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Decarboxylative Coupling of α-Keto Acids with *ortho*-Phenylenediamines Promoted by an Electrochemical Method in Aqueous Media

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Abstract: An electrochemical method for the decarboxylative coupling of α-keto acids with *ortho*-phenylenediamines was developed. The reaction proceeded smoothly in aqueous solution under air and metal catalyst-free conditions to afford 2-substituted benzimidazoles in good yields. Benzothiazoles could also be synthesized by this protocol.

Keywords: aqueous media; decarboxylative coupling; electrochemical reaction; 2-substituted benzoxazoles

Introduction

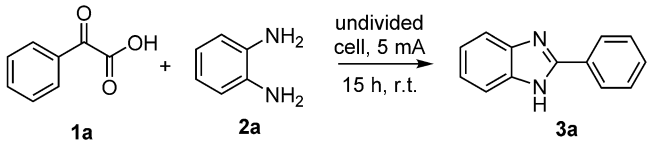
The decarboxylative coupling reaction has recently emerged as a powerful tool to construct C–C or C–heteroatom bonds in synthetic organic chemistry. This reaction typically involves transition metal catalytic systems and high reaction temperatures are necessary.[1] A Kolbe-type reaction through anodic oxidative decarboxylation of a carboxylic acid represents the seminal study of electroorganic synthesis that allows one-step C–C or C–heteroatom bond formation, which is difficult to be attained through other routes.[2] Despite the convenience and clean chemistry that electrochemistry could bestow in the field of contemporary organic synthesis,[3,4] its applications in decarboxylative cross-coupling reactions remain challenging and the reported methods are nonetheless limited.

2-Substituted benzimidazoles are important building blocks for pharmaceutical agents, natural products and functional materials.[5] Hence, tremendous efforts have been made to explore efficient methods for the construction of this type of heterocyclic ring.[6] However, the preparation of benzimidazoles from α-keto acids has received less attention. Very recently, Lei et al. demonstrated an elegant photocatalyzed decarboxylation of α-keto acids with amines to form amides and benzazoles by visible light.[7] In continuation of our interest in the development of new electrochemical process in aqueous solution,[8] herein we report the first highly efficient electrochemical decarboxylative coupling of α-keto acids with *o*-phenylenediamines to form 2-substituted benzimidazoles in aqueous solution.

Results and Discussion

We commenced our study with benzoylformic acid (**1a**) and *ortho*-phenylenediamine (**2a**) as model substrates. The two compounds were treated with TFA (trifluoroacetic acid, 0.5 mmol) and DIPEA (*N*,*N*-diisopropylethylamine, 1.0 mmol) in 4.0 mL DMF (*N*,*N*-dimethylformamide)–0.2 M NH_4ClO_4 solution in a one-compartment cell under a constant current (5 mA) for 15 h at room temperature. The desired product **3a** was obtained in 48% isolated yield (Table 1, entry 1). The solvent effect was then studied (entries 2–4). To our delight, the desired product was formed in 88% yield (entry 3) by using DMSO (dimethyl sulfoxide, AR grade, water content ≤0.2%) as the solvent. However, when the reaction was carried out in anhydrous DMSO, the product was only obtained in 53% yield (Table 1, entry 4). When the combination DMSO/H_2O (3/1, v/v) was employed, the yield could be further increased to 94% (Table 1, entry 5). Switching the Pt foils with graphite electrodes led to a yield of 85% (Table 1, entry 6). Studies on the effect of current density revealed that an increase or decrease of the current led to a decrease of

Table 1. Optimization of the reaction conditions.[a]



1a 2a 3a

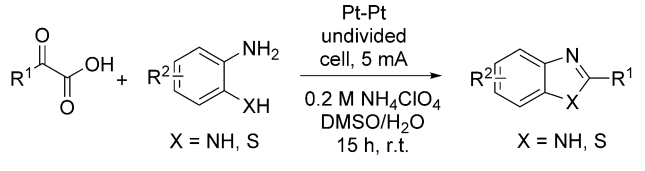
Entry	Anode-Cathode	Solvent	Yield [%][b]
1	Pt-Pt	DMF	48
2	Pt-Pt	CH_3OH	54
3	Pt-Pt	DMSO	88
4[c]	Pt-Pt	DMSO	53
5	Pt-Pt	DMSO/H_2O (3/1, v/v)	94
6	C-C[d]	DMSO/H_2O (3/1, v/v)	85
7[e]	Pt-Pt	DMSO/H_2O (3/1, v/v)	63
8[f]	Pt-Pt	DMSO/H_2O (3/1, v/v)	68
9[g]	Pt-Pt	DMSO/H_2O (3/1, v/v)	40
10[h]	Pt-Pt	DMSO/H_2O (3/1, v/v)	48

[a] the mixture of **1a** (0.4 mmol), **2a** (1.2 mmol), TFA (0.5 mmol) and DIPEA (1.0 mmol) in solvent (4.0 mL) with 0.2 M NH_4ClO_4 as supporting electrolyte was electrolyzed at constant current (5 mA) in an undivided cell at room temperature for 15 h under air, anode: Pt foil (1×1.5 cm^2), cathode: Pt foil (1×1.5 cm^2).
[b] Yields of isolated products.
[c] Anhydrous DMSO (4.0 mL).
[d] Graphite rod electrode (diameter = 0.5 cm, height = 1.8 cm).
[e] The current was 3 mA.
[f] The current was 8 mA.
[g] In the absence of TFA.
[h] In the absence of DIPEA.

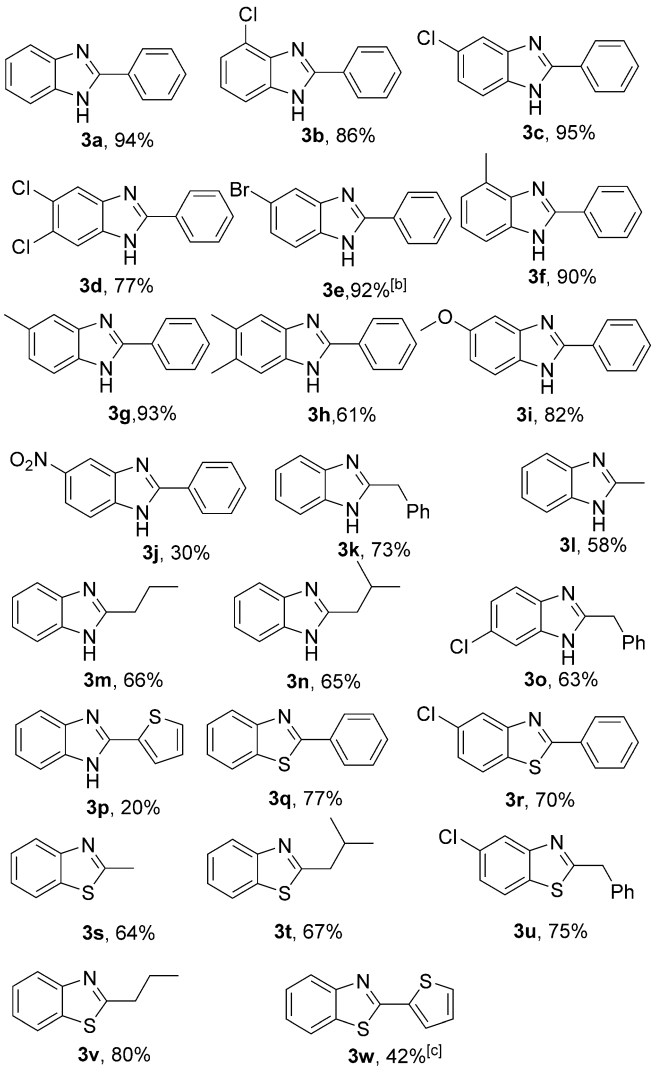
the product yield (Table 1, entries 7 and 8). Hence, 5 mA was the optimal current for this reaction. Also, the absence of TFA or DIPEA both led to decreases of the chemical yield (Table 1, entries 9 and 10).

The reaction scope was explored by employing the optimized reaction conditions. First, the reactivities of various substituted aromatic diamines under our reaction protocol were examined. As can be seen in Table 2, most of the phenylenediamines, which bore electron-deficient or electron-rich groups on the aromatic rings, gave the corresponding products in good to excellent yields. It is noteworthy that the halide substituents could be well tolerated under the electrochemical conditions and could thus provide an opportunity for further transformations at the halide position. However, the reaction of 4-nitro-*o*-phenylenediamine yielded only 30% of respective product, **3j**. It was speculated that the reduction of the nitro group could have occurred on the cathode. Next, the reactions of different α-keto acids, including aliphatic and heteroaromatic α-keto acids were studied. Besides the aromatic keto acids, the aliphatic keto acids underwent decarboxylative coupling with **2a** smoothly to afford the desired benzimidazoles in moderate to good yields (**3k–o**). The 2-thiopheneglyoxylic acid was not compatible for this transformation under the standard conditions (**3p**). Finally, this method was extended to the synthesis of benzothiazoles and it was found that these useful compounds could also be synthesized in good yields (**3q–w**).

Table 2. Scope of substrates.[a]



1 2 3



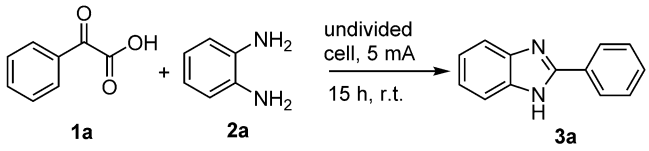
[a] *Reaction conditions:* **1** (0.4 mmol), **2** (1.2 mmol), DMSO (3.0 mL), H_2O (1.0 mL), TFA (0.5 mmol), DIPEA (1.0 mmol), 0.2 M NH_4ClO_4 as supporting electrolyte, 15 h at room temperature under air, anode: Pt foil (1×1.5 cm^2), cathode: Pt foil (1×1.5 cm^2), constant current (5 mA), undivided cell. Yields of isolated products.
[b] DMSO (3.5 mL) and H_2O (0.5 mL).
[c] After 22 h.

Control experiments were carried out in order to obtain useful insights into the mechanism. The standard conditions include the presence of electric supply, water together with air, as listed in entry 1, Table 3. The reaction yield was decreased to 85% under a nitrogen atmosphere (Table 3, entry 2). Only a trace amount of product was obtained in the absence of the power supply (Table 3, entry 3). When anhydrous DMSO was used without addition of water, the reaction gave a 53% yield of product (Table 3, entry 4). Furthermore, it was observed that if the conditions listed in entry 4 were repeated under a nitrogen atmosphere instead of air, a lower yield of product was observed (Table 3, entry 5). Some other control reactions were also carried out by using the preformed imine from benzaldehyde and *ortho*-phenylenediamine **2a**. The imine was subjected to the cyclization and dehydrogenation reactions under different control conditions (see the Supporting Information, Scheme S1 for the results and discussion). Very recently, Cheon and co-workers had verified that water could act as a nucleophilic catalyst for the synthesis of benzimidazoles.[9] Hence, in our reaction system, it was demonstrated that electrochemical current, oxygen and water have all played important roles in this decarboxylative coupling process.

Further studies on the mechanism of the reaction were performed. When two equivalents of 2,2,6,6-tetramethylpiperidine *N*-oxyl (TEMPO) were added into the reaction mixture under the standard conditions, the desired product was obtained in 58% yield (Scheme 1A). However, the (2,2,6,6-tetramethylpiperidin-1-yl) benzoate was not detected by NMR, GC-MS and LC-MS analysis. On the other hand, when only benzoylformic acid **1a** was added to the reaction mixture under the standard conditions, 12% conversion of benzoylformic acid **1a** was observed with 6% of benzaldehyde and 6% benzoic acid being formed (Scheme 1B). The Kolbe coupling product, benzil was not detected by TLC and GC-MS post reaction.[10] Cyclic voltammetry (CV) experiments were carried out (Figure 1, for more details, please refer to the Supporting Information). An obvious oxidative peak (peak potential at 1.01 V *vs.* $Ag/AgNO_3$, curve b) was detected in the solution of PhCOCOOK, but the corresponding reductive peak was not detected. These experimental results showed that $PhCOCOO^-$ could be oxidized to form $PhCOCOO^{\cdot}$ followed by an irreversible extrusion of CO_2. The CV studies on the effect of CF_3COOH were also carried out. In the absence of CF_3COOH, the oxidation peak of 1,2-phenylenediamine was observed at $E_p = 0.41$ V *vs.* SCE (Supporting Information, Figure S1, curve f) and at $E_p = 0.63$ V *vs.* SCE (Supporting Information, Figure S1, curve g) in its presence. This implies that in our reaction system the acid could have partially protonated the 1,2-phenylenediamine and hampered its oxidation.[11]

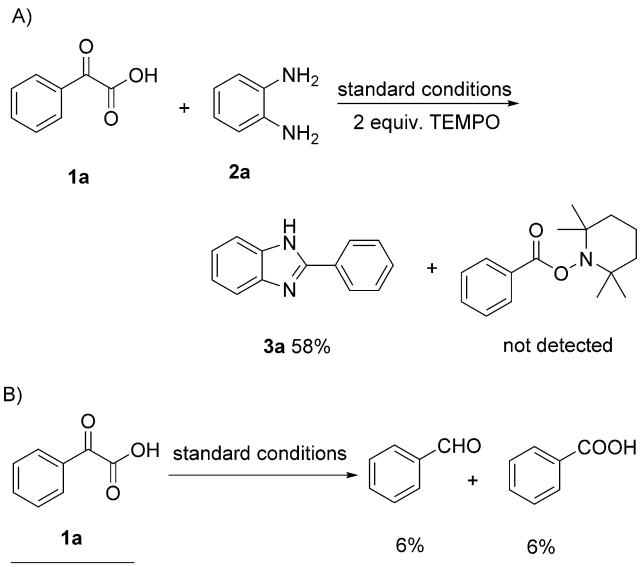
Based on the above described results and reported works,[12] we proposed two mechanistic pathways for the reaction (Scheme 2, Paths A and B). In Path A, according to the cyclic voltammetry (CV) experiments (Figure 1), α-keto acid anion[13] loses an electron to generate radical **5. 5** then undergoes decarboxylation to produce the acyl radical **6**, which couples with partially protonated diamine **2a** and a hydrogen atom transfers from the electrogenerated amine radi-

Table 3. Control experiments.[a]



Entry	Current	Water	Air	Yield [%][b]
1	+	+	+	94
2[c]	+	+	–	85
3	-	+	+	12
4[d]	+	–	+	53
5[c,d]	+	–	–	47

[a] *Reaction conditions:* **1a** (0.4 mmol), **2a** (1.2 mmol), DMSO (3.0 mL), H_2O (1.0 mL), TFA (0.5 mmol), DIPEA (1.0 mmol), 0.2 M NH_4ClO_4 as supporting electrolyte, 15 h at room temperature, anode: Pt foil (1×1.5 cm^2), cathode: Pt foil (1×1.5 cm^2), constant current (5 mA), undivided cell.
[b] Yields of isolated products.
[c] Reaction was carried out under N_2.
[d] Anhydrous DMSO (4.0 mL).



The yields were determined by ^{1}H NMR of the crude reaction mixture with CH_3NO_2 as the internal standard.

Scheme 1. Studies on the mechanism of the reaction.

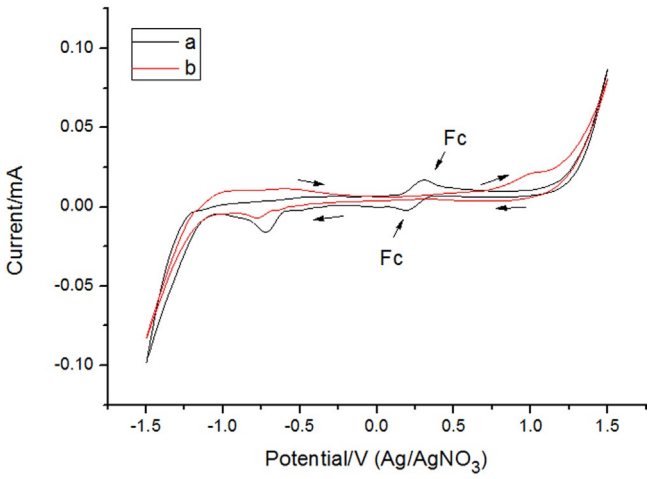
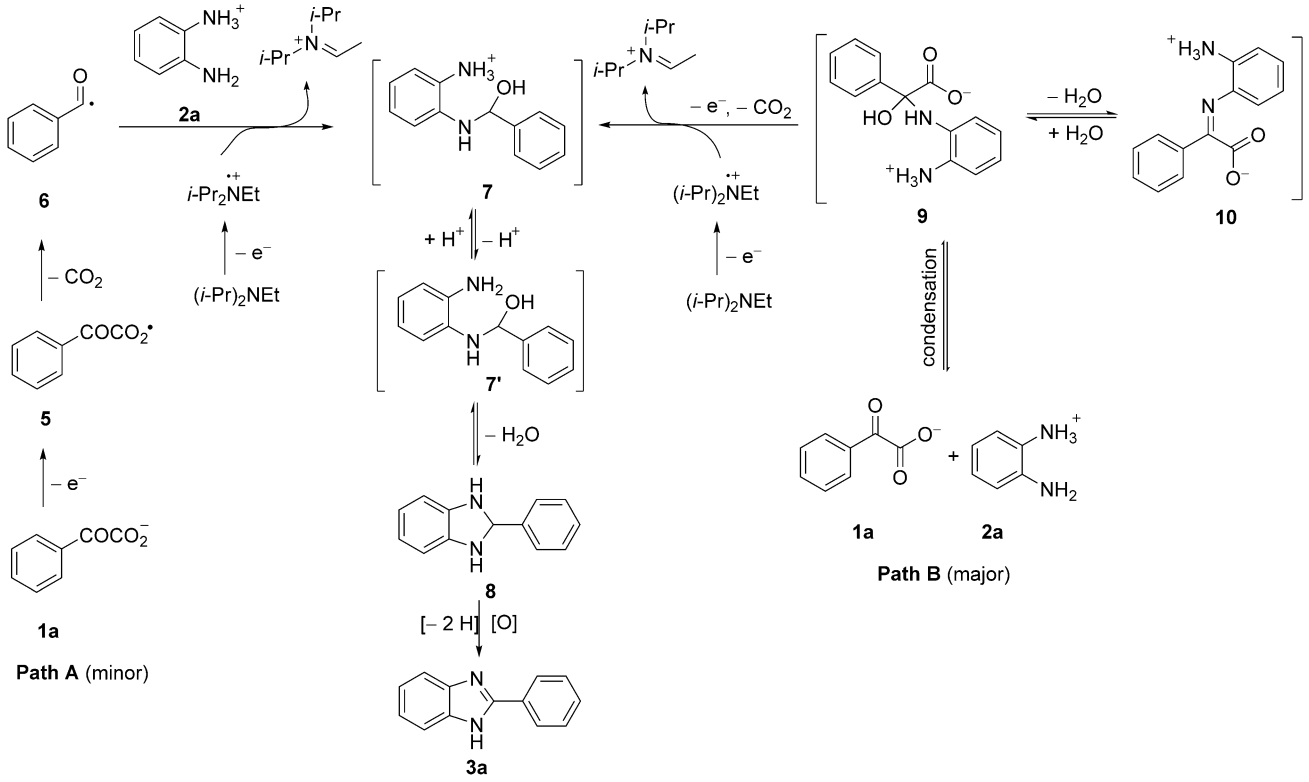


Figure 1. Cyclic voltammograms in DMSO–0.1 M NH_4ClO_4 solution at room temperature: (a) 0.05 M ferrocene, (b) 0.01 M PhCOCOOK. The voltammogram was obtained with Pt wire as auxiliary electrode and $Ag/AgNO_3$ as reference electrode. The scan rate was 0.1 Vs^{-1} on a platinum disk electrode ($d = 2$ mm).

cal cation [$(i\text{-Pr})_2NEt^{\bullet+}$)] to afford the product **7**.[14] **7** is then transformed to the intermediate benzimidazoline **8**. Subsequent dehydrogenation of **8** has proceeded through a synergistic action of O_2 and anodic oxidation (Path A). Alternatively, in Path B, hemiaminal **9** is formed by the condensation of *o*-phenylenediamine with α-oxocarboxylate which is catalyzed by TFA.[15] Then the decarboxylation of **9** was assisted by the anodic oxidation followed by H atom abstraction from $(i\text{-Pr})_2NEt^{\bullet+}$ to form **7**. Subsequent transformation of intermediate **7** to final product **3a** follows the same process as described in Path A. Noteworthily, α-iminocarboxylate **10** was detected during the reaction (see the Supporting Information for details). It had been reported that the activation barrier of the decarboxylation of **9** would be reduced after condensation of *o*-phenylenediamine with α-oxocarboxylate. Hence, it could extrude CO_2 more easily than α-oxocarboxylate.[15e] Therefore, we propose that Path B is the more favorable process for our reaction.

Conclusions

In summary, a novel electrochemical-promoted decarboxylative coupling of α-keto acids with *o*- benzimidazoles has been developed. This reaction protocol accommodates the use of undivided-cell equipment, aqueous media without the need of inert atmosphere, rendering it a mild and easily-operated reaction protocol. Under metal catalyst-free conditions, the reaction afforded the desired products in good to excellent yields with a wide substrate scope. Further investigations on the mechanism and the synthetic applications are in progress.



Scheme 2. Proposed reaction mechanism.

Experimental Section

General Information

Cyclic voltammetric (CV) experiments were carried out in a classical undivided cell in the presence of a supporting electrolyte. A platinum disk electrode ($d=2$ mm) and a platinum wire electrode ($d=0.2$ mm) were employed as the anodic electrode and cathodic electrode, respectively. An $Ag/AgNO_3$ electrode was used as the reference electrode in the CV experiments. Analytical thin-layer chromatography (TLC) plates and the silica gel for column chromatography were commercially available.

Commercial solvents and reagents were used without further purification, and tap water was used for the reaction. GC-MS analyses were carried out on a GC apparatus coupled with a single quadrupole mass spectrometer (EI, 70 eV) and a TG-5MS (30 m × 0.25 mm i.d. × 0.25 μm) capillary column. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts of ^{1}H NMR and ^{13}C NMR spectra are reported in units of parts per million (ppm) downfield from $SiMe_4$ ($\delta=0.0$ ppm) and relative to the signal of $CDCl_3$ ($\delta=7.26$ ppm for ^{1}H NMR and $\delta=77.1$ ppm for ^{13}C NMR) and $(CD_3)_2SO$ ($\delta=2.50$ ppm for ^{1}H NMR and $\delta=39.5$ ppm for ^{13}C). Multiplicities are given as s (singlet); br s (broad singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); m (multiplets), etc. The number of protons (n) for a given resonance is indicated by nH.

General Procedure for the Electrochemical Decarboxylative Coupling of α-Keto Acids with *ortho*-Phenylenediamines

In a round-bottom flask cell, α-keto acid (0.4 mmol), *o*-phenylenediamine (1.2 mmol), TFA (0.5 mmol) and DIPEA (1.0 mmol) were dissolved in 4 mL DMSO/H_2O (v/v = 3:1) with NH_4ClO_4 (0.2 M) as electrolyte. The reaction flask was equipped with Pt foils as anode and cathode (1.5 cm^2). The solution was electrolyzed at a constant current (5 mA) for 15 h (270 C of charge passed based on the standard conditions) at ambient temperature. After electrolysis, the mixture was quenched by water and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. Pure product was obtained after column chromatography on silica gel using a solvent mixture of petroleum ether and ethyl acetate.

Characterization Data of 2-Substituted Benzoxazoles

2-Phenyl-1*H*-benzo[*d*]imidazole (3a):[7] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3a** as a yellow solid; yield: 72.9 mg (94%); $R_f=0.44$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=13.00$ (br s, 1H), 8.23 (d, $J=7.3$ Hz, 2H), 7.64–7.64 (m, 2H), 7.58–7.55 (m, 2H), 7.51–7.50 (m, 1H), 7.24–7.23 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=151.2$, 130.2, 129.8, 128.9, 126.4, 122.1.

4-Chloro-2-phenyl-1*H*-benzo[*d*]imidazole (3b):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3b** as a yellow solid; yield: 78.4 mg (86%); $R_f=0.48$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=13.30$ (br s, 1H), 8.24 (d, $J=6.5$ Hz, 2H), 7.58–7.53 (m, 4H), 7.30–7.28 (m, 1H), 7.24–7.20 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=152.1$, 130.2, 129.6, 128.9, 126.8, 123.2, 121.7.

5-Chloro-2-phenyl-1*H*-benzo[*d*]imidazole (3c):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3c** as a yellow solid; yield: 86.7 mg (95%); $R_f=0.54$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=13.12$ (br s, 1H), 8.19 (d, $J=7.6$ Hz, 2H), 7.66–7.66 (m, 1H), 7.62–7.49 (m, 4H), 7.23 (d, $J=8.4$ Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=152.6$, 130.2, 129.7, 129.0, 126.7, 126.6, 122.3.

5,6-Dichloro-2-phenyl-1*H*-benzo[*d*]imidazole (3d):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3d** as a yellow solid; yield: 80.7 mg (77%); $R_f=0.50$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=13.20$ (br s, 1H), 8.17–8.17 (m, 2H), 7.83–7.83 (m, 2H), 7.56–7.54 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=153.8$, 130.4, 129.3, 128.9, 126.7, 124.5.

5-Bromo-2-phenyl-1*H*-benzo[*d*]imidazole (3e):[16b] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3e** as a yellow solid; yield: 100.1 mg (92%); $R_f=0.54$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=13.13$ (br s, 1H), 8.19 (d, $J=7.6$ Hz, 2H), 7.81 (s, 1H), 7.58–7.50 (m, 4H), 7.36–7.32 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=$ 152.5, 130.2, 129.6, 129.0, 126.6, 124.9.

4-Methyl-2-phenyl-1*H*-benzo[d]imidazole (3f):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3f** as a yellow solid; yield: 74.9 mg (90%); $R_f=0.63$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=12.68$ (br s, 1H), 8.24 (d, $J=7.6$ Hz, 2H), 7.58–7.56 (m, 2H), 7.54–7.48 (m, 1H), 7.42 (d, $J=7.7$ Hz, 1H), 7.13–7.09 (m, 1H), 7.02–7.00 (m, 1H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=$ 150.7, 130.3, 129.6, 128.8, 126.5, 122.4, 122.1, 16.9.

5-Methyl-2-phenyl-1*H*-benzo[*d*]imidazole (3g):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3g** as a yellow solid; yield: 77.4 mg (93%); $R_f=0.44$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=12.79$ (s, 1H), 8.20 (d, $J=7.4$ Hz, 2H), 7.57–7.53 (m, 3H), 7.50–7.48 (m, 1H), 7.41 (m, 1H), 7.05–7.03 (m, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=150.9$, 131.3, 130.3, 129.6, 128.9, 126.3, 123.5, 21.3.

5,6-Dimethyl-2-phenyl-1*H*-benzo[*d*]imidazole (3h):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3h** as a yellow solid; yield: 54.2 mg (61%); $R_f=0.46$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=12.33$ (br s, 1H), 8.24 (d, $J=7.5$ Hz, 2H), 7.54–7.50 (m, 2H), 7.46–7.43 (m, 3H), 2.31 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): $\delta=$ 150.5, 130.4, 129.4, 128.8, 126.3, 19.9.

5-Methoxy-2-phenyl-1*H*-benzo[*d*]imidazole (3i):[6b] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3i** as a yellow solid; yield: 73.5 mg (82%); $R_f=0.33$ (PE/EA = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=9.83$ (br s, 1H), 8.18–8.16 (m, 2H), 7.46 (d, $J=8.8$ Hz, 1H), 7.34–7.33 (m, 3H), 6.97–6.97 (m, 1H), 6.86–6.84 (m, 1H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=156.7$, 152.3, 139.4, 134.5, 130.1, 129.9, 129.1, 126.8, 116.2, 112.6, 97.5, 55.7.

5-Nitro-2-phenyl-1*H*-benzo[*d*]imidazole (3j):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3j** as a brown solid; yield: 28.7 mg (30%); R_f = 0.40 (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 13.44 (br s, 1H), 8.45 (s, 1H), 8.21–8.19 (m, 2H), 8.11–8.09 (m, 1H), 7.75–7.73 (m, 1H), 7.59–7.57 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 155.7, 142.7, 130.9, 129.1, 129.0, 126.9, 117.9.

2-Benzyl-1*H*-benzo[*d*]imidazole (3k):[16c] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3k** as a yellow solid; yield: 60.8 mg (73%); R_f = 0.39 (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.36 (br s, 1H), 7.53–7.53 (m, 2H), 7.36–7.32 (m, 4H), 7.25–7.23 (m, 1H), 7.16–7.15 (m, 2H), 4.22 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.5, 137.6, 128.7, 128.5, 126.5, 34.9.

2-Methyl-2-phenyl-1*H*-benzo[*d*]imidazole (3l):[16d] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3l** as a brown liquid; yield: 30.6 mg (58%); R_f = 0.61 (PE/EA = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.53 (m, 2H), 7.22–7.29 (m, 2H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.4, 138.6, 122.2, 114.5, 14.8.

2-Propyl-1*H*-benzo[*d*]imidazole (3m):[16e] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3m** as a yellow liquid; yield: 42.3 mg (66%); R_f = 0.58 (PE/EA = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (br s,1H), 7.58–7.51 (m, 2H), 7.24–7.22 (m, 2H), 2.97 (t, J = 7.2 Hz, 2H), 1.97–1.88 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 138.7, 122.1, 114.6, 31.3, 21.8, 13.9.

2-Isobutyl-1*H*-benzo[*d*]imidazole (3n):[16a] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3n** as a yellow liquid; yield: 45.3 mg (65%); R_f = 0.64 (PE/EA = 2/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.16 (br s, 1H), 7.57–7.56 (m, 2H), 7.23–7.21 (m, 2H), 2.86 (d, J = 7.2 Hz, 2H), 2.29–2.25 (m, 1H), 0.98 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.0, 138.6, 122.1, 114.6, 38.5, 28.6, 22.5.

6-Chloro-2-phenyl-1*H*-benzo[*d*]imidazole (3o):[16f] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3o** as a white solid; yieöld: 61.0 mg (63%); R_f = 0.43 (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.51 (s, 1H), 7.57–7.52 (m, 2H), 7.34–7.30 (m, 4H), 7.25–7.22 (m, 1H), 7.17–7.15 (m, 1H), 4.21 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 155.1, 137.3, 128.8, 128.5, 126.6, 125.8, 121.5, 34.9.

2-(Thiophen-2-yl)-1*H*-benzo[*d*]imidazole (3p):[6b] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give **3p** as a white solid; yield: 16.0 mg (20%); R_f = 0.74 (PE/EA = 2/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.93 (s, 1H), 7.84–7.84 (m, 1H), 7.74–7.72 (m, 1H), 7.61–7.61 (m, 1H), 7.52–7.52 (m, 1H), 7.24–7.20 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 147.0, 133.6, 128.7, 128.2, 126.7, 122.2.

2-Phenylbenzo[*d*]thiazole (3q):[7] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3q** as a white solid; yield: 65.0 mg (77%); R_f = 0.72 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13–8.13 (m, 3H), 7.91 (d, J = 7.4 Hz, 1H), 7.52–7.51 (m, 4H), 7.42–7.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 154.2, 135.1, 133.7, 131.0, 129.1, 127.6, 126.4, 125.2, 123.3, 121.7.

5-Chloro-2-phenylbenzo[*d*]thiazole (3r):[6b] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3r** as a white solid; yield: 68.6 mg (70%); R_f = 0.75 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08–8.06 (m, 3H), 7.80 (d, J = 8.8 Hz, 1H), 7.51–7.50 (m, 3H), 7.37–7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.9, 150.0, 133.3, 133.2, 132.4, 131.3, 129.1, 127.6, 125.7, 123.1, 122.3.

2-Methylbenzo[*d*]thiazole (3s):[16g] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3s** as a yellow liquid; yield: 38.1 mg (64%); R_f = 0.72 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.90 (m, 1H), 7.75–7.73 (m, 1H), 7.40–7.34 (m, 1H), 7.29–7.25 (m, 1H), 2.76–2.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.8, 153.4, 135.6, 125.8, 124.6, 122.3, 121.3, 20.0.

2-Isobutylbenzo[*d*]thiazole (3t):[16h] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3t** as a yellow liquid; yield: 51.2 mg (67%); R_f = 0.69 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.82 (m, 1H), 7.84–7.82 (m, 1H), 7.46–7.42 (m, 1H), 7.36–7.32 (m, 1H), 2.99 (d, J = 6.6 Hz, 2H), 2.28–2.18 (m, 1H), 1.04 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 153.3, 135.3, 125.8, 124.6, 122.6, 121.4, 43.3, 29.7, 22.4.

5-Chloro-2-methylbenzo[*d*]thiazole (3u):[16i] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3u** as a yellow liquid; yield: 54.9 mg (75%); R_f = 0.65 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.90 (m, 1H), 7.70–7.68 (m, 1H), 7.31–7.29 (m, 1H), 2.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 154.3, 133.9, 132.0, 125.2, 122.3, 122.1, 20.2.

2-Propylbenzo[*d*]thiazole (3v):[16j] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3v** as a yellow liquid; yield: 56.6 mg (80%); R_f = 0.71 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.1 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 3.08 (t, J = 7.6 Hz, 2H), 1.95–1.86 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1, 153.3, 135.2, 125.8, 124.6, 122.5, 121.4, 36.2, 23.1, 13.7.

2-(Thiophen-2-yl)benzo[*d*]thiazole (3w):[6b] The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3w** as a white solid; yield: 36.4 mg (42%); R_f = 0.78 (PE/EA = 10/1); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.10 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.87 (d, J = 5.0 Hz, 1H), 7.84 (d, J = 3.6 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.25 (t, J = 4.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.8, 153.1, 136.3, 134.2, 129.6, 128.7, 128.6, 126.7, 125.5, 122.4, 122.2.

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References

[1] a) O. Baudoin, *Angew. Chem.* **2007**, *119*, 1395–1397; *Angew. Chem. Int. Ed.* **2007**, *46*, 1373–1375; b) N. Rodríguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030–5048; c) R. Shang, L. Liu, *Sci. China Chem.* **2011**, *54*, 1670–1687; d) J. D. Weaver, A. Recio III, A. J. Grenning, J. A. Tunge, *Chem. Rev.* **2011**, *111*, 1846–1913; e) W. I. Dzik, P. P. Lange, L. J. Goossn, *Chem. Sci.* **2012**, *3*, 2671–2678.

[2] For reviews, see: a) H. J. Schäfer, *Angew. Chem.* **1981**, *93*, 978–1000; *Angew. Chem. Int. Ed.* **1981**, *20*, 911–934; b) E. Klocke, A. Matzeit, M. Gockeln, H. J. Schäfer, *Chem. Ber.* **1993**, *126*, 1623–1630; c) J. Utley, *Chem. Soc. Rev.* **1997**, *26*, 157–167; d) K. D. Moeller, *Tetrahedron* **2000**, *56*, 9527–9554; e) H. Lund, *J. Electrochem. Soc.* **2002**, *149*, 21–33.

[3] a) G. W. Morrow, in: *Organic Electrochemistry*, 4th edn., (Eds.: H. Lund, O. Hammerich), Marcel Dekker, New York, **2001**. For reviews, see: b) J. B. Sperry, D. L. Wright, *Chem. Soc. Rev.* **2006**, *35*, 605–621; c) J. Yoshida, K. Kataoka, R. Horcajada, A. Nagaki, *Chem. Rev.* **2008**, *108*, 2265–2299; d) B. A. Frontana-Uribe, R. D. Little, J. G. Ibanez, A. Palma, R. Vasquez-Medrano, *Green Chem.* **2010**, *12*, 2099–2119.

[4] For examples, see: a) G. Hilt, K. I. Smolko, *Angew. Chem.* **2001**, *113*, 3514–3516; *Angew. Chem. Int. Ed.* **2001**, *40*, 3399–3402; b) G. Hilt, *Angew. Chem.* **2003**, *115*, 1760–1762; *Angew. Chem. Int. Ed.* **2003**, *42*, 1720–1721; c) B. H. Nguyen, A. Redden, K. D. Moeller, *Green Chem.* **2014**, *16*, 69–72; d) A. Kirste, B. Elsler, G. Schnakenburg, S. R. Waldvogel, *J. Am. Chem. Soc.* **2012**, *134*, 3571–3576; e) W.-C. Li, C.-C. Zeng, L.-M. Hu, H.-Y. Tian, R. D. Little, *Adv. Synth. Catal.* **2013**, *355*, 2884–2890; f) B. Elsler, D. Schollmeyer, K. M. Dyballa, R. Franke, S. R. Waldvogel, *Angew. Chem.* **2014**, *126*, 5079, *Angew. Chem. Int. Ed.* **2014**, *53*, 5210–5213; g) K. Xu, Z. Zhang, P. Qian, Z. Zha, Z. Wang, *Chem. Commun.* **2015**, *51*, 11108–11111.

[5] a) Y. Bansal, O. Silakari, *Bioorg. Med. Chem.* **2012**, *20*, 6208–6236; b) P. Singla, V. Luxami, K. Paul, *RSC Adv.* **2014**, *4*, 12422–12440.

[6] a) A. Correa, O. G. Mancheño, C. Bolm, *Chem. Soc. Rev.* **2008**, *37*, 1108–1117; b) X. Shi, J. Guo, J. Liu, M. Ye, Q. Xu, *Chem. Eur. J.* **2015**, *21*, 9988–9993, and references cited therein.

[7] J. Liu, Q. Liu, H. Yi, C. Qin, R. Bai, X. Qi, Y. A.-W. Lei, *Angew. Chem.* **2014**, *126*, 512–516; *Angew. Chem. Int. Ed.* **2014**, *53*, 502–506.

[8] a) J.-M. Huang, X.-X. Wang, Y. Dong, *Angew. Chem.* **2011**, *123*, 954–957; *Angew. Chem. Int. Ed.* **2011**, *50*, 924–927; b) J.-M. Huang, Z.-Q. Lin, D.-S. Chen, *Org. Lett.* **2012**, *14*, 22–25; c) J.-M. Huang, Y. Dong, *Chem. Commun.* **2009**, 3943–3945; d) J.-M. Huang, H.-R. Ren, *Chem. Commun.* **2010**, *46*, 2286–2288; e) H.-L. Qi, D.-S. Chen, J.-S. Ye, J.-M. Huang, *J. Org. Chem.* **2013**, *78*, 7482–7487; f) W.-B. Wu, J.-M. Huang, *J. Org. Chem.* **2014**, *79*, 10189–10195; g) W.-B. Wu, M.-L. Li, J.-M. Huang, *Tetrahedron Lett.* **2015**, *56*, 1520–1523.

[9] Y.-S. Lee, Y.-H. Cho, S. Lee, J.-K. Bin, J. Yang, G. Chae, C.-H. Cheon, *Tetrahedron* **2015**, *71*, 532–538.

[10] No homo-coupling product was detected at all experiments done during the optimization study (Table 1) and screening of the substrate scope (Table 2).

[11] I. Y. Sapurina, J. Stejskal, *Russ. J. Gen. Chem.* **2012**, *82*, 256- 275.

[12] a) Z.-J. Cai, S.-Y. Wang, S.-J. Ji, *Org. Lett.* **2012**, *14*, 6068–6071; b) H.-Q. Luo, W. Dong, T.-P. Loh, *Tetrahedron Lett.* **2013**, *54*, 2833–2836; c) I. Thomé, C. Besson, T. Kleine, C. Bolm, *Angew. Chem.* **2013**, *125*, 7657–7661; *Angew. Chem. Int. Ed.* **2013**, *52*, 7509–7513; d) S. R. Waldvogel, S. Möhle, *Angew. Chem.* **2015**, *127*, 6496–6497; *Angew. Chem. Int. Ed.* **2015**, *54*, 6398–6400.

[13] The pH value of the reaction mixture was 8.5. In the presence of *ortho*-phenylenediamine and $(i\text{-Pr})_2$NEt, α-keto acid was converted to α-keto acid anion which was more easily oxidized to form radical **5**.

[14] Formation of *N,N*-diisopropylamine which was oxidized from $(i\text{-Pr})_2$NEt was observed in the reaction system after the reaction. On the other hand, it was also proposed that a hemi-aminal carbon radical could undergo an electron transfer followed by protonation to form **7** as a minor process; a) G. Pandey, P. Y. Reddy, U. T. Bhalerao, *Tetrahedron Lett.* **1991**, *32*, 5147–5150; b) Y. Yoshimi, T. Itou, M. Hatanaka, *Chem. Commun.* **2007**, 5244–5246; c) J. M. R. Narayanam, J. W. Tucker, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2009**, *131*, 8756–8875; d) J. M. Allen, T. H. Lambert, *J. Am. Chem. Soc.* **2011**, *133*, 1260–1262; e) J. Du, L. R. Espelt, I. A. Guzei, T. P. Yoon, *Chem. Sci.* **2011**, *2*, 2115–2119; f) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322–5363; g) J. D. Griffin, M. A. Zeller, D. A. Nicewicz, *J. Am. Chem. Soc.* **2015**, *137*, 11340–11348.

[15] a) J. E. Baldwin, R. M. Adlington, J. C. Bottaro, J. N. Kolhe, M. W. D. Perry, A. U. Jain, *Tetrahedron* **1986**, *42*, 4223–4234; b) M. F. Aly, R. Grigg, *Tetrahedron* **1988**, *44*, 7271–7282; c) J. W. Bode, R. M. Fox, K. D. Baucom, *Angew. Chem.* **2006**, *118*, 1270–1274; *Angew. Chem. Int. Ed.* **2006**, *45*, 1248–1252; d) C.-C. Cho, J.-N. Liu, C.-H. Chien, J.-J. Shie, Y.-C. Chen, J.-M. Fang, *J. Org. Chem.* **2009**, *74*, 1549–1556; e) F. B. Song, L. J. Gooßen, *Adv. Synth. Catal.* **2011**, *353*, 337–342.

[16] a) D. Xue, Y.-Q. Long, *J. Org. Chem.* **2014**, *79*, 4727–4734; b) T. B. Nguyen, J. L. Bescont, L. Ermolenko, A. Al-Mourabit, *Org. Lett.* **2013**, *15*, 6218–6221; c) R.-G. Xing, Y.-N. Li, Q. Liu, Q.-Y. Meng, J. Li, X.-X. Shen, Z. Liu, B. Zhou, X. Yao, Z.-L. Liu, *Eur. J. Org. Chem.* **2010**, *34*, 6627–6632; d) B. Yu, H. Zhang, Y. Zhao, S. Chen, J. Xu, C. Huang, Z. Liu, *Green Chem.* **2013**, *15*, 95–99; e) C. Mukhopadhyay, S. Ghosh, S. Sengupta, S. De, *RSC Adv.* **2011**, *1*, 1033–1037; f) X. Diao, Y. Wang, Y. Jiang, D. Ma, *J. Org. Chem.* **2009**, *74*, 7974–7977; g) Y. Sun, H. Jiang, W. Wu, W. Zeng, X. Wu, *Org. Lett.* **2013**, *15*, 1598–1601; h) M. Bala, P. K. Verma, U. Sharma, N. Kumarb, B. Singh, *Green Chem.* **2013**, *15*, 1687–1693; i) M. S. Mayo, X. Yu, X. Zhou, X. Feng, Y. Yamamoto, M. Bao, *Org. Lett.* **2014**, *16*, 764–767; j) Y. Cheng, Q. Peng, W. Fan, P. Li, *J. Org. Chem.* **2014**, *79*, 5812–5819.

