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Graphical Abstract

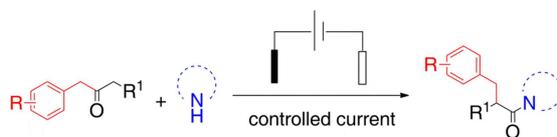
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Synthesis of α -benzylated amides via electrocatalytic Favorskii rearrangement of 1, 3-diarylacetonnes

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ABSTRACT

Electrolysis of 1,3-diarylacetonnes with aliphatic amines in Bu₄NI/CH₃CN to racemic Favorskii amides via benzyl group rearrangement has been developed. The electroconversion is easily conducted in a simple undivided cell under constant-current conditions at room temperature. The electrocatalytic Favorskii rearrangement of 1,3-diarylacetonnes including electron-withdrawing substituents was favored and gave a good yield of α -benzylated amides. When several unsymmetrical ketones were employed as substrates, this rearrangement with moderate regioselectivity was observed. This chemistry also provides an efficient approach to construct a chiral center at α -position of amides.

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1. Introduction

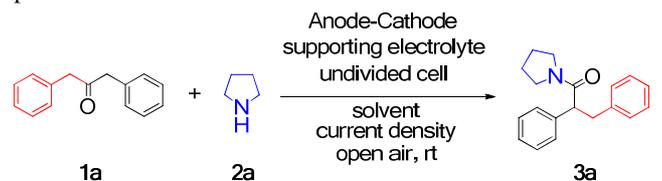
The Favorskii rearrangement is a well-known organic name reaction that uses α -haloketones as substrates.¹ When α -haloketones are treated with a nucleophilic base, carboxylic acids, esters and amides are usually obtained as reaction products via the C-C skeletal rearrangement. Besides base, by the employment of hypervalent iodine reagents,² acid,³ enzyme,⁴ photochemistry⁵ or electrochemistry,⁶ some novel Favorskii rearrangements have been also developed. To date, some reviews by Butkus⁷ and Yus⁸ discussed synthetic applications of this rearrangement.

In the past decade, electroorganic synthesis that employs electrons as reagents, has been developed to be a versatile and environment-friendly synthetic tool and become increasingly attractive. A search of the literature based around the electrochemically induced Favorskii rearrangement revealed only a few references to similar rearrangements of ketones or α -halo ketones in the presence of base. Among them, electrochemically induced Favorskii rearrangement of ketones under iodides-methanol system formed mainly the corresponding esters. For example, electrolysis of aliphatic cyclic ketones in methanol in the presence of sodium halides in an undivided cell resulted in ring-contracted esters as main products.^{9,10} In addition, aliphatic open-chain ketones under similar reaction conditions formed α,β -unsaturated carboxylic esters.^{11,12} The above several reactions need high constant current density which was more than 100 mA/cm². When α -polyhaloketones took the place of ketones as substrates through controlled potential electrolysis, the corresponding α,β -unsaturated amides as the Favorskii rearranged products were obtained in aprotic solvents such as DMF¹³ and CH₃CN¹⁴. To the best of our knowledge, a direct one-pot transformation of ketones into saturated amides via electrochemically induced Favorskii rearrangement has not been reported. Our group's research has been focused on the development of green and efficient electrochemical methodologies for C-H activation reactions. Herein, the synthesis of α -benzylated amides from 1,3-diarylacetonates is achieved via Favorskii rearrangement, in which migration of benzyl group led to formation of one chiral center at α -position of amides through electrochemical methods.

2. Results and discussion

We began our investigation with optimizing the reaction conditions for the electrocatalytic rearrangement of the easily available dibenzyl ketone **1a**, which was chosen as a model substrate and electrolyzed (Table 1). Cyclic voltammetry (CV) experiments of the substrates in acetonitrile were conducted (see ESI, Fig. S1). The constant current electrolysis of a mixture of **1a** (1 mmol) and pyrrolidine **2a** (2 mmol) using platinum electrodes was carried out in Bu₄Ni/CH₃CN at room temperature in a simple undivided cell. To our delight, the desired product **3a** was obtained in 75% yield (entry 1). The yield decreased when graphite rod was used as electrode material. Moreover, a dramatic corrosion of graphite rod cathode was observed under this electrolysis condition (entry 2-3). Other solvents such as methanol (entry 4) and DMF (entry 5) could not promote this transformation. The choice of supporting electrolyte has also a substantial impact on the reaction outcome. When Bu₄Ni was replaced by another halide salt, such as Bu₄NBr, product **3a** was obtained in 50% yield (entry 6), indicating that bromide is also efficient for this reaction. However, Bu₄NCl didn't lead to acceptable result (entry 7). The use of Bu₄NBF₄ (entry 8) or LiClO₄ (entry 9) led to almost no product formation. Further

Table 1
Optimization of the reaction conditions.^a



Entry	Anode-Cathode	Supporting electrolyte (equiv)	Solvent	Current density (mA/cm ²)	Yield ^b (%)
1	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	6	75
2	C-C	Bu ₄ Ni(1)	CH ₃ CN	6	63
3	C-Pt	Bu ₄ Ni(1)	CH ₃ CN	6	64
4	Pt-Pt	Bu ₄ Ni(1)	CH ₃ OH	6	37
5	Pt-Pt	Bu ₄ Ni(1)	DMF	6	42
6	Pt-Pt	Bu ₄ NBr(1)	CH ₃ CN	6	50
7	Pt-Pt	Bu ₄ NCl(1)	CH ₃ CN	6	trace
8	Pt-Pt	Bu ₄ NBF ₄ (1)	CH ₃ CN	6	0
9	Pt-Pt	LiClO ₄ (1)	CH ₃ CN	6	0
10 ^c	Pt-Pt	KI(1)	CH ₃ CN+H ₂ O	6	73
11	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	4	81
12	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	12	61
13	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	2	67
14 ^d	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	4	66
15	Pt-Pt	Bu ₄ Ni(2)	CH ₃ CN	4	78
16	Pt-Pt	Bu ₄ Ni(0.5)	CH ₃ CN	4	65
17 ^e	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	4	67
18 ^f	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	4	76
19 ^g	Pt-Pt	Bu ₄ Ni(1)	CH ₃ CN	4	0

^a Reaction conditions: dibenzyl ketone **1a** (1 mmol), pyrrolidine **2a** (2 mmol), and supporting electrolyte in 25 mL of solvent, undivided cell, the constant-current electrolysis, 4.5 F/mol.

^b ¹H NMR yields using 1,3,5-trimethoxybenzene as an internal standard.

^c 1 mL H₂O as co-solvent.

^d 8 F/mol was passed.

^e **2a** (1 mmol).

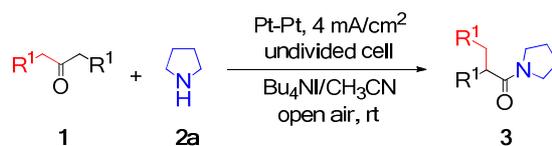
^f **2a** (3 mmol).

^g H-type cell, the distance between two electrodes is about 4 cm.

electrolyte screening disclosed that Bu₄Ni provided the best yields of **3a**, although KI (entry 10) and Bu₄Ni were almost equally effective. The above results reveal that the iodide ion is more important for the electrocatalytic Favorskii rearrangement reaction than others.

The effect of current density on the reaction was also examined. The reaction did not proceed without electrolysis. It was found that yield of **3a** was improved to 81% when a current density of 4 mA/cm² was employed instead of 6 mA/cm² (entry 11-13). In addition, extending electrolysis time (8 F/mol) could not improve the yield (entry 14). Though 0.5 equiv Bu₄Ni also gave the good result (65%, entry 16), the assay of the amount of Bu₄Ni disclosed that 1 equiv of Bu₄Ni was fit in order to obtain the highest yield (81%, entry 11) in Table 1. It suggested 0.5 equiv Bu₄Ni was not enough due to side reactions which could also consume Bu₄Ni. Attempt on decreasing and increasing the amount of amine **2a** led to decreased reaction yields (entry 17 and 18). No desired product **3a** could be obtained in two-compartment cell (entry 19).

Table 2
Synthesis of α -benzylated arylacetamides from symmetrical ketones.^a



Entry	Substrate	Product	Yield ^b (%)	Entry	Substrate	Product	Yield ^b (%)
1			73	8 ^d			38
2			66	9 ^d			40
3			79	10			29
4			69	11			37
5 ^c			77	12			60
6			64	13			mess
7 ^d			32	14			mess

^a Reaction conditions: ketones **1** (1 mmol), pyrrolidine **2a** (2 mmol), and Bu₄NI (1 mmol) as supporting electrolyte in 25 mL of CH₃CN, undivided cell, Pt-Pt, the constant-current electrolysis, 4.5 F/mol.

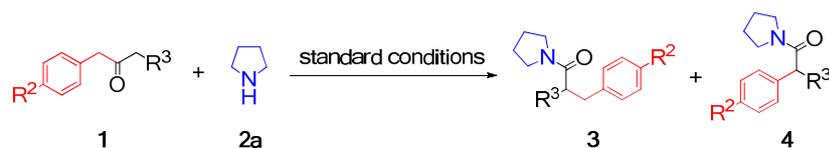
^b Isolated yields.

^c 2 mA/cm² was used.

^d 8 mA/cm² was used and 6 F/mol was consumed.

With the optimized conditions in hand (Table 1, entry 11), the scope of this electrochemical transformation was surveyed next. As shown in Table 2, changing the substituent of substrate **1** on the phenyl ring was carried out. Simple dibenzyl ketone could obtain the desired product **3a** in good yield. Halide substituents including F, Cl, and Br were well tolerated under electrochemical conditions, obtaining corresponding product **3b-d** in good yields too. When iodine was as the substituent, a current density of 2 mA/cm² was employed instead of 4 mA/cm² in order to avoid cleavage of C-I bond (**3e**). Beside of halide, dibenzyl ketones including strong electron-withdrawing substituents such as nitro group proceeded smoothly to afford the corresponding product **3f** in good yield. However, dibenzyl ketones including electron-donating substituents such as methyl group, which is substituted

at different positions of the phenyl ring, gave drastically decreased reaction yields (**3g-i**). Furthermore, it was found that dibenzyl ketones containing methoxyl group did not undergo the Favorskii rearrangement even though the longer reaction time and higher current density was used. The simple amides **3j** and **3k** were obtained instead of the desired products, respectively. Further investigation revealed that the steric size of naphthyl ring slightly affected the efficiency of the reaction (**3l**). Besides 1,3-diaryllactones, aliphatic ketones without benzyl group such as cyclohexanone (Table 2, entry 13) and heptan-4-one (Table 2, entry 14) were also electrolyzed under our optimized conditions, no desired Favorskii rearrangement product was isolated due to the form of many intractable by-products. Based upon these observations, we suggested that substrates including benzyl

Table 3
Synthesis of α -benzylated amides from unsymmetrical ketones.^a

Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield (%)
1			44	4			31
2			32	5			28
3			25				

^a Reaction conditions were the same as those of Table 2. Isolated yields were shown.

Table 4
Substrate scope of other amines.^a

Entry	Amine	Product	Yield (%)	Entry	Amine	Product	Yield (%)
1			61	7			49
2			63	8			mess
3			52	9			mess
4			0	10			0
5			29	11			0
6			35	12			mess

^a Reaction conditions were the same as those of Table 2. Isolated yields were shown.

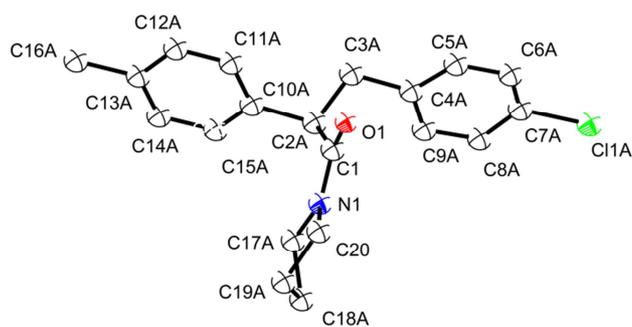


Figure 1. Structure of molecules **3m** with the atoms being represented as displacement ellipsoids at 30% probability level.

group were necessary for this rearrangement and electron-withdrawing substituents on phenyl ring were favored.

With the successful synthesis of α -benzylated arylacetamides **3** from symmetrical ketones, we next applied the electrochemical method to the more challenging attempt of constructing complex product **3** (Table 3). Surprisingly, the amides **3m-q** as the sole rearrangement products from unsymmetrical ketones **1** were obtained in acceptable yields and their isomers **4** were not detected *in situ* ^1H NMR monitoring. We found that the migration capability of benzyl group depended on electronic effect of substituents in this transformation. As a result, the migration of benzyl group including electron-withdrawing substituents happened more easily than benzyl group including electron-donating substituents under the standard conditions. For example, *p*-chlorobenzyl group (**3m**) and *p*-nitrobenzyl group (**3o**) migrated to α -C position of carbonyl group prior to *p*-methylbenzyl group, respectively. The structure of **3m** was confirmed by single-crystal X-ray diffraction studies.¹⁵ Similarly, *p*-nitrobenzyl group migrated prior to *p*-chlorobenzyl group in product **3n**. It is noteworthy that the benzyl alkyl ketones could also undergo benzyl group migration to furnish α -benzylated amides in acceptable yields (**3p** and **3q**, 31% and 28% yields, respectively).

As shown in Table 4, the reactions of dibenzyl ketone **1a** with various amines were investigated. Cyclic secondary aliphatic amines proceeded smoothly and afforded the corresponding α -benzylated amides **3r-t** in 52-63% isolated yield. The structure of **3t** was confirmed by single-crystal X-ray diffraction studies (Figure 2).¹⁶ X-ray crystallography revealed that compound **3t** crystallized as a racemic mixture in the solid state. However, 2,2,6,6-tetramethylpiperidine (entry 4) was not a suitable coupling partner owing to the steric hindrance. Acyclic aliphatic amine also reacted with **1a**, albeit in a bit lower yield (**3u-x**). On the contrary, arylamines were unreactive due to poor nucleophilicity (entry 8-12).

To further demonstrate the practicability of this transformation, the gram-scale electrolysis was also explored using 5 mmol of **1a** (1.05 g) under the standard reaction conditions. Product **3a** was isolated in a 69 % yield without significant loss of reaction efficiency.

In order to better understand the reaction mechanism, two control experiments were conducted. As shown in Scheme 1, when molecular iodine took place of Bu_4NI , the desired product **3a** was obtained in a 37% yield without electrolysis (eq. 1). Therefore, the *in situ* generated molecular iodine was suggested to be one of the active species. Moreover, the reaction of 1-iodo-

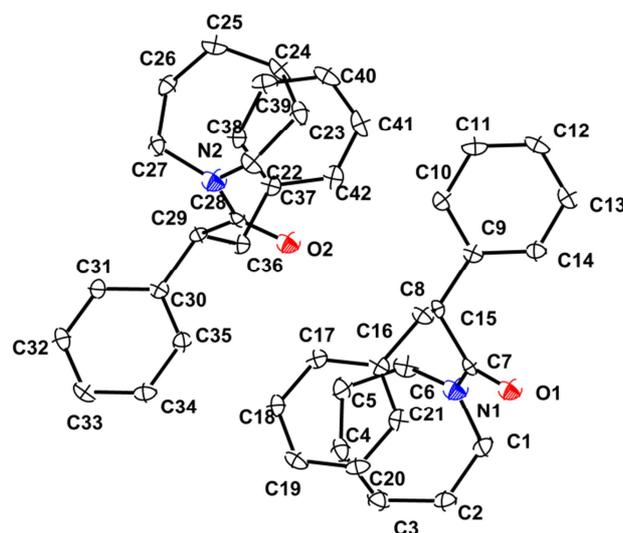
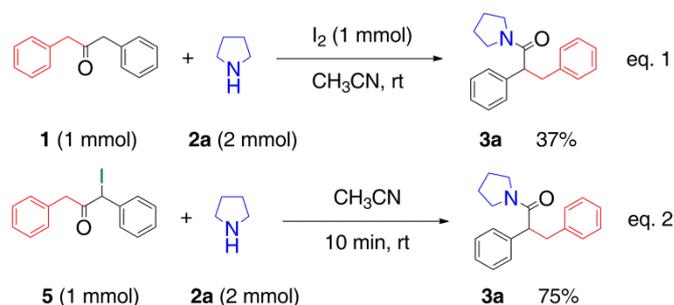


Figure 2. Structure of molecules **3t** and its enantiomer with the atoms being represented as displacement ellipsoids at 30% probability level.

1,3-diphenylpropan-2-one **5** and pyrrolidine finished in 10 minutes under room temperature and gave good yield of **3a** (eq. 2), which suggests that **5** may be a key intermediate in this transformation.

Based on the experimental results and literature reports,¹⁷ a plausible mechanism of the reaction between ketone **1** and pyrrolidine **2a** is proposed. As illustrated in Scheme 1, the reaction begins with the anodic oxidation of iodide to generate molecular iodine, which undergoes reaction with ketone **1** to form α -iodo ketone **A**. Secondary amines **2a** can promote Favorskii rearrangements by the formation of an enamine **B**. In the general case, the cyclopropanone intermediate **C** attacked by **2a** should open on the side that gives the more stable carbanion **D**. Finally, α -Benzylated amides **3** are obtained by hydrolysis of **D**.

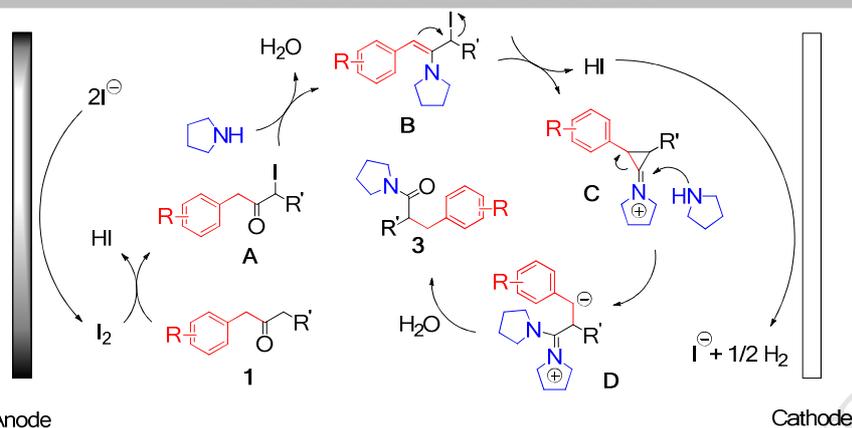


Scheme 1. Control experiments. ^1H NMR yields using 1,3,5-trimethoxybenzene as an internal.

3. Conclusions

In conclusion, an efficient electrochemical protocol for the synthesis of α -benzylated amides via the Favorskii rearrangement of 1,3-diarylacetonates has been developed. Neither high current density nor α -halo ketones were needed in this transformation. Importantly, the experimental set-up, with an undivided cell at ambient conditions, is very simple. Gram-scale reaction demonstrated the practicality of the protocol.

It was found that iodide ion and aliphatic amines play a significant role in the transformation. The electrocatalytic Favorskii rearrangement of symmetrical 1,3-diarylacetonates



Scheme 2. Proposed reaction mechanism.

including electron-withdrawing substituents was favored and gave a good yield of racemic α -benzylated arylacetamides. Notably, the unsymmetrical ketones were also suitable for this reaction, affording the sole products in acceptable yields with moderate regioselectivity.

4. Experimental

4.1 General

All chemicals were purchased from Sigma-Aldrich and were used without further purification. All products were purified through silica gel chromatography (200-300 mesh). Column chromatography was carried out with light petroleum ether (bp. 60-90 °C)/ethyl acetate as eluent. Melting points were determined using an SGW-X4B digital melting point apparatus and were uncorrected. ^1H and ^{13}C spectra were recorded in CDCl_3 on a 400 MHz Bruker Avance DPX spectrometer. Coupling constants were referred to as J values in Hz. X-ray single-crystal diffraction data collected on a Rigaku SuperNova dual four-circle diffractometer. ESI mass spectra were acquired using a Bruker ESQUIRELCTM ESI ion trap spectrometer. High-resolution mass spectral (HRMS) analysis data were measured on a Waters Synapt G1 UPLC-Q-TOF instrument.

Preparative electrolysis and cyclic voltammetry was performed using a CHI605D Electrochemical Analyser (Chenhua Co. Ltd., Shanghai, China). Cyclic voltammetry was performed in a three-compartment cell. The working electrode used in the voltammetry experiments was a platinum disk (2 mm in diameter) and platinum sheet was used as counter electrode. All potentials were referred to Ag/AgCl electrode.

4.2 Preparative electrolysis

The preparative-scale electrolysis was performed in an undivided cell fitted with Pt sheet electrodes having an area of 3 cm^2 (the distance is about 1 cm). A 25 ml solution of acetonitrile containing $n\text{-Bu}_4\text{NI}$ (1 mmol), dibenzyl ketone derivatives **1** (1 mmol) and amine **2** (2 mmol) was stirred magnetically. The constant-current electrolysis was carried out at current density of 4 mA/cm^2 at room temperature. The electrolysis was stopped when 4.5 or 6 F/mol of electricity was passed. The final electrolyte was concentrated under reduced pressure; a saturated aqueous sodium chloride solution was then added and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate and concentrated. The products were purified by column chromatography on silica gel using ethyl acetate/petroleum ether as the eluent.

4.2.1. 2,3-Diphenyl-1-(1-pyrrolidinyl)-1-propanone (**3a**)

Purification by chromatography (petroleum ether/EtOAc = 6:1, R_f = 0.25) afforded **3a** as a white solid (224 mg, 73%); mp: 83-84 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.28 (d, J = 4 Hz, 4H), 7.25-7.12 (m, 4H), 7.10 (d, J = 6.9 Hz, 2H), 3.82 (t, J = 7.3 Hz, 1H), 3.49 (dd, J = 13.4, 6.5 Hz, 1H), 3.40 (d, J = 27.3 Hz, 2H), 3.20 (d, J = 27.3 Hz, 2H), 2.95 (dd, J = 13.4, 6.5 Hz, 1H), 1.73 (s, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.0, 140.0, 139.5, 129.1, 128.5, 128.2, 128.1, 126.9, 126.0, 53.0, 46.2, 45.9, 40.9, 25.9, 24.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{19}\text{H}_{21}\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 302.1515, found 302.1515.

4.2.2. 2,3-Bis(4-fluorophenyl)-1-(1-pyrrolidinyl)-1-propanone (**3b**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, R_f = 0.18) afforded **3b** as a white solid (208 mg, 66%); mp: 90-92 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.25-7.18 (m, 2H), 7.03-7.00 (m, 2H), 6.99-6.94 (t, J = 8.4 Hz, 2H), 6.93-6.85 (t, J = 8.8 Hz, 2H), 3.74 (t, J = 7.6 Hz, 1H), 3.49-3.34 (m, 3H), 3.26-3.22 (m, 1H), 3.20-3.10 (m, 1H), 2.89 (dd, J = 13.6, 7.0 Hz, 1H), 1.85-1.68 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 161.9 (d, $J_{\text{C-F}}$ = 244 Hz, 1C), 161.5 (d, $J_{\text{C-F}}$ = 242 Hz, 1C), 135.4 (d, $J_{\text{C-F}}$ = 3.3

Hz, 1C), 134.9 (d, $J_{\text{C-F}}$ = 3.3 Hz, 1C), 130.6 (d, $J_{\text{C-F}}$ = 7.8 Hz, 1C), 129.7 (d, $J_{\text{C-F}}$ = 8.0 Hz, 1C), 115.5 (d, $J_{\text{C-F}}$ = 21.3 Hz, 1C), 114.9 (d, $J_{\text{C-F}}$ = 21.1 Hz, 1C), 52.4, 46.3, 46.0, 40.2, 26.0, 24.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{19}\text{H}_{19}\text{F}_2\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 338.1327, found 338.1325.

4.2.3. 2,3-Bis(4-chlorophenyl)-1-(pyrrolidin-1-yl)propan-1-one (**3c**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, R_f = 0.21) afforded **3c** as a white solid (274 mg, 79%); mp: 94-96 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.25 (d, J = 8.0 Hz, 2H), 7.20-7.17 (m, 4H), 7.00 (d, J = 7.9 Hz, 2H), 3.73 (t, J = 7.4 Hz, 1H), 3.43-3.38 (m, 3H), 3.25 (s, br 1H), 3.13 (s, br, 1H), 2.88 (dd, J = 13.5, 6.9 Hz, 1H), 1.75 (s, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 138.1, 137.5, 133.0, 132.0, 130.5, 129.5, 128.8, 128.3, 52.4, 46.2, 46.0, 40.2, 25.9, 24.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{19}\text{H}_{21}\text{Cl}_2\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 370.0736, found 370.0736.

4.2.4. 2,3-Bis(4-bromophenyl)-1-(1-pyrrolidinyl)-1-propanone (**3d**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, R_f = 0.30) afforded **3d** as a white solid (301 mg, 69%); mp: 101-103 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.41 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 8.3

Hz, 2H), 3.71 (t, $J = 7.4$ Hz, 1H), 3.52-3.31 (m, 3H), 3.26 (s, br, 1H), 3.13 (s, br, 1H), 2.86 (dd, $J = 13.5, 6.9$ Hz, 1H), 1.75 (d, $J = 2.8$ Hz, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 138.6, 138.1, 131.8, 131.3, 130.9, 129.9, 121.1, 120.1, 52.4, 46.3, 46.1, 40.2, 25.9, 24.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{19}\text{H}_{21}\text{Br}_2\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 457.9726, found 457.9724.

4.2.5. 2,3-Bis(4-iodophenyl)-1-(1-pyrrolidinyl)-1-propanone (**3e**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, $R_f = 0.23$) afforded **3e** as a white solid (409 mg, 77%); mp: 149-151 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, $J = 8.3$ Hz, 2H), 7.53 (d, $J = 8.2$ Hz, 2H), 7.01 (d, $J = 8.3$ Hz, 2H), 6.83 (d, $J = 8.2$ Hz, 2H), 3.69 (t, $J = 7.4$ Hz, 1H), 3.50-3.32 (m, 3H), 3.25 (s, br, 1H), 3.12 (s, br, 1H), 2.84 (dd, $J = 13.5, 6.8$ Hz, 1H), 1.75 (s, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.1, 139.3, 138.8, 137.8, 137.3, 131.3, 130.2, 92.7, 91.5, 52.5, 46.3, 46.1, 40.3, 25.9, 24.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{19}\text{H}_{19}\text{I}_2\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 553.9448, found 553.9442.

4.2.6. 2,3-Bis(4-nitrophenyl)-1-(1-pyrrolidinyl)-1-propanone (**3f**)

Purification by chromatography (petroleum ether/EtOAc = 2:1, $R_f = 0.2$) afforded **3f** as a yellow solid (237 mg, 64%); mp: 160-161 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.18 (d, $J = 8.7$ Hz, 2H), 8.10 (d, $J = 8.7$ Hz, 2H), 7.47 (d, $J = 8.8$ Hz, 2H), 7.28 (d, $J = 8.6$ Hz, 2H), 3.95 (dd, $J = 8.3, 6.6$ Hz, 1H), 3.61 (dd, $J = 13.5, 8.3$ Hz, 1H), 3.50-3.37 (m, 2H), 3.34-3.28 (m, 1H), 3.14-3.10 (m, 1H), 3.06 (dd, $J = 13.5, 8.3$ Hz, 1H), 1.87-1.77 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.8, 147.3, 146.8, 146.7, 145.9, 123.0, 129.0, 124.1, 123.7, 52.5, 46.4, 46.3, 40.5, 25.9, 24.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{19}\text{H}_{19}\text{N}_3\text{O}_5\text{Na}^+$ [$\text{M}+\text{Na}^+$] 392.1217, found 392.1220.

4.2.7. 2,3-bis(2-methylphenyl)-1-(1-pyrrolidinyl)-1-propanone (**3g**)

Purification by chromatography (petroleum ether/EtOAc = 6:1, $R_f = 0.25$) afforded **3g** as a colorless oil (98 mg, 32%); ^1H NMR (400 MHz, CDCl_3) δ 7.56-7.50 (m, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 7.12 (td, $J = 7.6, 1.2$ Hz, 1H), 7.06 (d, $J = 3.9$ Hz, 2H), 7.04-6.95 (m, 2H), 6.88 (d, $J = 7.4$ Hz, 1H), 4.02 (t, $J = 7.2$ Hz, 1H), 3.52-3.52 (m, 3H), 3.23-3.19 (m, 1H), 2.95-2.90 (m, 2H), 2.19 (s, 3H), 1.93 (s, 3H), 1.79-1.67 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.8, 138.04, 138.02, 136.5, 135.8, 130.03, 130.00, 129.9, 127.7, 126.8, 126.7, 126.2, 125.7, 46.9, 46.1, 45.6, 37.7, 26.0, 24.1, 19.4, 19.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{21}\text{H}_{25}\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 330.1828, found 330.1830.

4.2.8. 2,3-Bis(3-methylphenyl)-1-(1-pyrrolidinyl)-1-propanone (**3h**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, $R_f = 0.23$) afforded **3h** as a colorless oil (118 mg, 38%); ^1H NMR (400 MHz, CDCl_3) δ 7.18-7.10 (m, 3H), 7.08-7.03 (m, 2H), 6.97 (d, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 11.5$ Hz, 2H), 3.78 (dd, $J = 8.6, 6.0$ Hz, 1H), 3.48-3.43 (m, 2H), 3.42-3.33 (m, 1H), 3.24-3.15 (m, 2H), 2.87 (dd, $J = 13.4, 6.0$ Hz, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 1.77-1.70 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.1, 140.1, 139.6, 138.2, 137.6, 129.9, 128.7, 128.3, 128.0, 127.7, 126.7, 126.1, 125.3, 52.9, 46.2, 45.9, 40.9, 25.9, 24.1, 21.4, 21.3; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{21}\text{H}_{25}\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 330.1828, found 330.1831.

4.2.9. 2,3-Bis(4-methylphenyl)-1-(1-pyrrolidinyl)-1-propanone (**3i**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, $R_f = 0.25$) afforded **3i** as a white solid (126 mg, 40%); mp: 71-73 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.18 (d, $J = 8.0$ Hz, 2H),

7.09 (d, $J = 7.9$ Hz, 2H), 7.03-6.98 (m, 4H), 3.76 (t, $J = 7.6$ Hz, 1H), 3.50-3.33 (m, 3H), 3.29-3.21 (m, 1H), 3.20-3.12 (m, 1H), 2.87 (dd, $J = 13.5, 6.4$ Hz, 1H), 2.31 (s, 3H), 2.28 (s, 3H), 1.78-1.67 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.3, 137.2, 136.7, 136.5, 135.4, 129.3, 129.0, 128.8, 128.1, 52.7, 46.2, 45.9, 40.6, 25.9, 24.1, 21.1, 21.0; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{21}\text{H}_{25}\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 330.1828, found 330.1832.

4.2.10. (4-Methoxyphenyl)(pyrrolidin-1-yl)methanone (**3j**)

Purification by chromatography (petroleum ether/EtOAc = 1:1, $R_f = 0.23$) afforded **3j** as a yellow oil (60 mg, 29%); ^1H NMR (400 MHz, CDCl_3) δ 7.52 (d, $J = 8.4$ Hz, 2H), 6.90 (d, $J = 8.7$ Hz, 2H), 3.83 (s, 3H), 3.63 (t, $J = 6.8$ Hz, 2H), 3.48 (t, $J = 6.5$ Hz, 2H), 1.97-1.92 (m, 2H), 1.90-1.85 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.4, 160.7, 129.3, 129.1, 113.3, 55.3, 49.8, 46.3, 26.4, 24.4; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_2\text{Na}^+$ [$\text{M}+\text{Na}^+$] 228.0995, found 228.1007.

4.2.11. benzo[d][1,3]dioxol-5-yl(pyrrolidin-1-yl)methanone (**3k**)

Purification by chromatography (petroleum ether/EtOAc = 1:1, $R_f = 0.28$) afforded **3k** as a yellow oil (81 mg, 37%); ^1H NMR (400 MHz, CDCl_3) δ 7.06 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.03 (d, $J = 1.2$ Hz, 1H), 6.81 (d, $J = 8.0$ Hz, 1H), 5.99 (s, 2H), 3.62 (t, $J = 6.9$ Hz, 2H), 3.46 (t, $J = 6.6$ Hz, 2H), 1.97-1.85 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.0, 148.8, 147.4, 131.0, 121.8, 108.1, 107.9, 101.4, 49.8, 46.4, 26.5, 24.5; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_3\text{Na}^+$ [$\text{M}+\text{Na}^+$] 242.0788, found 242.0787.

4.2.12. 2,3-Dinaphthyl-1-(1-pyrrolidinyl)-1-propanone (**3l**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, $R_f = 0.2$) afforded **3l** as a white solid (227 mg, 60%); mp: 54-56 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.0$ Hz, 1H), 7.83 (d, $J = 7.8$ Hz, 2H), 7.80-7.70 (m, 3H), 7.64 (d, $J = 7.8$ Hz, 1H), 7.52-7.45 (m, 3H), 7.40 (t, $J = 7.2$ Hz, 1H), 7.29 (td, $J = 7.6, 1.2$ Hz, 1H), 7.23-7.16 (m, 2H), 4.77 (dd, $J = 7.9, 5.8$ Hz, 1H), 4.20 (dd, $J = 14.2, 8.0$ Hz, 1H), 3.54-3.39 (m, 3H), 3.10-3.04 (m, 1H), 2.78-2.73 (m, 1H), 1.71-1.52 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.5, 136.3, 136.1, 133.78, 133.77, 132.0, 131.4, 129.0, 128.8, 127.5, 127.2, 126.8, 126.0, 125.9, 125.8, 125.6, 125.4, 125.4, 125.3, 123.6, 122.4, 46.8, 46.2, 37.3, 26.9, 25.9, 24.0; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{27}\text{H}_{25}\text{NONa}^+$ [$\text{M}+\text{Na}^+$] 402.1828, found 402.1829.

4.2.13. 2-(4-Methylphenyl)-3-(4-chlorophenyl)-1-(1-pyrrolidinyl)-1-propanone (**3m**)

Purification by chromatography (petroleum ether/EtOAc = 5:1, $R_f = 0.27$) afforded **3m** as a white solid (144 mg, 44%); mp: 93-95 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.19-7.13 (m, 4H), 7.09 (d, $J = 7.6$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 3.72 (dd, $J = 8.4, 6.8$ Hz, 1H), 3.46-3.39 (m, 3H), 3.27 (s, br, 1H), 3.15 (s, br, 1H), 2.88 (dd, $J = 13.5, 6.8$ Hz, 1H), 2.32 (s, 3H), 1.73 (s, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 138.7, 136.7, 136.1, 131.7, 130.6, 129.3, 128.2, 128.0, 52.7, 46.2, 46.0, 40.3, 25.9, 24.1, 21.1; HRMS(ESI-TOF) m/z : calcd for $\text{C}_{20}\text{H}_{22}\text{ClNONa}^+$ [$\text{M}+\text{Na}^+$] 350.1282, found 350.1282.

4.2.14. 2-(4-Nitrophenyl)-3-(4-chlorophenyl)-1-(1-pyrrolidinyl)-1-propanone (**3n**)

Purification by chromatography (petroleum ether/EtOAc = 3:1, $R_f = 0.18$) afforded **3n** as a yellow solid (115 mg, 32%); mp: 115-116 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.08 (d, $J = 8.8$ Hz, 2H), 7.29-7.26 (m, 2H), 7.24 (d, $J = 7.4$ Hz, 2H), 7.18 (d, $J = 8.8$ Hz, 2H), 3.78 (t, $J = 7.4$ Hz, 1H), 3.54 (dd, $J = 13.5, 8.0$ Hz, 1H), 3.49-3.36 (m, 2H), 3.32-3.26 (m, 1H), 3.13-3.08 (m, 1H), 3.02 (dd, $J = 13.5, 6.9$ Hz, 1H), 1.85-1.73 (m, 4H); ^{13}C NMR (100

MHz, CDCl₃) δ 169.7, 147.5, 146.6, 137.0, 133.3, 130.1, 129.4, 129.1, 123.5, 52.1, 46.3, 46.1, 40.7, 25.9, 24.1; HRMS(ESI-TOF) m/z: calcd for C₁₉H₁₉ClN₂O₃Na⁺ [M+Na⁺] 381.0976, found 381.0978.

4.2.15. 2-(4-Nitrophenyl)-3-(4-methylphenyl)-1-(1-pyrrolidinyl)-1-propanone (**3o**)

Purification by chromatography (petroleum ether/EtOAc = 3:1, R_f = 0.22) afforded **3o** as a yellow solid (85 mg, 25%); mp: 115–116 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.13–7.08 (m, 4H), 3.76 (t, *J* = 7.4 Hz, 1H), 3.55 (dd, *J* = 13.4, 8.0 Hz, 1H), 3.50–3.36 (m, 2H), 3.33–3.27 (m, 1H), 3.15–3.10 (m, 1H), 3.02 (dd, *J* = 13.5, 6.8 Hz, 1H), 2.32 (s, 3H), 1.84–1.69 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 170.3, 148.2, 146.5, 137.0, 135.4, 130.1, 129.5, 127.9, 123.4, 52.4, 46.2, 46.1, 40.8, 25.9, 24.1, 21.1; HRMS(ESI-TOF) m/z: calcd for C₂₀H₂₂N₂O₃Na⁺ [M+Na⁺] 361.1523, found 361.1528.

4.2.16. 2-Methyl-3-phenyl-1-(1-piperidinyl)-1-propanone (**3p**)

Purification by chromatography (petroleum ether/EtOAc = 3:1, R_f = 0.17) afforded **3p** as a colorless oil (67.9 mg, 31%); ¹H NMR (400 MHz, CDCl₃) δ 7.28–7.23 (m, 2H), 7.18 (d, *J* = 7.6 Hz, 3H), 3.45–3.40 (m, 2H), 3.31–3.25 (m, 1H), 3.01–2.92 (m, 2H), 2.82–2.74 (m, 1H), 2.64 (dd, *J* = 13.0, 6.4 Hz, 1H), 1.83–1.64 (m, 4H), 1.17 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 174.3, 140.1, 128.9, 128.1, 126.1, 46.2, 45.5, 40.5, 40.4, 25.9, 24.1, 17.3; HRMS(ESI-TOF) m/z: calcd for C₁₄H₁₉NONa⁺ [M+Na⁺] 240.1359, found 240.1357.

4.2.17. 2-Butyl-3-phenyl-1-(1-piperidinyl)-1-propanone (**3q**)

Purification by chromatography (petroleum ether/EtOAc = 3:1, R_f = 0.27) afforded **3q** as a colorless oil (70 mg, 28%); ¹H NMR (400 MHz, CDCl₃) δ 7.27–7.22 (m, 2H), 7.28–7.16 (m, 3H), 3.43–3.31 (m, 2H), 3.24–3.18 (m, 1H), 2.95–2.88 (m, 1H), 2.76–2.67 (m, 3H), 1.83–1.21 (m, 8H), 0.89 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.8, 140.2, 128.9, 128.1, 126.0, 46.5, 46.3, 45.4, 39.6, 35.1, 25.8, 24.1, 20.8, 14.1; HRMS(ESI-TOF) m/z: calcd for C₁₆H₂₃NONa⁺ [M+Na⁺] 268.1672, found 268.1670.

4.2.18. 2,3-Diphenyl-1-(1-azetidiny)-1-propanone (**3r**)

Purification by chromatography (petroleum ether/EtOAc = 3:1, R_f = 0.2) afforded **3r** as a white solid (162 mg, 61%); mp: 85–86 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.30 (d, *J* = 4.3 Hz, 4H), 7.27–7.22 (m, 3H), 7.19–7.16 (m, 1H), 7.12 (d, *J* = 7.5 Hz, 2H), 3.97–3.87 (m, 2H), 3.83 (t, *J* = 7.6 Hz, 2H), 3.57 (dd, *J* = 8.7, 6.2 Hz, 1H), 3.44 (dd, *J* = 13.3, 8.7 Hz, 1H), 2.92 (dd, *J* = 13.3, 6.0 Hz, 1H), 2.14–1.97 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 172.2, 139.9, 139.3, 129.1, 128.6, 128.2, 128.1, 127.0, 126.2, 50.0, 49.9, 47.8, 40.2, 14.9; HRMS(ESI-TOF) m/z: calcd for C₁₈H₁₉NONa⁺ [M+Na⁺] 288.1363, found 288.1363.

4.2.19 2,3-Diphenyl-1-(1-piperidinyl)-1-propanone (**3s**)

Purification by chromatography (petroleum ether/EtOAc = 10:1, R_f = 0.22) afforded **3s** as a white solid (186 mg, 63%); mp: 75–76 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.25 (m, 2H), 7.23–7.19 (m, 5H), 7.17–7.13 (m, 1H), 7.08 (d, *J* = 7.2 Hz, 2H), 3.98 (t, *J* = 7.2 Hz, 1H), 3.63–3.57 (m, 1H), 3.50 (dd, *J* = 13.6, 7.9 Hz, 1H), 3.44–3.41 (m, 1H), 3.26 (t, *J* = 5.6 Hz, 2H), 2.94 (dd, *J* = 13.5, 6.8 Hz, 1H), 1.50–1.37 (m, 4H), 1.17–1.07 (m, 1H), 0.97–0.86 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 170.6, 140.2, 140.1, 129.2, 128.6, 128.1, 127.9, 126.8, 126.0, 50.9, 46.7, 43.3, 41.1, 25.9, 25.5, 24.5; HRMS(ESI-TOF) m/z: calcd for C₂₀H₂₃NONa⁺ [M+Na⁺] 316.1672, found 316.1673.

4.2.20. 2,3-Diphenyl-1-(1-azepanyl)-1-propanone (**3t**)

Purification by chromatography (petroleum ether/EtOAc = 10:1, R_f = 0.23) afforded **3t** as a white solid (160 mg, 52%); mp: 92–94 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.31–7.27 (m, 4H), 7.25–7.20 (m, 3H), 7.17–7.13 (m, 3H), 3.95 (dd, *J* = 8.7, 5.9 Hz, 1H), 3.72–3.66 (m, 1H), 3.52 (dd, *J* = 13.3, 8.6 Hz, 1H), 3.47–3.41 (m, 1H), 3.25–3.19 (m, 1H), 3.16–3.09 (m, 1H), 2.92 (dd, *J* = 13.3, 5.9 Hz, 1H), 1.65–1.56 (m, 2H), 1.43–1.30 (m, 3H), 1.29–1.17 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.7, 140.2, 140.1, 129.3, 128.6, 128.1, 128.0, 126.9, 126.0, 51.4, 47.7, 46.4, 41.6, 29.1, 27.4, 26.6, 26.2; HRMS(ESI-TOF) m/z: calcd for C₂₁H₂₅NOH⁺ [M+H⁺] 308.2009, found 308.2017.

4.2.21. *N,N*-diethyl-*o*-phenylbenzenepropanamide (**3u**)

Purification by chromatography (petroleum ether/EtOAc = 10:1, R_f = 0.25) afforded **3u** as a yellow oil (83 mg, 29%); ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, *J* = 4.4 Hz, 4H), 7.25–7.19 (m, 3H), 7.17–7.09 (m, 3H), 3.90 (dd, *J* = 8.4, 6.1 Hz, 1H), 3.49 (dd, *J* = 13.4, 8.4 Hz, 1H), 3.39–3.18 (m, 3H), 3.06–2.96 (m, 1H), 2.92 (dd, *J* = 13.3, 6.2 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.5, 140.1, 140.1, 129.2, 128.6, 128.1, 127.9, 126.9, 126.0, 51.2, 41.7, 41.6, 40.6, 14.2, 12.8; HRMS(ESI-TOF) m/z: calcd for C₁₉H₂₃NONa⁺ [M+Na⁺] 304.1672, found 304.1680.

4.2.22. 2,3-Diphenyl-*N*-propyl-propionamide (**3v**)

Purification by chromatography (petroleum ether/EtOAc = 8:1, R_f = 0.22) afforded **3v** as a white solid (94 mg, 35%); mp: 63–65 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.27 (m, 4H), 7.25–7.12 (m, 4H), 7.13–7.08 (m, 2H), 5.29 (s, br, 1H), 3.58–3.50 (m, 2H), 3.19–3.03 (m, 2H), 3.01–2.94 (m, 1H), 1.40–1.31 (m, 2H), 0.74 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.6, 139.8, 139.8, 129.0, 128.7, 128.2, 128.1, 127.3, 126.1, 55.8, 41.3, 39.7, 22.7, 11.1; HRMS(ESI-TOF) m/z: calcd for C₁₈H₂₁NOH⁺ [M+H⁺] 268.1696, found 268.1697.

4.2.23. *N*-hexyl-2,3-diphenyl-propionamide (**3x**)

Purification by chromatography (petroleum ether/EtOAc = 10:1, R_f = 0.22) afforded **3x** as a white solid (152 mg, 49%); mp: 52–54 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, *J* = 4.3 Hz, 4H), 7.25–7.18 (m, 3H), 7.16–7.09 (m, 3H), 5.37 (s, br, 1H), 3.57–3.51 (m, 2H), 3.20–3.04 (m, 2H), 3.00–2.94 (m, 1H), 1.35–1.08 (m, 8H), 0.84 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.5, 139.8, 139.8, 128.9, 128.6, 128.2, 128.0, 127.2, 126.1, 55.7, 39.7, 39.6, 31.3, 29.3, 26.3, 22.4, 13.9; HRMS(ESI-TOF) m/z: calcd for C₂₁H₂₇NONa⁺ [M+Na⁺] 332.1985, found 332.1990.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at

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An efficient electrochemical protocol for the synthesis of racemic α -benzylated amides via the Favorskii rearrangement of 1,3-diarylacetonnes

Highlights:

non-halogenated ketones

undivided cell

low current density

electron-withdrawing substituents favored

moderate regioselectivity