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Nickel-Catalyzed Arylation/Alkenylation of *tert*-Cyclobutanols with Aryl/Alkenyl Triflates *via* a C−C Bond Cleavage

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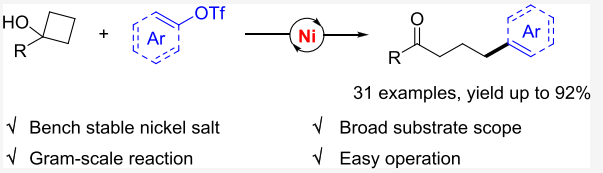
ABSTRACT: Herein, we first present a nickel-catalyzed arylation and alkenylation of *tert*-cyclobutanols with aryl/alkenyl triflates *via* a C−C bond cleavage. An array of γ-substituted ketones was obtained in moderate-to-good yields, thus featuring earth-abundant nickel catalysis, broad substrate scope, and simple reaction conditions. Preliminary mechanistic experiments indicated that β-carbon elimination pathways might be involved in the catalytic cycle.



INTRODUCTION

Carbon−carbon (C−C) bond is ubiquitous and usually inert in most organic molecules. The direct transformation of the C−C bond into new C−C or C−X (X = heteroatom) enables an unusual disconnection of the carbon chain and then reassembles with other coupling partners. However, it is still challenging to achieve a selective C−C bond activation since the C−C bond is usually co-existence with the C−H bond and the transition-metal catalyst tends to interact with the C−H bond.[1] Up to now, considerable endeavors have been devoted to the development of competent catalytic systems and viable substrates.[2] *tert*-Cyclobutanol is among the most useful precursors[3] for the synthesis of γ-substituted ketone *via* a C−C bond cleavage.[4] Also, it is routinely considered as an ideal model substrate proceeding single-electron oxidation reaction followed by a radical-mediated β-fragmentation process in the presence of a stoichiometric amount of strong oxidant. The formed alkyl radical could be further functionalized known as halogenation,[5] azidation,[6] alkynylation,[7] cyanation,[7b] thiolation,[8] hydrazination,[9] and selenation (Scheme 1a).[10] In addition, this radical pathway can also be accessed through a visible-light-induced photocatalytic strategy, enabling the formation of γ-H,[11] Br,[12] allyl/formyl,[13] aryl,[14] or alkynyl[15] substituted ketones under mild reaction conditions (Scheme 1a). An alternative transformation of *tert*-cyclobutanol to γ-substituted ketone relies on organometallic catalysis through a β-carbon elimination process (Scheme 1b). In 1999, Uemura group presented a pioneering work on the palladium-catalyzed dehydrogenation reaction of *tert*-cyclobutanols to give α, β-unsaturated ketones.[16a] After that, the extended research work based on palladium catalysis has been successively reported by the same group,[16b−e] Orellana,[17] Martin,[18] and Jia and Ma[19] groups. In 2012, Murakami group[20] disclosed a rhodium-catalyzed C−C cleavage/intramolecular C−Br coupling reaction of 1-(2-haloaryl)cyclobutanols affording 3,3-disubstituted α-tetralones. An asymmetric reaction could be realized by using 3,3-disubstituted 1-(2-haloaryl)-cyclobutanols as substrates. In spite of these intriguing achievements, precious metals such as palladium or rhodium are used as catalysts to realize a β-carbon elimination process and the development of base metal-catalyzed C−C bond activation/functionalization is highly desirable.

Scheme 1. Transformations of *tert*-Cyclobutanols to γ-Substituted Ketones

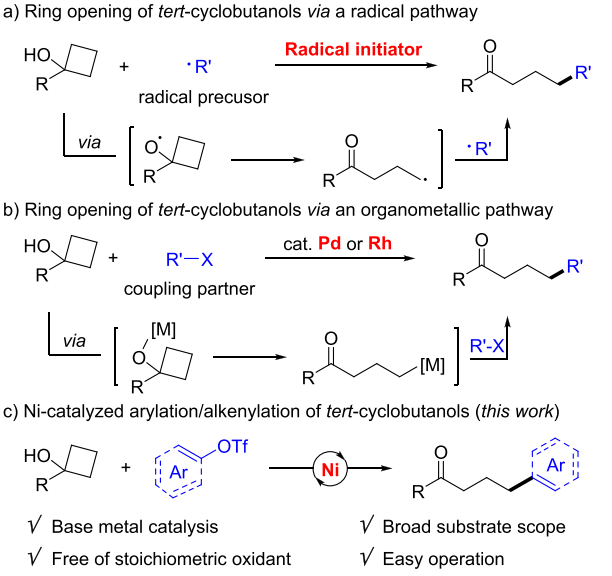


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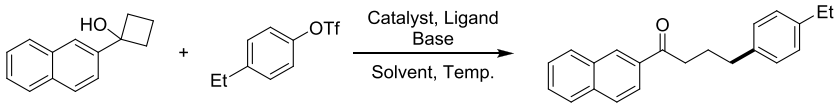
Table 1. Reaction Parameter Screening[a]



1k 2c 3c

entry	catalyst (mol %)	ligand	base	temp (°C)	solvent	yield (%)
1	$NiBr_2$ (10)	PPh_3	NaO^tBu	90	toluene	5
2	$NiBr_2$ (10)	PCy_3	NaO^tBu	90	toluene	37
3	$NiBr_2$ (10)	IMes·HCl	NaO^tBu	90	toluene	0
4	$NiBr_2$ (10)	XantPhos	NaO^tBu	90	toluene	0
5	$NiBr_2$ (10)	1,10-Phen	NaO^tBu	90	toluene	0
6	$Ni(PPh_3)_2Br_2$ (10)	[b]	NaO^tBu	90	toluene	70
7	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	90	toluene	78
8	$Ni(PCy_3)Cl_2$ (10)	[b]	NaO^tBu	90	toluene	64
9	$Ni(dppe)Cl_2$ (10)	[b]	NaO^tBu	90	toluene	65
10	$Ni(dppp)Cl_2$ (10)	[b]	NaO^tBu	90	toluene	62
11	$Ni(PPh_3)_2(CO)_2$ (10)	[b]	NaO^tBu	90	toluene	18
12	$Ni(PPh_3)_2Cl_2$ (5)	[b]	NaO^tBu	90	toluene	63
13	[c]	[b]	NaO^tBu	90	toluene	0
14	$Ni(PPh_3)_2Cl_2$ (10)	[b]	LiO^tBu	90	toluene	0
15	$Ni(PPh_3)_2Cl_2$ (10)	[b]	KO^tBu	90	toluene	0
16	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaOEt	90	toluene	0
17	$Ni(PPh_3)_2Cl_2$ (10)	[b]	Na_2CO_3	90	toluene	0
18	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	90	THF	0
19	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	90	MeCN	0
20	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	90	dioxane	0
21	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	90	xylene	43
22	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	120	toluene	61
23	$Ni(PPh_3)_2Cl_2$ (10)	[b]	NaO^tBu	60	toluene	60

[a]Reaction conditions unless otherwise noted: **1k** (0.2 mmol), **2c** (0.3 mmol), catalyst (0.02 mmol), ligand (0.04 mmol), base (0.4 mmol), solvent (1 mL), at 90 °C for 12 h. [b]No ligand. [c]No catalyst.

Nickel salts are rich abundant in earth crust and display fantastic reactivity in catalytic coupling reactions due to the diverse mechanistic pathways.[21] To the best of our knowledge, nickel-catalyzed ring-opening reactions of strained cyclic ketones[3g] and cyclopropanols[22] have been described previously while the corresponding reaction of less-strained cyclobutanols is still underdeveloped. Herein, we first report a nickel-catalyzed arylation/alkenylation of *tert*-cyclobutanols with aryl/alkenyl triflates (Scheme 1c). The reaction avoids the use of the stoichiometric oxidant and utilizes readily available nickel salt as a catalyst instead of precious metals such as palladium and rhodium.

RESULTS AND DISCUSSION

Initially, the model reaction of 1-(naphthalen-2-yl)cyclobutan-1-ol **1k** with 4-ethylphenyl trifluoromethanesulfonate **2c** was carried out using $NiBr_2$ as a catalyst, PPh_3 as a ligand, NaO^tBu as a base, and toluene as a solvent at 90 °C for 12 h. To our delight, the desired product was isolated and characterized albeit in a low yield (entry 1, Table 1). The yield was improved to 37% when PCy_3 was used as a ligand while other ligands such as IMes·HCl, XantPhos, 1,10-phenanthroline failed to produce the product (entries 2−5, Table 1, see the Supporting Information for details). Several phosphine-ligated nickel salts were then screened (entries 6−11, Table 1), and $Ni(PPh_3)_2Cl_2$ gave the product in a 78% yield (entry 7, Table 1). Halving the catalyst loading or removal of the nickel salt resulted in a decreased yield and no reaction, respectively (entries 12 and 13, Table 1). Next, we examined a series of bases and solvents in the model reaction. Surprisingly, only NaO^tBu (2 equiv) in combination with toluene was proved to be efficient (entries 14−21, Table 1). Finally, either elevating or lowering the reaction temperature gave inferior yields compared with the optimal reaction condition at 90 °C (entries 22 and 23 *vs* 7, Table 1).

We then evaluated the scope of aryl/alkenyl triflates under the optimized reaction conditions (Scheme 2). Aryl triflates with a range of electron-varied substitutes at the *para*-position of phenyl ring proceeded smoothly (**3a**−**3g**, Scheme 2). In general, aryl triflates with electron-donating groups exhibited higher reactivity than those with electron-withdrawing ones while the stronger electron-donating groups such as methoxy (−OMe) and dimethylamino ($-NMe_2$) groups could not further promote the yields (**3e** and **3f**, Scheme 2). This result indicated that an appropriate electron effect on the phenyl ring is preferable. More steric *o*-tolyl trifluoromethanesulfonate and naphthalen-1-yl trifluoromethanesulfonate also worked efficiently compared with less steric ones (**3h** *vs* **3b**, **3i** *vs* **3e**, Scheme 2). The terminal alkenyl group was found to be compatible with the nickel catalysis giving the product **3l** in 62% yield. Additionally, alkenyl triflates were also viable substrates furnishing the reaction in good yields (**3n** and **3o**, Scheme 2).

Next, we continued to investigate the generality of *tert*-cyclobutanols by reacting with *p*-tolyl trifluoromethanesulfonate **2b** (Scheme 3). An array of *tert*-cyclobutanols bearing different *para*-substituted phenyl rings were readily converted into the corresponding ketones in moderate-to-good yields

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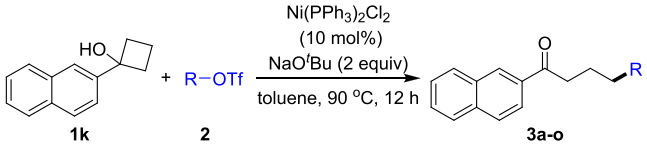
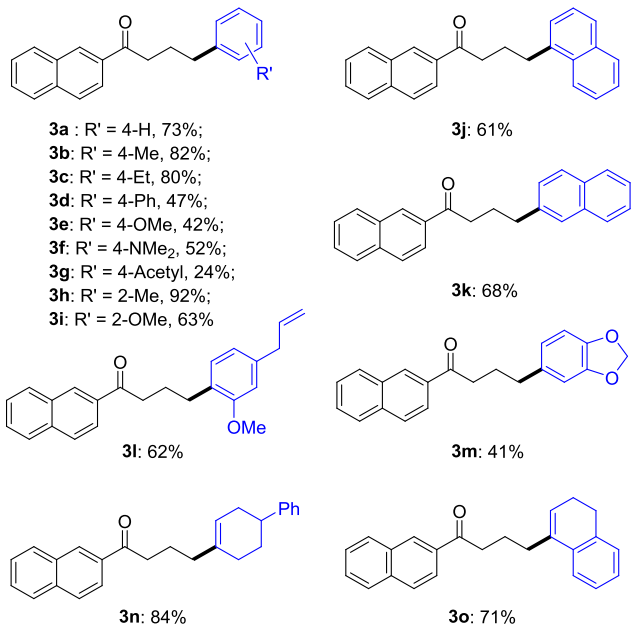
Scheme 2. Substrate Scope of Aryl/Alkenyl Triflates[a]





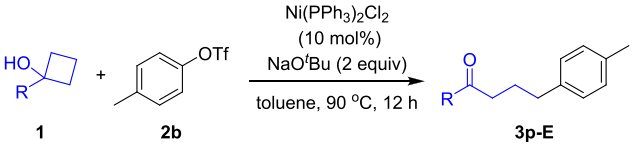
[a]Conditions: **1k** (0.4 mmol), **2** (0.6 mmol), $Ni(PPh_3)_2Cl_2$ (0.04 mmol), NaO^tBu (0.8 mmol), toluene (2 mL), at 90 °C for 12 h.

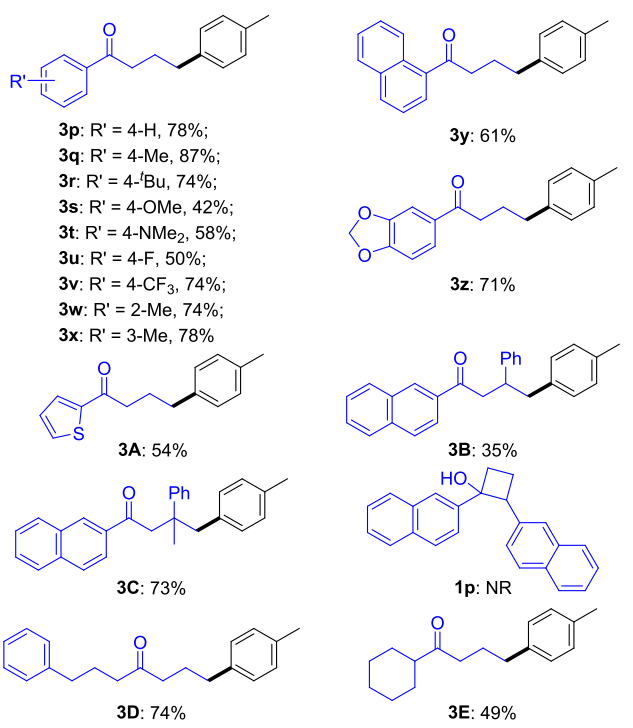
(**3p**−**3v**, Scheme 3). Again, the methoxy and dimethylamino groups at cyclobutanols were still unable to increase the yields (**3s** and **3t**, Scheme 3). Gratefully, the *tert*-cyclobutanols with electron withdrawing groups such as −F and $-CF_3$ at the phenyl ring were workable in this case, which shaped a sharp contrast to substrate scope of aryl triflates (**3u** and **3v**, Scheme 3). 1-Naphthyl and thienyl cyclobutanols were suitable substrates to deliver the products in satisfying yields (**3y** and **3A**, Scheme 3). Furthermore, 3-mono/di-substituted aryl cyclobutanols proceeded smoothly while 2-phenyl-substituted one failed to give the desired products presumably due to the facile isomerization to ketone (**3B** and **3C**, **1p**, Scheme 3). At last, less steric alkyl cyclobutanols were chosen as substrates and subjected to the standard reaction conditions. Expectedly, unsymmetric dialkyl ketones were accessed in 74 and 49% yields, respectively (**3D** and **3E**, Scheme 3).

To examine the synthetic utility of this reaction, a gram-scale reaction of 1-(naphthalen-2-yl)cyclobutan-1-ol **1k** with *p*-tolyl trifluoromethanesulfonate **2b** was performed under the optimized reaction conditions and the product **3b** could be isolated in 87% yield (Scheme 4). This gram-scale reaction might provide a practically useful method for the synthesis of γ-substituted ketones.

Further experiments were conducted to clarify the possible reaction mechanism. 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) was used as a radical trapper and added to the model reaction (Scheme 5a). Unexpectedly, the reaction was inhibited and neither product **3b** nor TEMPO-trapped ketone **4a** could be detected although **1k** was totally consumed. In contrast, a messy mixture was isolated and their structures could not be characterized by ^1H NMR and MS analysis (see

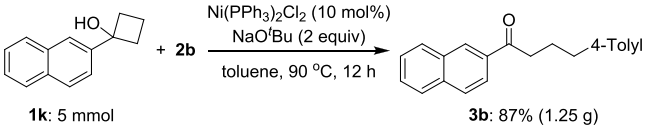
Scheme 3. Substrate Scope of *tert*-Cyclobutanols



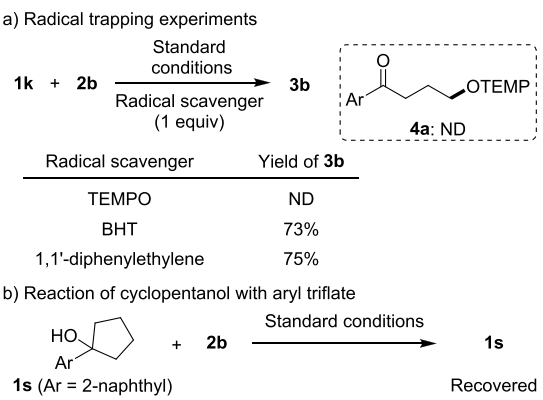


[a]Conditions: **1** (0.4 mmol), **2b** (0.6 mmol), $Ni(PPh_3)_2Cl_2$ (0.04 mmol), NaO^tBu (0.8 mmol), toluene (2 mL), at 90 °C for 12 h. NR = No Reaction.

Scheme 4. Gram-Scale Reaction



Scheme 5. Mechanistic Experiments



the Supporting Information for details). In addition, both BHT and 1,1′-diphenylethylene were examined. To our surprise, the reaction was not suppressed and the products were obtained in 73 and 75%, respectively. Furthermore, the reaction *tert*-

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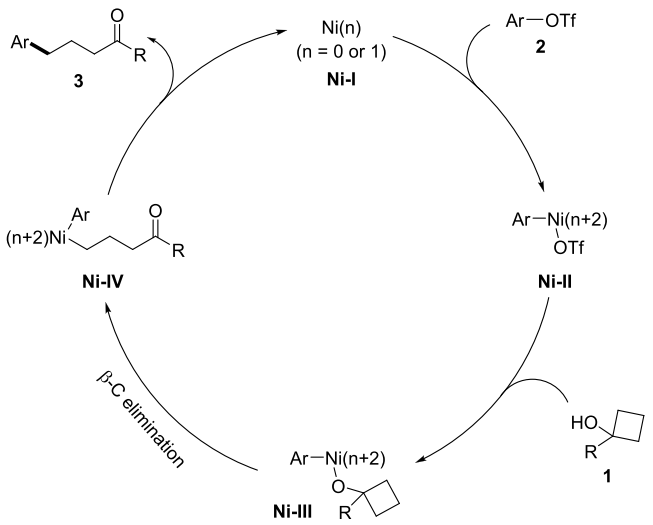
cycolpentanol **1s** with aryl triflate **2b** was examined and no product was detected and the starting material **1s** was recovered (Scheme 5b). It suggested that the C−C bond cleavage might not undergo a radical β-fragmentation process.[23,24]

We proposed the plausible reaction mechanism based on the above experiments and previous literature (Scheme 6).[25,26]

Scheme 6. Plausible Reaction Mechanism



The active nickel species **Ni-I** was generated *in situ* from the reduction of $Ni(PPh_3)Cl_2$.[25] An oxidative addition of aryl triflate with **Ni-I** took place to form intermediate **Ni-II**, which then underwent a radical process with *tert*-cyclobutanol in the presence of a base. The generated nickel alcoholate **Ni-III** further proceeded a β-C elimination, producing an alkylnickel intermediate **Ni-IV**.[26] Finally, the reductive elimination of **Ni-IV** fulfilled the whole catalytic cycle to regenerate the **Ni-I** and provide the product **3**.

CONCLUSIONS

In conclusion, we have developed a nickel-catalyzed arylation/alkenylation of *tert*-cyclobutanols with aryl/alkenyl triflates *via* β-carbon elimination process. A number of γ-substituted ketones were successfully obtained in moderate-to-good yields. The present protocol features earth abundant nickel salt, broad functional group tolerance, and easy operation. The further exploration for the nickel-catalyzed C−C bond activation of less-strained *tert*-cycloalcohols is underway in our laboratory.

EXPERIMENTAL SECTION

Unless otherwise noted, all reactions were carried out in flame-dried reaction vessels with Teflon screw caps under nitrogen. Solvents were purified and dried according to standard methods prior to use. All commercially available reagents were obtained from chemical suppliers and used after proper purification if necessary. Flash column chromatography was performed on silica gel (200−300 mesh) with the indicated solvent mixtures. TLC analysis was performed on precoated, glass-backed silica gel plates, and visualized with UV light. An oil bath was used as a heat source.

The ^1H and ^{13}C NMR spectra were recorded on a Bruker 500 AV spectrometer. Chemical shifts (δ) were reported as parts per million (ppm) downfield from tetramethylsilane, and the following abbreviations were used to identify the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, br = broad, and all combinations thereof can be explained by their integral parts. Coupling constant (J) was reported in hertz unit (Hz). The high-resolution mass spectra (HRMS) were recorded on an Agilent 6210 LC/TOF spectrometer.

General Procedure for Synthesizing Cyclobutanols.[27] Cyclobutanone (5 mmol) was dissolved in 10 mL of dried THF in a 50 mL Schlenk tube under N_2. The mixture was cooled to 0 °C, and Grignard reagent (1.1 equiv) was added dropwise with stirring under an ice bath. Then, it was allowed to warm to room temperature and stirred overnight. After completion, the mixture was quenched with NH_4Cl (aq). The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. After the removal of the solvent *in vacuo*, the crude mixture was purified by flash column chromatography on silica gel to give the desired cyclobutanols. All the *tert*-cyclobutanols were synthesized according to this general procedure. **1s** was synthesized from cyclopentanone according to this procedure. Substrates **1n** and **10** are new compounds.

*1-(Naphthalen-2-yl)-3-phenylcyclobutan-1-ol (**1n**).* Purified by flash column chromatography (petroleum ether/EtOAc = 20:1 to 5:1) as white solid and obtained as a diastereomer mixture. ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.98−7.85 (m, 4H), 7.79 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.62−7.50 (m, 3H), 7.42−7.33 (m, 5H), 7.33−7.23 (m, 2H), 3.23−3.14 (m, 3H), 2.93−2.76 (m, 1H), 2.72−2.63 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.99, 144.6, 143.8, 128.7, 128.4, 128.4, 128.3, 128.1, 128.08, 127.59, 127.6, 126.7, 126.5, 126.3, 126.2, 126.1, 126.1, 126.0, 126.0, 124.4, 123.5, 123.5, 123.0, 75.2, 72.6, 44.4, 43.1, 33.6, 30.1. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{20}H_{18}O$ 274.1358; found 274.1367.

*3-Methyl-1-(naphthalen-2-yl)-3-phenylcyclobutan-1-ol (**1o**).* Purified by flash column chromatography (petroleum ether/EtOAc = 20:1 to 5:1) as white solid and obtained as a diastereomer mixture. ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.97−7.88 (m, 1H), 7.84−7.77 (m, 1H), 7.74−7.69 (m, 1H), 7.59−7.52 (m, 1H), 7.51−7.45 (m, 1H), 7.45−7.36 (m, 1H), 7.36−7.32 (m, 1H), 7.29−7.24 (m, 1H), 7.24−7.17 (m, 1H), 7.16−7.07 (m, 1H), 3.20−3.07 (m, 1H), 3.01 (d, J = 13.1 Hz, 1H), 2.78−2.66 (m, 1H), 1.81 (s, 1H), 1.33 (s, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 153.6, 151.6, 151.5, 144.5, 143.5, 133.1, 132.9, 132.7, 132.4, 129.7, 128.7, 128.4, 128.3, 128.2, 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 127.1, 126.4, 126.3, 126.3, 126.1, 126.1, 126.1, 126.0, 125.9, 125.5, 125.3, 125.3, 125.2, 125.1, 124.4, 124.0, 123.6, 123.6, 123.4, 122.8, 117.9, 109.4, 73.1, 72.5, 49.5, 48.6, 48.3, 36.1, 34.3, 32.8, 31.4, 29.4. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{21}H_{20}O$ 288.1514; found 288.1537.

General Procedure for Synthesizing Aryl Triflates.[28] A 100 mL Schlenk tube was charged successively with phenol derivative (10 mmol), dry DCM (30 mL), and pyridine (2 equiv) under N_2. The solution was cooled to 0 °C in an ice bath and then treated with the dropwise addition of triflic anhydride (1.2 equiv). The resulting mixture was allowed to warm up to room temperature (rt) and stirred for additional 5 h. At the end of the reaction, the mixture was filtered. The filtrate was concentrated *in vacuo* and the residue was subjected to flash chromatography (200−300 mesh silica gel, PE or PE/EtOAc as an eluent) to afford the desired aryl triflate. Aryl triflates were prepared from this procedure. General procedure for synthesizing alkenyl triflates[29] under N2, trifluoromethanesulfonic anhydride (20 mmol) in dichloromethane (15 mL) was added to a solution of ketone (10 mmol) and anhydrous sodium carbonate (16.0 mmol) in dichloromethane (15 mL) over a period of 10 min. The reaction was stirred for an addition 24 h at room temperature. After completion, the reaction mixture was washed with sodium hydrogen carbonate (2 × 50 mL), water (2 × 50 mL), dried with Na_2SO_4, and then filtered. Then, the filtrate was concentrated and purified by silica gel column chromatography to get the alkenyl triflates.

Typical Procedure for Preparation of γ-Substituted Ketones. To a 25 mL flame-dried Schlenk tube containing a stirring bar were added $Ni(PPh_3)_2Cl_2$ (0.04 mmol, 26.1 mg), NaO^t-Bu (0.8 mmol, 76.8 mg), 1-(naphthalen-2-yl)cyclobutan-1-ol **1k** (0.4 mmol, 79.2 mg), toluene (2.0 mL), and 4-ethylphenyl trifluoromethanesul-

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fonate **2c** (0.6 mmol, 152.4 mg), sequentially under nitrogen. The tube was sealed and stirred at 90 °C for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (5.0 mL) and filtered through a short pad silica gel washing with ethyl acetate (20 mL). The filtrate was concentrated and purified by silica gel column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) to provide the product **3c** in 80% yield.

Experimental Procedure for Gram-Scale Reaction. To a 100 mL flame-dried Schlenk tube containing a stirring bar were added $Ni(PPh_3)_2Cl_2$ (0.5 mmol, 327 mg), NaO^tBu (10 mmol, 961 mg), 1-(naphthalen-2-yl)cyclobutan-1-ol **1k** (5 mmol, 991.3 mg), toluene (25.0 mL), and *p*-tolyl trifluoromethanesulfonate **2b** (7.5 mmol, 1800 mg), sequentially under nitrogen. The tube was sealed and stirred at 90 °C for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (30 mL) and filtered through a short pad silica gel washing with ethyl acetate (50 mL). The filtrate was concentrated and purified by silica gel column chromatography (petroleum ether: EtOAc = 60:1) to provide the product **3b** in 87% yield (1.25 g) as white solid.

*1-(Naphthalen-2-yl)-4-phenylbutan-1-one (**3a**).*[30a] Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (80 mg, 73% yield). mp: 72−74 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.00 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.94−7.89 (m, 1H), 7.85 (dd, J_1 = 8.1 Hz, J_2 = 6.5 Hz, 2H), 7.61−7.49 (m, 2H), 7.33−7.27 (m, 2H), 7.26−7.17 (m, 3H), 3.09 (t, J = 7.3 Hz, 2H), 2.75 (t, J = 7.5 Hz, 2H), 2.20−2.07 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.0, 141.7, 135.5, 134.2, 132.5, 129.6, 129.5, 128.5, 128.4, 128.3, 128.3, 127.7, 126.7, 125.9, 123.8, 37.7, 35.2, 25.8.

*1-(Naphthalen-2-yl)-4-(p-tolyl)butan-1-one (**3b**).*[30a] Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (95 mg, 82% yield). mp: 81−83 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.99 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.85 (dd, J_1 = 8.2 Hz, J_2 = 5.7 Hz, 2H), 7.60−7.48 (m, 2H), 7.15−7.06 (m, 4H), 3.08 (t, J = 7.3 Hz, 2H), 2.71 (t, J = 7.5 Hz, 2H), 2.32 (s, 3H), 2.16−2.07 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.1, 138.5, 135.5, 135.3, 134.3, 132.5, 129.6, 129.5, 129.1, 128.4, 128.3, 128.3, 127.7, 126.6, 123.8, 37.7, 34.7, 25.9, 21.0.

*4-(4-Ethylphenyl)-1-(naphthalen-2-yl)butan-1-one (**3c**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (94 mg, 80% yield). mp: 54−56 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.99−7.94 (m, 1H), 7.88−7.84 (m, 1H), 7.82−7.77 (m, 2H), 7.54−7.46 (m, 2H), 7.15−7.07 (m, 4H), 3.04 (t, J = 7.3 Hz, 2H), 2.69 (t, J = 7.5 Hz, 2H), 2.60 (q, J = 7.6 Hz, 2H), 2.13−2.07 (m, 2H), 1.21 (t, J = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.8, 141.6, 138.7, 135.3, 134.1, 132.3, 129.4, 129.3, 128.3, 128.2, 128.1, 127.7, 127.6, 126.5, 123.7, 37.6, 34.6, 28.3, 25.8, 15.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}O$ 303.1749; found 303.1743.

*4-([1,1′-Biphenyl]-4-yl)-1-(naphthalen-2-yl)butan-1-one (**3d**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (66 mg, 47% yield). mp: 138−140 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.01 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.94−7.89 (m, 1H), 7.86 (t, J = 8.2 Hz, 2H), 7.61−7.55 (m, 3H), 7.55−7.49 (m, 3H), 7.45−7.39 (m, 2H), 7.35−7.28 (m, 3H), 3.13 (t, J = 7.3 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H), 2.22−2.14 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.0, 141.0, 140.8, 138.9, 135.5, 134.3, 132.5, 129.6, 129.5, 129.0, 128.7, 128.4, 128.3, 127.7, 127.1, 127.0, 127.0, 126.7, 123.9, 37.7, 34.8, 25.8. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{22}NaO$ 373.1568; found 373.1563.

*4-(4-Methoxyphenyl)-1-(naphthalen-2-yl)butan-1-one (**3e**)*[29a]. Purified by flash column chromatography (petroleum ether/EtOAc = 60:1 to 30:1) as white solid (51 mg, 42% yield). mp: 95−97 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.99 (dd, J_1 = 8.6, J_2 = 1.7 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.85 (dd, J_1 = 8.1 Hz, J_2 = 6.1 Hz, 2H), 7.61−7.46 (m, 2H), 7.17−7.06 (m, 2H), 6.87−6.80 (m, 2H), 3.77 (s, 3H), 3.07 (t, J = 7.3 Hz, 2H), 2.69 (t, J = 7.5 Hz, 2H), 2.15−2.05 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.0, 157.8, 135.4, 134.2, 133.7, 132.4, 129.6, 129.5, 129.4, 128.3, 128.3, 127.7, 126.6, 123.8, 113.8, 55.2, 37.6, 34.2, 26.1.

*4-(4-(Dimethylamino)phenyl)-1-(naphthalen-2-yl)butan-1-one (**3f**).* Purified by flash column chromatography (petroleum ether/EtOAc = 60:1 to 20:1) as pale-yellow solid (66 mg, 52% yield). mp: 104−106 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.00 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.85 (dd, J_1 = 8.3 Hz, J_2 = 4.9 Hz, 2H), 7.60−7.49 (m, 2H), 7.10 (d, J = 8.7 Hz, 2H), 6.74−6.68 (m, 2H), 3.08 (t, J = 7.3 Hz, 2H), 2.91 (s, 6H), 2.67 (t, J = 7.4 Hz, 2H), 2.13−2.06 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.4, 149.2, 135.5, 134.4, 132.5, 129.8, 129.6, 129.5, 129.1, 128.3, 128.3, 127.7, 126.6, 123.9, 113.0, 40.9, 37.8, 34.2, 26.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}NO$ 318.1852; found 318.1852.

*4-(4-Acetylphenyl)-1-(naphthalen-2-yl)butan-1-one (**3g**).* Purified by flash column chromatography (petroleum ether/EtOAc = 10:1 to 5:1) as white solid (31 mg, 24% yield). mp: 119−121 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.00 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.95−7.84 (m, 5H), 7.62−7.51 (m, 2H), 7.31 (d, J = 8.3 Hz, 2H), 3.11 (t, J = 7.2 Hz, 2H), 2.81 (t, 2H), 2.57 (s, 3H), 2.20−2.11 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.6, 197.8, 147.5, 135.5, 135.2, 134.2, 132.4, 129.5, 129.5, 128.7, 128.6, 128.4, 127.7, 126.7, 123.7, 37.5, 35.1, 26.5, 25.4. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{20}NaO_2$ 339.1361; found 339.1356.

*1-(Naphthalen-2-yl)-4-(o-tolyl)butan-1-one (**3 h**).*[30b] Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (106 mg, 92% yield). mp: 55−57 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.00 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 8.2 Hz, 2H), 7.60−7.46 (m, 2H), 7.19−7.07 (m, 4H), 3.13 (t, J = 7.2 Hz, 2H), 2.76−2.67 (m, 2H), 2.32 (s, 3H), 2.13−2.03 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.9, 139.9, 136.0, 135.5, 134.2, 132.5, 130.2, 129.5, 129.5, 128.9, 128.3, 128.3, 127.7, 126.7, 126.0, 125.9, 123.8, 37.9, 32.6, 24.6, 19.3.

*4-(2-Methoxyphenyl)-1-(naphthalen-2-yl)butan-1-one (**3i**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as colorless oil (77 mg, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.00 (dd, J_1 = 8.6 Hz, J_2 = 1.6 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.86 (dd, J_1 = 8.3 Hz, J_2 = 5.5 Hz, 2H), 7.60−7.50 (m, 2H), 7.23−7.11 (m, 2H), 6.93−6.86 (m, 1H), 6.83 (d, J = 8.1 Hz, 1H), 3.74 (s, 3H), 3.10 (t, J = 7.4 Hz, 2H), 2.77 (t, J = 7.4 Hz, 2H), 2.15−2.07 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.3, 157.5, 135.5, 134.4, 132.5, 130.1, 130.0, 129.6, 129.5, 128.3, 128.2, 127.7, 127.2, 126.6, 124.0, 120.4, 110.2, 55.1, 38.0, 29.5, 24.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}O_2$ 305.1542; found: 305.1536.

*4-(Naphthalen-1-yl)-1-(naphthalen-2-yl)butan-1-one (**3j**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as colorless oil (79 mg, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.12 (d, J = 8.3 Hz, 1H), 7.97 (dd, J_1 = 8.6 Hz, J_2 = 1.6 Hz, 1H), 7.85−7.77 (m, 4H), 7.69 (d, J = 8.0 Hz, 1H), 7.54−7.42 (m, 4H), 7.38−7.30 (m, 2H), 3.19−3.14 (m, 2H), 3.11 (t, J = 7.1 Hz, 2H), 2.27−2.20 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.8, 137.8, 135.4, 134.2, 133.8, 132.4, 131.8, 129.5, 129.4, 128.7, 128.3, 128.3, 127.6, 126.7, 126.6, 126.1, 125.8, 125.4, 125.4, 123.9, 123.7, 37.9, 32.3, 25.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{20}NaO$, 347.1412; found 347.1406.

*4-(Naphthalen-1-yl)-1-(naphthalen-2-yl)butan-1-one (**3k**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (88 mg, 68% yield).mp: 136−138 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.99 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.89−7.82 (m, 3H), 7.82−7.74 (m, 3H), 7.65 (s, 1H), 7.60−7.55 (m, 1H), 7.54−7.49 (m, 1H), 7.47−7.39 (m, 2H), 7.37 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 3.12 (t, J = 7.3 Hz, 2H), 2.92 (t, J = 7.5 Hz, 2H), 2.30−2.17 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 200.1, 139.2, 135.5, 134.3, 133.6, 132.5, 132.1, 129.6, 129.5, 128.4, 128.3, 128.0, 127.7, 127.6, 127.4, 127.3, 126.7, 126.6, 125.9, 125.2, 123.9, 37.6, 35.3, 25.7. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{20}NaO$ 347.1412; found 347.1413.

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*4-(4-Allyl-2-methoxyphenyl)-1-(naphthalen-2-yl)butan-1-one (**3l**).* Purified by flash column chromatography (petroleum ether/EtOAc = 60:1 to 30:1) as yellow solid (85 mg, 62% yield). mp: 59−61 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.00 (dd, J_1 = 8.6 Hz, J_2 = 1.6 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.85 (m, 2H), 7.54 (m, 2H), 7.08 (d, J = 7.5 Hz, 1H), 6.72 (d, J = 7.5 Hz, 1H), 6.66 (s, 1H), 6.05−5.91 (m, 1H), 5.15−5.03 (m, 2H), 3.73 (s, 3H), 3.36 (d, J = 6.7 Hz, 2H), 3.09 (t, J = 7.4 Hz, 2H), 2.73 (t, J = 7.4 Hz, 2H), 2.18−2.05 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.3, 157.5, 139.3, 137.5, 135.4, 134.4, 132.5, 129.9, 129.5, 129.5, 128.3, 128.2, 127.7, 127.7, 126.6, 123.9, 120.4, 115.7, 110.6, 55.1, 40.2, 38.0, 29.2, 24.6. HRMS (ESI) m/z: [M + Na]$^+$ $C_{24}H_{24}NaO_2$ Calcd for 367.1674; found 367.1669.

*4-(Benzo[d][1,3]dioxol-5-yl)-1-(naphthalen-2-yl)butan-1-one (**3m**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (52 mg, 41% yield). mp: 86−88 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.02 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.90−7.84 (m, 2H), 7.62−7.52 (m, 2H), 6.78−6.73 (m, 2H), 6.70−6.66 (m, 1H), 5.92 (s, 2H), 3.09 (t, J = 7.3 Hz, 2H), 2.69 (t, J = 7.5 Hz, 2H), 2.14−2.07 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.0, 147.6, 145.7, 135.5, 135.5, 134.2, 132.5, 129.5, 129.5, 128.3, 128.3, 127.7, 126.6, 123.8, 121.2, 108.9, 108.1, 100.7, 37.5, 34.9, 26.0. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{18}NaO$ 341.1154; found 341.1150.

*1-(Naphthalen-2-yl)-4-(1,2,3,6-tetrahydro-[1,1′-biphenyl]-4-yl)-butan-1-one (**3n**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (119 mg, 84% yield). mp: 89−91 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.04 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.88 (dd, J_1 = 11.3 Hz, J_2 = 8.4 Hz, 2H), 7.61−7.50 (m, 2H), 7.31−7.25 (m, 2H), 7.24−7.14 (m, 4H), 5.55−5.51 (m, 1H), 3.09 (t, J = 7.3 Hz, 2H), 2.79−2.66 (m, 1H), 2.30−2.06 (m, 6H), 2.01−1.90 (m, 2H), 1.82−1.71 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.3, 147.1, 136.9, 135.5, 134.4, 132.5, 129.6, 129.5, 128.4, 128.3, 128.28, 127.74, 126.8, 126.7, 125.9, 123.9, 121.4, 40.1, 38.0, 37.1, 33.5, 30.0, 28.7, 22.4. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{26}H_{26}NaO$ 377.1881; found 377.1876.

*4-(3,4-Dihydronaphthalen-1-yl)-1-(naphthalen-2-yl)butan-1-one (**3o**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as yellow oil (92 mg, 71% yield). mp: 89−91 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.01 (dd, J_1 = 8.6 Hz, J_2 = 1.7 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.86 (dd, J_1 = 8.2 Hz, J_2 = 5.7 Hz, 2H), 7.60−7.49 (m, 2H), 7.31 (d, J = 7.6 Hz, 1H), 7.22−7.17 (m, 1H), 7.16−7.11 (m, 2H), 5.90 (t, J = 4.5 Hz, 1H), 3.13 (t, J = 7.2 Hz, 2H), 2.74 (t, J = 8.0 Hz, 2H), 2.62−2.55 (m, 2H), 2.27−2.20 (m, 2H), 2.10−1.99 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.2, 136.7, 135.8, 135.5, 134.6, 134.3, 132.5, 129.6, 129.5, 128.3, 128.3, 127.7, 127.6, 126. 7, 126.6, 126.4, 125.6, 123.9, 122.7, 38.0, 32.2, 28.4, 23.1, 23.1. HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{24}H_{23}O$ 327.1743; found; 327.1743.

*1-Phenyl-4-(p-tolyl)butan-1-one (**3p**).*[30c] Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as colorless oil (74 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94−7.88 (m, 2H), 7.55−7.49 (m, 1H), 7.46−7.39 (m, 2H), 7.09 (s, 4H), 2.96 (t, J = 7.3 Hz, 2H), 2.71−2.61 (m, 2H), 2.31 (s, 3H), 2.10−2.01 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.1, 138.5, 137.0, 135.3, 132.8, 129.0, 128.5, 128.3, 128.0, 37.6, 34.7, 25.7, 20.9.

*1,4-Di-p-tolylbutan-1-one (**3q**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (88 mg, 87% yield). mp: 73−75 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84−7.79 (m, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.09 (s, 4H), 2.93 (t, J = 7.3 Hz, 2H), 2.72−2.61 (m, 2H), 2.39 (s, 3H), 2.31 (s, 3H), 2.08−2.01 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 199.8, 143.6, 138.6, 135.3, 134.6, 129.2, 129.0, 128.4, 128.1, 37.6, 34.8, 25.9, 21.6, 21.0. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{20}NaO$ 275.1412; found 275.1406.

*1-(4-(tert-Butyl)phenyl)-4-(p-tolyl)butan-1-one (**3r**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as colorless oil (86 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88−7.84 (m, 2H), 7.46−7.42 (m, 2H), 7.09 (s, 4H), 2.94 (t, J = 7.3 Hz, 2H), 2.70−2.65 (m, 2H), 2.31 (s, 3H), 2.10−2.01 (m, 2H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, CDCl3) δ 199.8, 156.5, 138.6, 135.2, 134.4, 129.0, 128.3, 127.9, 125.4, 37.6, 35.0, 34.7, 31.0, 25.9, 20.9. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{26}NaO$ 317.1881; found 317.1876.

*1-(4-Methoxyphenyl)-4-(p-tolyl)butan-1-one (**3s**).*[30c] Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (44 mg, 42% yield). mp: 76−78 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91−7.87 (m, 2H), 7.09 (s, 4H), 6.92−6.88 (m, 2H), 3.83 (s, 3H), 2.90 (t, J = 7.3 Hz, 2H), 2.66 (t, J = 7.6 Hz, 2H), 2.31 (s, 3H), 2.07−2.00 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 198.7, 163.3, 138.6, 135.2, 130.2, 130.1, 129.0, 128.3, 113.6, 55.3, 37.3, 34.8, 26.0, 20.9.

*1-(4-(Dimethylamino)phenyl)-4-(p-tolyl)butan-1-one (**3t**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (65 mg, 58% yield). mp: 94−96 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86−7.82 (m, 2H), 7.14−7.05 (m, 4H), 6.67−6.60 (m, 2H), 3.04 (s, 6H), 2.87 (m, 2H), 2.66 (t, 2H), 2.31 (s, 3H), 2.07−2.00 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 198.4, 153.3, 138.9, 135.2, 130.2, 129.0, 128.4, 125.1, 110.6, 40.0, 37.0, 35.0, 26.5, 21.0. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{19}H_{23}NNaO$ 304.1677; found 304.1672.

*1-(4-Fluorophenyl)-4-(p-tolyl)butan-1-one (**3u**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (51 mg, 50% yield). mp: 49−51 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96−7.89 (m, 2H), 7.15−7.04 (m, 6H), 2.92 (t, J = 7.3 Hz, 2H), 2.67 (t, J = 7.5 Hz, 2H), 2.31 (s, 3H), 2.08−2.02 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 198.5, 165.6 (d, $^1J_{C-F}$ = 254.3 Hz), 138.4, 135.4, 133.4 (d, $^4J_{C-F}$ = 3.0 Hz), 130.6 (d, $^3J_{C-F}$ = 9.2 Hz), 129.1, 128.3, 115.6 (d, $^2J_{C-F}$ = 21.8 Hz), 37.5, 34.7, 25.7, 20.9. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{17}FNaO$ 279.1161; found 279.1156.

*4-(p-Tolyl)-1-(4-(trifluoromethyl)phenyl)butan-1-one (**3v**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (90 mg, 74% yield). mp: 89−91 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 7.15−7.03 (m, 4H), 2.98 (t, J = 7.3 Hz, 2H), 2.69 (t, J = 7.5 Hz, 2H), 2.32 (s, 3H), 2.10−2.04 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 199.1, 139.7, 138.3, 135.5, 134.2 (q, $^2J_{C-F}$ = 32.6 Hz), 129.1, 128.4, 128.3, 125.6 (q, $^3J_{C-F}$ = 3.7 Hz), 123.6 (q, $^1J_{C-F}$ = 271.1 Hz), 37.9, 34.6, 25.5, 21.0. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{17}F_3NaO$ 329.1129; found 329.1124.

*1-(o-Tolyl)-4-(p-tolyl)butan-1-one (**3w**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as yellow oil (74 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57−7.51 (m, 1H), 7.37−7.29 (m, 1H), 7.21 (dd, J_1 = 9.5 Hz, J_2 = 4.2 Hz, 2H), 7.12−7.01 (m, 4H), 2.87 (t, J = 9.5 Hz, J_2 = 5.1 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H), 2.47 (s, 3H), 2.31 (s, 3H), 2.05−1.98 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.4, 138.5, 138.2, 137.7, 135.3, 131.8, 131.0, 129.0, 128.3, 128.2, 125.5, 40.7, 34.7, 25.9, 21.1, 20.9. HRMS (ESI) [M + Na]$^+$ Calcd for $C_{18}H_{20}NaO$ 275.1412; found 275.1406.

*1-(m-Tolyl)-4-(p-tolyl)butan-1-one (**3x**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as colorless oil (78 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, J_1 = 6.1 Hz J_2 = 5.0 Hz, 2H), 7.37−7.29 (m, 2H), 7.09 (s, 4H), 2.94 (t, J = 7.3 Hz, 2H), 2.67 (t, J = 7.5 Hz, 2H), 2.39 (s, 3H), 2.31 (s, 3H), 2.08−2.01 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.4, 138.6, 138.3, 137.0, 135.3, 133.6, 129.0, 128.5.128.4, 125.2, 37.7, 34.7, 25.9, 21.3, 21.0. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{20}NaO$ 275.1412; found 275.1407.

*1-(Naphthalen-1-yl)-4-(p-tolyl)butan-1-one (**3y**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as yellow oil (70 mg, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J = 8.6 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.55 (m, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.45−7.39 (m, 1H), 7.08 (s, 4H), 3.02 (t, J = 7.3 Hz, 2H), 2.69 (t, J = 7.6 Hz, 2H), 2.30 (s, 3H), 2.13−2.06 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.5, 138.4, 136.2, 135.3, 133.9, 132.3, 130.1, 129.0, 128.3, 127.7, 127.1, 126.3, 125.7, 124.3, 41.3, 34.7, 26.2, 20.9. HRMS

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(ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{20}NaO$ 311.1412; found 311.1406.

*1-(Benzo[d][1,3]dioxol-5-yl)-4-(p-tolyl)butan-1-one (**3z**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (80 mg, 71% yield). mp: 59−61 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.52−7.47 (m, 1H), 7.40 (d, J = 1.7 Hz, 1H), 7.08 (s, 4H), 6.80 (d, J = 8.1 Hz, 1H), 6.00 (s, 2H), 2.87 (t, J = 7.3 Hz, 2H), 2.65 (t, J = 7.5 Hz, 2H), 2.31 (s, 3H), 2.07−1.99 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 198.2, 151.5, 148.1, 138.5, 135.3, 131.9, 129.0, 128.3, 124.1, 107.8, 107.7, 101.7, 37.4, 34.7, 26.0, 20.9. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{18}NaO_3$ 305.1154; found 305.1148.

*1-(Thiophen-2-yl)-4-(p-tolyl)butan-1-one (**3A**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as yellow oil (52 mg, 54% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, J_1 = 3.8, J_2 = 1.1 Hz, 1H), 7.59 (dd, J_1 = 5.0 Hz, J_2 = 1.1 Hz, 1H), 7.12−7.05 (m, 5H), 2.89 (t, J = 7.3 Hz, 2H), 2.69−2.65 (m, 2H), 2.31 (s, 3H), 2.09−2.02 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 193.1, 144.4, 138.4, 135.4, 133.3, 131.7, 129.0, 128.3, 128.0, 38.5, 34.7, 26.1, 21.0. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{16}NaOS$ 267.0820; found 267.0814.

*1-(Naphthalen-2-yl)-3-phenyl-4-(p-tolyl)butan-1-one (**3B**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as white solid (50 mg, 35% yield). mp: 118−120 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.92−7.86 (m, 2H), 7.82 (dd, J_1 = 8.2 Hz, J_2 = 5.0 Hz, 2H), 7.58−7.50 (m, 2H), 7.26−7.21 (m, 4H), 7.17−7.13 (m, 1H), 7.05−6.98 (m, 4H), 3.76−3.65 (m, 1H), 3.44−3.37 (m, 2H), 2.98 (d, J = 7.4 Hz, 2H), 2.28 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 198.9, 144.3, 136.7, 135.5, 135.5, 134.5, 132.4, 129.6, 129.5, 129.2, 128.9, 128.4, 128.3, 128.3, 127.7, 127.7, 126.7, 126.4, 123.9, 44.2, 43.4, 42.6, 21.0. HRMS(ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{24}NaO$ 387.1725; found 387.1720.

*3-Methyl-1-(naphthalen-2-yl)-3-phenyl-4-(p-tolyl)butan-1-one (**3C**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as light yellow oil (110 mg, 73% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.90 (dd, J_1 = 15.3 Hz, J_2 = 8.4 Hz, 2H), 7.82 (t, J = 7.0 Hz, 2H), 7.60−7.47 (m, 2H), 7.33−7.24 (m, 4H), 7.19−7.10 (m, 1H), 6.95 (d, J = 7.6 Hz, 2H), 6.76 (d, J = 7.3 Hz, 2H), 3.66 (d, J = 16.5 Hz, 1H), 3.37 (d, J = 16.5 Hz, 1H), 3.17 (q, J = 13.1 Hz, 2H), 2.26 (s, 3H), 1.51 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 198.7, 147.1, 135.6, 135.5, 135.3, 134.9, 132.4, 130.6, 129.5, 129.4, 128.3, 128.2, 128.2, 128.0, 127.7, 126.6, 126.2, 125.8, 123.8, 48.5, 47.9, 41.5, 25.1, 21.0. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{26}NaO$ 401.1881; found 401.1876.

*1-Phenyl-7-(p-tolyl)heptan-4-one (**3D**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as colorless oil (83 mg, 74% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, J = 7.4 Hz, 2H), 7.19−7.12 (m, 3H), 7.05 (dd, J_1 = 20.7 Hz, J_2 = 8.0 Hz, 4H), 2.61−2.53 (m, 4H), 2.37−2.33 (m, 4H), 2.30 (s, 3H), 1.91−1.82 (m, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 210.6, 141.6, 138.4, 135.3, 129.0, 128.4, 128.3, 128.3, 125.9, 41.9, 41.9, 35.0, 34.6, 25.2, 25.1, 20.9. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{24}NaO$ 303.1725; found 303.1719.

*1-Cyclohexyl-4-(p-tolyl)butan-1-one (**3E**).* Purified by flash column chromatography (petroleum ether/EtOAc = 100:1 to 50:1) as yellow oil (47 mg, 49% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.11−7.03 (m, 4H), 2.56 (t, J = 7.6 Hz, 2H), 2.42 (t, J = 7.3 Hz, 2H), 2.31 (s, 3H), 1.90−1.83 (m, 2H), 1.81−1.74 (m, 4H), 1.68−1.63 (m, 1H), 1.38−1.08 (m, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 213.9, 138.6, 135.2, 129.0, 128.3, 50.8, 39.7, 34.7, 28.5, 25.8, 25.6, 25.2, 20.9. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{24}NaO$ 267.1725; found 267.1719.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02209.

List of starting materials, table of optimization, and copies of ^1H and ^{13}C NMR spectra of all compounds (PDF)

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All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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