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Visible Light-Driven, Copper-Catalyzed Aerobic Oxidative Cleavage of Cycloalkanones

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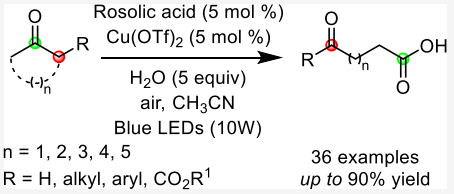
ABSTRACT: A visible light-driven, copper-catalyzed aerobic oxidative cleavage of cycloalkanones has been presented. A variety of cycloalkanones with varying ring sizes and various α-substituents reacted well to give the distal keto acids or dicarboxylic acids with moderate to good yields.

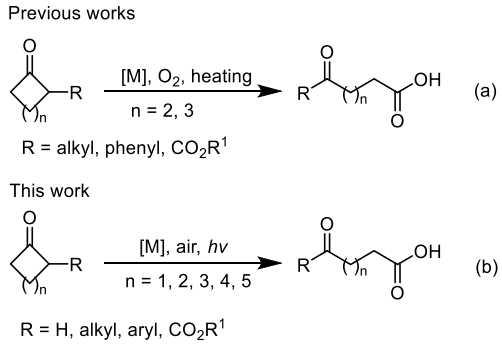


INTRODUCTION

Oxidative transformation is one of the most fundamental reactions, and is widely used in modern organic synthesis and chemical industries. For example, adipic acid is an important industrial material for Nylon 66, which could be obtained by oxidation of cyclohexanol and cyclohexanone or by two-step oxidation of cyclohexane.[1] Although impressive progress has been made in kinds of oxidation reactions, replacing precious metal catalysts and (over)stoichiometric amounts of hazardous oxidants with low-cost and more sustainable oxidants is still highly demanding. In view of its abundant, environmentally benign, and waste-free characters, molecular oxygen (O_2) is undoubtedly the best oxidant. Furthermore, O_2 possesses powerful oxidation property, which could oxidize not only the organic molecules but also the transition metals [from a low valence state to a high valence state, e.g., Pd(0) to Pd(II)].[2] So far, considerable catalytic aerobic oxidation reactions have been developed.[3] In this field, the catalytic oxidative cleavage of C−C bonds with O_2 has drawn a lot of attention for a long time because it provides straightforward and sustainable routes to high-value fine chemicals.[4] On the other hand, visible light is another natural and infinite energy. Since 2008, visible light photoredox catalysis has displayed great potential in organic synthesis.[5] Thus, visible light-driven, aerobic oxidative C−C bond cleavage reactions are desirable and aroused great interest of chemists.[6]

The keto acids are important synthetic building blocks in organic chemistry, which could undergo diverse chemical transformations, such as esterification, acylation, decarboxylic reactions, and so on. Compared with the stoichiometric oxidation, the catalytic oxidative cleavage of α-substituted cycloalkanones with O_2 provided an attractive alternative to access these compounds. Over the past few decades, different catalytic systems including iron (III), copper (II), vanadium (V), heteropolyacids, or other catalysts have been developed under the traditional heating conditions (Scheme 1a).[7] Therein, only a few examples of cycloalkanones were reported. Recently,

Scheme 1. Oxidative Cleavage of α-Substituted Cycloalkanones



we demonstrated a metal-free, visible light-induced oxidative C−C bond cleavage of α-substituted cycloalkanones with singlet molecular oxygen ($^1O_2$), which provides a mild and atom-economy route to a series of γ-, δ-, and ε-keto esters.[6b] However, the corresponding keto acids were obtained in very low yield even using water as the nucleophile. Herein, we describe a new visible light-driven, copper catalytic system for the oxidative cleavage of cycloalkanones under an air atmosphere (Scheme 1b). Remarkably, the unsubstituted cycloalkanone could also be oxidized to the corresponding dicarboxylic acids.

RESULTS AND DISCUSSION

Initially, we began with the oxidative cleavage of 2-phenylcyclohexan-1-one **1a** with molecular oxygen in the presence of

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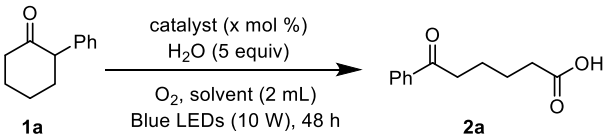
10 mol % $Fe(OTf)_2$ and 5.0 equiv of water in MeCN under irradiation of a blue LED (10 W). To our delight, the desired ε-keto acid **2a** was isolated in 56% yield (Table 1, entry 1). Among

Table 1. Optimization of the Reaction Conditions[a]



1a 2a

entry	catalyst (mol %)	solvent	yield (%)[b]
1	$Fe(OTf)_2$ (10)	MeCN	56 (58)[b]
2	$Fe(OTf)_3$ (10)	MeCN	53 (54)[b]
3	$FeCl_3$ (10)	MeCN	23 (25)[b]
4	$Fe(OAc)_2$ (10)	MeCN	trace (trace)[b]
5	$Cu(OTf)_2$ (10)	MeCN	66
6	$CuCl_2$ or $Cu(OAc)_2$ (10)	MeCN	13, trace
7	$Cu(NO_3)_2{\cdot}3H_2O$ (10)	MeCN	12 (20)[b]
8	$Cu(OTf)_2$ (10)	DMF or NMP	38, 45 (51)[b]
9	$Cu(OTf)_2$ (10)	HOAc	47
10	$Cu(OTf)_2$ (10)	acetone	33
11	$Cu(OTf)_2$ (10)	toluene	n.r.[c]
12	**Cu**$(OTf)_2$ (5)	**MeCN**	**73 (72)**[b]
13	$Cu(OTf)_2$ (3)	MeCN	20
14		MeCN	n.r.[c]
15[d]	$Cu(OTf)_2$ (5)	MeCN	trace
16[e]	$Cu(OTf)_2$ (5)	MeCN	39
17	$Cu(OTf)_2$ (5)	MeCN	trace[f], 70[g]
18	$Cu(OTf)_2$ (5)	MeCN	17[h]

[a]Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), H_2O (1.0 mmol, 5.0 equiv), 5 mol % of $Cu(OTf)_2$, CH_3CN (2.0 mL), blue LED (10 W), for 48 h, under O_2. Yields of the isolated product. [b]Under air. [c]n.r. = no reaction. [d]Without light irradiation. [e]Without light irradiation, heating to 60 °C in an oil bath. [f]10 mol % of bipyridine as the ligand. [g]10 mol % of PPh_3 as the ligand. [h]Irradiation by sunlight.

the iron (II) and (III) salts tested, $Fe(OTf)_3$ gave a similar yield with $Fe(OTf)_2$ (entries 2−4). Some copper salts were also examined instead of the iron catalyst. It was found that $Cu(OTf)_2$ is superior to $Fe(OTf)_2$, raising the yield of **2a** to 66% (entries 5−7). Solvent screening revealed that MeCN was the optimal one. It should be noted that the reaction of **1a** in a mixed solvent of MeCN and H_2O (9:1) only delivered a trace amount of **2a** (not shown). Satisfactorily, decreasing the catalyst loading to 5 mol % led to an improved yield of **2a** (73%), while further reducing resulted in a diminished yield due to low conversion of **1a** (entries 12 and 13). Notably, this oxidation reaction proceeded well in air, furnishing comparable yields of **2a** (entries 1−4, 7, 8, and 12). Finally, control experiments revealed that the copper catalyst and visible light both were essential for the success of this oxidation reaction (entries 14 and 15). Without light irradiation, the reaction resulted in 39% yield of **2a** by heating to 60 °C in an oil bath (entry 16). Some ligands, such as bipyridine and PPh_3, were added into the reaction system, respectively, but none of them gave better results (entry 17). It should be noted that using H_2O_2 (2 equiv) instead of O_2 as the oxidant only led to 28% yield of **2a**, along with 55% of **1a** recovered (not shown). Finally, the reaction of **1a** with O_2 could also be conducted in a normal flask under sunlight, albeit with relatively low yield (entry 18).

With the optimal conditions in hand, the generality and limitation of the α-substituted cycloalkanones were evaluated (Scheme 2). A variety of 2-aryl cyclohexan-1-ones underwent the visible light-induced oxidative cleavage regioselectively to give the desired ε-keto acids **2a**−**2o** in moderate to good yields. Both electron-donating groups (Me, OMe, and OCF_3) and electron-withdrawing groups (F, Cl, and CF_3) on the *p*-, *m*-, and *o*-positions of aromatic ring were compatible with the reaction conditions. 1-Naphthyl- and 2-naphthyl-substituted cyclohexanones gave the desired oxidation products **2n** and **2o** in moderate yields. Unfortunately, 2-methyl cyclohexan-1-one **1p** only furnished the desired product **2p** in 11% yield under the present conditions. As we know, the photocatalytic energy transfer could activate the molecular oxygen to more reactive singlet molecular oxygen ($^1O_2$).[8] Thus, some photosensitizers were examined as the cocatalyst. After several trials, we were delighted to find that the addition of a catalytic amount of photosensitizer such as 5 mol % rosolic acid (RA) or 5 mol % *meso*-tetraphenylporphyrin (TPP) is beneficial for enhancing the reaction efficiency (for details, see Supporting Information). The yield of **2p** could be improved from 11% to 87% under the synergistic Cu/RA catalysis. Other 2-alkyl cyclohexan-1-ones were also efficient substrates under this new dual catalytic system. 2,6-dimethyl cyclohexan-1-one and menthone reacted well to yield the anticipated ε-keto acids **2r** and **2s** in 63 and 81% yields, respectively. Satisfactorily, the 2-ester-substituted substrate was also compatible with the reaction, affording the desired product **2t** in 80% yield. When 2-(2-hydroxyethyl)-cyclohexan-1-one **1u** was subjected to the reaction system, the lactone **2u** was obtained in 39% yield, along with 50% of **1u** recovered and other unidentified byproducts detected. 2-Isobutyrylcyclohexan-1-one gave the unexpected adipic acid **2v** in 79% yield. Surprisingly, when 2-methyl-1-tetralone was used, no desired product was isolated and 94% of starting material **1w** was recovered.

Subsequently, cycloalkanones with varying ring sizes and various R substituents were examined (Scheme 3). Both 2-aryl- and 2-alkyl-substituted cyclopentanones underwent the oxidative C−C bond cleavage efficiently to provide the δ-keto acids **3a**−**3g** in 64−90% yields. The simple cyclopentanone also gave the glutaric acid **3h** in 38% isolated yield. Unfortunately, 2,2-dimethyl cyclopentanone did not work under the present reaction conditions (not shown). More strained 2-phenyl and 2-thienyl cyclobutanone delivered the anticipated γ-keto acids **3i** and **3j** in 68 and 54% yields, respectively. 2-Phenyl cycloalkanones with seven- and eight-membered rings were also compatible substrates, furnishing the desired acids **3k** and **3m** in acceptable yields. 2-Hydroxyethyl cycloheptanone was engaged in the reaction efficiently to afford the lactone **3l** in 77% yield. Drug molecule loxoprofen derivative was also amenable, providing the target product **3n** in 30% yield due to low conversion. Unfortunately, 2-phenyl cycloalkanone with 12-membered ring failed to give the expected product.

To demonstrate the application of this protocol, the reactions of **1a** and **1p** were conducted on a larger scale (10 mmol), respectively (Scheme 4). After prolonging the reaction time, both **1a** and **1p** gave the desired products in good yields. Furthermore, the products displayed a wide range of applications in diverse chemical transformations. For instance, the complex bioactive molecules, such as memantine and leelamine could be acylated with **2a** to afford desired products **4a** and **4b** in satisfied yields. ε-Keto acid **2a** also underwent the oxidative decarboxylation reaction smoothly to give the 5-fluoro-1-phenylpentan-1-one **5a** and 5-azido-1-phenylpentan-1-one **5b** in moderate yields.[9] In addition, δ-keto acid **3a** could be

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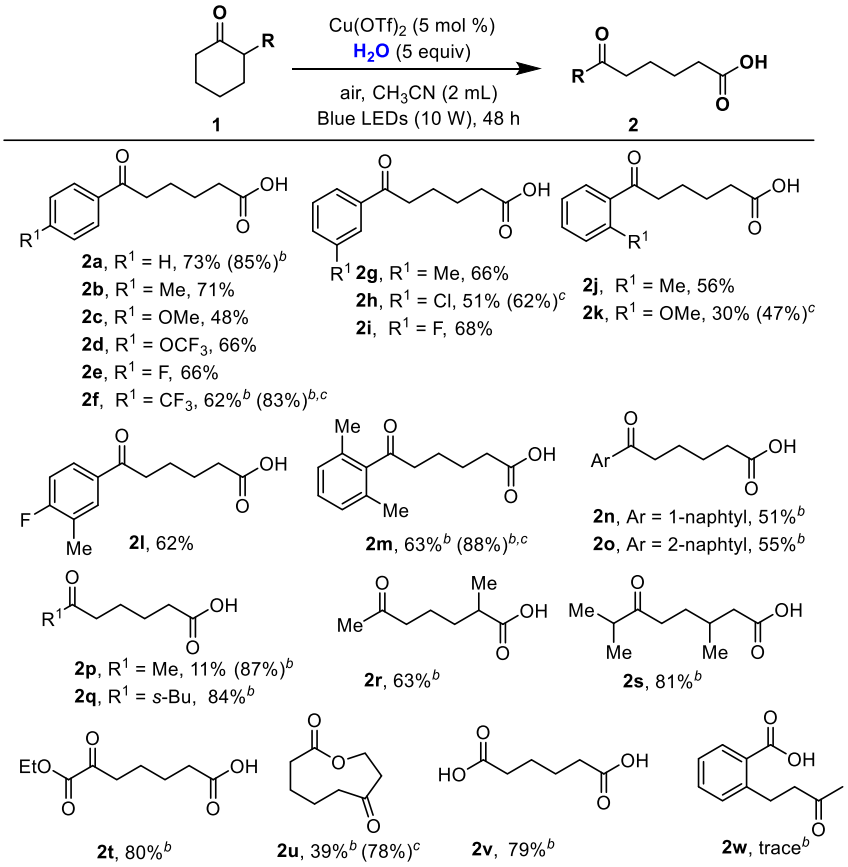
Scheme 2. Scope of the α-Substituted Cyclohexan-1-ones[a]



[a]Reaction conditions A: **1a** (0.2 mmol, 1.0 equiv), H_2O (1.0 mmol, 5.0 equiv), 5 mol % of $Cu(OTf)_2$, CH_3CN (2.0 mL), blue LED (10 W), for 48 h, under air. Yields of the isolated product. [b]Reaction conditions B: **1a** (0.2 mmol, 1.0 equiv), H_2O (1.0 mmol, 5.0 equiv), 5 mol % of $Cu(OTf)_2$, 5 mol % of RA, CH_3CN (2.0 mL), blue LED (10 W), for 48 h, under air. [c]Yields were based on the recovered starting material.

reduced with $NaBH_4$, and then made to undergo intramolecular esterification to deliver the lactone **7a** in 77% yield.[10]

To elucidate the mechanism, control experiments were conducted (Scheme 5). When 2.0 equiv of TEMPO was added into the reaction of **1a**, the reaction was completely inhibited, and the TEMPO-adduct could be detected by high-resolution mass spectrometry (Scheme 5, eq 1). The addition of BHT also prevented this reaction completely (Scheme 5, eq 2). Both results suggest a radical pathway for this oxidative C−C bond cleavage reaction. Furthermore, in the presence of 2.0 equiv of 1,4-diazabicyclo[2.2.2]octane, a well-known singlet oxygen quencher, the reaction of **1p** was greatly inhibited, indicating that the singlet oxygen species was probably involved in this transformation [Scheme 5, eq 3]. The use of NaN_3 led to the same conclusion [Scheme 5, eq 4].[11] In all these cases, a large amount of unreacted substituted cycloalkanones **1a** and **1p** was recovered, respectively. In addition, when the singlet oxygen generator TPP[12] was used instead of RA as the photocatalyst, the reaction of **1p** also took place well, affording **2p** in 75% yield [Scheme 5, eq 5]. We thought that the more active $^1O_2$ was formed through an energy transfer process with hv/RA during the reaction. Finally, it should be mentioned that the reactant of **1p** did not work in the presence of TPP, without the copper catalyst. Maybe, the copper catalyst is helpful to form the enol intermediate. Although the exact mechanism remains unclear, two tentative reaction pathways were proposed for the reactions under conditions A and conditions B, respectively (Schemes 6 and 7).

Based on the results mentioned above and previous reports,[19] a possible reaction mechanism of conditions A is shown in Scheme 6. Enolization of **1** forms the enol **A** in the presence of $Cu^{(II)}$, then photoexcitation of enol **A** generates excited-state complex **B**, which undergoes a SET process to radical intermediate **C**. Intermediate **C** could readily react with molecular oxygen to form complex **D**. Isomerization rearrangement of **D** to form the peroxide **E**. Then, peroxide **E** undergoes homolytic O−O bond scission promoted by visible light, followed by the C−C bond fragment to afford the acetyl radical intermediate **F**. The radical **F** rapidly converts acid **2** and **3** via an oxidation/H_2O attack cascade.

On the other hand, a possible reaction mechanism of conditions B was proposed, where enolization of **1** forms the enol **A** in the presence of $Cu^{(II)}$. Meanwhile, excited-state RA* would undergo energy transfer to form the singlet $^1O_2$ through the activation $^3O_2$ process. Subsequently, the reaction of singlet $^1O_2$ with complex **A** leads to dioxetane intermediate **B**. Finally, fragmentation of the C−C bond and the O−O bond of dioxetane **B** produces the target acid **2** or **3**.

CONCLUSIONS

In conclusion, we described an efficient visible light-driven oxidative C−C bond cleavage of cycloalkanones with O_2. This protocol provides a simple and easily handled approach to a

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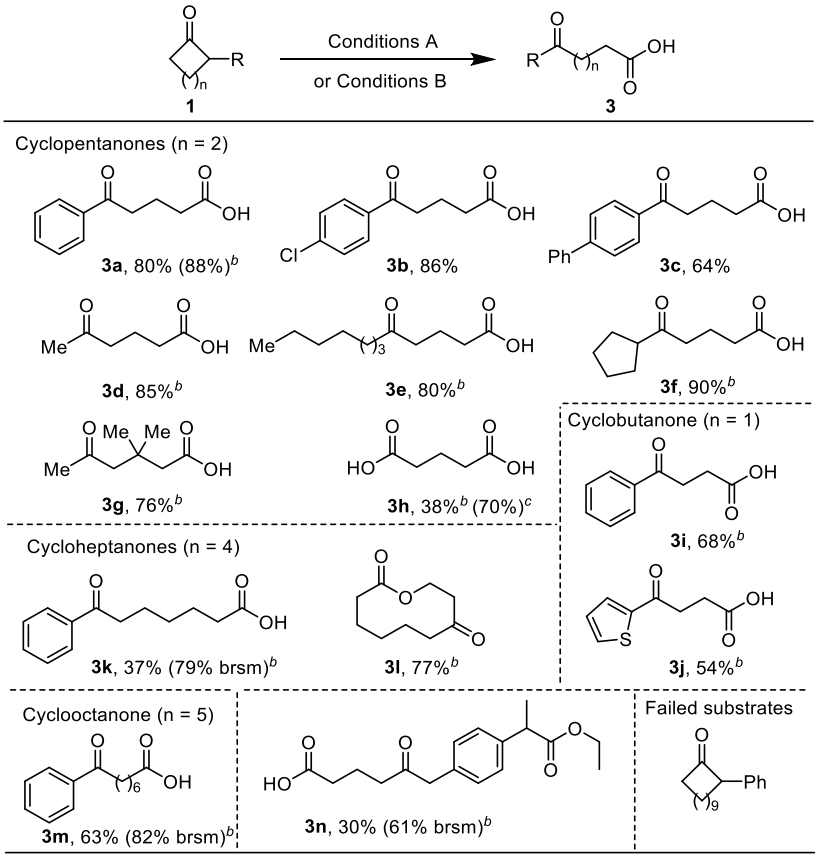
Scheme 3. Scope of the Cycloalkanones with Varying Ring Sizes[a]



[a]Reaction conditions A: **1a** (0.2 mmol, 1.0 equiv), H_2O (1.0 mmol, 5.0 equiv), 5 mol % of $Cu(OTf)_2$, CH_3CN (2.0 mL), blue LED (10 W), for 48 h, under air. Yields of isolated product. [b]Reaction conditions B: **1a** (0.2 mmol, 1.0 equiv), H_2O (1.0 mmol, 5.0 equiv), 5 mol % of $Cu(OTf)_2$, 5 mol % of RA, CH_3CN (2.0 mL), blue LED (10 W), for 48 h, under air. [c]Yield was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard.

wide range of γ-, δ-, and ε-keto acids and dicarboxylic acids with good yields, which are versatile building blocks for organic synthesis.

EXPERIMENTAL SECTION

General Methods. The reactions were conducted in an oven-dried Schlenk-tube. The photoinduced reactions were carried out in the oven-dried Schlenk-tube connected with a Wattecs blue LED for irradiation. Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. ^1H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz (100 MHz for ^{13}C NMR) spectrometer at ambient temperature. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard ($CDCl_3$: ^1H NMR: δ = 7.26; ^{13}C NMR: δ = 77.0; DMSO-d_6: ^1H NMR: δ = 2.50; ^{13}C NMR: δ = 39.5). Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), and m (multiplet). Except **2v** and **3h**, active hydrogen of other carboxylic acids did not present due to hydrogen deuterium exchange in $CDCl_3$. The Fourier transform infrared spectra were recorded on a Bruker V 70 spectrometer and only major peaks are reported in cm^{-1}. High-resolution mass spectra (HRMS) were obtained on a WATERS I-Class VION IMS Q-Tof mass spectrometer. Melting points were measured using open glass capillaries on a SGW X-4A apparatus. Analytical thin-layer chromatography: aluminum-backed plates were precoated (0.25 mm) with Merck silica gel 60F-254. Compounds were visualized by exposure to UV light or by dipping the plates in $KMnO_4$, bromocresol green, or 2,4-dinitrophenylhydrazine stain, followed by heating.

Starting Materials. All of 2-aryl cycloalkanones were prepared according to the literature.[13] The NMR spectra of known compounds were in full accordance with the data reported in the literature.

Detailed Optimization of Reaction Conditions. *General Procedure for the Oxidative Cleavage of **1a** without Photocatalyst.* A 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with 2-phenylcyclohexanone **1a** (0.20 mmol, 1.0 equiv), catalyst (see Table S1). Then, the tube was evacuated and backfilled with oxygen (three times). Subsequently, a solution of water (1.0 mmol, 5.0 equiv) in the solvent (2.0 mL) was added using a syringe. The reaction mixture was stirred under the irradiation of a 10 W blue LED (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 2:1 to 1:1) furnishes the ε-keto acid **2a** as light yellow oil.

*General Procedure for the Oxidative Cleavage of **1p** with Photocatalyst.* A 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with $Cu(OTf)_2$ (5 mol %), photocatalyst (see Table S2). Then, the tube was evacuated and backfilled with oxygen (three times). Subsequently, a solution of 2-methylcyclohexanone **1p** (0.20 mmol, 1.0 equiv) in CH_3CN (1.0 mL), followed by water (1 mmol, 5.0 equiv) in CH_3CN (1 mL) were added using a syringe. The reaction mixture was stirred under the irradiation of a 10 W blue LED (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 2:1 to 1:1) furnishes ε-keto acid **2p** as light yellow oil.

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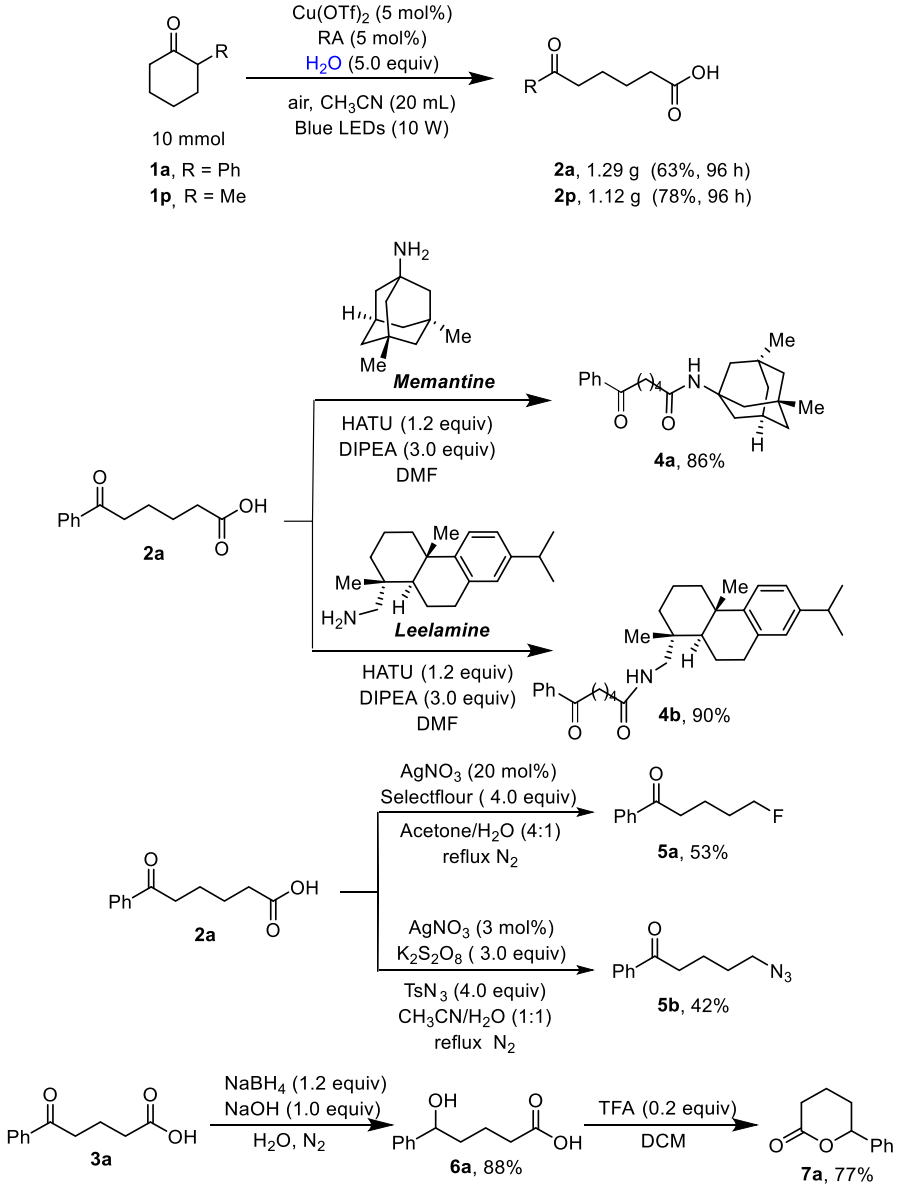
Scheme 4. Scale-up and Application of Products



General Procedure for the Oxidative Cleavage of 1 without Photocatalyst (Conditions A). A 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with cyclohexanone **1** (0.20 mmol, 1.0 equiv) and $Cu(OTf)_2$ (3.6 mg, 5 mol %). Subsequently, a solution of water (1 mmol, 5.0 equiv) in CH_3CN (2.0 mL) was added using a syringe. The reaction mixture was stirred in air under the irradiation of a 10 W blue LED (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 2:1 to 1:1) furnishes acid **2** or **3** in yields listed in Schemes 2 and 3.

General Procedure for the Oxidative Cleavage of 1 with Photocatalyst (Conditions B). A 10 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with $Cu(OTf)_2$ (3.6 mg, 5 mol %) and RA (2.9 mg, 5 mol %). Subsequently, a solution of cyclohexanone **1** (0.20 mmol, 1.0 equiv) in CH_3CN (1.0 mL), followed by water (1 mmol, 5.0 equiv) in CH_3CN (1.0 mL) were added using a syringe. The reaction mixture was stirred in air under the irradiation of a 10 W blue LED (λ = 460−470 nm; distance app. 1.0 cm from the bulb) for a specified time. After that, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 2:1 to 1:1) furnishes acid **2** or **3** in yields listed in Schemes 2 and 3.

Scale-up Reaction. A 200 mL oven-dried Schlenk-tube equipped with a magnetic stirrer was charged with $Cu(OTf)_2$ (180 mg, 5 mol %) and RA (145 mg, 5 mol %). Subsequently, a solution of cyclohexanone (**1a** or **1p**) (10 mmol, 1.0 equiv) in CH_3CN (40 mL), followed by water (50 mmol, 5.0 equiv) in CH_3CN (60 mL) were added using a syringe. The reaction mixture was stirred in air under the irradiation of a 10 W blue LED for a specified time. After that, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (petroleum ether/EtOAc: 2:1 to 1:1) furnishes ε-keto acid **2a** (1.29 g, 63%) or **2p** (1.12 g, 78%).

Characterization of Products 2, 3, 4, 5, 6a, and 7a. *6-Oxo-6-phenylhexanoic Acid (**2a**).* Reaction conditions B. Known compound, light yellow oil (85%, 35.0 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96−7.94 (m, 2H), 7.58−7.54 (m, 1H), 7.48−7.44 (m, 2H), 3.01 (t, J = 7.2 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.84−1.72 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 199.8, 178.8, 136.9, 133.0, 128.6, 128.0, 38.1, 33.7, 24.3, 23.5 ppm. Spectral data match those previously reported.[14]

*6-Oxo-6-(p-tolyl)hexanoic Acid (**2b**).* Reaction conditions A. White solid (71%, 31.2 mg); m.p. 42−43 °C; R_f = 0.15 (EtOAc/petroleum

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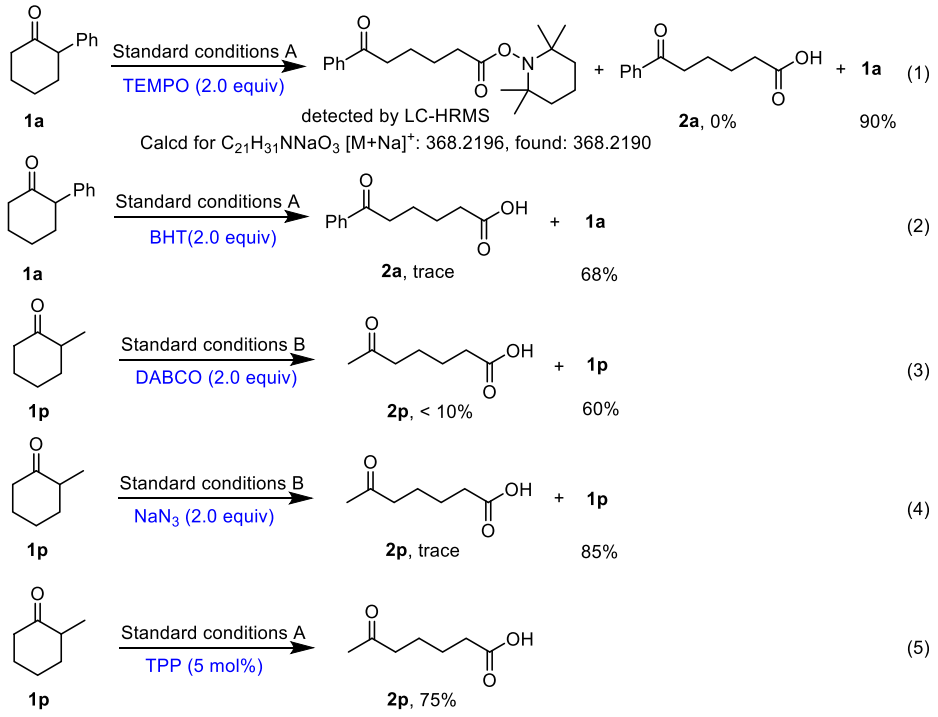
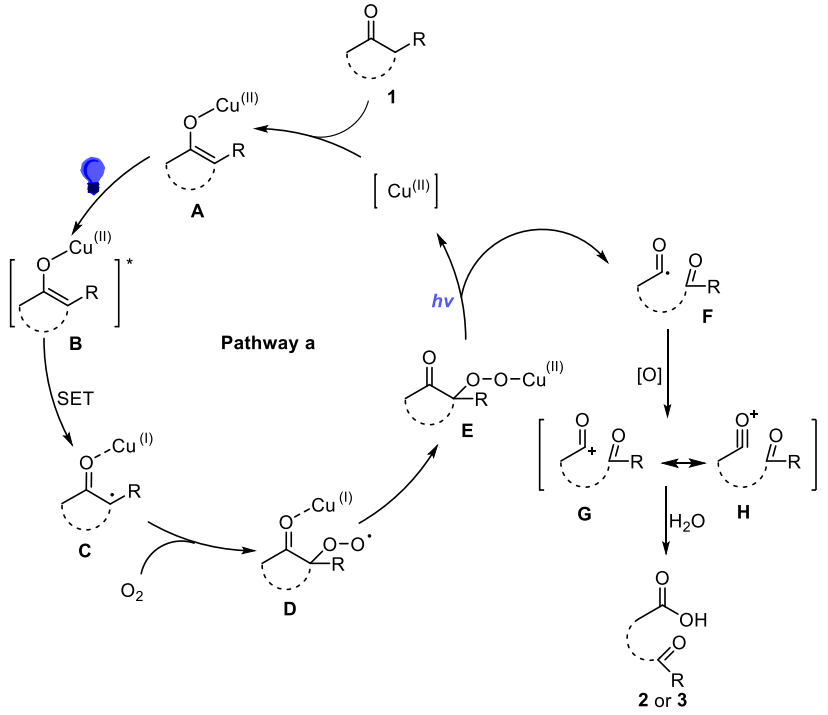
Scheme 5. Control Experiments



Scheme 6. Tentative Reaction Mechanism of Conditions A



ether = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.0 Hz, 2H), 7.26−7.24 (m, 2H), 2.98 (t, J = 7.2 Hz, 2H), 2.43−2.41 (m, 5H), 1.83−1.71 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 199.5, 178.6, 143.8, 134.4, 129.3, 128.1, 37.9, 33.7, 24.3, 23.6, 21.6 ppm; IR (neat): υ_{max} 3053, 2957, 2923, 1694, 1606, 1508, 1459, 1080, 798 cm^{-1}; HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{13}H_{16}O_3Na$, 243.0992; found 243.0991.

*6-(4-Methoxyphenyl)-6-oxohexanoic Acid (**2c**).* Reaction conditions A. White solid (48%, 22.7 mg); m.p. 84−85 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.8 Hz, 2H), 6.3 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 2.95 (t, J = 7.2 Hz, 2H), 2.42 (t, J = 7.2 Hz, 2H), 1.83−1.71 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 198.5, 178.6, 163.4, 130.3, 130.0, 113.7, 55.5, 37.7, 33.7, 24.4, 23.7 ppm; IR (neat): υ_{max} 3051, 2924, 2856, 1700, 1599, 1511, 1457, 1106, 835 cm^{-1}; HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{13}H_{16}O_4Na$, 259.0941; found, 259.0937.

*6-Oxo-6-(4-(trifluoromethoxy)phenyl)hexanoic Acid (**2d**).* Reaction conditions A. Light yellow oil (66%, 38.3 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 2.99 (t, J = 6.8 Hz, 2H), 2.43 (t, J

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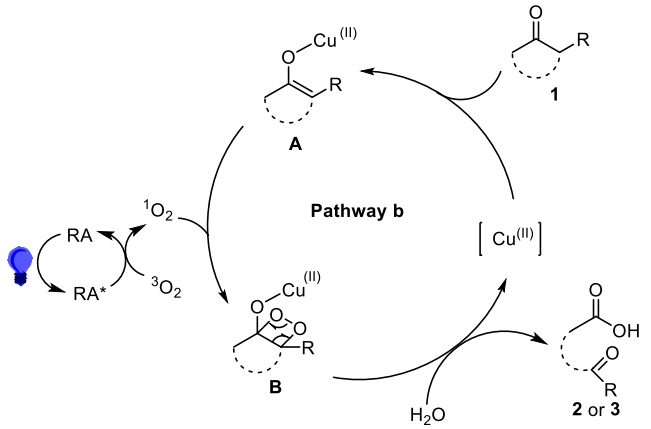
Scheme 7. Tentative Reaction Mechanism of Conditions B



= 6.8 Hz, 2H), 1.84−1.69 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.2, 179.5, 152.6, 135.0, 130.0, 120.4, 120.2 (q, J = 257.2 Hz), 38.1, 33.8, 24.2, 23.4 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −57.60 (s, 3F); IR (neat): υ_{max} 3041, 2931, 2873, 1694, 1679, 1605, 1509, 1463, 1109, 843 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{13}F_3O_4Na$, 313.0658; found, 313.0657.

*6-(4-Fluorophenyl)-6-oxohexanoic Acid (**2e**).* Reaction conditions A. White solid (66%, 29.6 mg); m.p. 83−84 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00−7.96 (m, 2H), 7.15−7.11 (m, 2H), 2.98 (t, J = 7.2 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.83−1.71 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.2, 179.2, 165.7 (d, J = 253.1 Hz), 133.3 (d, J = 3.0 Hz), 130.6 (d, J = 9.2 Hz), 115.7 (d, J = 21.7 Hz), 38.0, 33.8, 24.2, 23.5 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −105.36 (s, 1F); IR (neat): υ_{max} 3045, 2931, 2874, 1699, 1679, 1600, 1508, 1464, 1094, 841 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{13}FO_3Na$, 247.0741; found, 247.0752.

*6-Oxo-6-(4-(trifluoromethyl)phenyl)hexanoic Acid (**2f**).* Reaction conditions B. White solid (62%, 34.0 mg); m.p. 85−86 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 3.04 (t, J = 7.2 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.86−1.70 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.7, 179.4, 139.5, 134.3 (q, J = 32.5 Hz), 128.3, 125.7 (q, J = 3.7 Hz), 123.6 (q, J = 271.0 Hz), 38.4, 33.7, 24.1, 23.2 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.08 (s, 3F); IR (neat): υ_{max} 3067, 2925, 2866, 1697, 1682, 1584, 1509, 1460, 832 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{13}F_3O_3Na$, 297.0709; found, 297.0708.

*6-Oxo-6-(m-tolyl)hexanoic Acid (**2g**).* Reaction conditions A. Light yellow oil (66%, 29.0 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76−7.73 (m, 2H), 7.38−7.32 (m, 2H), 2.99 (t, J = 7.2 Hz, 2H), 2.44−2.41 (m, 5H), 1.84−1.69 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.1, 179.0, 138.4, 136.9, 133.8, 128.5, 125.2, 38.1, 33.8, 24.3, 23.6, 21.4 ppm; IR (neat): υ_{max} 3051, 2957, 2854, 1709, 1685, 1604, 1587, 1488, 788, 690 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{16}O_3Na$, 243.0992; found, 243.0985.

*6-(3-Chlorophenyl)-6-oxohexanoic Acid (**2h**).* Reaction conditions A. Light yellow oil (51%, 24.5, 7.3 mg starting material was recovered); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.92−7.91 (m, 1H), 7.83−7.81 (m, 1H), 7.54−7.52 (m, 1H), 7.43−7.39 (m, 1H), 2.98 (t, J = 7.2 Hz, 2H), 2.43 (t, J = 7.2 Hz, 2H), 1.84−1.71 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.4, 178.8, 138.4, 133.0, 130.0, 128.1, 126.1, 38.2, 33.7, 24.2, 23.3 ppm; IR (neat): υ_{max} 3050, 2926, 2871, 1703, 1689, 1593, 1461, 784, 680 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{13}ClO_3Na$, 263.0445; found, 263.0447.

*6-(3-Fluorophenyl)-6-oxohexanoic Acid (**2i**).* Reaction conditions A. White solid (68%, 30.5 mg); m.p. 49−50 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.74−7.72 (m, 1H), 7.64−7.61 (m, 1H), 7.47−7.42 (m, 1H), 7.28−7.24 (m, 1H), 2.99 (t, J = 6.8 Hz, 2H), 2.43 (t, J = 6.8 Hz, 2H), 1.84−1.71 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.4, 178.8, 162.9 (d, J = 246.4 Hz), 138.9 (d, J = 5.9 Hz), 130.3 (d, J = 7.6 Hz), 123.7 (d, J = 3.0 Hz), 120.1 (d, J = 21.4 Hz), 114.8 (d, J = 22.1 Hz), 38.2, 33.7, 24.2, 23.3 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −111.84 (s, 1F); IR (neat): υ_{max} 3078, 2944, 2872, 1698, 1681, 1589, 1485, 784, 681 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{13}FO_3Na$, 247.0741; found, 247.0748.

*6-Oxo-6-(o-tolyl)hexanoic Acid (**2j**).* Reaction conditions A. Light yellow oil (56%, 24.6 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, J = 8.0 Hz, 1H), 7.39−7.35 (m, 1H), 7.27−7.23 (m, 2H), 2.93 (t, J = 6.8 Hz, 2H), 2.49 (s, 3H), 2.41 (t, J = 6.8 Hz, 2H), 1.81−1.69 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 204.0, 178.5, 138.0, 132.0, 131.2, 128.3, 125.7, 41.0, 33.7, 24.3, 23.7, 21.3 ppm; IR (neat): υ_{max} 3053, 2926, 2857, 1704, 1683, 1601, 1571, 1486, 752 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{16}O_3Na$, 243.0992; found, 243.0992.

*6-(2-Methoxyphenyl)-6-oxohexanoic Acid (**2k**).* Reaction conditions A. Light yellow oil (30%, 14.2 mg, 14.7 mg starting material was recovered); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68−7.65 (m, 1H), 7.45−7.43 (m, 1H), 7.01−6.95 (m, 2H), 3.90 (s, 3H), 3.00 (t, J = 7.2 Hz, 2H), 2.40 (t, J = 7.2 Hz, 2H), 1.78−1.69 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 202.5, 179.0, 158.4, 133.4, 130.2, 128.3, 120.6, 111.5, 55.5, 43.3, 33.8, 24.3, 23.7 ppm; IR (neat): υ_{max} 3058, 2927, 2871, 1707, 1672, 1597, 1462, 1114, 758 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{16}O_4Na$, 259.0941; found, 259.0939.

*6-(4-Fluoro-3-methylphenyl)-6-oxohexanoic Acid (**2l**).* Reaction conditions A. White solid (62%, 29.5 mg); m.p. 50−51 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.83−7.76 (m, 2H), 7.08−7.04 (m, 1H), 2.96 (t, J = 7.2 Hz, 2H), 2.42 (t, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.83−1.70 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.5, 178.8, 164.3 (d, J = 251.8 Hz), 133.0 (d, J = 3.3 Hz), 131.8 (d, J = 6.5 Hz), 127.9 (d, J = 9.2 Hz), 125.3 (d, J = 17.7 Hz), 115.2 (d, J = 22.9 Hz), 38.0, 33.7, 24.3, 23.5, 14.6 (d, J = 3.4 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −109.52 (s, 1F); IR (neat): υ_{max} 3055, 2921, 2850, 1719, 1683, 1589, 1500, 1466, 811 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{15}FO_3Na$, 261.0897; found, 261.0896.

*6-(2,6-Dimethylphenyl)-6-oxohexanoic Acid (**2m**).* Reaction conditions B. Light yellow oil (63%, 29.5, 11.5 mg starting material was recovered); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.17−7.14 (m, 1H), 7.02−7.00 (m, 2H), 2.74 (t, J = 6.8 Hz, 2H), 2.41 (t, J = 6.8 Hz, 2H), 2.21 (s, 6H), 1.81−1.71 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 210.1, 178.8, 142.3, 132.3, 128.5, 127.7, 44.2, 33.7, 24.2, 22.7, 19.1 ppm; IR (neat): υ_{max} 3064, 2926, 1705, 1595, 1511, 1460, 781, 728 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{14}H_{18}O_3Na$, 257.1148; found, 257.1148.

*6-(Naphthalen-1-yl)-6-oxohexanoic Acid (**2n**).* Reaction conditions B. Light yellow oil (51%, 26.1 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.56 (d, J = 8.4 Hz, 1H), 8.00−7.97 (m, 1H), 7.89−7.84 (m, 2H), 7.61−7.48 (m, 3H), 3.10 (t, J = 7.2 Hz, 2H), 2.44 (t, J = 7.2 Hz, 2H), 1.91−1.75 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 204.2, 178.8, 136.1, 134.0, 132.5, 130.1, 128.4, 127.9, 127.3, 126.4, 125.7, 124.4, 41.7, 33.7, 24.3, 24.0 ppm; IR (neat): υ_{max} 3052, 2921, 2853, 1707, 1683, 1594, 1509, 1461, 780, 728 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{16}H_{16}O_3Na$, 279.0992; found, 279.0988.

*6-(Naphthalen-2-yl)-6-oxohexanoic Acid (**2o**).* Reaction conditions B. White solid (55%, 28.2 mg); m.p. 138−139 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.47 (s, 1H), 8.02−7.87 (m, 4H), 7.62−7.54 (m, 2H), 3.15 (t, J = 7.2 Hz, 2H), 2.45 (t, J = 7.2 Hz, 2H), 1.91−1.76 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 199.8, 178.6, 135.6, 134.2, 132.5, 129.6, 129.5, 128.5, 128.4, 127.8, 126.8, 123.8, 38.1, 33.7, 24.3, 23.7 ppm; IR (neat): υ_{max} 3060, 2929, 1699, 1670, 1598, 1464, 865, 832 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{16}H_{16}O_3Na$, 279.0992; found, 279.0984.

*6-Oxoheptanoic Acid (**2p**).* Reaction conditions B. Known compound, light yellow oil (87%, 25.1 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.46 (t, J = 6.8 Hz, 2H), 2.37 (t, J = 6.8 Hz, 2H), 2.14 (s, 3H), 1.64−1.60 (m, 4H);

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$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 208.7, 178.9, 43.2, 33.6, 29.9, 24.0, 23.0 ppm. Spectral data match those previously reported.[15]

*7-Methyl-6-oxononanoic Acid (**2q**).* Reaction conditions B. Light yellow oil (84%, 31.2 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.47−2.40 (m, 3H), 2.37 (t, J = 6.8 Hz, 2H), 1.70−1.62 (m, 5H), 1.41−1.32 (m, 1H), 1.05 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 214.4, 179.2, 47.9, 40.6, 33.8, 25.9, 24.2, 22.9, 15.9, 11.7 ppm; IR (neat): υ_{max} 2937, 2877, 1708, 1276 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{10}H_{18}O_3Na$, 209.1148; found, 209.1148.

*2-Methyl-6-oxoheptanoic Acid (**2r**).* Reaction conditions B. Known compound, light yellow oil (63%, 19.9 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.49−2.43 (m, 3H), 2.14 (s, 3H), 1.68−1.57 (m, 3H), 1.47−1.40 (m, 1H), 1.19 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 208.7, 182.4, 43.4, 39.2, 32.8, 29.9, 21.3, 16.8 ppm. Spectral data match those previously reported.[7]

*3,7-Dimethyl-6-oxooctanoic Acid (**2s**).* Reaction conditions B. Light yellow oil (81%, 30.1 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.64−2.57 (m, 1H), 2.50−2.45 (m, 2H), 2.35 (dd, J = 9.2 Hz, 6.0 Hz, 1H), 2.18 (dd, J = 8.0 Hz, 7.2 Hz, 1H), 1.97−1.92 (m, 1H), 1.68−1.62 (m, 1H), 1.53−1.45 (m, 1H), 1.09 (d, J = 7.2 Hz, 6H), 0.97 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 214.6, 178.7, 41.2, 40.9, 37.8, 30.2, 29.8, 19.5, 18.3, 18.2 ppm; IR (neat): υ_{max} 2933, 2876, 1704, 1259 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{10}H_{18}O_3Na$, 209.1148; found, 209.1140.

*7-Ethoxy-6,7-dioxoheptanoic Acid (**2t**).* Reaction conditions B. Known compound, colorless oil (80%, 32.3 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 4.31 (q, J = 7.2 Hz, 2H), 2.87 (t, J = 6.8 Hz, 2H), 2.39 (t, J = 6.8 Hz, 2H), 1.68−1.60 (m, 4H), 1.36 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 194.1, 179.2, 161.0, 62.5, 38.8, 33.6, 23.8, 22.2, 14.0 ppm. Spectral data match those previously reported.[16]

*Oxonane-2,7-dione (**2u**).* Reaction conditions B. Known compound, colorless oil (39%, 12.2 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$): δ = 4.57 (t, J = 6.8 Hz, 2H), 2.78 (t, J = 6.8 Hz, 2H), 2.43−2.35 (m, 4H), 1.92−1.77 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 211.0, 174.7, 60.5, 42.1, 41.4, 34.9, 24.4, 23.7 ppm. Spectral data match those previously reported.[6a]

*Adipic Acid (**2v**).* Reaction conditions B. Known compound, white solid (45%, 13.1 mg); R_f = 0.10 (EtOAc/petroleum ether = 2:1); ^1H NMR (400 MHz, DMSO-d_6): δ = 12.03 (s, 2H), 2.20 (t, J = 6.0 Hz, 4H), 1.50−1.47 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ = 174.4, 33.4, 24.1 ppm. Spectral data match those previously reported.[17]

*5-Oxo-5-phenylpentanoic Acid (**3a**).* Reaction conditions B. Known compound, light yellow oil (88%, 33.8 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97−7.95 (m, 2H), 7.58−7.55 (m, 1H), 7.48−7.44 (m, 2H), 3.09 (t, J = 7.2 Hz, 2H), 2.51 (t, J = 7.2 Hz, 2H), 2.13−2.06 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 199.3, 178.6, 136.7, 133.1, 128.6, 128.0, 37.3, 32.9, 19.0 ppm. Spectral data match those previously reported.[10]

*5-(4-Chlorophenyl)-5-oxopentanoic Acid (**3b**).* Reaction conditions A. White solid (86%, 38.9 mg); m.p. 117−118 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 3.06 (t, J = 7.2 Hz, 2H), 2.51 (t, J = 7.2 Hz, 2H), 2.11−2.04 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.0, 178.0, 139.6, 135.0, 129.4, 128.9, 37.2, 32.7, 18.9 ppm; IR (neat): υ_{max} 3056, 2927, 2871, 1705, 1588, 834 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{11}H_{11}ClO_3Na$, 249.0289; found, 249.0287.

*5-([1,1′-Biphenyl]-4-yl)-5-oxopentanoic Acid (**3c**).* Reaction conditions A. White solid (64%, 34.3 mg); m.p. 158−159 °C; R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, J = 8.4 Hz, 2H), 7.70−7.62 (m, 4H), 7.49−7.39 (m, 3H), 3.12 (t, J = 7.2 Hz, 2H), 2.54 (t, J = 7.2 Hz, 2H), 2.16−2.09 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 198.9, 177.8, 145.8, 139.8, 135.4, 129.0, 128.6, 128.2, 127.3, 37.3, 32.8, 19.1 ppm; IR (neat): υ_{max} 3059, 2922, 1701, 1674, 1605, 1563, 1450, 831 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}O_3Na$, 291.0992; found, 291.0990.

*5-Oxohexanoic Acid (**3d**).* Reaction conditions B. Known compound, light yellow oil (85%, 22.1 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.54 (t, J = 7.2 Hz, 2H), 2.40 (t, J = 7.2 Hz, 2H), 2.15 (s, 3H), 1.93−1.86 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 208.1, 178.9, 42.2, 32.8, 30.0, 18.5 ppm. Spectral data match those previously reported.[15]

*5-Oxododecanoic Acid (**3e**).* Reaction conditions B. Light yellow oil (80%, 34.2 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.50 (t, J = 7.2 Hz, 2H), 2.41−2.37 (m, 4H), 1.94−1.88 (m, 2H), 1.59−1.54 (m, 2H), 1.33−1.21 (m, 8H), 0.87 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 210.5, 178.1, 42.9, 41.3, 32.8, 31.7, 29.2, 29.0, 23.8, 22.6, 18.6, 14.1 ppm; IR (neat): υ_{max} 2926, 2855, 1712, 1260 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{22}O_3Na$, 237.1461; found, 237.1454.

*5-Cyclopentyl-5-oxopentanoic Acid (**3f**).* Reaction conditions B. Light yellow oil (90%, 33.1 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.89−2.81 (m, 1H), 2.54 (t, J = 7.2 Hz, 2H), 2.39 (t, J = 7.2 Hz, 2H), 1.94−1.84 (m, 2H), 1.82−1.55 (m, 8H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 212.5, 179.1, 51.4, 40.3, 33.0, 28.9, 26.0, 18.6 ppm; IR (neat): υ_{max} 2952, 2869, 1703 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{10}H_{16}O_3Na$, 207.0992; found, 207.0989.

*3,3-Dimethyl-5-oxohexanoic Acid (**3g**).* Reaction conditions B. Known compound, light yellow oil (76%, 24.0 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.59 (s, 2H), 2.50 (s, 2H), 2.16 (s, 3H), 1.12 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 209.4, 176.3, 52.1, 44.4, 32.7, 32.2, 28.3 ppm. Spectral data match those previously reported.[18]

*Glutaric Acid (**3h**).* Reaction conditions B. Known compound, white solid (38%, 10.0 mg); R_f = 0.10 (EtOAc/petroleum ether = 2:1); ^1H NMR (400 MHz, DMSO-d_6): δ = 12.12 (s, 2H), 2.24 (t, J = 7.2 Hz, 4H), 1.71−1.68 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ = 174.1, 32.7, 20.0 ppm. Spectral data match those previously reported.[17]

*4-Oxo-4-Phenylbutanoic Acid (**3i**).* Reaction conditions B. Known compound, light yellow oil (68%, 24.2 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00−7.98 (m, 2H), 7.60−7.56 (m, 1H), 7.49−7.46 (m, 2H), 3.33 (t, J = 6.8 Hz, 2H), 2.82 (t, J = 6.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 197.9, 177.8, 136.3, 133.3, 128.6, 128.0, 33.2, 27.9 ppm. Spectral data match those previously reported.[10]

*4-Oxo-4-(thiophen-2-yl)butanoic Acid (**3j**).* Reaction conditions B. White solid (54%, 19.9 mg); m.p. 81−82 °C; R_f = 0.10 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, J = 3.6 Hz, 1H), 7.66 (d, J = 4.8 Hz, 1H), 7.16−7.13 (m, 1H), 3.27 (t, J = 6.8 Hz, 2H), 2.82 (t, J = 6.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 190.7, 177.6, 143.4, 133.8, 132.1, 128.1, 33.7, 27.8 ppm; IR (neat): υ_{max} 3101, 2923, 1706, 1662 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_8H_8O_3SNa$, 207.0086; found, 207.0087.

*7-Oxo-7-phenylheptanoic Acid (**3k**).* Reaction conditions B. Light yellow oil (37%, 16.3, 20.0 mg starting material was recovered); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96−7.95 (m, 2H), 7.58−7.54 (m, 1H), 7.48−7.44 (m, 2H), 2.99 (t, J = 7.2 Hz, 2H), 2.39 (t, J = 7.2 Hz, 2H), 1.77−1.67 (m, 4H), 1.49−1.41 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.2, 179.0, 136.9, 133.0, 128.6, 128.0, 38.2, 33.7, 28.7, 24.5, 23.8 ppm; IR (neat): υ_{max} 3053, 2941, 2867, 1708, 1684, 1591, 1446, 754, 689 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{16}O_3Na$, 243.0992; found, 243.0988.

*Oxecane-2,8-dione (**3l**).* Reaction conditions B. Known compound, colorless oil (77%, 26.2 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$): δ = 4.46 (t, J = 6.0 Hz, 2H), 2.75 (t, J = 6.0 Hz, 2H), 2.46 (t, J = 6.4 Hz, 2H), 2.34 (t, J = 6.4 Hz, 2H), 1.74−1.66 (m, 4H), 1.45−1.38 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 211.9, 173.3, 61.6, 43.2, 39.6, 34.8, 25.2, 23.1, 22.2 ppm. Spectral data match those previously reported.[6a]

*8-Oxo-8-phenyloctanoic Acid (**3m**).* Reaction conditions B. Light yellow oil (63%, 29.5 mg, 9.3 mg starting material was recovered); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96−7.94 (m, 2H), 7.57−7.54 (m, 1H), 7.48−7.44 (m, 2H), 2.97 (t, J = 7.2 Hz, 2H), 2.36 (t, J = 7.2 Hz, 2H), 1.76−1.64 (m, 4H), 1.42−1.39

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(m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.4, 179.6, 137.0, 132.9, 128.6, 128.0, 38.4, 33.9, 28.9, 28.8, 24.5, 24.0 ppm; IR (neat): υ_{max} 3057, 2932, 2856, 1708, 1685, 1597, 1467, 730, 688 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{18}O_3Na$, 257.1148; found, 257.1147.

*6-(4-(1-Ethoxy-1-oxopropan-2-yl)phenyl)-5-oxohexanoic Acid (**3n**).* Reaction conditions B. Light yellow oil (30%, 18.4 mg, 27.5 mg starting material was recovered); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.21−7.25 (d, *J* = 8.0 Hz, 2H), 7.16−7.14 (d, *J* = 8.0 Hz, 2H), 4.15−4.08 (m, 2H), 3.72−3.66 (m, 3H), 2.55 (t, *J* = 7.2 Hz, 2H), 2.33 (t, *J* = 7.2 Hz, 2H), 1.90−1.85 (m, 2H), 1.48 (d, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 207.5, 178.2, 174.6, 139.4, 132.7, 129.6, 127.9, 60.8, 49.7, 45.2, 40.5, 32.6, 18.5, 18.4, 14.1 ppm; IR (neat): υ_{max} 3033, 2916, 1716, 1685, 1584, 1467 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{22}O_5Na$, 329.1359; found, 329.1367.

*N-((1r,3R,5S,7r)-3,5-Dimethyladamantan-1-yl)-6-oxo-6-phenylhexanamide (**4a**).* Light yellow oil (86%, 63.1 mg); R_f = 0.25 (EtOAc/petroleum ether = 1:2); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.95−7.93 (m, 2H), 7.56−7.52 (m, 1H), 7.46−7.42 (m, 2H), 5.30 (s, 1H), 2.99 (t, *J* = 7.2 Hz, 2H), 2.15−2.10 (m, 3H), 1.80−1.65 (m, 6H), 1.62 (s, 4H), 1.30 (dd, *J* = 26.0 Hz, 12.0 Hz, 4H), 1.30 (dd, *J* = 12.4 Hz, 8.4 Hz, 2H), 0.82 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.2, 172.0, 136.9, 133.0, 128.6, 128.0, 53.5, 50.5, 47.5, 42.6, 40.1, 38.2, 37.4, 32.3, 30.1, 30.0, 25.3, 23.6 ppm; IR (neat): υ_{max} 3308, 3065, 2902, 1682, 1647, 1598, 1452, 747, 692 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{24}H_{33}NO_2Na$, 390.2404; found, 390.2404.

*N-(((1R,4aS,10aR)-7-Isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)-6-oxo-6-phenylhexanamide (**4b**).* Light yellow oil (90%, 85.1 mg); R_f = 0.20 (EtOAc/petroleum ether = 1:2); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96−7.92 (m, 2H), 7.57−7.54 (m, 1H), 7.47−7.43 (m, 2H), 7.18−7.15 (m, 1H), 7.00−6.98 (m, 1H), 6.89 (s, 1H), 5.64 (s, 1H), 3.23 (dd, *J* = 7.6 Hz, 6.0 Hz, 1H), 3.13 (dd, *J* = 7.2 Hz, 6.4 Hz, 1H), 3.03−2.78 (m, 5H), 2.30−2.21 (m, 3H), 1.84−1.64 (m, 8H), 1.44−1.22 (m, 4H), 1.21 (d, *J* = 6.0 Hz, 6H), 0.94 (s, 3H), 0.85 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 200.0, 172.7, 147.1, 145.5, 136.8, 134.7, 133.0, 128.5, 128.0, 126.9, 124.1, 123.8, 49.7, 45.2, 38.3, 38.1, 37.4, 37.3, 36.7, 36.1, 33.4, 30.1, 25.3, 25.2, 24.0, 23.9, 23.6, 18.9, 18.7, 18.5 ppm; IR (neat): υ_{max} 3309, 3065, 2929, 1683, 1646, 1500, 1451, 747, 693 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{32}H_{43}NO_2Na$, 496.3186; found, 496.3186.

*5-Fluoro-1-phenylpentan-1-one (**5a**).* Colorless oil (53%, 19.1 mg); R_f = 0.45 (EtOAc/petroleum ether = 1:20); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97−7.95 (m, 2H), 7.59−7.55 (m, 1H), 7.49−7.45 (m, 2H), 4.56 (t, *J* = 5.6 Hz, 1H), 4.44 (t, *J* = 5.6 Hz, 1H), 3.05 (t, *J* = 7.2 Hz, 2H), 1.92−1.75 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 199.8, 136.9, 133.0, 128.6, 128.0, 83.9 (d, *J* = 163.7 Hz), 37.9, 29.9 (d, *J* = 19.5 Hz), 20.0 (d, *J* = 5.2 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −218.45 (s, 1F); IR (neat): υ_{max} 3053, 2905, 1683, 1594, 1449, 755, 690 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_{13}FONa$, 203.0843; found, 203.0841.

*5-Azido-1-phenylpentan-1-one (**5b**).* Colorless oil (42%, 17.1 mg); R_f = 0.40 (EtOAc/petroleum ether = 1:20); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97−7.95 (m, 2H), 7.59−7.55 (m, 1H), 7.49−7.45 (m, 2H), 3.34 (t, *J* = 6.8 Hz, 2H), 3.03 (t, *J* = 6.8 Hz, 2H), 1.88−1.80 (m, 2H), 1.73−1.66 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 199.6, 136.8, 133.1, 128.6, 128.0, 51.3, 37.8, 28.4, 21.3 ppm; IR (neat): υ_{max} 3051, 2926, 1685, 1597, 1449, 753, 690 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_{13}N_3ONa$, 226.0951; found, 226.0951.

*5-Hydroxy-5-phenylpentanoic Acid (**6a**).* Known compound, light yellow oil (88%, 34.1 mg); R_f = 0.15 (EtOAc/petroleum ether = 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40−7.31 (m, 5H), 5.36 (dd, *J* = 7.2, 3.6 Hz, 1H), 2.76−2.54 (m, 2H), 2.20−2.14 (m, 1H), 2.05−1.82 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 171.4, 139.7, 128.6, 128.3, 125.7, 81.7, 30.5, 29.5, 18.6 ppm. Spectral data match those previously reported.[10]

*6-Phenyltetrahydro-2H-pyran-2-one (**7a**).* Known compound, colorless oil (77%, 27.1 mg); R_f = 0.50 (EtOAc/petroleum ether = 1:2); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40−7.32 (m, 5H), 5.36 (dd, *J* = 7.2, 3.2 Hz, 1H), 2.75−2.53 (m, 2H), 2.18−2.15 (m, 1H), 2.02−1.84 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 171.3, 139.7, 128.6, 128.2, 125.7, 81.6, 30.5, 29.5, 18.6 ppm. Spectral data match those previously reported.[10]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00708.

^1H and ^{13}C spectra of all new compounds and the primary mechanistic studies of the reactions (PDF)

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Notes

The authors declare no competing financial interest.

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