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Note

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Multifunctionalization of Unactivated Cyclic Ketones via an Electrochemical Process: Access to Cyclic α-Enaminones

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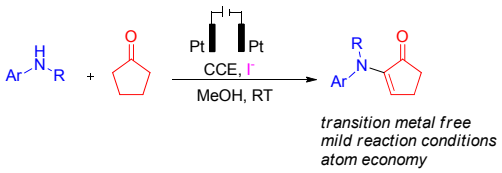
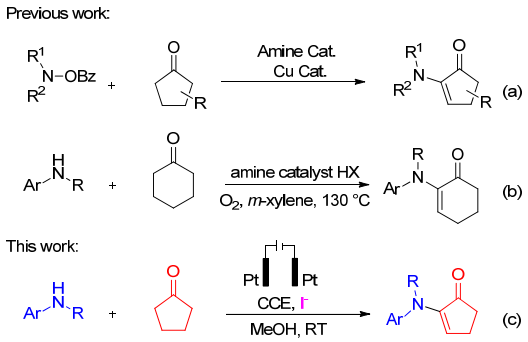


ABSTRACT: The multifunctionalization of unactivated cyclic ketones was developed via an electrochemically intermolecular α-amination under metal free conditions. The reaction can be carried out smoothly with a broad scope of the aromatic amines substrates under mild conditions, affording a variety of α-enaminones with good to excellent yields in one step.

α-Amino ketones are prevalent substructures, widely exist in biologically active natural products, biomolecules and therapeutic agents.[1] Since the extensive utility of the synthon, development of efficient and atom-economical method is a longstanding goal in organic synthesis.[2] Various methods have been developed for α-amination, mainly divided into two types: 1) transition metal catalyzed α-amination reaction,[3] 2) chemical oxidants under metal-free conditions.[4] Recently, significant progress was made in β-functionalization of unactivated cyclic ketones by MacMillan's group using cooperative organocatalysis and photoredox catalysis.[5] Despite the great achievement of monofunctionalization of unactivated cyclic ketones, direct multifunctionalization of cyclic ketones in one step are rarely studied. Fu's group reported multifunctionalization of unactivated ketones by employing *O*-benzoylhydroxylamines as both amination and oxidation reagents via a cooperative Cu and an organocatalyst to generate α-enaminone (Scheme 1a).[6] Zhao's group reported the acid/base co-catalyzed α-amination of cyclic ketones, in which dioxygen as an oxidant (Scheme 1b).[7] Although considerable progress has been made in α-amination reaction,[8] development of direct oxidative α-amination of ketones with different amines in the absence of metals and chemical oxidants remains challenging.



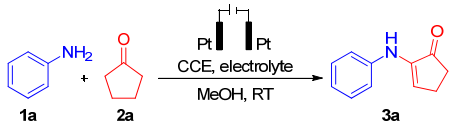
Scheme 1. Methods for the mono- and multi-functionalization of (cyclic) ketones.

Our group has been focusing on elegant electrochemical catalysis for a long time.[9] For instance, we synthesized benzoylhydrazines,[10] α-ketoamides,[11] α-enaminone[12] by virtue of electrochemistry. Herein, we report a directly intermolecular oxidative α-amination of cyclic ketone by virtue of electrochemistry under metal free conditions (Scheme 1c).

First of all, the reaction of aniline with cyclopentaone was employed as the model reaction. Initially, the reaction was conducted in an undivided cell with KI as electrolyte and EtOH as solvent at a constant current of 20 mA. To our delight, the desired product was obtained in 60% isolated yield (entry 1, Table 1), which encouraged us to optimize the reaction conditions further. First, different kinds of solvents were examined in this reaction (entries 1-6, Table 1). The experimental results indicated that the alcohol solvents favored the reaction and MeOH was the best choice, while other solvents could not promote the reaction, which can be ascribed to the conductivity of the solvent, the polarity of the solvent and the solubility of the reaction mixtures in the solvent (see page S3 of supporting information). Then various electrolytes were investigated. The experimental results showed that the iodide ion was necessary for the reaction, the reaction did not work without iodide ion (entries 7-12, Table 1). Among the different iodide salts, KI proved to be the optimal electrolyte for the reaction while the other iodide salts, such as $^{n}Bu_4NI$, Et_4NI, Me_4NI, NH_4I and NaI gave low electrolytic efficiency (entries 8-11, Table 1), which can be

ascribed to the good solubility and the high ion activity of KI in methanol (see page S3 of supporting information).

Table 1. Optimization of reaction conditions



Entry[a]	Electrode	Electrolyte	Solvent	Yield[b]
1	Pt|Pt	KI	EtOH	60 %
2	Pt|Pt	KI	MeOH	76 %
3	Pt|Pt	KI	DMF	n.d.
4	Pt|Pt	KI	DMSO	n.d.
5	Pt|Pt	KI	CH_3CN	n.d.
6	Pt|Pt	KI	CH_2Cl_2	n.d.
7	Pt|Pt	NaI	MeOH	63 %
8	Pt|Pt	Bu_4NI	MeOH	64 %
9	Pt|Pt	Et_4NI	MeOH	57 %
10	Pt|Pt	Me_4NI	MeOH	11 %
11	Pt|Pt	NH_4I	MeOH	trace
12	Pt|Pt	$LiClO_4$	MeOH	n.d.
13	C|Pt	KI	MeOH	55 %
14	Pt|C	KI	MeOH	31 %
15	C|C	KI	MeOH	17 %
16[c)]	Pt|M	KI	MeOH	< 40 %
17[d)]	Pt|Pt	KI	MeOH	43 %
18[e)]	Pt|Pt	KI	MeOH	50 %
19[f)]	Pt|Pt	KI	MeOH	76 %
20[g)]	Pt|Pt	KI	MeOH	73 %
21[h)]	Pt|Pt	KI	MeOH	69 %
22[i)]	Pt|Pt	KI	MeOH	86 %
23[j)]	Pt|Pt	KI	MeOH	58 %
24[k)]	Pt|Pt	KI	MeOH	87 %
25[l)]	Pt|Pt	KI	MeOH	65 %

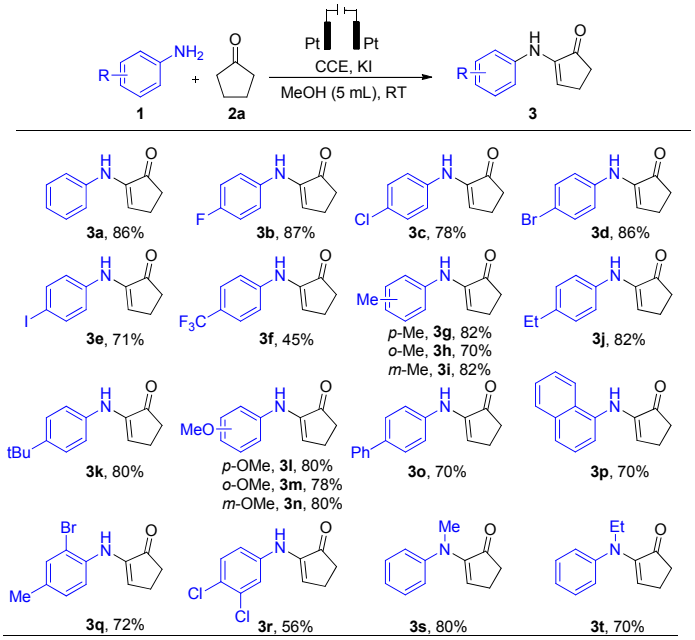
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), electrolyte (1.0 mmol), solvent (5 mL), two platinum electrodes, electrolyze at a constant current in an undivided cell at room temperature, CCE = constant current. [b] Isolated yield. [c] Metal electrode: Al , Ni, Cu. [d] I = 10 mA. [e] I = 30 mA. [f] I = 40 mA. [g] I = 50 mA. [h] I = 60 mA. [i] 0.1 M. [j] 0.2 M. [k] N_2 atmosphere. [l] O_2 atmosphere.

Subsequently, the different electrodes were studied in the reaction, including graphite, platinum, and other metal electrodes. Of them, the platinums gave the best result (entries 13-16, Table 1), which may due to its proper cell voltage. The current intensity was also optimized, 40 mA was turned out to be the best constant current (entries 17-21, Table 1). We also modulated the substrate concentration and ratio (entries 22-24, Table 1). It was found that 0.1 M of substrate concentration

gave the desired product with a higher yield. When the reaction was conducted under nitrogen atmosphere, the yield was slightly improved in comparison with the reaction under air (entries 24 and 22, Table 1). In contrast, the yield was decreased under oxygen atmosphere (entries 25, Table 1). Therefore, the optimal reaction conditions were established as follows: KI as electrolyte, MeOH as solvent, and the reaction being carried out at a constant current of 40 mA for 3 h with two platinum electrodes in an undivided cell at room temperature under air atmosphere.

Having established the optimal reaction conditions, the substrate scope of the reaction was investigated by evaluating a variety of aromatic amines and cyclic ketones under standard conditions. As shown in Table 2, the reaction proceeded smoothly with different aromatic amines to afford α-enaminones in moderate to good yields. The electronic effect of aromatic amines had a great influence on the reaction. Generally, the strong electron-withdrawing groups disfavoured the reaction. For example, the substrate 4-nitro-substituted aniline didn't work in the reaction. The moderate electron-withdrawing groups (CF_3, *di*-halide substitution) led to the decrease of the yield

Table 2. Scope of aromatic amines.[a, b]

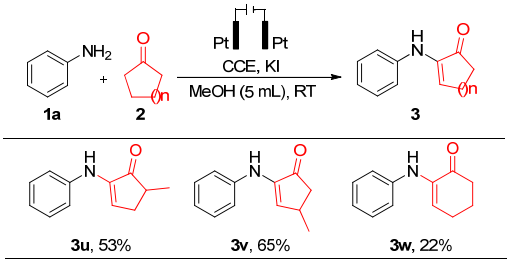


[a] Reaction conditions: **1** (0.5 mmol), **2a** (1.0 mmol), KI (1.0 mmol), MeOH (5 mL), two platinum electrodes, electrolyze at a constant current of 40 mA in an undivided cell at room temperature. [b] Isolated yield.

remarkably (**3f**, **3r**, Table 2), while the weak electron-withdrawing groups gave moderate to good yields under standard conditions (**3b-3e**, **3i**, **3n**, **3q**, Table 2). On the other hand, the steric effect had little effect on the reaction. For instance, the *ortho*-substituted methoxyl gave the cyclic α-enaminone **3l** with a similar yield in comparison with **3m, 3n**. Both electronic effect and steric effect influenced the yield of the corresponding substrate. Moreover, the aromatic secondary amines were also employed in the reaction to give **3s** and **3t** with moderate yields as long as there was no electron-withdrawing group on the amino substitution. Subsequently, the scope of cyclic ketones were also investigated, and the results were listed in Table 3. The cyclopentanone, substituted cyclopentanone and cyclohexane could be employed as the substrates to afford the corresponding α-enaminones with moderate yields. Nevertheless, indanone and other linear

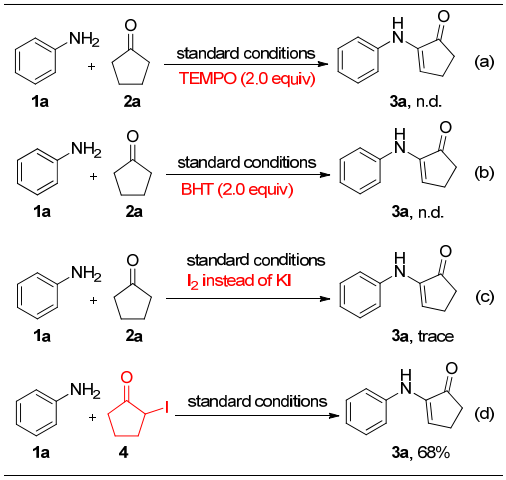
ketones didn't work in this reaction, perhaps due to the lower oxidation potential and poor nucleophility of iodo-ketones to amines (see the transformation of **4** to **6** in the Scheme 3).

Table 3. Scope of cyclic ketones.[a, b]



[a] Reaction conditions: **1a** (0.5 mmol), **2** (1.0 mmol), KI (1.0 mmol), MeOH (5 mL), two platinum electrodes, electrolyze at a constant current of 40 mA in an undivided cell at room temperature. [b] Isolated yield.

To understand the reaction mechanism, a series of control experiments were performed (Scheme 2). When the radical scavengers 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) were added to the reaction system respectively under standard conditions, the reaction was completely suppressed (Scheme 2a, 2b). This suggested that the reaction might go through a radical pathway. When 2.0 equivalent of molecular iodine was added instead of KI, we detected a trace amount of target product (Scheme 2c), which excluded that molecular iodine promoted the reaction. When 2-iodocyclopentanone **4** was employed as the coupling partner with aniline under standard conditions, the corresponding α-enaminone was obtained in 68% yield (Scheme 2d), which indicated that 2-iodocyclopentanone was likely to be the intermediate of the reaction.



Scheme 2. Control experiments.

To further study the reaction process, electron paramagnetic resonance (EPR) experiments were conducted to capture the possible free radicals involved in the reaction. As shown in Figure 1, a complicated spectra **a** was obtained in the presence of the radical trapper 5,5-dimethyl-1-proline-N-oxide (DMPO). Two signals were identified by the characteristic hyperfine constants for nitrogen and β-proton. One was assigned to be DMPO-**5** with the $A_{14}N$ =

15.6 G and A_1H = 22.6 G, g = 2.0046. Another signal can be ascribed to DMPO-OH and the hyperfine constants for nitrogen and proton were $A_{14}N = A_1H$ = 14.8 G, g = 2.0047. Spectra **c** and **d** were their corresponding simulations (DMPO-**5** and DMPO-OH), respectively (see page S2-S3 of supporting information). When we overlapped the spectra **c** and **d** with an intensity ratio of 5:1, the complicated spectra **b** were obtained, which was consistent with the experimental result **a**. Therefore, these results further provided evidence for a radical process in the reaction.

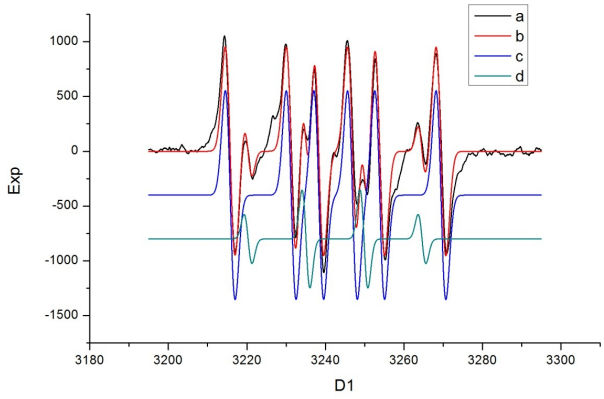
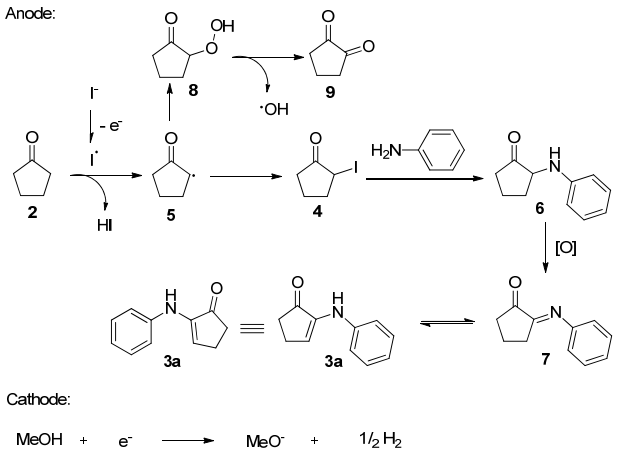


Figure 1. EPR spectra (X band, 9.7 GHz, room temperature) for reaction mixtures in the presence of the radical trapper DMPO and their simulations (**b-d**). (a) Spectrum **a** was the experimental spectrum. (b) Simulation of DMPO-**5** and DMPO-OH. (c) DMPO-**5**. (d) Simulation of DMPO-OH. (e) Overlapping of spectra **c** and **d** with an intensity ratio of 5:1 led to the complicated **b**, which was consistent with the experimental result **a**.

Based on the above experimental results and related reports, we proposed a possible mechanism (Scheme 3). Initially, the iodide anion is oxidized to be iodine free radical in the anode, and then reacts with cyclopentanone **2** to generate the radical **5**, which was captured by DMPO and the generated DMPO-**5** radical was detected by EPR, with the liberation of one molecule of HI. The radical coupling between radical **5** and iodine free radical yields 2-iodocyclopentanone **4**. At the same time, the radical **5** might be captured by oxygen molecular to give molecule **8**, which is unstable and easily transformed into **9**, accompanying the loss of hydroxyl radical. Subsequent nucleophilic attack of the intermediate **4** with aniline provides 2-(phenylamino)-cyclopentanone **6**, which undergoes anodic oxidation to form the intermediate 2-(phenylimino)-cyclopentanone **7**. Finally, the imine interconverts mainly to the target product α-enaminone **3a**. Simultaneously, methanol is reduced in the cathode to give methoxide and hydrogen gas.



Scheme 3. Plausible mechanism.

In summary, we developed an electrochemically oxidative α-amination of ketones to afford the α-enaminones from facile starting materials via cross-coupling between (sp^3) C-H/N-H under metal-free conditions. The reaction features atom economic efficiency and good functional tolerance. Additionally, the reaction intermediate was identified by EPR. Further studies will focus on other types of substrates and applications in organic synthesis.

Experimental Section

General Information: All products were characterized by ^{1}H NMR and $^{13}C\{^1H\}$ NMR, using TMS as an internal reference (^{1}H NMR: 400 MHz, $^{13}C\{^1H\}$ NMR: 100 MHz). The chemical shifts (δ) and coupling constants (*J*) were expressed in ppm and Hz, respectively. HRMS (ESI) were recorded on a Q-TOF Premier. Commercially available compounds were used without further purification. Solvents were purified according to the standard procedures unless otherwise noted.

Representative Experimental Procedures: A mixture of electrolyte (1.0 mmol), amine (0.5 mmol), cyclic ketone (1.0 mmol) and MeOH (5 mL) were added to an undivided cell (15 mL). The cell was equipped with platinum electrodes (1.5 cm × 1.5 cm × 0.3 cm) as both the anode and cathode. The reaction mixture was stirred and electrolyzed at a constant current of 40 mA at room temperature for corresponding time. The reaction was monitored by TLC. When the reaction was finished, the solvent was removed with a rotary evaporator. The residue was purified by column chromatography on silica gel to afford the desired product.

EPR measurements and simulations for the capture of radicals:

An undivided cell was equipped with a magnet stirrer, two platinum electrodes (1.5 cm × 1.5 cm × 0.3 cm) as both the working electrode and the counter electrode, respectively. A mixture of electrolyte (1.0 mmol), amine (0.5 mmol), cyclic ketone (1.0 mmol) and MeOH (5 mL) were added to an undivided cell (15 mL). The cell was equipped with platinum electrodes (1.5 cm × 1.5 cm × 0.3 cm) as both the anode and cathode. The reaction mixture was stirred and electrolyzed at a constant current of 40 mA at room temperature for 30 min. A 0.05 mL reaction solution was taken out into a small tube and mixed well with 0.03 mL of DMPO aqueous solution. Then the mixture was quick-frozen with liquid nitrogen and measured by EPR at room temperature. EPR simulation was performed with EasySpin software package in Mathlab. The simulation parameters were microwave frequency 9.097 GHz, g-2.0047 (without calibration). The hyperfine constants

were shown in the main text.

2-(phenylamino)cyclopent-2-enone (**3a**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 74.5 mg, 86% yield; mp = 110-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.31-7.27 (m, 2H), 7.04-7.02 (m, 2H), 6.94-6.91 (m, 1H), 6.75 (s, 1H), 6.24 (br, 1H), 2.65 (t, J = 3.8 Hz, 2H), 2.47 (t, J = 4.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.8, 142.1, 140.2, 129.6, 124.8, 120.7, 116.6, 32.6, 24.2. HRMS (ESI) calcd for $C_{11}H_{12}NO$ $[M + H]^+$ 174.0919, found 174.0915.

2-((4-fluorophenyl)amino)cyclopent-2-enone (**3b**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 83.2 mg, 87% yield; mp = 123-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.00-6.99 (m, 4H), 6.65 (t, J = 3.2 Hz, 1H), 6.13 (br, 1H), 2.65-2.62 (m, 2H), 2.49-2.46 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.7, 158.6, 140.6, 138.0 (d, $^{3}J_{C\text{-}F}$ = 10.4 Hz), 123.9, 118.3 (d, $^{2}J_{C\text{-}F}$ = 30.0 Hz), 116.1 (d, $^{1}J_{C\text{-}F}$ = 89.2 Hz), 32.6, 23.9. Decoupling ^{19}F NMR (377 MHz, $CDCl_3$, ppm): -122.5. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): -122.5 (m, J = 6.6 Hz). HRMS (ESI) calcd for $C_{11}H_{11}FNO$ $[M + H]^+$ 192.0825, found 192.0821.

2-((4-chlorophenyl)amino)cyclopent-2-enone (**3c**). The compound was prepared according to the general procedure (3.5 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 80.9 mg, 78% yield; mp = 156-157 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.26-7.23 (m, 2H), 6.97-6.95 (m, 2H), 6.70 (t, J = 2.6 Hz, 1H), 6.23 (br, 1H), 2.66-2.64 (m, 2H), 2.48 (t, J = 3.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.5, 140.4, 139.5, 129.3, 125.7, 125.1, 117.9, 32.6, 24.1. HRMS (ESI) calcd for $C_{11}H_{11}ClNO$ $[M + H]^+$ 208.0529, found 208.0522.

2-((4-bromophenyl)amino)cyclopent-2-enone (**3d**). The compound was prepared according to the general procedure (3.5 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 108.1 mg, 86% yield; mp = 156-157 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.39-7.37 (m, 2H), 6.92-6.90 (m, 2H), 6.70 (t, J = 3.0 Hz, 1H), 6.23 (br, 1H), 2.66-2.65 (m, 2H), 2.47 (t, J = 4.2 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.6, 140.8, 139.9, 132.4, 125.3, 118.1, 113.0, 32.1, 24.2. HRMS (ESI) calcd for $C_{11}H_{11}BrNO$ $[M + H]^+$ 252.0024, found 252.0020.

2-((4-iodophenyl)amino)cyclopent-2-enone (**3e**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 106.2 mg, 71% yield; mp = 157-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.56-7.54 (m, 2H), 6.82-6.79 (m, 2H), 6.70 (t, J = 3.0 Hz, 1H), 6.24 (br, 1H), 2.66-2.65 (m, 2H), 2.48-2.46 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.5, 141.5, 139.7, 138.2, 125.5, 118.6, 82.6, 32.4, 24.1. HRMS (ESI) calcd for $C_{11}H_{11}INO$ $[M + H]^+$ 299.9885, found 299.9901.

2-((4-(trifluoromethyl)phenyl)amino)cyclopent-2-enone (**3f**). The compound was prepared

according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 53.8 mg, 45% yield; mp = 144-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.54-7.52 (m, 2H), 7.08-7.06 (m, 2H), 6.83 (t, *J* = 3.2 Hz, 1H), 6.47 (br, 1H), 2.71-2.68 (m, 2H), 2.51-2.48 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.4, 144.6, 139.3, 126.8 (q, $^{2}J_{C\text{-}F}$ = 14.9 Hz), 124.5, 122.7 (q, $^{1}J_{C\text{-}F}$ = 130.2 Hz), 115.8, 114.5, 32.3, 24.2. Decoupling ^{19}F NMR (377 MHz, $CDCl_3$, ppm): -61.6. ^{19}F NMR (377 MHz, $CDCl_3$, ppm): -61.6. HRMS (ESI) calcd for $C_{12}H_{11}F_3NO$ $[M + H]^+$ 242.0793, found 242.0796.

2-(p-tolylamino)cyclopent-2-enone (**3g**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 77.1 mg, 82% yield; mp = 115-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.11-7.09 (m, 2H), 6.96-6.92 (m, 2H), 6.67 (t, *J* = 3.3 Hz, 1H), 2.65-2.62 (m, 2H), 2.48-2.45 (m, 2H), 2.29 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.9, 140.5, 139.3, 130.5, 129.9, 124.0, 116.9, 32.6, 24.0, 20.7. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M + H]^+$ 188.1075, found 188.1075.

2-(o-tolylamino)cyclopent-2-enone (**3h**). The compound was prepared according to the general procedure (4 h) and purified by column chromatography (PE/EA = 30/1) to give the product as yellow oil: 65.5 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.25-7.16 (m, 3H), 6.88 (t, *J* = 7.1 Hz, 1H), 6.67 (m, 1H), 6.05 (br, 1H), 2.65-2.64 (m, 2H), 2.50-2.48 (m, 2H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.8, 140.3, 139.8, 130.8, 126.8, 126.1, 124.5, 121.1, 115.8, 32.5, 23.9, 17.5. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M + H]^+$ 188.1075, found 188.1074.

2-(m-tolylamino)cyclopent-2-enone (**3i**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 76.8 mg, 82% yield; mp = 89-90 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.20-7.16 (m, 1H), 6.86-6.84 (m, 2H), 6.76-6.73 (m, 2H), 6.19 (br, 1H), 2.66-2.63 (m, 2H), 2.48-2.45 (m, 2H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.8, 141.8, 140.2, 139.3, 129.3, 124.6, 121.8, 117.5, 113.8, 32.5, 24.0, 21.7. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M + H]^+$ 188.1075, found 188.1072.

2-((4-ethylphenyl)amino)cyclopent-2-enone (**3j**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 82.7 mg, 82% yield; mp = 83-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.14-7.11 (m, 2H), 6.98-6.95 (m, 2H), 6.69 (t, *J* = 3.3 Hz, 1H), 6.15 (br, 1H), 2.65-2.56 (m, 4H), 3.48-2.45 (m, 2H), 1.21 (t, *J* = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.1, 140.4, 139.4, 136.9, 128.6, 123.9, 116.8, 32.4, 28.1, 23.9, 15.7. HRMS (ESI) calcd for $C_{13}H_{16}NO$ $[M + H]^+$ 202.1232, found 202.1232.

2-((4-(tert-butyl)phenyl)amino)cyclopent-2-enone (**3k**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 119.7 mg, 80% yield; mp = 103-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.33-7.30 (m, 2H), 7.00-6.97 (m, 2H), 6.70 (t, *J* = 3.3 Hz, 1H), 6.16 (br, 1H), 2.65-2.62 (m, 2H), 2.48-2.46 (m, 2H), 1.30 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.9, 143.8, 140.4, 139.3, 126.2, 124.0, 116.5, 34.2, 32.5, 31.5, 24.0. HRMS (ESI) calcd for $C_{15}H_{20}NO$ $[M + H]^+$

230.1545, found 230.1543.

2-((4-methoxyphenyl)amino)cyclopent-2-enone (**3l**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 81.3 mg, 80% yield; mp = 90-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.01-6.97 (m, 2H), 6.88-6.84 (m, 2H), 6.59 (t, *J* = 3.3 Hz, 1H), 6.00 (br, 1H), 3.78 (s, 3H), 2.63-2.60 (m, 2H), 2.48-2.46 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.8, 154.4, 141.2, 135.4, 123.0, 118.8, 114.8, 55.7, 32.7, 23.9. HRMS (ESI) calcd for $C_{12}H_{14}NO_2$ $[M + H]^+$ 204.1025, found 204.1021.

2-((2-methoxyphenyl)amino)cyclopent-2-enone (**3m**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a white solid: 79.3 mg, 78% yield; mp = 84-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.21-7.19 (m, 1H), 6.95-6.91 (m, 1H), 6.88-6.85 (m, 2H), 6.76 (t, *J* = 3.3 Hz, 1H), 3.88 (s, 3H), 2.67-2.64 (m, 2H), 2.48-2.46 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.9, 148.1, 139.9, 131.6, 124.6, 120.8, 120.3, 114.2, 110.2, 55.6, 32.4, 24.1. HRMS (ESI) calcd for $C_{12}H_{14}NO_2$ $[M + H]^+$ 204.1025, found 204.1020.

2-((3-methoxyphenyl)amino)cyclopent-2-enone (**3n**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a white solid: 80.9 mg, 80% yield; mp = 91-93 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.21-7.17 (m, 1H), 6.76-6.74 (m, 1H), 6.64-6.59 (m, 2H), 6.49-6.47 (m, 1H), 6.24 (br, 1H), 3.80 (s, 3H), 2.66-2.63 (m, 2H), 2.48-2.45 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.7, 160.7, 143.0, 140.0, 130.2, 125.2, 109.4, 106.1, 102.8, 55.3, 32.4, 24.1. HRMS (ESI) calcd for $C_{12}H_{14}NO_2$ $[M + H]^+$ 204.1025, found 204.1022.

2-([1, 1'-biphenyl]-4-ylamino)cyclopent-2-enone (**3o**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 87.8 mg, 70% yield; mp = 205-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.57-7.53 (m, 4H), 7.44-7.40 (m, 2H), 7.32-7.28 (m, 1H), 7.12-7.10 (m, 2H), 6.79 (m, 1H), 6.31 (br, 1H), 2.69-2.68 (m, 2H), 2.50-2.48 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.8, 141.1, 140.7, 140.1, 133.8, 128.9, 128.1, 126.8, 126.7, 125.0, 116.9, 32.5, 24.1. HRMS (ESI) calcd for $C_{17}H_{16}NO$ $[M + H]^+$ 250.1232, found 250.1230.

2-(naphthalen-1-ylamino)cyclopent-2-enone (**3p**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a yellow solid: 78.1 mg, 70% yield; mp = 89-91 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 8.01-7.98 (m, 1H), 7.86-7.84 (m, 1H), 7.54-7.48 (m, 3H), 7.44-7.40 (m, 1H), 7.33-7.31 (m, 1H), 6.73 (br, 1H), 6.70 (t, *J* = 3.2 Hz, 1H), 2.68-2.66 (m, 2H), 2.55-2.53 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.9, 141.0, 137.1, 134.5, 128.7, 126.3, 125.9, 125.9, 125.9, 125.5, 122.1, 120.9, 112.8, 32.8, 24.0. HRMS (ESI) calcd for $C_{15}H_{14}NO$ $[M + H]^+$ 224.1075, found 224.1073.

2-((2-bromo-4-methylphenyl)amino)cyclopent-2-enone (**3q**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1)

to give the product as a yellow solid: 95.8 mg, 72% yield; mp = 112-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.36 (s, 1H), 7.18-7.16 (m, 1H), 7.07-7.05 (m, 1H), 6.70 (m, 1H), 6.66 (br, 1H), 2.65-2.64 (m, 2H), 2.49-2.47 (m, 2H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.4, 140.1, 136.9, 133.5, 131.6, 128.9, 125.0, 116.2, 112.7, 32.5, 24.1, 20.4. HRMS (ESI) calcd for $C_{12}H_{13}BrNO$ $[M + H]^+$ 266.0181, found 266.0184.

2-((3, 4-dichlorophenyl)amino)cyclopent-2-enone (**3r**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as a white solid: 67.8 mg, 56% yield; mp = 147-148 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.31 (d, J = 8.7 Hz, 1H), 7.14 (s, 1H), 6.84 (d, J = 8.7 Hz, 1H), 6.74-6.73 (m, 1 H), 6.26 (br, 1H), 2.68-2.67 (m, 2H), 2.48 (t, J = 4.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.3, 141.3, 139.5, 133.1, 130.9, 126.1, 123.7, 117.7, 116.2, 32.3, 24.1. HRMS (ESI) calcd for $C_{11}H_{10}Cl_2NO$ $[M + H]^+$ 242.0139, found 242.0158.

2-(methyl(phenyl)amino)cyclopent-2-enone (**3s**). The compound was prepared according to the general procedure (3 h) and purified by column chromatography (PE/EA = 30/1) to give the product as yellow oil: 74.9 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.27-7.23 (m, 2H), 6.97-6.92 (m, 3H), 6.83-6.82 (m, 1H), 3.19 (s, 3H), 2.61-2.60 (m, 2H), 2.50-2.48 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.7, 149.1, 147.7, 140.0, 128.9, 121.9, 120.0, 39.6, 34.8, 23.7. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M + H]^+$ 188.1075, found 188.1071.

2-(ethyl(phenyl)amino)cyclopent-2-enone (**3t**). The compound was prepared according to the general procedure (4 h) and purified by column chromatography (PE/EA = 30/1) (PE:EtOAc, 30/1) to give the product as yellow oil: 70.4 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.26-7.21 (m, 2H), 6.97-6.90 (m, 2H), 6.79-6.78 (m, 1H), 3.70-3.65 (m, 2H), 2.61-2.58 (m, 2H), 2.48-2.45 (m, 2H), 1.14 (t, J = 8.0 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 205.0, 147.8, 146.3, 139.1, 128.9, 122.0, 121.0, 46.2, 34.9, 23.8, 12.6. HRMS (ESI) calcd for $C_{13}H_{16}NO$ $[M + H]^+$ 202.1232, found 202.1233.

5-methyl-2-(phenylamino)cyclopent-2-enone (**3u**). The compound was prepared according to the general procedure (4 h) and purified by column chromatography (PE/EA = 30/1) to give the product as yellow oil: 49.6 mg, 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.32-7.26 (m, 2H), 7.05-7.02 (m, 2H), 6.94-6.90 (m, 1H), 6.21 (br, 1H), 2.94-2.87 (m, 1H), 2.50-2.43 (m, 1H), 2.26-2.20 (m, 1H), 1.24 (d, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 207.4, 141.8, 139.0, 129.4, 123.2, 120.9, 116.7, 38.0, 33.4, 16.5. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M + H]^+$ 188.1075, found 188.1070.

4-methyl-2-(phenylamino)cyclopent-2-enone (**3v**). The compound was prepared according to the general procedure (4 h) and purified by column chromatography (PE/EA = 30/1) to give the product as yellow oil: 60.8 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.31-7.27 (m, 2H), 7.04-7.01 (m, 2H), 6.94-6.90 (m, 1H), 6.52 (d, J = 3.0 Hz, 1H), 6.18 (br, 1H), 3.01-2.96 (m, 1H), 2.73-2.67 (m, 1H), 2.03-1.98 (m, 1H), 1.22 (d, J = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm): 204.6, 141.7, 139.3, 130.5, 129.4, 120.9, 116.7, 41.2, 31.3, 21.8. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M + H]^+$ 188.1075, found 188.1074.

2-(phenylamino)cyclohex-2-enone (**3w**)[7]. The compound was prepared according to the general procedure (4 h) and purified by column chromatography (PE/EA = 30/1) to give the product as yellow oil: 20.1 mg, 22% yield. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.27-7.23 (m, 1H), 7.03-7.01 (m, 2H), 6.92-6.88 (m, 1H), 6.41 (t, J = 4.7 Hz, 1H), 2.55 (t, J = 6.6 Hz, 2H), 2.45 (q, J = 5.5 Hz, 2H), 2.05-1.98 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm): 195.7, 142.0, 136.4, 129.3, 121.2, 118.7, 116.5, 37.8, 24.7, 23.0.

ASSOCIATED CONTENT

^{1}H NMR and $^{13}C\{^{1}H\}$ NMR spectra for all the products (PDF)

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Notes

The authors declare no competing financial interest.

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References

[1] (a) Carrol, F. I.; Blough, B. E.; Abraham , P.; Mills, A. C.; Holleman, J. A.; Wolchenhauer, S. A.; Decker, A. M.; Landavazo, A. K.; McElroy, T.; Navarro, H. A.; Gatch, M. B.; Forster, M. J. Synthesis and Biological Evaluation of Bupropion Analogues as Potential Pharmacotherapies for Cocaine Addiction. *J. Med. Chem.* **2009**, *52*, 6768. (b) Meltzer, P. C.; Butler, D.; Deschamps, J. R.; Madras, B. K. 1-(4-Methylphenyl)-2-pyrrolidin-1-yl-pentan-1-one (Pyrovalerone) Analogues: A Promising Class of Monoamine Uptake Inhibitors. *J. Med. Chem.* **2006**, *49*, 1420. (c) Meyers, M. C.; Wang, J.; lera, J. A.; Bang, J. K.; Hara, T.; Saito, S.; Zambetti, G. P.; Appella, D. H. A New Family of Small Molecules to Probe the Reactivation

of Mutant p53. *J. Am. Chem. Soc.* **2005**, *127*, 6152. (d) Pettit, G. R.; Moser, B. R.; Mendonca, R. F.; Knight, J. C.; Hogan, F. The Cephalostatins. 22. Synthesis of Bis-steroidal Pyrazine Pyrones. *J. Nat. Prod.* **2012**, *75*, 1063. (e) Bouteiller, C.; Becerril-Ortega, J.; Marchand, P.; Nicole, O.; Barre, L.; Buisson, A.; Perrio, C. Copper-catalyzed amination of (bromophenyl)ethanolamine for a concise synthesis of aniline-containing analogues of NMDA NR2B antagonist ifenprodil. *Org. Biomol. Chem,* **2010**, *8*, 1111.

[2] For reviews, see: (a) Stevenazzi, A.; Marchini, M.; Sandrone, G.; Vergani, B.; Lattanzio, M. Amino acidic scaffolds bearing unnatural side chains: An old idea generates new and versatile tools for the life sciences. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5349. (b) Vogt, H.; Brase, S. Recent approaches towards the asymmetric synthesis of α, α-disubstituted α-amino acids. *Org. Biomol. Chem.* **2007**, *5*, 406. (c) Perdih, A.; Sollner Dolenc, M. Recent Advances in the Synthesis of Unnatural α-Amino Acids. *Curr. Org. Chem.* **2007**, *11*, 801.

[3] (a) Smith, A. M. R.; Hii, K. K. Transition Metal Catalyzed Enantioselective α-Heterofunctionalization of Carbonyl Compounds. *Chem. Rev.* **2011**, *111*, 1637. (b) Maji, B.; Yamamoto, H. Use of In Situ Generated Nitrosocarbonyl Compounds in Catalytic Asymmetric α-Hydroxylation and α-Amination Reactions. *Bull. Chem. Soc. Jpn.* **2015**, *88*, 753. (c) Janey, J. M. Fortschritte bei katalytischen enantioselektiven α-Aminierungen und α-Oxygenierungen von Carbonylverbindungen. *Angew. Chem.* **2005**, *117*, 4364. (d) Tokumasu, K.; Yazaki, R.; Ohshima, T. Direct Catalytic Chemoselective α-Amination of Acylpyrazoles: A Concise Route to Unnatural α-Amino Acid Derivatives. *J. Am. Chem. Soc.* **2016**, *138*, 2664. (e) Xu, C.; Zhang, L.; Luo, S. Merging Aerobic Oxidation and Enamine Catalysis in the Asymmetric α-Amination of β-Ketocarbonyls Using N-Hydroxycarbamates as Nitrogen Sources. *Angew. Chem.* **2014**, *126*, 4233. (f) Baidya, M.; Griffin, K. A.; Yamamoto, H. Direct Catalytic Chemoselective α-Amination of Acylpyrazoles: A Concise Route to Unnatural α-Amino Acid Derivatives. *J. Am. Chem. Soc.* **2012**, *134*, 18566. (g) Liu, X. X.; Wu, Z. Y.; He, Y. Q.; Zhou, X. Q.; Hu, T.; Ma, C. W.; Huang, G. S. Copper-Catalyzed C-N Bond Formation *via* Oxidative Cross Coupling of Amines with α-Aminocarbonyl Compounds. *Adv. Synth. Catal,* **2016**, *358*, 2385. (h) Murru, S.; Lott, C. S.; Fronczek, F. R.; Srivastava, R. S. Fe-Catalyzed Direct α C−H Amination of Carbonyl Compounds. *Org. Lett.* **2015**, *17*, 2122. (i) Jiang, Q.; Xu, B.; Zhao, A.; Jia, J.; Liu, T.; Guo, C. Transition-Metal-Free Oxidative α C−H Amination of Ketones via a Radical Mechanism: Mild Synthesis of α-Amino Ketones. *J. Org. Chem.* **2014**, *79*, 8750.

[4] (a) Zhou, F.; Liao, F. M.; Yu, J. S.; Zhou, J. Catalytic Asymmetric Electrophilic Amination Reactions To Form NitrogenBearing Tetrasubstituted Carbon Stereocenters. *Synthesis*. **2014**, *46*, 2983. (b) Vilaivan, T.; Bhanthumnavin, W. Organocatalyzed Asymmetric α-Oxidation, α-Aminoxylation and α-Amination of Carbonyl Compounds. *Molecules*. **2010**, *15*, 917. (c) Yang, X.; Toste, F. D. Direct Asymmetric Amination of α-Branched Cyclic Ketones Catalyzed by a Chiral Phosphoric Acid. *J. Am. Chem. Soc.* **2015**, *137*, 3205. (d) Shang, M.; Wang, X.; Koo, S. M.; Youn, J.; Chan, J. Z.; Yao, W.; Hastings, B. T.; Wasa, M. Frustrated Lewis Acid/Brønsted Base Catalysts for Direct Enantioselective α-Amination of Carbonyl Compounds. *J. Am. Chem. Soc.* **2017**, *139*, 95. (e) Tian, J. S.; Ng, K. W. J.; Wong, J. R.; Loh, T. P. α-Amination of Aldehydes Catalyzed by In Situ Generated Hypoiodite. *Angew. Chem.* **2012**, *124*, 9239. (f) Lv, Y.; Li, Y.; Xiong, T.; Lu, Y.; Liu, Q.; Zhang, Q. nBu_4NI-Catalyzed oxidative imidation of ketones with imides: synthesis of α-amino ketones. *Chem. Commun.* **2014**, *50*, 2367. (g) Jiang, Q.; Xu, B.; Zhao, A.; Jia, J.; Liu, T.; Guo, C. Transition-Metal-Free Oxidative α-C−H Amination of Ketones via a Radical Mechanism: Mild Synthesis of α-Amino Ketones. *J. Org. Chem.* **2014**, *79*, 8750. (h) Jia, W. G.; Li, D. D.; Dai, Y. C.; Zhang, H.; Yan, L. Q.; Sheng, E. H.; Wei, Y.; Mu, X. L.; Huang, K. W. Synthesis and characterization of bisoxazolinesand pybox-copper (II) complexes and their application in the coupling of α-carbonyls with functionalized amines. *Org. Biomol. Chem.* **2014**, *12*, 5509.

[5] (a) Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D. W. C. Photoredox Activation for the Direct β-Arylation of Ketones and Aldehydes. *Science*. **2013**, *339*, 1593. (b) Petronijevic, F. R.; Nappi, M.; MacMillan, D. W. Direct β-Functionalization of Cyclic Ketones with Aryl Ketones via the Merger of Photoredox and Organocatalysis. *J. Am. Chem. Soc.* **2013**, *135*, 18323. (c) Jeffrey, J. L.; Petronijevic, F. R.; MacMillan, D. W. C. Selective Radical-Radical Cross-Couplings: Design of a Formal β-Mannich Reaction. *J. Am. Chem. Soc.* **2015**, *137*, 8404. For some other examples for direct functionalization of cyclic ketones, see: (d) Huang, Z.; Dong, G. Catalytic Direct β-Arylation of Simple Ketones with Aryl Iodides. *J. Am. Chem. Soc.* **2013**, *135*, 17747. (e) Okada, M.; Fukuyama, T.; Yamada, K.; Ryu, I.; Ravelli,

D. Fagnoni, M. Sunlight photocatalyzed regioselective β-alkylation and acylation of cyclopentanones. *Chem. Sci.* **2014**, *5*, 2893.

[6] Li, Y.; Zhang, R.; Bi, X. H.; & Fu, J. K. Multifunctionalization of Unactivated Cyclic Ketones via Synergistic Catalysis of Copper and Diarylamine: Access to Cyclic α-Enaminone. *Org. Lett*. **2018**, *20*, 1207-1211.

[7] Li, Y. J.; Zhang, L.; Yan, N.; Meng, X. H.; Zhao, Y. L. Acid/Base-Co-catalyzed Direct Oxidative α-Amination of Cyclic Ketones: Using Molecular Oxygen as the Oxidant. *Adv. Synth. Catal*. **2018**, *360*, 455.

[8] For some examples, see: (a) Xie, J.; Huang, Z. Z. Cross-Dehydrogenative Coupling Reactions by Transition-Metal and Aminocatalysis for the Synthesis of Amino Acid Derivatives. *Angew. Chem., Int. Ed.* **2010**, *49*, 10181. (b) Xu, Z.; Liu, L.; Wheeler, K.; Wang, H. Asymmetric Inverse-Electron-Demand Hetero-Diels–Alder Reaction of Six-membered Cyclic Ketones: An Enamine/Metal Lewis Acid Bifunctional Approach. *Angew. Chem., Int. Ed.* **2011**, *50*, 3484. (c) Liu, L.; Sarkisian, R.; Xu, Z.; Wang, H. Asymmetric Michael Addition of Ketones to Alkylidene Malonates and Allylidene Malonates via Enamine−Metal Lewis Acid Bifunctional Catalysis. *J. Org. Chem.* **2012**, *77*, 7693.

[9] (a) Zhang, L.; Zha, Z. G.; Zhang, Z. L.; Li, Y. F. and Wang, Z. Y. An electrochemical tandem reaction: one-pot synthesis of homoallylic alcohols from alcohols in aqueous media. *Chem. Commun.* **2010**, *46*, 7196. (b) Zhang, L.; Su, J. H.; Wang, S. J.; Wan, C. F.; Zha, Z. G.; Du, J. F. and Wang, Z. Y. Direct electrochemical imidation of aliphatic amines *via* anodic oxidation. *Chem. Commun*. **2011**, *47*, 5488. (c) Zhang, L.; Chen, H.; Zha, Z. G. and Wang, Z. Y. Electrochemical tandem synthesis of oximes from alcohols using KNO_3 as the nitrogen source, mediated by tin microspheres in aqueous medium. *Chem. Commun.*, **2012**, *48*, 6574. (d) Meng, L.; Su, J. H.; Zha, Z. G.; Zhang, L.; Zhang, Z. L. and Wang, Z. Y. Direct Electrosynthesis of Ketones from Benzylic Methylenes by Electrooxidative C-H Activation. *Chem. -Eur. J*., **2013**, *19*, 5542. (e) Xu, K.; Zhang, Z. L.; Qian, P.; Zha, Z. G. and Wang, Z. Y. Electrosynthesis of enaminones directly from methyl ketones and amines with nitromethane as a carbon source. *Chem. Commun.*, **2015**, *51*, 11108. (f) Qian, P.; Bi, M. X.; Su, J. H.; Zha, Z. G. and Wang, Z. Y. Electrosynthesis of (*E*)-Vinyl Sulfones Directly from Cinnamic Acids and Sodium Sulfinates via Decarboxylative Sulfono Functionalization. *J. Org. Chem*. **2016**, *81*, 11, 4876-4882. (g) Qian, P.; Su, J. H.; Wang, Y. K.; Bi, M. X.; Zha, Z. G. and Wang, Z. Y. Electrocatalytic C−H/N−H Coupling of 2′-Aminoacetophenones for the Synthesis of Isatins. *J. Org. Chem*. **2017**, *82*, 12, 6434-6440.

[10] Ma, H. Y.; Zha, Z. G.; Zhang, Z. L.; Meng, L. and Wang, Z. Y. Electrosynthesis of oxadiazoles from benzoylhydrazines. *Chin. Chem. Lett.,* **2013**, *24*, 780.

[11] Zhang, Z. L.; Su, J. H.; Zha, Z. G. and Wang, Z. Y. A novel approach for the one-pot preparation of α-ketoamides by anodic oxidation. *Chem. Commun.,* **2013**, *49*, 8982.

[12] Li, Y. N.; Gao, H. H.; Zhang, Z. L.; Qian, P.; Bi, M. X.; Zha, Z. G. and Wang, Z. Y. Electrochemical synthesis of α-enaminones from aryl ketones. *Chem. Commun.,* **2016**, *52*, 8600-8603.

[13] Makhija, M. T.; Kasliwal, R. T.; Kulkarni, V. M.; Neamati, N. De novo design and synthesis of HIV-1 integrase inhibitors. *Bioorg. Med. Chem*. **2004**, *12*, 2317.