.6, 123.0, 122.6, 120.0, 119.4, 116.9, 55.7, 55.2, 42.2, 29.8, 29.2; IR (neat) ν = 3313, 2872, 1682, 1619, 1508, 1445, 1399, 1369, 1245, 1210, 1148, 1052, 1015, 896, 826, 787, 735, 685; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{14}F_3N_3O_2$ 301.1038, found 301.1039.

(±)-(*R*,*S*)-1,3-Dimethyl-11-phenyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*a*][4,7]phenanthrolin-2(11c*H*)-one (3j): yellow solid; yield 44% (76 mg); mp 204−206 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 8.71 (d, J = 4.0 Hz, 1H), 7.96 (d, J = 8.8 Hz, 1H), 7.61−7.60 (m, 2H), 7.45−7.44 (m, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.21 (d, J = 4.4 Hz, 1H), 7.16 (d, J = 8.8 Hz, 1H), 4.54 (d, J = 10.4 Hz, 1H), 4.32 (br 1H), 3.77 (dd, J_1 = 2.8 Hz, J_2 = 10.4 Hz, 1H), 3.44 (d, J = 12.4 Hz, 1H), 2.86 (dd, J_1 = 3.6 Hz, J_2 = 12.4 Hz, 1H), 2.76 (s, 3H), 1.95 (s, 3H); ^{1}H NMR (400 M Hz, CD_3COCD_3) δ 8.65 (d, J = 4.0 Hz, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 7.2 Hz, 1H), 7.66 (t, J = 6.8 Hz, 1H),7.50−7.44 (m, 2H), 7.41 (d, J = 6.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 7.25 (d, J = 4.0 Hz, 1H), 4.57 (d, J = 10.4 Hz, 1H), 3.87 (dd, J_1 = 2.4 Hz, J_2 = 10.4 Hz, 1H), 3.54 (d, J = 12.8 Hz, 1H), 2.84 (dd, J_1 = 2.8 Hz, J_2 = 12.4 Hz, 1H), 2.67 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.0, 150.4, 145.9, 144.9, 142.6, 131.0, 130.3, 128.5, 128.4, 127.8, 124.4, 121.8, 113.5, 59.8, 51.2, 41.1, 28.3, 28.2; IR (neat) ν = 3304, 2884, 1680, 1616, 1520, 1451, 1400, 1338, 1257, 1040, 996, 853, 763, 702; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{21}H_{20}N_4O$ 344.1637, found 344.1642.

(±)-(*R*,*S*)-11-(2-Methoxyphenyl)-1,3-dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*a*][4,7]phenanthrolin-2(11c*H*)-one (3k): yellow solid; yield 40% (75 mg); mp 211−212 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 8.71 (d, J = 4.4 Hz, 0.5H), 8.67 (d, J = 4.4 Hz, 0.5H), 7.96 (d, J = 8.8 Hz, 0.5H), 7.93 (d, J = 8.8 Hz, 0.5H), 7.48−7.40 (m, 1.5H), 7.28 (d, J = 5.6 Hz, 0.5H), 7.19−7.12 (m, 2.5H), 7.04 (dd, J_1 = 2.0 Hz, J_2 = 7.6 Hz, 0.5H), 6.97 (t, J = 7.6 Hz, 0.5H), 6.91 (d, J = 8.4 Hz, 0.5H), 4.77 (d, J = 10.4 Hz, 0.5H), 4.44 (d, J = 10.4 Hz, 0.5H), 4.30 (br, 0.5H), 4.24 (br, 0.5H), 3.88 (s, 1.5H), 3.77−3.69 (m, 1.0H), 3.61 (s, 1.5H), 3.44−3.39 (m, 1.0H), 2.77 (s, 1.5H), 2.75 (s, 1.5H), 1.98 (s, 1.5H), 1.97 (s, 1.5H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.1, 156.5, 154.8, 150.3, 149.2, 146.0, 145.5, 145.3, 144.5, 142.1, 140.9, 131.5, 131.0, 130.4, 130.31, 130.27, 130.1, 130.0, 129.3, 128.4, 125.4, 121.8, 121.6, 121.5, 120.7, 115.2, 113.5, 112.1, 110.1, 60.0, 55.3, 55.1, 51.3, 49.8, 44.3, 44.0, 28.3, 28.1, 28.0; IR (neat) ν = 3306, 1893, 1681, 1617, 1519, 1456, 1400, 1338, 1262, 1121, 1026, 853, 805, 757; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{22}H_{22}N_4O_2$ 374.1743, found 374.1753.

(±)-(*R*,*S*)-1,3-Dimethyl-7-(trifluoromethyl)-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3l): light yellow solid; yield 18% (26 mg); mp 206−208 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.25 (d, J = 7.6 Hz, 1H), 6.99 (d, J = 8.0 Hz, 1H), 6.70 (s, 1H), 4.35 (d, J = 8.0 Hz, 1H), 4.26 (br, 1H), 3.88−3.83 (m, 1H), 3.33 (dd, J_1 = 4.0 Hz, J_2 = 11.6 Hz, 1H), 3.21 (dd, J_1 = 6.8 Hz, J_2 = 11.2 Hz, 1H), 2.88 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.3, 146.3, 131.5, 125.1, 122.4, 121.0, 114.23, 114.19, 112.13, 112.09, 54.9, 54.2, 41.2, 29.2, 28.5; IR (neat) ν = 3293, 2955, 1684, 1623, 1510, 1451, 1417, 1341, 1318, 1286, 1248, 1168, 1112, 1073, 1016, 963, 877, 800, 760, 740, 700, 663; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{14}F_3N_3O$ 285.1089, found 285.1092.

(±)-(*R*,*S*)-1,3,5-Trimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo-[4,5-*c*]quinolin-2(9b*H*)-one (3m): yellow solid; yield 39% (45 mg); mp 137−138 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.24 (t, J = 8.4 Hz, 1H), 7.15 (d, J = 7.2 Hz, 1H), 6.80 (t, J = 8.0 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 4.36 (d, J = 8.8 Hz, 1H), 3.95−3.90 (m, 1H), 3.11 (dd, J_1 = 5.6 Hz, J_2 = 12.4 Hz, 1H), 3.02 (dd, J_1 = 4.0 Hz, J_2 = 11.6 Hz, 1H), 2.89 (s, 3H), 2.86 (s, 3H), 2.69 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.3, 148.5, 130.6, 129.2, 119.8, 117.7, 112.4, 55.7, 55.4, 51.1, 39.4, 28.9, 28.4; IR (neat) ν = 2868, 1693, 1603, 1501, 1451, 1396, 1339, 1286, 1214, 1122, 1047, 999, 757, 697; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1373.

(±)-(*R*,*S*)-5-Ethyl-1,3-dimethyl-3,3a,4,5-tetrahydro-1*H*-imidazo[4,5-*c*]quinolin-2(9b*H*)-one (3n): light yellow liquid; yield 30% (37 mg); ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.21 (t, J = 8.0 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 6.77−6.72 (m, 2H), 4.30 (d, J = 8.0 Hz, 1H), 3.89−3.84 (m, 1H), 3.49−3.40 (m, 1H), 3.29−3.20 (m, 1H),

dx.doi.org/10.1021/jo400979h | J. Org. Chem. 2013, 78, 8155−8160

3.16 (dd, J_1 = 6.8 Hz, J_2 = 12.0 Hz, 1H), 3.06 (dd, J_1 = 3.6 Hz, J_2 = 11.6 Hz, 1H), 2.89 (s, 3H), 2.72 (s, 3H), 1.15 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 160.4, 146.7, 131.2, 129.1, 119.2, 116.8, 112.3, 55.8, 54.9, 47.2, 45.0, 28.9, 28.4, 10.5; IR (neat) ν = 2970, 1685, 1603, 1499, 1444, 1395, 1265, 1187, 1049, 1007, 922, 838, 750, 730, 694, 664, 648; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{14}H_{19}N_3O$ 245.1528, found 245.1525.

(±)-(*R*,*S*)-1,3-Dimethyl-1,4,4a,5,6,10b-hexahydropyrimido-[5,4-*c*]quinolin-2(3*H*)-one (3o): yellow solid; yield 37% (43 mg); mp 204−206 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.10−7.04 (m, 2H), 6.43 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 6.49 (dd, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1H), 4.42 (d, J = 4.0 Hz, 1H), 3.94 (br, 1H), 3.48 (dd, J_1 = 4.4 Hz, J_2 = 11.6 Hz, 1H), 3.33 (dd, J_1 = 6.0 Hz, J_2 = 12 Hz, 1H), 3.29−3.21 (m, 2H), 3.10 (s, 3H), 2.89 (s, 3H), 2.52−2.47 (m, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 155.6, 142.9, 128.9, 128.8, 119.4, 116.9, 113.8, 56.8, 48.8, 41.8, 36.0, 35.8, 29.5; IR (neat) ν = 3321, 2868, 1697, 1612, 1515, 1458, 1398, 1361, 1270, 1055, 750; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{17}N_3O$ 231.1372, found 231.1378.

(±)-(*R*,*S*)-1,3,9-Trimethyl-1,4,4a,5,6,10b-hexahydropyrimido-[5,4-*c*]quinolin-2(3*H*)-one (3p): brown solid; yield 35% (43 mg); mp 179−180 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 6.91 (s, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.41 (d, J = 8.4 Hz, 1H), 4.40 (d, J = 3.2 Hz, 1H), 3.49 (dd, J_1 = 4.4 Hz, J_2 = 12.0 Hz, 1H), 3.31−3.20 (m, 3H), 3.14 (s, 3H), 2.89 (s, 3H), 2.50−2.48 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 155.5, 140.3, 129.2, 128.8, 126.2, 119.7, 113.8, 56.8, 48.6, 42.1, 36.4, 35.7, 29.5, 20.5; IR (neat) ν = 3326, 2919, 1613, 1514, 1458, 1402, 1357, 1297, 1264, 1129, 1053, 910, 814, 729, 643; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{14}H_{19}N_3O$ 245.1528, found 245.1531.

(±)-(*R*,*S*)-9-Chloro-1,3-dimethyl-1,4,4a,5,6,10b-hexahydropyrimido[5,4-*c*]quinolin-2(3*H*)-one (3q): light yellow solid; yield 50% (66 mg); mp 202−204 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.06 (dd, J_1 = 0.4 Hz, J_2 = 2.4 Hz, 1H), 6.99 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 6.42 (d, J = 8.4 Hz, 1H), 4.38 (d, J = 4.0 Hz, 1H), 3.50 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 3.31 (dd, J_1 = 5.2 Hz, J_2 = 12 Hz, 1H), 3.24 (d, J = 7.6 Hz, 2H), 3.14 (s, 3H), 2.89 (s, 3H), 2.52−2.47 (m, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 155.3, 141.2, 128.5, 128.0, 121.3, 120.8, 114.8, 56.6, 48.4, 41.8, 36.4, 35.7, 28.8; IR (neat) ν = 3297, 2933, 1603, 1514, 1460, 1406, 1359, 1297, 1254, 1109, 1053, 929, 883, 811, 735, 700; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{13}H_{16}ClN_3O$ 265.0982, found 265.0981.

(±)-(*R*,*S*)-8-Chloro-1-methyl-3,3a,4,5-tetrahydro-1*H*-pyrrolo-[3,2-*c*]quinolin-2(9b*H*)-one (3r): gray solid; yield 43% (51 mg); mp 118−119 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.17 (d, J = 2.4 Hz, 1H), 7.12 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 4.45 (d, J = 6.0 Hz, 1H), 4.01 (br, 1H), 3.22 (dd, J_1 = 4.4 Hz, J_2 = 11.6 Hz, 1H), 2.98 (dd, J_1 = 9.2 Hz, J_2 = 11.6 Hz, 1H), 2.83 (s, 3H), 2.77−2.63 (m, 2H), 2.31 (dd, J_1 = 2.4 Hz, J_2 = 16.8 Hz, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 173.8, 144.8, 131.1, 129.2, 121.8, 118.3, 116.7, 58.1, 43.2, 35.1, 30.8, 27.9; IR (neat) ν = 3330, 2957, 1674, 1607, 1503, 1456, 1422, 1299, 1273, 1180, 1121, 969, 896, 820, 739, 677; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{13}ClN_2O$ 236.0716, found 236.0713.

(±)-(*R*,*S*)-8-Bromo-1-methyl-3,3a,4,5-tetrahydro-1*H*-pyrrolo-[3,2-*c*]quinolin-2(9b*H*)-one (3s): brown solid; yield 45% (63 mg); mp 133−135 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.27 (d, J = 2.4 Hz, 1H), 7.20 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.52 (d, J = 8.4 Hz, 1H), 4.43 (d, J = 6.0 Hz, 1H), 4.06 (br, 1H), 3.19 (dd, J_1 = 4.4 Hz, J_2 = 11.6 Hz, 1H), 2.99 (dd, J_1 = 8.4 Hz, J_2 = 11.4 Hz, 1H), 2.83 (s, 3H), 2.75−2.61 (m, 2H), 2.28 (d, J = 14.4 Hz, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 172.6, 144.1, 132.9, 130.9, 117.8, 116.0, 107.6, 57.0, 42.0, 34.0, 29.6, 26.8; IR (neat) ν = 3325, 2958, 1676, 1602, 1502, 1456, 1422, 1298, 1268, 1179, 1061, 969, 893, 818, 751, 671; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{13}BrN_2O$ 280.0211, found 280.0212.

(±)-(*R*,*S*)-8-Fluoro-1-methyl-3,3a,4,5-tetrahydro-1*H*-pyrrolo-[3,2-*c*]quinolin-2(9b*H*)-one (3t): brown solid; yield 35% (39 mg); mp 82−84 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 6.92−6.85 (m, 2H), 6.59 (dd, J_1 = 4.8 Hz, J_2 = 8.8 Hz, 1H), 4.45 (d, J = 6.4 Hz, 1H), 3.71 (br, 1H), 3.18 (dd, J_1 = 4.4 Hz, J_2 = 11.6 Hz, 1H), 3.00 (dd, J_1 = 8.4 Hz, J_2 = 11.2 Hz, 1H), 2.84 (s, 3H), 2.77−2.71 (m, 1H), 2.64 (dd, J_1 = 8.0 Hz, J_2 = 16.4 Hz, 1H), 2.35 (dd, J_1 = 3.2 Hz, J_2 = 16.8 Hz, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 174.4, 155.9 (d, J_{C-F} =234.3 Hz), 143.1, 118.9 (d, J_{C-F} =6.2 Hz), 118.0 (d, J_{C-F} =22.3 Hz), 117.1 (d, J_{C-F} =8.1 Hz), 116.9 (d, J_{C-F} =21.8 Hz), 59.0, 44.4, 35.6, 31.7, 28.6; IR (neat) ν = 3331, 2923, 1677, 1509, 1457, 1426, 1394, 1301, 1254, 1207, 1148, 1121, 1061, 959, 880, 820, 760, 667; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{13}FN_2O$ 220.1012, found 220.1010.

(±)-(*R*,*S*)-1-Methyl-3,3a,4,5-tetrahydro-1*H*-pyrrolo[3,2-*c*]-quinolin-2(9b*H*)-one (3u): gray solid; yield 30% (30 mg); mp 144−145 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.19 (d, J = 7.6 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 6.77 (t, J = 7.2 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 4.50 (d, J = 6.0 Hz, 1H), 3.78 (br, 1H), 3.21 (dd, J_1 = 4.4 Hz, J_2 = 11.2 Hz, 1H), 3.02 (dd, J_1 = 9.2 Hz, J_2 = 11.2 Hz, 1H), 2.82 (s, 3H), 2.77−2.74 (m, 1H), 2.71−2.63 (m, 1H), 2.30 (dd, J_1 = 2.4 Hz, J_2 = 16.4 Hz, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 172.8, 145.1, 130.8, 128.2, 116.4, 115.9, 114.4, 57.3, 42.2, 34.3, 29.9, 26.8; IR (neat) ν = 3331, 2956, 1672, 1609, 1502, 1419, 1394, 1338, 1299, 1182, 1124, 967, 862, 756, 663; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{14}N_2O$ 202.1106, found 202.1108.

(±)-(*R*,*S*)-1-Methyl-8-nitro-3,3a,4,5-tetrahydro-1*H*-pyrrolo-[3,2-*c*]quinolin-2(9b*H*)-one (3v): yellow solid; yield 50% (62 mg); mp 177−178 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 8.12 (d, J = 2.0 Hz, 1H), 8.03 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 6.64 (d, J = 8.8 Hz, 1H), δ 5.31 (br, 1H), 4.53 (d, J = 5.2 Hz, 1H), 3.37 (dd, J_1 = 4.0 Hz, J_2 = 12.4 Hz, 1H), 3.07 (dd, J_1 = 10.0 Hz, J_2 = 12.0 Hz, 1H), 2.85 (s, 3H), 2.75−2.67 (m, 2H), 2.23 (d, J = 14.8 Hz, 1H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 174.1, 151.9, 138.2, 129.4, 126.6, 115.3, 115.0, 58.4, 42.6, 36.0, 30.2, 28.4; IR (neat) ν = 3308, 2966, 1677, 1613, 1588, 1539, 1512, 1473, 1419, 1394, 1321, 1290, 1184, 1097, 973, 915, 830, 752, 674; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{13}N_3O_3$ 247.0957, found 247.0956.

(±)-(*R*,*S*)-8-Chloro-1-ethyl-4-methyl-3,3a,4,5-tetrahydro-1*H*-pyrrolo[3,2-*c*]quinolin-2(9b*H*)-one (3w): gray solid; yield 18% (24 mg); mp 84−85 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 7.10 (d, J = 2.4 Hz, 1H), 7.04 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 6.56 (d, J = 8.8 Hz, 1H), 4.76 (d, J = 8.4 Hz, 1H), 3.88−3.79 (m, 1H), 3.41−3.35 (m, 1H), 3.09−3.04 (m, 1H), 2.90−2.75 (m, 2H), 2.31−2.24 (dd, J_1 = 8.4 Hz, J_2 = 15.6 Hz, 1H), 1.20 (d, J = 6.4 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 M Hz, $CDCl_3$) δ 173.8, 145.6, 129.3, 128.4, 123.09, 123.07, 117.1, 56.1, 49.8, 39.2, 35.3, 29.3, 18.9, 12.2; IR (neat) ν = 3310, 2973, 2930, 1667, 1605, 1490, 1453, 1422, 1380, 1299, 1259, 1213, 1187, 1078, 937, 899, 823, 790, 703, 659; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{14}H_{17}ClN_2O$ 264.1029, found 264.1033.

1,3-Dimethyl-1*H*-imidazo[4,5-*c*]quinolin-2(3*H*)-one (4). To a solution of **3a** (0.2 mmol, 43 mg) and potassium iodide (0.04 mmol, 6 mg) in 2 mL of CH_3CN was added a solution of *t*-BHP (0.6 mmol, 108 μL, 5−6 M in water) dropwise at room temperature. After reaction at 75 °C for 4 h, the mixture was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography with ethyl acetate to give the gray solid **4** in 50% yield (21 mg): mp 210−212 °C; ^{1}H NMR (400 M Hz, $CDCl_3$) δ 8.59 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.55 (t, J = 8.4 Hz, 1H), 7.48 (t, J = 8.0 Hz, 1H), 3.82 (s, 3H), 3.51 (s, 3H);^{13}C NMR (100 M Hz, $CDCl_3$) δ 153.9, 144.9, 132.0, 130.5, 129.7, 126.9, 126.4, 122.2, 120.1, 115.7, 30.5, 27.6; IR (neat) ν = 2958, 2922, 2851, 1706, 1583, 1503, 1460, 1432, 1391, 1263, 1232, 1154, 1016, 982, 882, 761, 741, 659; HRMS (TOF MS EI$^+$) $[M]^+$ calcd for $C_{12}H_{11}N_3O$ 213.0902, found 213.0901.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of the ^{1}H and ^{13}C NMR spectra for all compounds, X-ray crystal structure of **3m** (CIF), and checkCIF/PLATON report for **3m**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wlbao@css.zju.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work is financially supported by the Natural Science Foundation of China (No. 21072168).

■ REFERENCES

(1) For recent reviews, see: (a) Cho, S. H.; J. Kim, Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (b) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879.

(2) (a) Karthikeyan, J.; Cheng, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 9880. (b) Wang, G.; Yuan, T.; Li, D. *Angew. Chem., Int. Ed.* **2011**, *50*, 1380. (c) Wang, Z.; Song, F.; Zhao, Y.; Huang, Y.; Yang, L.; Zhao, D.; Lan, J.; You, J. *Chem.—Eur. J.* **2012**, *18*, 16618.

(3) (a) Zhang, X.; Liu, B.; Shu, X.; Gao, Y.; Lv, H.; Zhu, J. *J. Org. Chem.* **2012**, *77*, 501. (b) Frolova, L. V.; Evdokimov, N. M.; Hayden, K.; Malik, I.; Rogelj, S.; Kornienko, A.; Magedov, I. V. *Org. Lett.* **2011**, *13*, 1118.

(4) (a) Campos, K. R. *Chem. Soc. Rev.* **2007**, *36*, 1069. (b) Murahashi, S.; Zhang, D. *Chem. Soc. Rev.* **2008**, *37*, 1490.

(5) (a) Li, Z.; Li, C. *Eur. J. Org. Chem.* **2005**, 3173. (b) Xie, J.; Huang, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 10181. (c) Baslé, O.; Li, C. *Green Chem.* **2007**, *9*, 1047. (d) Shen, Y.; Li, M.; Wang, S.; Zhan, T.; Tan, Z.; Guo, C. *Chem. Commun.* **2009**, 953. (e) Li, Z.; Li, C. *J. Am. Chem. Soc.* **2005**, *127*, 3672. (f) Yang, F.; Li, J.; Xie, J.; Huang, Z. *Org. Lett.* **2010**, *12*, 5214.

(6) (a) Liu, P.; Zhou, C.; Xiang, S.; Che, C. *Chem. Commun.* **2010**, *46*, 2739. (b) Li, Z.; Li, C. *J. Am. Chem. Soc.* **2005**, *127*, 6968. (c) Shirakawa, E.; Uchiyama, N.; Hayashi, T. *J. Org. Chem.* **2011**, *76*, 25. (d) Huang, L.; Niu, T.; Wu, J.; Zhang, Y. *J. Org. Chem.* **2011**, *76*, 1759. (e) Ghobrial, M.; Harhammer, K.; Mihovilovic, M. D.; Schnurch, M. *Chem. Commun.* **2010**, *46*, 8836.

(7) (a) Li, Z.; Li, C. *J. Am. Chem. Soc.* **2004**, *126*, 11810. (b) Niu, M.; Yin, Z.; Fu, H.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2008**, *73*, 3961. (c) Xu, X.; Li, X. *Org. Lett.* **2009**, *11*, 1027. (d) Rao Volla, C. M.; Vogel, P. *Org. Lett.* **2009**, *11*, 1701.

(8) (a) Zhang, C.; Kanta, De, C.; Mal, R.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 416. (b) Wan, C.; Zhang, J.; Wang, S.; Fan, J.; Wang, Z. *Org. Lett.* **2010**, *12*, 2338. (c) Han, G.; LaPorte, M. G.; McIntosh, M. C.; Weinreb, S. M. *J. Org. Chem.* **1996**, *61*, 9483.

(9) The coupling of the sp^3 C−H bond α to a nitrogen atom with an unactivated sp^3 C−H bond has not been found, but unactivated sp^3 C−H bonds have been coupled with other types of C−H or X−H bonds, such as: (a) Wasa, M.; Engle, K. M.; Lin, D. W.; Yoo, E.; Yu, J. *J. Am. Chem. Soc.* **2011**, *133*, 19598. (b) Gephart, R. T., III; Huang, D. L.; Aguila, M. B.; Schmidt, G.; Shahu, A.; Warren, T. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 6488.

(10) (a) Li, H.; He, Z.; Guo, X.; Li, W.; Zhao, X.; Li, Z. *Org. Lett.* **2009**, *11*, 4176. (b) Yang, J.; Wang, Z.; Pan, F.; Li, Y.; Bao, W. *Org. Biomol. Chem.* **2010**, *8*, 2975.

(11) Sridharan, V.; Suryavanshi, P. A.; Menendez, J. C. *Chem. Rev.* **2011**, *111*, 7157.

(12) Fish, R. H.; Tan, J. L.; Thormodsen, A. D. *J. Org. Chem.* **1984**, *49*, 4500.

(13) (a) Gigant, N.; Gillaizeau, I. *Org. Lett.* **2012**, *14*, 4622. (b) Cho, H.; Iwama, Y.; Sugimoto, K.; Mori, S.; Tokuyama, H. *J. Org. Chem.* **2010**, *75*, 627. (c) Babu, G.; Perumal, P. T. *Tetrahedron Lett.* **1998**, *39*, 3225. (d) Omar-Amrani, R.; Thomas, A.; Brenner, E.; Schneider, R.; Fort, Y. *Org. Lett.* **2003**, *5*, 2311.

(14) (a) Fabio, R. D.; Alvaro, G.; Bertani, B.; Donati, D.; Giacobbe, S.; Marchioro, C.; Palma, C.; Lynn, S. M. *J. Org. Chem.* **2002**, *67*, 7319. (b) Comesse, S.; Sanselme, M.; Daïch, A. *J. Org. Chem.* **2008**, *73*, 5566. (c) Yee, Ng, P.; Masse, C. E.; Shaw, J. T. *Org. Lett.* **2006**, *8*, 3999. (d) Vicente-García, E.; Catti, F.; Ramón, R.; Lavilla, R. *Org. Lett.* **2010**, *12*, 860.

(15) (a) Yi, C. S.; Yun, S. Y.; Guzei, I. A. *J. Am. Chem. Soc.* **2005**, *127*, 5782. (b) Yi, C. S.; Yun, S. Y. *J. Am. Chem. Soc.* **2005**, *127*, 17000. (c) Zeng, L.; Yi, W.; Cai, C. *Eur. J. Org. Chem.* **2012**, 559.

(16) (a) Shukla, N. M.; Kimbrell, M. R.; Malladi, S. S.; David, S. A. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2211. (b) van Galen, P. J. M.; Nissen, P.; van Wijngaarden, I.; IJzerman, A. P.; Soudijnt, W. *J. Med. Chem.* **1991**, *34*, 1202. (c) Göblyös, A.; Gao, Z.; Brussee, J.; Connestari, R.; Santiago, S. N.; Ye, K.; IJzerman, A. P.; Jacobson, K. A. *J. Med. Chem.* **2006**, *49*, 3354.

(17) (a) Nieman, J. A.; Ennis, M. D. *Org. Lett.* **2000**, *2*, 1395. (b) Hadden, M.; Nieuwenhuyzen, M.; Potts, D.; Stevenson, P. J.; Thompson, N. *Tetrahedron* **2001**, *57*, 5615.