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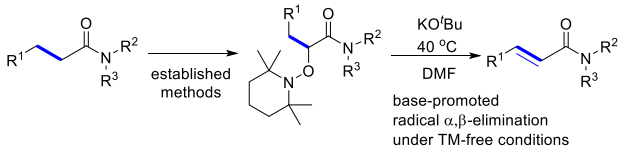
Radical α,β-Dehydrogenation of Saturated Amides via α-Oxidation with TEMPO under Transition Metal-Free Conditions

Mei-Mei Wang,[†] Guo-Hui Sui,[‡] Xian-Chao Cui,[†] Hui Wang,[†] Jian-Ping Qu,*[‡] and Yan-Biao Kang*[†]

[†] Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China

[‡] Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Jiangsu National Synergetic Innovation Center for Advanced Materials, Nanjing Tech University, Nanjing 211816, China

Supporting Information Placeholder

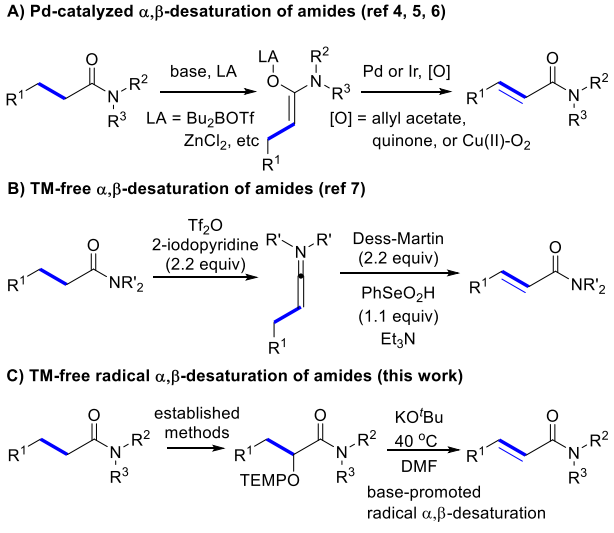


ABSTRACT: A transition metal-free radical process for the selective α,β-dehydrogenation of saturated amides under mild conditions is developed. Utilizing radical activation strategy, the challenging issue associated with the low α-acidity of amides is resolved. For the first time, α,β-unsaturated Weinreb amides and acrylamides could be efficiently prepared directly from corresponding saturated amides. Mechanistic studies confirm the radical nature of this transformation. Two gram scale α,β-dehydrogenation have also been performed to demonstrate the utility of this method.

α,β-Unsaturated amides are useful synthetic intermediates with remarkable chemical versatility. Considering the easy availability of the precursor amides, methods to access such building blocks directly from the α,β-dehydrogenation of the corresponding saturated amides are the most straightforward and therefore highly desired. Compared to the dehydrogenative synthesis of α,β-unsaturated ketones, aldehydes, and esters,[1-3] the analogical synthesis of α,β-unsaturated amides has been much less reported (Scheme 1, A).[4] In the palladium-catalysed dehydrogenation, Newhouse et al. combined the Lewis acids promoted enonation and the oxidative C-H cleavage of such enonate intermediates to achieve desired unsaturated amides.[4a] Dong further accomplished dehydrogenation of lactams.[4b] An iridium-catalysed dehydrogenation of double activated enamides has also been reported shortly.[4c] During our preparation of this manuscript, we noticed Maulide et al. reported a selenium-based dehydrogenative synthesis of α,β-unsaturated amides with Dess-Martin periodinane (DMP) as oxidant (Scheme 1, B).[5] With respect to the transition metal-free radical dehydrogenation using non-selenium-based α,β-dehydrogenation of saturated amides, there still undiscovered space remains.

TEMPO (2,2,6,6-Tetramethylpiperidine-*N*-oxyl) are well-known for its utilizations as oxidants and radical scavengers in oxidation synthesis. The alkoxyamines derived from TEMPO could generate C-centered radicals and has demonstrated applications in polymer chemistry.[6] As part of our ongoing research interest on base-promoted reaction,[7] we envisioned that it is possible to use base or thermal conditions to accomplish α,β-dehydrogenation of saturated amides via a radical β-elimination (Scheme 1, C). To our glad, the α-oxygenation of amides under radical pathways have been established by Maulide and Jiao et al.[8-9] The challenge is how to avoid enolization through the α-deprotonation by base. In previous work, ^{t}BuOK, a bulky strong base, has proven to be an efficient electron donor to initiate radical reactions.[10] After carefully controlling the reaction conditions, we finally established a new method for the synthesis α,β-unsaturated amides from dehydrogenation of saturated amides. We herein present the results in details.

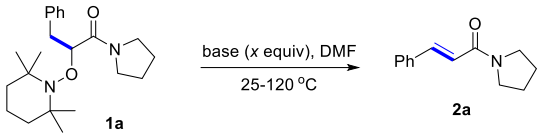
Scheme 1. α,β-Dehydrogenation of Saturated Amides



Initially, the reaction conditions were investigated. The thermos-elimination at 120 °C gave the target unsaturated amide **2a** in 92% yield, whereas the lowering down the reaction temperature from 120

°C to 40 °C gave rise to the remarkable decrease of yields from 92% to 0% (Table 1, entries 1-3). In the further investigation, it was found that 1.2 equiv KO^{t}Bu dramatically promoted the reaction (entry 6), achieving comparable yield under heating conditions (entry 4 vs 1). The reactions in the presence of other bases such as NaO^{t}Bu, KHMDS resulted in much lower yields (entries 7-8). Lowering reaction temperature from 40 °C to 25 °C decreased the yields to moderate level (entries 9-10). The reaction conditions demonstrated in entry 6 were chosen as the standard reaction conditions.

Table 1. Reaction Conditions[a]



entry	base	x	T (°C)	t (h)	2a (%)[b]
1	–	–	120	24	**92**
2	–	–	90	24	20
3	–	–	40	24	0
4	KO^{t}Bu	1.0	90	5	70
5	KO^{t}Bu	1.0	60	5	72
6	KO^{t}Bu	1.2	40	1.5	**90**
7	NaO^{t}Bu	1.2	40	5	19
8	KHMDS	1.2	40	24	5
9	KO^{t}Bu	1.2	25	5	56
10	KO^{t}Bu	1.5	25	5	46

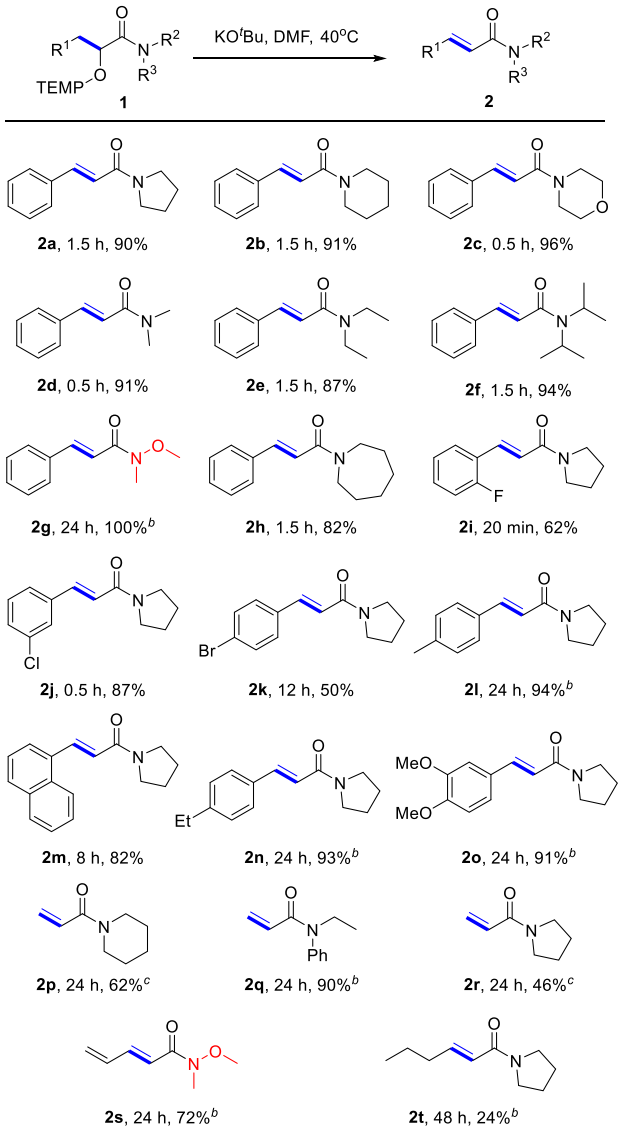
[a]Reaction conditions: **1a** (0.25 mmol), base (1.0-1.5 equiv), DMF (1 mL), argon, 25-120 °C.

With the standard conditions in hand, the reaction scope was investigated (Scheme 2). Various *N*-substituted α-OTEMP amides, prepared according to the literature reported methods,[8-9] were examined, affording the corresponding unsaturated amides in generally high yields. With respect to the aryl substituents (**2a**-**2o**), (*o*)-fluoro-substituted **2i** was obtained in lower yields than **2j** with meta-substituents. Unsaturated *N*-hydroxyl amide **2g** could also be synthesized by this method. What should be mentioned is that terminal alkenes **2p**-**2s** were achieved from the corresponding *N*-substituted propionamides under base-promotion or thermo-elimination at 120 °C. Such acrylamides (**2p**, **2q**, **2s**) bearing terminal double bonds were not reported in previous work via dehydrogenation methods.

Base effect was then investigated using **1a** under conditions described in Table 1, entry 6. As shown in Figure 1, conversion of α, β-dehydrogenation product depends on the loading of ^{t}BuOK. When the usage of ^{t}BuOK is less than 0.5 equivalent, conversion of **1a** is less than 5%. Nevertheless, when the loading of ^{t}BuOK is more than 0.6 equivalent, conversion of **1a** and the isolated yields of **2a** increases dramatically.

Although ^{t}BuOK is crucial to the reaction, the mechanism of this deprotonation reaction is not clear so far. However, the elimination can go through either radical pathway or anionic (E2) pathway. The deprotonation of less acidic β-proton over α-proton seems to be unlikely; actually, the steric hindrance at α-position is too big for bulky ^{t}BuOK.

Scheme 2. Reaction Scope



[a] Condition: **1** (0.25 mmol), ^{t}BuOK (1.0-1.5 equiv), DMF (1 mL), argon, 40 °C. [b] The reaction was performed without ^{t}BuOK in DMF (1 mL) at 120 °C. [c] The reaction was performed at 120 °C.

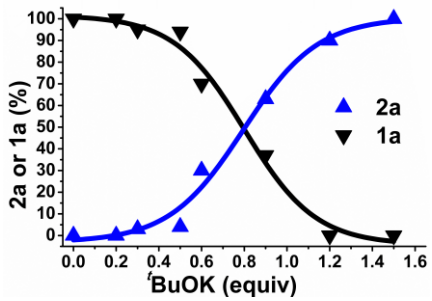
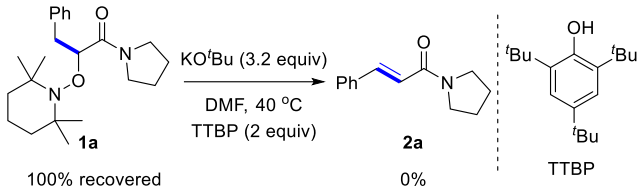


Figure 1. Base Effect of the α,β-Dehydrogenation of 1a to 2a.

To understand the mechanism, the base promoted α, β-dehydrogenation of saturated amide **1a** was performed in the presence of 2 equivalents of TTBP (2,4,6-tri-tert-butylphenol) (Scheme 3). The

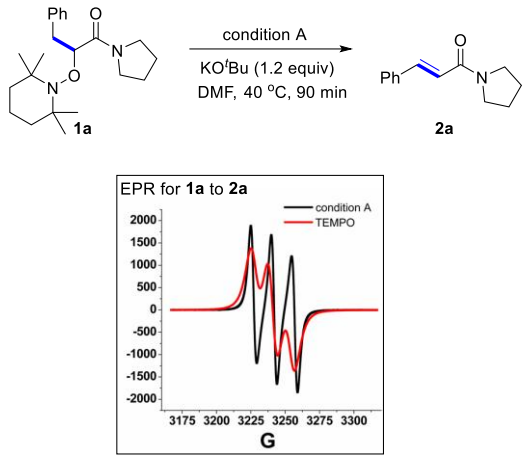
α, β-dehydrogenation was completed inhibited and no dehydrogenation product **2a** was detected with 100% recovery of **1a**. This indicates the involvement of radicals in this transformation.

Scheme 3. Radical Trapping Experiments



The EPR experiment demonstrated that abundant TEMPO was existing in the reaction mixture during the reaction (Scheme 4). This further confirms the radical nature of this reaction.

Scheme 4. EPR Experiments

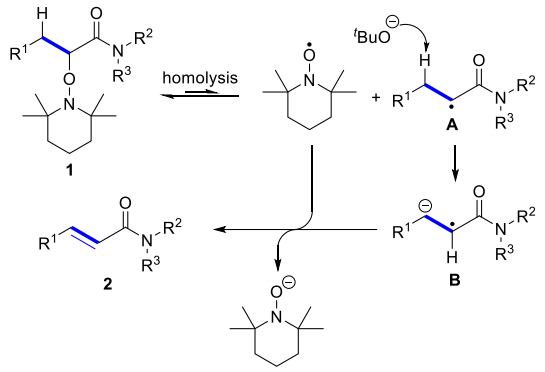


Based on the abovementioned results, a radical pathway for α, β-dehydrogenation of saturated amide **1** is proposed (Scheme 5). First, the C-O bond homolysis in DMF can occur to a small extend already at 40 °C generating the radical C-centered radical **A** and TEMPO. The radical **A** can then be deprotonated with ^{t}BuOK to give a radical anion **B**. The radical anion **B** could be finally oxidized by the TEMPO formed in the homolysis step affording the desired α, β-dehydrogenation product **2**.

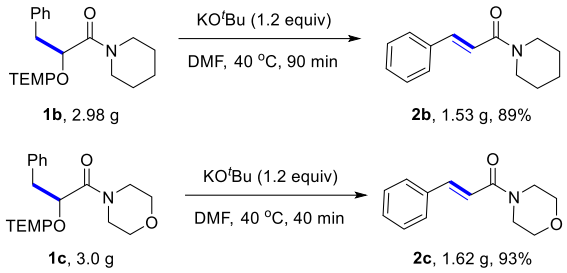
To demonstrate the utility of this method, we then performed this transition metal-free radical process of dehydrogenation of amide **1b** and **1c** in gram scale (Scheme 6). Both α,β-unsaturated amide **2b** and **2c** were regioselectivity obtained in 89% and 93% yields, respectively. There is no obvious decrease in yield compared to the standard reaction conditions.

In conclusion, we have developed a transition metal-free radical process for the selective α,β-dehydrogenation of saturated amides under mild conditions. For the first time, α,β-unsaturated Weinreb amides and acrylamides could be efficiently prepared directly from corresponding amides in moderate to excellent yields under transition metal free dehydrogenation conditions. The radical assistant "autocatalytic" process enables an efficient synthetically practical method for the synthesis of α,β-unsaturated amides via dehydrogenation of corresponding saturated amides.

Scheme 5. Reaction Mechanism



Scheme 6. Gram Scale Synthesis of 2b and 2c.



EXPERIMENTAL SECTION

General information. Solvents were pre-dried over activated 4 Å molecular sieves and heated to reflux over sodium (toluene, THF, hexane), CaH_2 (CH_2Cl_2 and DMF) under argon atmosphere and collected by distillation. ^1H, $^{13}C\{^1H\}$ NMR spectra were recorded on a 400 spectrometer; chemical shifts are reported in δ units relative to TMS [^1H, δ = 0.00] and $CDCl_3$ [^{13}C, δ = 77.16]. Starting material 1 were prepared according to the known procedure.[8,9]

General procedure for dehydrogenation of amides. Amide **1** (0.25 mmol) and KO^{t}Bu (1.2 equiv) in a 25 mL tube was dried under high vacuum for 10 min, DMF (1 mL) was added and the mixture was heated at 40 - 120 °C by oil bath under N_2 for desired time. The reaction was monitored by TLC. The reaction mixture was quenched by H_2O and extracted with ethyl acetate (4 mL×3). The combined organic layers were concentrated and purified by column chromatography to afford **2**.

Gram-scale preparation of 2b Amide **1b** (8 mmol, 2.98 g) and KO^{t}Bu (1.2 equiv, 1.08 g) in a 100 mL tube was dried under high vacuum for 10 min, DMF (16 mL) was added and the mixture was heated at 40 under N_2 for 1.5 h. The reaction mixture was quenched by H_2O and extracted with ethyl acetate (50 mL×3). The combined organic layers were concentrated and purified by column chromatography (PE/EA = 2:1) to afford **2b**, yellow solid (1.53 g, 89%).

Gram-scale preparation of 2c. Amide **1c** (8 mmol, 3.00 g) and KO^{t}Bu (1.2 equiv, 1.08 g) in a 100 mL tube was dried under high vacuum for 10 min, DMF (16 mL) was added and the mixture was heated at 40 under N_2 for 40 min. The reaction mixture was quenched by H_2O and extracted with ethyl acetate (50 mL×3). The combined organic layers were concentrated and purified by column chromatography (PE/EA = 2:1) to afford **2c**, white solid (1.62 g, 93%).

(E)-3-phenyl-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2a***). This compound was prepared according to the general procedure at 40 °C, 90 min and purified by flash column chromatography (PE/EA = 2:1); yellow solid (45.3 mg, 90%), mp 97-98°C ^1H NMR ($CDCl_3$, 400 MHz) δ 1.86–1.93 (m, 2 H), 1.97–2.03 (m, 2 H), 3.57–3.64 (m, 4 H), 6.73 (d, J = 15.6

Hz, 1 H), 7.32–7.39 (m, 3 H), 7.52–7.54 (m, 2 H), 7.70 (d, *J* = 15.6 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.5, 26.3, 46.2, 46.7, 118.9, 128.0, 128.9, 129.7, 135.4, 141.8, 164.9.[11]

(E)-3-phenyl-1-(piperidin-1-yl)prop-2-en-1-one (***2b***). This compound was prepared according to the general procedure at 40 °C, 90 min and purified by flash column chromatography (PE/EA = 3:1); yellow solid (49.0 mg, 91%), mp 116-117°C ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.58–1.70 (m, 6 H), 3.62 (d, *J* = 33.6 Hz, 2 H), 6.90 (d, *J* = 15.6 Hz, 1 H), 7.33–7.39 (m, 3 H), 7.51–7.53 (m, 2 H), 7.64 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.8, 25.7, 26.9, 43.4, 47.1, 117.9, 127.8, 128.9, 129.5, 135.6, 142.2, 165.5.[11]

(E)-1-morpholino-3-phenylprop-2-en-1-one (***2c***). This compound was prepared according to the general procedure at 40 °C, 30 min, and purified by flash column chromatography (PE/EA = 2:1); white solid (52.1 mg, 96%) mp 89-90°C ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.64–3.70 (m, 8 H), 6.83 (d, *J* = 15.6 Hz, 1 H), 7.34–7.35 (m, 3 H), 7.49–7.51 (m, 2 H), 7.68 (d, *J* = 15.6 Hz. 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 42.5, 46.2, 66.9 (two peaks), 116.6, 127.8, 128.9, 129.8, 135.1, 143.2, 165.6.[11]

N,N-dimethylcinnamamide (***2d***). This compound was prepared according to the general procedure at 40 °C, 30 min, and purified by flash column chromatography (PE/EA = 5:1); white solid (39.9 mg, 91%). mp 87-89°C ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.06 (s, 3 H), 3.17 (s, 3 H), 6.86 (d, *J* = 14 Hz, 1 H), 7.35–7.37 (m, 3 H), 7.51–7.53 (m, 2 H), 7.67 (d, *J* = 14.8 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 36.0, 37.5, 117.5, 127.9, 128.9, 129.6, 135.5, 142.4, 166.8.[11]

N,N-diethylcinnamamide (***2e***). This compound was prepared according to the general procedure at 40 °C, 90 min, and purified by flash column chromatography (PE/EA = 3:1); white solid (44.2 mg, 87%) mp 61-63°C ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18 (t, *J* = 7.0 Hz, 3 H), 1.26 (t, *J* = 7.0 Hz, 3 H), 3.48 (m, 4 H), 6.82 (d, *J* = 15.2 Hz, 1 H), 7.31–7.39 (m, 3 H), 7.50–7.53 (m, 2 H), 7.70 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.3, 15.2, 41.2, 42.4, 117.9, 127.9, 128.9, 129.5, 135.6, 142.4, 165.8.[11]

N,N-diisopropylcinnamamide (***2f***). This compound was prepared according to the general procedure at 40 °C, 90 min, and purified by flash column chromatography (PE/EA = 3:1); colorless oil (54.4 mg, 94%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.29 (s, 6 H), 1.38 (s, 6 H), 3.83 (s, 1 H), 4.10 (s, 1 H), 6.83 (d, *J* = 15.6 Hz, 1 H), 7.28–7.36 (m, 3. H), 7.47–7.50 (m, 2 H), 7.58 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 20.5 (two peaks), 21.5 (two peaks), 45.8, 47.9, 120.5, 127.4, 128.6, 129.1, 135.6, 140.7, 166.0.[12]

N-methoxy-N-methylcinnamamide (***2g***). This compound was prepared according to the general procedure without ^{t}BuOK at 120 °C, 24h, and purified by flash column chromatography (PE/EA = 5:1); white solid (47.8 mg, 100%) mp 56-58°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.29 (s, 3 H), 3.74 (s, 3 H), 7.03 (d, *J* = 15.6 Hz, 1 H), 7.34–7.37 (m, 3 H), 7.55 (s, 2 H), 7.72 (d, *J* = 16.0 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 32.5, 61.9, 115.8, 128.1, 128.8, 129.9, 135.2, 143.4, 167.0.[13]

(E)-1-(azepan-1-yl)-3-phenylprop-2-en-1-one (***2h***). This compound was prepared according to the general procedure at 40 °C, 90 min, and purified by flash column chromatography (PE/EA = 2:1); white solid (47.0 mg, 82%) mp 120-121°C ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.55–1.59 (m, 4 H), 1.77–1.79 (m, 4 H), 3.62 (dt, *J* = 16.8, 6.2 Hz, 4 H), 6.87 (d, *J* = 14.8 Hz, 1 H), 7.31–7.39 (m, 3 H), 7.51 -7.53 (m, 2 H), 7.70 (d, *J* = 15.6 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 26.7, 27.1, 27.8, 29.5, 46.6, 48.1, 117.9, 127.9, 128.9, 129.6, 135.7, 142.4, 166.4.[11]

(E)-3-(2-fluorophenyl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2i***). This compound was prepared according to the general procedure at 40 °C, 20 min, and purified by flash column chromatography (PE/EA = 2:1);yellow oil (34.0 mg, 62%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.87–1.93 (m, 2 H), 1.97–2.04 (m, 2 H), 3.58–3.64 (m, 4 H), 6.88 (d, *J* = 15.6 Hz, 1 H), 7.06–7.16 (m, 2 H), 7.28–7.33 (m, 1 H), 7.52 (t, *J* = 7.8 Hz, 1 H), 7.76 (d, *J* = 15.6 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.4, 26.2, 46.1, 46.6, 116.2 (d, *J* = 21.9 Hz), 122.0 (d, *J* = 8.4 Hz), 123.4 (d, *J* = 11.5 Hz), 124.4 (d, *J* = 3.5 Hz), 129.9 (d, *J* = 4.3 Hz), 130.8 (d, *J* = 8.8 Hz), 134.8, 161.2 (d, *J* = 243.5 Hz), 164.7. HRMS (ESI–TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{15}FNO$ 220.1138, found 220.1136.

(E)-3-(3-chlorophenyl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2j***). This compound was prepared according to the general procedure at 40 °C, 30 min, and purified by flash column chromatography (PE/EA = 2:1); white solid (51.3 mg, 87%) mp 141-143°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.88–1.95 (m, 2 H), 1.99–2.06 (m, 2 H), 3.60 (t, *J* = 6.8 Hz, 2 H), 3.64 (t, *J* = 6.8 Hz, 2 H), 6.74 (d, *J* = 15.6 Hz, 1 H), 7.30–7.33 (m, 2 H), 736–7.40 (m, 1 H), 7.52 (s, 1 H), 7.63 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.4, 26.3, 46.2, 46.8, 120.4, 126.5, 127.4, 129.5, 130.2, 134.9, 137.3, 140.3, 164.4.[14]

(E)-3-(4-bromophenyl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2k***). This compound was prepared according to the general procedure at 60 °C, 12 h, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (35.0 mg, 50%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.84–1.91 (m, 2 H), 1.95–2.02 (m, 2 H), 3.55–3.61 (m, 4 H), 6.70 (d, *J* = 15.2 Hz, 1 H), 7.35–7.38 (m, 2 H), 7.46–7.48 (m, 2 H), 7.60 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.4, 26.2, 46.2, 46.7, 119.6, 123.7, 129.3, 132.0, 134.4, 140.4, 164.4.[15]

(E)-1-(pyrrolidin-1-yl)-3-(p-tolyl)prop-2-en-1-one (***2l***). This compound was prepared according to the general procedure without ^{t}BuOK at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (50.6 mg, 94%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.86–1.92 (m, 2 H), 1.96 (m, 2 H), 2.36 (s, 3 H), 3.57–3.64 (m, 4 H), 6.68 (d, *J* = 15.6 Hz, 1 H), 7.17 (d, *J* = 8.0 Hz, 1 H), 7.43 (d, *J* = 8.0 Hz, 1 H), 7.67 (d, *J* = 15.6 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 21.5, 24.5, 26.3, 46.1, 46.7, 117.9, 128.0, 130.0, 132.7, 139.9, 141.8, 165.0.[16]

(E)-3-(naphthalen-1-yl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2m***). This compound was prepared according to the general procedure at 40 °C, 8 h, and purified by flash column chromatography (PE/EA = 2:1); white solid (51.5 mg, 82%) 131-132°C ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.88–1.95 (m, 2 H), 1.97–2.04 (m, 2 H), 3.62–3.66 (m, 4 H), 6.80 (d, *J* = 15.6 Hz, 1 H), 7.45–7.57 (m, 3 H), 7.71 (d, *J* = 7.2 Hz, 1 H), 7.86 (d, *J* = 8.4 Hz, 1 H), 8.25 (d, *J* = 8.4 Hz, 1 H), 8.53 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.4, 26.2, 46.2, 46.7, 122.1, 123.9, 124.6, 125.5, 126.2, 126.7, 128.6, 129.8, 131.6, 133.2, 133.7, 139.0, 164.7.[16]

(E)-3-(4-ethylphenyl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2n***). This compound was prepared according to the general procedure without ^{t}BuOK at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (53.3 mg, 93%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.23 (t, *J* = 7.6 Hz, 3 H), 1.85–1.92 (m, 2 H), 1.96–2.03 (m, 2 H), 2.65 (q, *J* = 7.6 Hz, 2 H), 3.57–3.64 (m, 4 H), 6.69 (d, *J* = 15.6 Hz, 1 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 7.68 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 15.5, 24.5, 26.3, 28.9, 46.1, 46.7, 118.0, 128.0, 128.4, 133.0, 141.8, 146.2, 165.0. HRMS (ESI–TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{20}NO$ 230.1545, found 230.1544.

(E)-3-(3,4-dimethoxyphenyl)-1-(pyrrolidin-1-yl)prop-2-en-1-one (***2o***). This compound was prepared according to the general procedure without ^{t}BuOK at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 2:1); white solid (59.5 mg, 91%), mp 142-143°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.86 -1.92 (m, 2 H), 1.96–2.03 (m, 2 H), 3.57 -3.66 (m, 4 H), 3.89–3.92 (m, 6 H), 6.59 (d, *J* = 15.6 Hz, 1 H), 6.85 (d, *J* = 8.4 Hz, 1 H), 7.03 (s, 1 H), 7.11–7.14 (m, 1 H), 7.63 (d, *J* = 15.2 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.5, 26.3, 46.1, 46.7, 56.1, 110.1, 111.2, 116.8, 121.9, 128.5, 141.7, 149.2, 150.6, 165.0.[15]

1-(piperidin-1-yl)prop-2-en-1-one (***2p***).

This compound was prepared according to the general procedure at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (21.6 mg, 62%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.50–1.58 (m, 6 H), 3.42 (s, 2 H), 3.53 (s, 2 H), 5.55 – 5.59 (m, 1 H), 6.13 - 6.19 (m, 1 H), 6.47 – 6.55 (m, 1 H), ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.5, 25.5, 26.6, 43.0, 46.9, 127.0, 128.2, 165.3.[17]

*N-ethyl-N-phenylacrylamide (**2q**).* This compound was prepared according to the general procedure without ^{t}BuOK at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (39.4 mg, 90%).^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (t, *J* = 7.0 Hz, 3 H), 3.84 (q, *J* = 7.2 Hz, 2 H), 5.48 (d, *J* = 10.0 Hz, 1 H), 5.99 (dd, *J* = 16.8, 10.4 Hz, 1 H), 6.35 (d, *J* = 16.8 Hz, 1 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 7.32–7.44 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 12.8, 44.1, 127.1, 127.6, 128.2, 128.8, 129.4, 141.6, 165.0.[18]

*1-(pyrrolidin-1-yl)prop-2-en-1-one (**2r**).* This compound was prepared according to the general procedure at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (14.4 mg, 46%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.84–1.90 (m, 2 H), 1.93–2.00 (m, 2 H), 3.51–3.55 (m, 4 H), 5.65 (s, *J* = 10 Hz, 1 H), 6.33–6.48 (m, 2 H), ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.4, 26.2, 46.0, 46.7, 127.4, 128.9, 164.6.[19]

*(E)-N-methoxy-N-methylpenta-2,4-dienamide (**2s**).* This compound was prepared according to the general procedure without ^{t}BuOK at 120 °C, 24 h, and purified by flash column chromatography (PE/EA = 5:1); yellow oil (25.4 mg, 72%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.26 (s, 3 H), 3.72 (s, 3 H), 5.47 (d, *J* = 10.8 Hz, 1 H), 5.61 (d, *J* = 16.4 Hz, 1 H), 6.47–6.56 (m, 2 H), 7.29–7.35 (m, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 32.5, 61.9, 120.0, 124.9, 135.3, 143.6, 167.0.[20]

*(E)-1-(pyrrolidin-1-yl)hex-2-en-1-one (**2t**).* This compound was prepared according to the general procedure, and purified by flash column chromatography (PE/EA = 2:1); yellow oil (10.0 mg, 24%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.89 (t, *J* = 7.4 Hz, 3 H), 1.40–1.49 (m, 2 H), 1.79–1.85 (m, 2 H), 1.89–1.95 (m, 2 H), 2.14 (q, *J* = 7.1 Hz, 2 H), 3.46–3.50 (m, 4 H), 6.06 (d, *J* = 15.1 Hz, 1 H), 6.86 (dt, *J* = 14.6, 7.3 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 13.7, 21.6, 24.3, 26.1, 34.4, 45.7, 46.5, 121.8, 145.5, 164.9.[21]

General procedure A for preparing 1. Amide **1** (2.0 mmol) and TEMPO (3.0 equiv) were added to a 25 mL tube with a magnetic stir bar. Then hexane (1 mL), ^{i}Pr$_3$SiOTf (3.3 equiv) and pyridine (5 equiv) were added to the tube and the mixture was heated at 60 °C under argon atmosphere for desired time. After cooling to room temperature, the saturated $CuSO_4$ aqueous solution (4 mL) was added to the mixture. The mixture was extracted with ethyl acetate (4 mL×3). The combined organic layers were concentrated and isolated by fast column chromatography to afford the imides **1a**-**1e**, **1h-1r**, and **1t**.[9]

General procedure B for preparing 1f, 1g, and 1s. To a solution of the amide (2.0 mmol) and TEMPO (2.2 equiv.) in DCM (0.1 M) with activated MS 3Å at 0 °C was added trifluoromethanesulfonic anhydride (1.1 equiv.). The resulting mixture was allowed to warm to room temperature (23 °C) over a period of 12 h. After this time, the reaction mixture was filtered from the MS 3Å with DCM and subsequently stirred with water for 15 min. The phases were separated and the aqueous phase was extracted with DCM. The combined organic phases were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel (heptane/ethyl acetate) to afford the imides **1f**, **1g**, and **1s**.[8]

*3-Phenyl-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1a**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); White solid (0.67 g, 94%), mp 56-58 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.01 (s, 3 H), 1.12 (s, 3 H), 1.14 (s, 3 H), 1.26 (s, 3 H), 1.31–1.38 (m, 2 H), 1.43–1.46 (m, 3 H), 1.55–1.56 (m, 3 H), 1.68–1.70 (m, 3 H), 2.60–2.66 (m, 1 H), 3.07–3.21 (m, 2 H), 3.27–3.31 (m, 2 H), 3.57–3.62 (m, 1 H), 4.59 (q, *J* = 5.2 Hz, 1 H), 7.17–7.27 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 16.8, 19.7, 20.0, 23.7, 25.5, 32.5, 33.2, 38.2, 40.0, 40.3, 45.0, 46.1, 59.0, 60.2, 84.0, 126.1, 127.8, 129.3, 136.5, 170.5. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{35}N_2O_2$ 359.2699, found 359.2702.

*3-Phenyl-1-(piperidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1b**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); White solid (0.59 g, 79%), mp 73-75 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.02 (s, 3 H), 1.12 (s, 3 H), 1.16 (s, 3 H), 1.20–1.58 (m, 15 H), 3.07–3.28 (m, 5 H), 3.58–3.63 (m, 1 H), 4.77 (dd, *J* = 10.8, 4.4 Hz, 1 H), 7.16–7.26 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 16.5, 19.5, 19.7, 23.7, 24.6, 25.1, 32.5, 33.2, 38.3, 39.7, 39.8, 41.8, 46.0, 58.7, 59.6, 81.8, 125.8, 127.6, 129.1, 136.2, 169.9. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{23}H_{37}N_2O_2$ 373.2855, found 373.2856.

*1-Morpholino-3-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1c**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); White solid (0.73 g, 97%), mp 89-91 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.04 (s, 3 H), 1.00 (s, 3 H), 1.10 (s, 3 H), 1.15 (s, 3 H), 1.30–1.53 (m, 9 H), 2.69–2.74 (m, 1 H), 2.99–3.10 (m, 2 H), 3.19–3.30 (m, 4 H), 3.35–3.38 (m, 1 H), 3.51–3.62 (m, 2 H), 7.15–7.24 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.1, 20.2, 20.5, 33.3, 34.0, 39.1, 40.4, 40.6, 41.8, 46.1, 59.6, 60.4, 66.1, 66.6, 82.7, 126.9, 128.6, 129.8, 136.6, 171.2. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{35}N_2O_3$ 375.2648, found 375.2645.

*N,N-dimethyl-3-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propanamide (**1d**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.59 g, 89%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00 (s, 3 H), 1.12 (s, 3 H), 1.15 (s, 3 H), 1.27 (s, 3 H), 1.30–1.47 (m, 6 H), 2.70 (s, 3 H), 2.77 (s, 3 H), 3.06–3.12 (m, 1 H), 3.20–3.24 (m, 1 H), 4.79 (dd, *J* = 10.0, 5.0 Hz, 1 H), 7.17–7.24 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 16.9, 19.9, 20.1, 32.5, 33.4, 35.2, 36.9, 38.5, 40.1, 40.3, 59.2, 60.3, 82.2, 126.2, 128.0, 129.4, 136.7, 172.2. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{20}H_{33}N_2O_2$ 333.2542, found 333.2549.

*N,N-diethyl-3-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propanamide (**1e**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.52 g, 72%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.75 (t, *J* = 7.2 Hz, 3 H), 0.97 (t, *J* = 7 Hz, 3 H), 1.03 (s, 3 H), 1.1 (s, 3 H), 1.14–1.16 (m, 3 H), 1.25 (s, 3 H), 1.31–1.58 (m, 6 H), 2.76–2.85 (m, 1 H), 3.08–3.23 (m, 4 H), 3.40–3.50 (m, 1 H), 4.61 (dd, *J* = 10.4, 4.4 Hz, 1 H), 7.16–7.24 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 12.3, 14.0, 17.1, 20.0, 20.3, 32.9, 33.4, 38.8, 40.4, 40.5, 40.6, 41.6, 59.2, 60.8, 81.6, 126.4, 128.2, 129.9, 136.9, 171.7. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{37}N_2O_2$ 361.2855, found 361.2856.

*N,N-diisopropyl-3-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propanamide (**1f**).* This compound was prepared according to the general procedure B and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.24 g, 31%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11–1.17 (m, 16 H), 1.25–1.58 (m, 14 H), 3.09–3.20 (m, 3 H), 4.12 (s, 1 H), 4.70 (q, *J* = 4.9 Hz, 1 H), 7.13–7.23 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.3, 20.2, 20.3, 20.4, 20.7, 33.8, 33.9, 39.1, 40.5, 40.6, 46.2, 59.3, 60.7, 82.0, 126.4, 128.3, 130.3, 137.1, 171.4. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{24}H_{41}N_2O_2$ 389.3168, found 389.3175.

*N-methoxy-N-methyl-3-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propanamide (**1g**)*. This compound was prepared according to the general procedure B and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.43 g, 61%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 3 H), 1.05 (s, 3 H), 1.07 (s, 3 H), 1.18 (s, 3 H), 1.23–1.48 (m, 6 H), 2.93 (s, 3 H), 2.97–3.03 (m, 1 H), 3.09–3.13 (m, 1 H), 3.23 (s, 3 H), 4.92 (dd, *J* = 9.8, 4.8 Hz, 1 H), 7.11–7.19 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.1, 20.1, 20.3, 31.7, 32.8, 33.5, 38.3, 40.4, 59.3, 60.6, 61.0, 80.6, 126.5, 128.2, 129.9, 136.6, 173.3. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{20}H_{33}N_2O_3$ 349.2491, found 349.2492.

*1-(azepan-1-yl)-3-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1h**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.43 g, 55%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00–1.54 (m, 26 H), 2.88–2.99 (m, 2 H), 3.12–3.27 (m, 2 H), 3.86–3.92 (m, 2 H), 4.69 -4.75 (m, 1 H), 7.21 -7.24 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 16.0, 18.9, 19.2, 24.9, 25.7, 26.4, 27.6, 31.5, 32.3, 37.3, 39.2, 39.4, 44.5, 46.0, 58.1, 59.6, 80.3, 125.3, 127.1, 128.9, 135.8, 170.7. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{24}H_{39}N_2O_2$ 387.3012, found 387.3009.

*3-(2-fluorophenyl)-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1i**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.46 g, 61%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97 (s, 3 H), 1.04 (s, 3 H), 1.07 (s, 3 H), 1.15 (s, 3 H), 1.22–1.76 (m, 10 H), 2.82–2.88 (m, 1 H), 2.93–2.98 (m, 1 H), 3.18–3.30 (m, 3 H), 3.69–3.75 (m, 1 H), 4.69 (dd, *J* = 9.8, 5.8 Hz, 1 H), 6.91–6.99 (m, 2 H), 7.10–7.20 (m, 2 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.0, 19.9, 20.2, 24.0, 25.8, 31.7, 32.8, 33.0, 40.4, 40.6, 45.3, 46.5, 59.3, 60.6, 81.7, 114.7 (d, *J* = 21.5 Hz), 123.8 (d, *J* = 2.8 Hz), 124.0, 128.3 (d, *J* = 7.9 Hz), 132.6 (d, *J* = 4.7 Hz), 161.5 (d, *J* = 243.7 Hz), 170.6. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{34}FN_2O_2$ 377.2604, found 377.2606.

*3-(3-chlorophenyl)-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1j**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.52 g, 66%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00 (s, 3 H), 1.12 (s, 6 H), 1.21 (s, 3 H), 1.27–1.76 (m, 10 H), 2.70–2.76 (m, 1 H), 3.04–3.17 (m, 2 H), 3.32 (t, *J* = 6.4 Hz, 2 H), 3.66–3.71 (m, 2 H), 4.57 (dd, *J* = 10.0, 5.6 Hz, 1 H), 7.08–7.12 (m, 1 H), 7.16–7.19 (m, 3 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.2, 20.1, 20.4, 24.2, 26.0, 32.9, 33.6, 38.2, 40.5, 40.7, 45.6, 46.7, 59.5, 60.8, 83.9, 126.8, 128.1, 129.6, 129.8, 134.0, 139.3, 170.6. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{34}ClN_2O_2$ 393.2309, found 393.2308.

*3-(4-bromophenyl)-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1k**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.86 g, 98%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (s, 3 H), 1.10 (s, 3 H), 1.11 (s, 3 H), 1.22 (s, 3 H), 1.30–1.79 (m, 10 H), 2.72–2.79 (m, 1 H), 3.02–3.13 (m, 2 H), 3.23–3.35 (m, 2 H), 3.67–3.72 (m, 1 H), 4.55 (dd, *J* = 10.0, 5.6 Hz, 1 H), 7.07 (d, *J* = 8.4 Hz, 2 H), 7.35 (d, *J* = 8.4 Hz, 2 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.1, 20.1, 20.4, 24.1, 25.9, 32.8, 33.6, 37.7, 40.4, 40.7, 45.5, 46.7, 59.5, 60.8, 83.8, 120.4, 131.3, 131.5, 136.1, 170.5. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{34}BrN_2O_2$ 437.1804, found 437.1804.

*1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-3-(p-tolyl)propan-1-one (**1l**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.57 g, 77%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00 (s, 3 H), 1.11 (s, 3 H), 1.13 (s, 3 H), 1.25 (s, 3 H), 1.30–1.72 (m, 10 H), 2.28 (s, 3 H), 2.63–2.69 (m, 1 H), 3.03–3.15 (m, 2 H), 3.23–3.34 (m, 2 H), 3.56–3.61 (m, 1 H), 4.55 (dd, *J* = 10.4, 5.2 Hz, 1 H), 7.01–7.08 (m, 4 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.2, 20.2, 20.5, 21.2, 24.1, 25.9, 33.0, 33.7, 38.1, 40.5, 40.8, 45.4, 46.5, 59.4, 60.6, 84.6, 129.0, 129.6, 133.9, 136.0, 171.0. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{22}H_{37}N_2O_2$ 373.2855, found 373.2856.

*3-(naphthalen-1-yl)-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1m**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.82 g, 100%) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.02 (s, 3 H), 1.07 (s, 3 H), 1.15 (s, 3 H), 1.22 (s, 3 H), 1.24–1.60 (m, 10 H), 2.17–2.23 (m, 1 H), 3.06–3.12 (m, 1 H), 3.19–3.26 (m, 1 H), 3.37–3.50 (m, 2 H), 3.76 (dd, *J* = 13.2, 5.6 Hz, 1 H), 4.80 (dd, *J* = 9.4, 5.8 Hz, 1 H), 7.35–7.38 (m, 1 H), 7.42–7.53 (m, 3 H), 7.71 (d, *J* = 8.4 Hz, 1 H), 7.82 (d, *J* = 8.0 Hz, 1 H), 8.15 (d, *J* = 8.4 Hz, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.0, 19.9, 20.3, 23.7, 25.6, 32.8, 33.5, 35.4, 40.3, 40.6, 45.2, 46.1, 59.3, 60.4, 83.3, 123.8, 125.3, 125.4, 125.8, 127.1, 128.3, 128.6, 132.4, 133.2, 133.5, 171.0. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{26}H_{37}N_2O_2$ 409.2855, found 409.2852.

*3-(4-ethylphenyl)-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1n**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.73 g, 95%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.01 (s, 3 H), 1.12 (s, 3 H), 1.14 (s, 3 H), 1.18 (t, *J* = 7.6 Hz, 3 H), 1.26 (s, 3 H), 1.34–1.58 (m, 8 H), 1.67–1.71 (m, 2 H), 2.55–2.64 (m, 3 H), 3.04–3.17 (m, 2 H), 3.28–3.31 (m, 2 H), 3.53–3.58 (m, 1 H), 4.56 (dd, *J* = 10.4, 5.2 Hz, 1 H), 7.04–7.12 (m, 4 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 15.6, 16.9, 19.8, 20.1, 23.7, 25.6, 28.3, 32.6, 33.4, 37.8, 40.1, 40.4, 45.1, 46.1, 59.0, 60.3, 84.3,127.4, 129.4, 133.7, 142.2,170.7. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{24}H_{39}N_2O_2$ 387.3012, found 387.3014.

*3-(3,4-dimethoxyphenyl)-1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1o**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.79 g, 94%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00 (s, 3 H), 1.12 (s, 3 H), 1.15 (s, 3 H), 1.26 (s, 3 H), 1.29 (s, 4 H), 1.43–1.46 (m, 2 H), 1.59–1.61 (m, 2 H), 1.67–1.74 (m, 2 H), 2.69–2.74 (m, 1 H), 3.02–3.14 (m, 2 H), 3.30–3.32 (m, 2 H), 3.64 (s, 1 H), 3.83–3.85 (m, 6 H), 4.57 (dd, *J* = 10.0, 5.2 Hz, 1 H), 6.73–6.75 (m, 3 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 17.0, 20.0, 20.3, 24.0, 25.8, 32.8, 33.5, 37.9, 40.3, 40.6, 45.4, 46.4, 55.8, 55.9, 59.3, 60.6, 84.3, 111.0, 112.9, 121.6, 129.5, 147.5, 148.5, 171.0. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{24}H_{39}N_2O_4$ 419.2910, found 419.2906.

*1-(piperidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1p**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.59 g, 99%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.05–1.28 (m, 13 H), 1.39–1.60 (m, 14 H), 3.31–3.36 (m, 1 H), 3.48–3.51 (m, 1 H), 3.65–3.68 (m, 4 H), 4.57–4.61 (m, 1 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 16.8, 18.2, 20.0, 20.2, 24.4, 25.3, 26.1, 32.8, 33.5, 39.8, 40.0, 42.5, 46.0, 59.2 (two peaks), 82.5, 171.7. HRMS (ESI–TOF) m/z: [M+H]$^+$ calcd for $C_{17}H_{33}N_2O_2$ 297.2542, found 297.2544.

*N-ethyl-N-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propanamide (**1q**)*. This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.47 g, 70%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.71 (s, 3 H), 1.04 (s, 3 H), 1.08–1.10 (m, 6 H), 1.15–1.23 (m, 6 H), 1.30–1.50 (m, 6 H), 3.61–3.69 (m, 1 H), 3.85–3.93 (m, 1 H), 4.23 (dd, *J* = 13.0, 6.6 Hz, 1 H), 7.21–7.45 (m, 5 H). ^{13}C {^{1}H} NMR ($CDCl_3$, 100 MHz) δ 11.1, 15.5, 16.0, 18.3, 18.6, 31.1, 31.6, 38.4, 39.0, 42.3, 57.4, 58.5, 75.0,

126.2, 127.2, 127.7, 140.2, 171.2. HRMS (ESI–TOF) m/z: $[M+Na]^+$ calcd for $C_{20}H_{32}N_2O_2Na$ 355.2361, found 355.2384.

*1-(Pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-1-one (**1r**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.46 g, 81%). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.94 (s, 3 H), 1.03–1.05 (m, 6 H), 1.14 (s, 3H), 1.19–1.39 (m, 9 H), 1.76–1.81 (m, 2 H), 1.84–1.91 (m, 2 H), 3.38 (t, *J* = 6.8 Hz, 2 H), 3.44–3.50 (m, 1 H), 3.72–3.78 (m, 1 H), 4.45 (q, *J* = 6.8 Hz, 1 H). ^{13}C {^1H} NMR ($CDCl_3$, 100 MHz) δ 16.1, 16.2, 19.1, 19.5, 23.0, 25.2, 31.7, 32.6, 39.2, 39.5, 44.8, 45.6, 58.3, 59.1, 79.5, 171.3. HRMS (ESI–TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{31}N_2O_2$ 283.2386, found 283.2390.

*N-methoxy-N-methyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-4-enamide (**1s**).* This compound was prepared according to the general procedure B and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.41 g, 68%). ^1H NMR ($CDCl_3$, 400 MHz) δ 1.01 (s, 3 H), 1.06 (s, 3 H), 1.10 (s, 3 H), 1.20–1.53 (m, 9 H), 2.54 (t, *J* = 7.0 Hz, 2 H), 3.11 (s, 3 H), 3.74 (s, 3 H), 4.81 (s, 1 H), 4.98–5.08 (m, 2 H), 5.64–5.74 (m, 1 H). ^{13}C {^1H} NMR ($CDCl_3$, 100 MHz) δ 17.0, 20.0, 20.3, 31.8, 32.8, 33.5, 36.5, 40.3, 40.4, 59.3, 60.5, 61.5, 117.8, 133.0, 173.7. HRMS (ESI–TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{31}N_2O_3$ 299.2335, found 299.2336.

*1-(pyrrolidin-1-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hexan-1-one (**1t**).* This compound was prepared according to the general procedure A and purified by flash column chromatography (PE/EA = 10:1); Yellow oil (0.60 g, 92%). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, *J* = 7.2 Hz, 3 H), 0.97 (s, 3 H), 1.05 (s, 3 H), 1.11 (s, 3 H), 1.51–1.20 (m, 13 H), 1.75–1.93 (m, 6 H), 3.90–3.95 (m, 1 H), 4.39 (q, *J* = 4.8 Hz, 1 H). ^{13}C {^1H} NMR ($CDCl_3$, 100 MHz) δ 13.8, 16.9, 19.8, 20.2, 22.7, 24.0, 26.0, 27.2, 31.2, 32.6, 33.2, 40.1, 40.4, 45.5, 46.6, 59.0, 60.3, 83.4. HRMS (ESI–TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{37}N_2O_2$ 325.2855, found 325.2846.

ASSOCIATED CONTENT

Supporting Information

NMR spectra for all products. This material is available free of charge *via* the Internet at http://pubs.acs.org.

NMR spectra (PDF)

AUTHOR INFORMATION

ybkang@ustc.edu.cn
ias_jpqu@njtech.edu.cn

Notes

The authors declare no competing financial interest.

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