

# Selective *cine*-Arylation of *tert*-Cyclobutanols with Indoles Enabled by Nickel Catalysis

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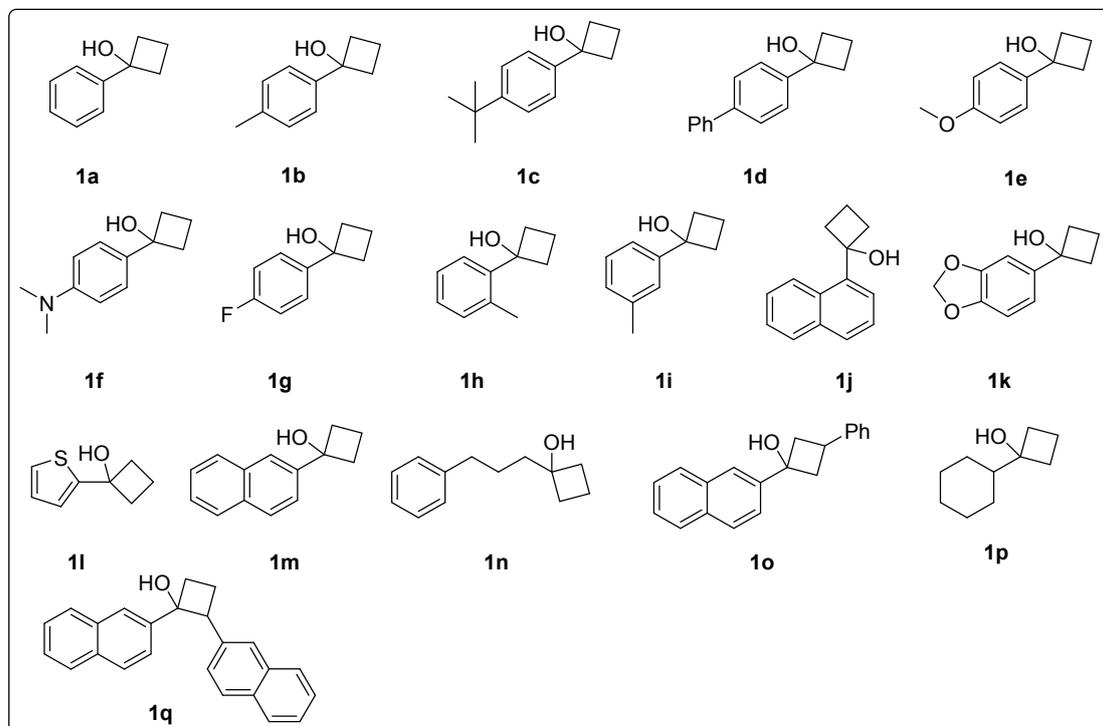
## 1. General Information

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 pre-coated, glass-backed silica gel plates and visualized with UV light.

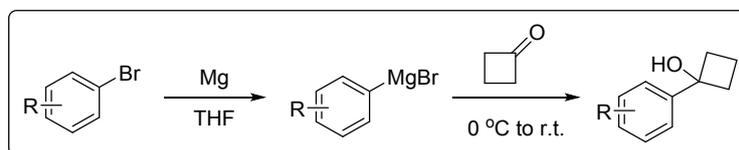
The  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker 500 AV spectrometers. Chemical shifts ( $\delta$ ) were reported as parts per million (ppm) downfield from tetramethylsilane (TMS) and the following abbreviations were used to identify the multiplicities: s = singlet, 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 a AB sciex TripleTOFTM 5600+ or Bruker Apex IV FTMS spectrometer.

## 2. Preparation of Substrates

### 2.1 General procedure for the preparation of *tert*-cyclobutanols



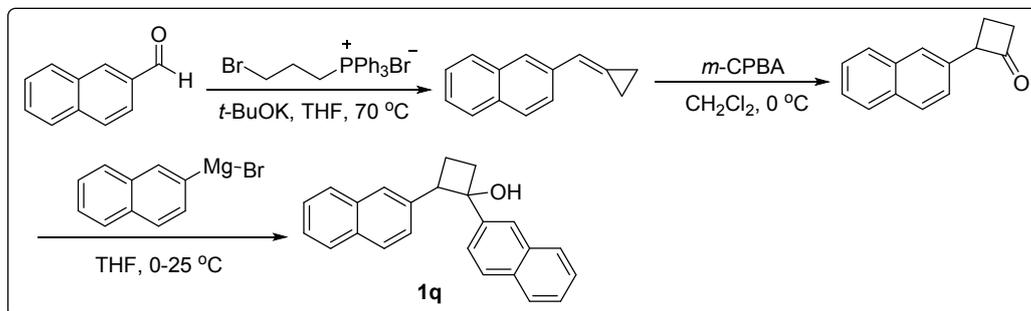
General procedure<sup>1</sup>:



To a 100 ml Schlenk tube was added magnesium (15 mmol, 0.36 g, 1.5 equiv) and anhydrous THF (30 ml) under the nitrogen. Aryl bromide (10 mmol) was added dropwise and the mixture was stirred until aryl bromide was completely converted into a Grignard reagent. The cyclobutanone was added slowly to the reaction mixture at 0 °C, and the reaction was allowed to warm to room temperature. When the starting materials were completely consumed, the mixture was quenched with NH<sub>4</sub>Cl (aq.). The aqueous layer was extracted with ethyl acetate (3×40 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. After removal of the solvent in vacuo, the crude material was purified by flash column chromatography on silica gel to give the desired *tert*-cyclobutanols. Substrates **1a**,<sup>2</sup> **1b**,<sup>2</sup> **1c**,<sup>2</sup> **1d**,<sup>2</sup> **1e**,<sup>2</sup> **1f**,<sup>3</sup> **1g**,<sup>2</sup> **1h**,<sup>2</sup> **1i**,<sup>2</sup> **1j**,<sup>2</sup> **1k**,<sup>4</sup> **1l**,<sup>5</sup> **1m**,<sup>2</sup> **1n**,<sup>5</sup> **1o**,<sup>6</sup> and **1p**,<sup>5</sup>

were prepared according to the general procedure and their structural characterization were in line with previous literature.

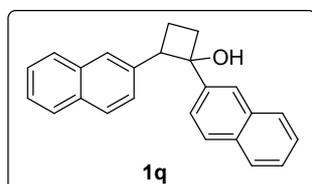
Procedure for the preparation of **1q**<sup>7</sup>.



A solution of *t*-BuOK (6.74 g, 60 mmol, 3.0 equiv) in dry THF (46 ml, 1.3 M) was slowly added to a solution of (3-bromopropyl)triphenylphosphonium bromide (13.92 g, 30 mmol, 1.5 equiv) in dry THF (60 ml, 0.5 M) and stirred at 70 °C for 1 h. The naphthaldehyde (3.12 g, dissolved in 10 ml THF) was then added dropwise and stirred for another 3h. After that, the suspension was cooled down to room temperature and filtered. The filtrate was concentrated under reduced pressure and purified by a silica gel column. A white solid was isolated in 45% yield.

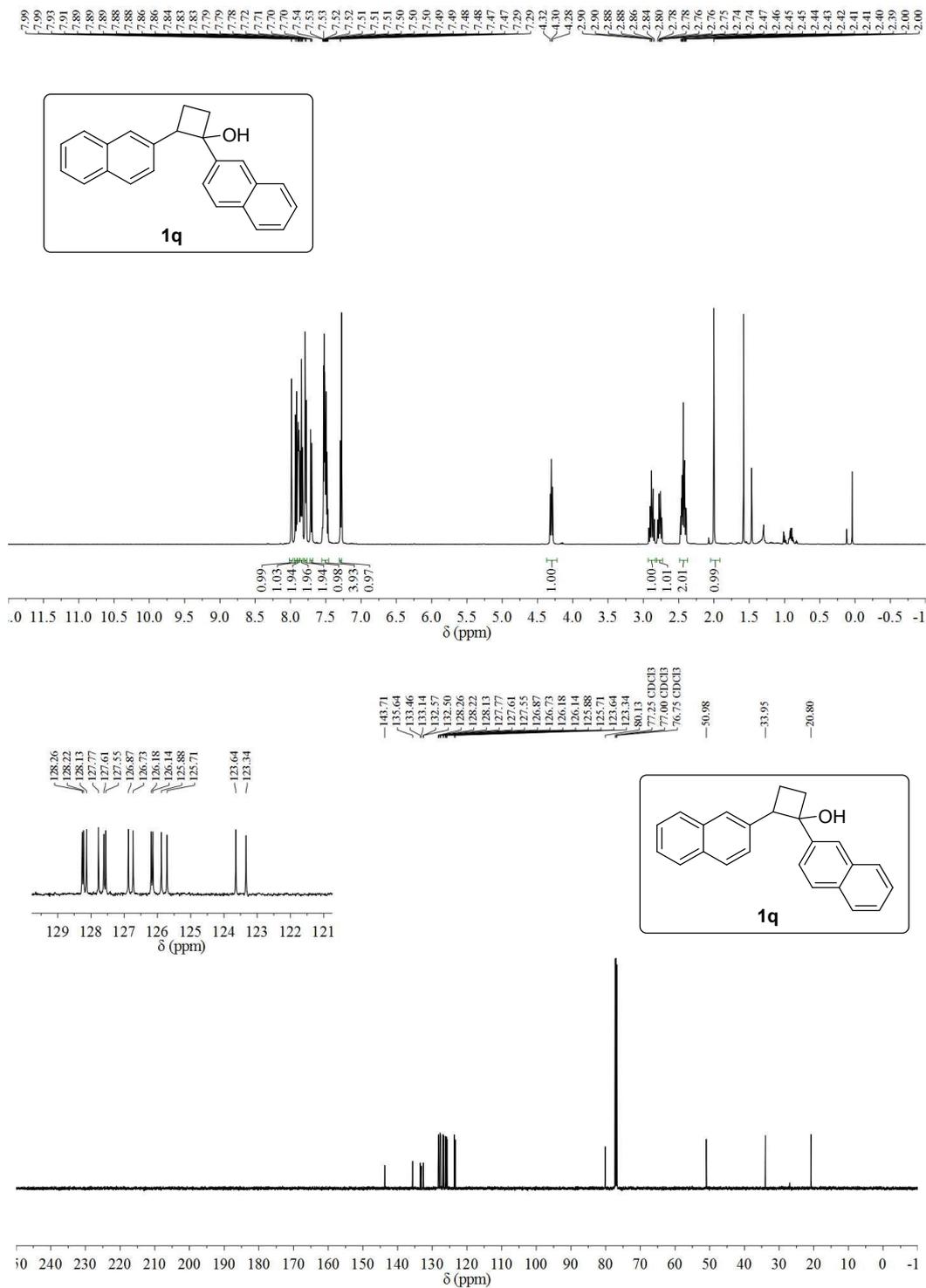
The obtained (phenylmethylene)cyclopropanes (9 mmol, 1.62 g) was dissolved in DCM (60 ml), and *m*-CPBA (2.07g, 9 mmol, dissolved in 25 ml DCM) was slowly added dropwise to the mixture at 0 °C and stirred for 1h. At the end of the reaction, it was diluted with a saturated solution of aqueous Na<sub>2</sub>SO<sub>3</sub> (15 ml) and extracted with DCM (3×10 ml). The organic layer was washed successively with a saturated NaHCO<sub>3</sub> (15 ml), brine (15 ml), and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was then purified by silica gel column chromatography using a mixture of petroleum ether and ethyl acetate (PE : EA = 20 : 1) as an eluent to give the cyclobutanone derivative (1.05 g, 60%). The procedure for the preparation of **1p** from cyclobutanone was in accordance with the above general procedure. The **1p** was obtained in 40% yield (0.7 g) as a light yellow solid.

### 1,2-di(naphthalen-2-yl)cyclobutan-1-ol (**1q**)

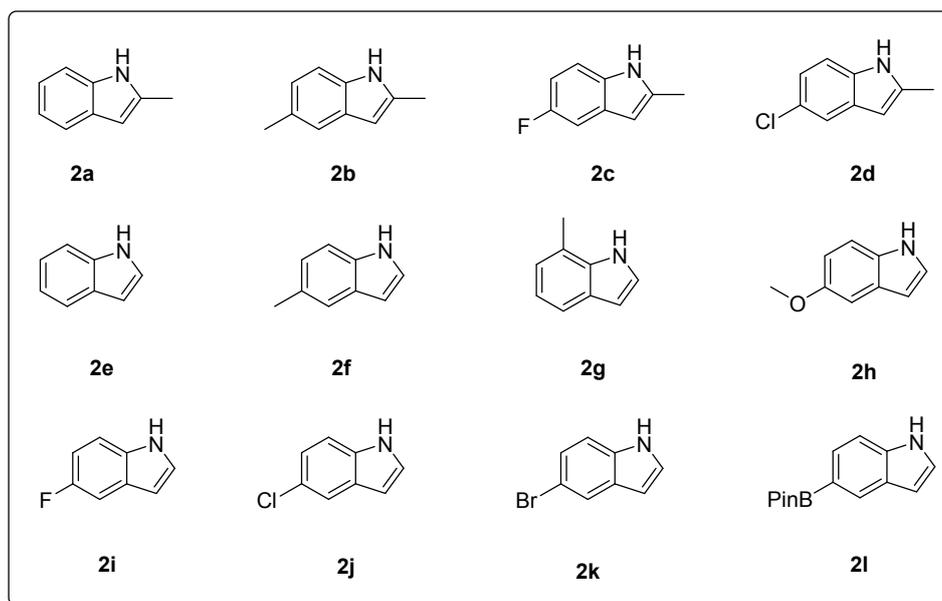


<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.98 (d, *J* = 1.5 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.90-7.87 (m, 2H), 7.87-7.82 (m, 2H), 7.80-7.77 (m,

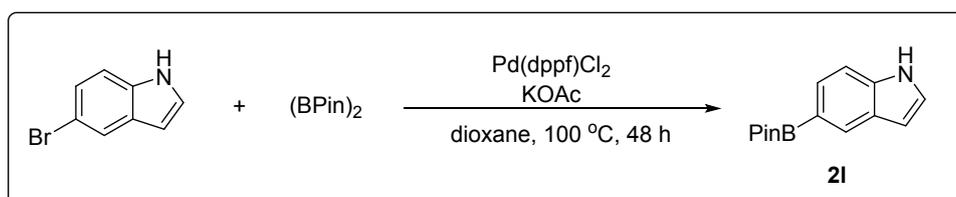
2H), 7.71 (dd,  $J_1 = 8.5$  Hz,  $J_2 = 2.0$  Hz, 1H), 7.54-7.48 (m, 4H), 7.30-7.27 (m, 1H), 4.30 (t,  $J = 8.0$  Hz, 1H), 2.93-2.84 (m, 1H), 2.80-2.73 (m, 1H), 2.48-2.39 (m, 2H), 2.00 (d,  $J = 1.5$  Hz, 1H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  143.7, 135.6, 133.5, 133.1, 132.6, 132.5, 128.3, 128.2, 128.1, 127.8, 127.6, 127.5, 126.9, 126.7, 126.2, 126.1, 125.9, 125.7, 123.6, 123.3, 80.1, 51.0, 34.0, 20.8. HRMS (-p ESI) Calculated for  $\text{C}_{24}\text{H}_{19}\text{O}^-$  ( $[\text{M}-\text{H}]^-$ ): 323.14414, found: 323.14423.



## 2.2 General procedure for the preparation of indoles.



Preparation of indole **2l**:<sup>8</sup>

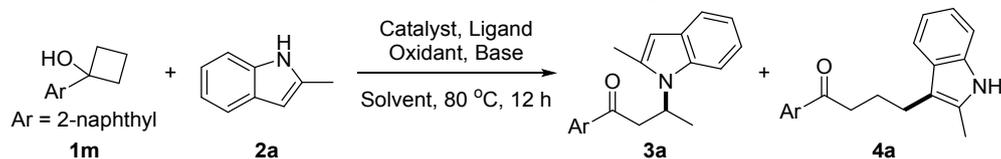


To a 100 ml Schlenk tube was added 5-bromoindole (5.1 mmol, 1.0 g), (Bpin)<sub>2</sub> (9.6 mmol, 1.1 equiv), Pd(dppf)Cl<sub>2</sub> (0.15 mmol, 3 mol%), KOAc (15.3 mmol, 3 equiv), and 1,4-dioxane (30 ml). The reaction was sealed and heated at 100 °C for 48 h. After the completion, the reaction mixture was cooled down to room temperature. The solvent was removed under reduced pressure and the residue was purified by a silica gel column to afford the product **2l** in 70% yield (0.87 g) as a white solid. Other indoles are commercially available and used as received.

### 3. Ni-Catalyzed *cine*-Arylation of *tert*-Cyclobutanols with Indoles

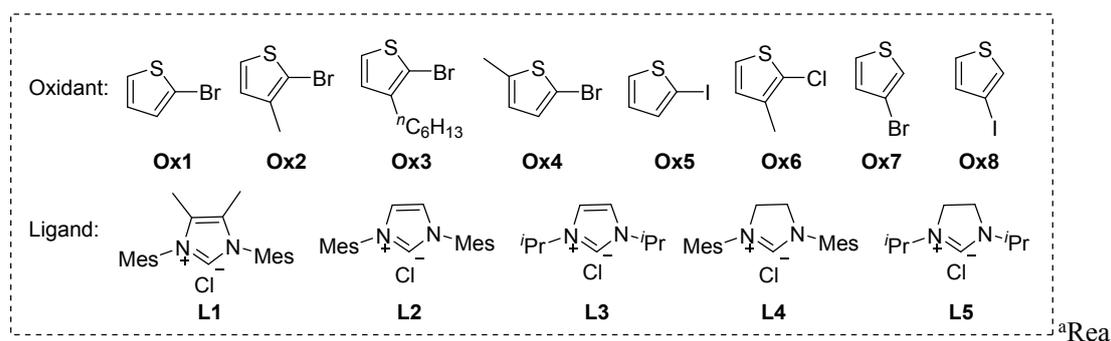
#### 3.1 Optimization of reaction conditions

**Table S1.** Survey of the reaction parameters<sup>a</sup>



Entry	Catalyst/mol%	Ligand/mol%	Oxidant	Base/equiv	Solvent	Yield/%
1	NiBr <sub>2</sub> /20	L1/20	- <sup>b</sup>	<sup>t</sup> BuONa/2	Toluene	8
2	NiBr <sub>2</sub> /20	L1/20	DDQ	<sup>t</sup> BuONa/2	Toluene	0
3	NiBr <sub>2</sub> /20	L1/20	AgNO <sub>3</sub>	<sup>t</sup> BuONa/2	Toluene	0
4	NiBr <sub>2</sub> /20	L1/20	<b>Ox1</b>	<sup>t</sup> BuONa/2	Toluene	55
5	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	76
6	NiBr <sub>2</sub> /20	L1/20	<b>Ox3</b>	<sup>t</sup> BuONa/2	Toluene	67
7	NiBr <sub>2</sub> /20	L1/20	<b>Ox4</b>	<sup>t</sup> BuONa/2	Toluene	58
8	NiBr <sub>2</sub> /20	L1/20	<b>Ox5</b>	<sup>t</sup> BuONa/2	Toluene	67
9	NiBr <sub>2</sub> /20	L1/20	<b>Ox6</b>	<sup>t</sup> BuONa/2	Toluene	trace
10	NiBr <sub>2</sub> /20	L1/20	<b>Ox7</b>	<sup>t</sup> BuONa/2	Toluene	35
11	NiBr <sub>2</sub> /20	L1/20	<b>Ox8</b>	<sup>t</sup> BuONa/2	Toluene	56
12	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuOK/2	Toluene	20
13	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuOLi/2	Toluene	0
14	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	K <sub>2</sub> CO <sub>3</sub> /2	Toluene	0
15	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	EtONa/2	Toluene	0
16	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	Na <sub>2</sub> CO <sub>3</sub> /2	Toluene	0
17	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	Cs <sub>2</sub> CO <sub>3</sub> /2	Toluene	trace
18	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/1	Toluene	25
19	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	- <sup>c</sup>	Toluene	0
20	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	THF	65
21	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	CH <sub>3</sub> CN	0
22	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	DCM	0
23	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Dioxane	57
24	NiBr <sub>2</sub> /20	L1/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Xylene	55
25	NiBr <sub>2</sub> /20	L2/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	61
26	NiBr <sub>2</sub> /20	L3/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	70
27	NiBr <sub>2</sub> /20	L4/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	26
28	NiBr <sub>2</sub> /20	L5/20	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	32
29	NiBr <sub>2</sub> /20	1,10-Phen/20%	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	0
30	NiBr <sub>2</sub> /20	Dppp/20%	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	0
31	NiBr <sub>2</sub> /20	L1/40%	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	55
32	NiBr <sub>2</sub> /20	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	7
33	Ni(OAc) <sub>2</sub> /20	L1	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	43

34	NiI <sub>2</sub> /20	<b>L1</b>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	40
35	Ni(acac) <sub>2</sub> /20	<b>L1</b>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	23
36	NiCl <sub>2</sub> /20	<b>L1</b>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	trace
37	Ni(cod) <sub>2</sub> /20	<b>L1</b>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	45
38	Ni(dppe)Cl <sub>2</sub> (20)	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	81
39	Ni(dppp)Cl <sub>2</sub> (20)	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	83
40	Ni(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> /20	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	78
41	Ni(PPh <sub>3</sub> ) <sub>2</sub> Br <sub>2</sub> /20	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	88
42	Ni(PCy <sub>3</sub> ) <sub>2</sub> Br <sub>2</sub> /20	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	83
43	Ni(PPh <sub>3</sub> ) <sub>2</sub> Br <sub>2</sub> /5	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	86
44	Ni(PPh <sub>3</sub> ) <sub>2</sub> Br <sub>2</sub> /2	- <sup>d</sup>	<b>Ox2</b>	<sup>t</sup> BuONa/2	Toluene	32

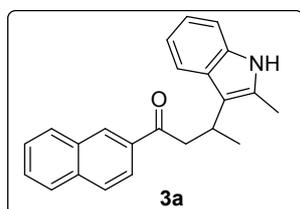


tion conditions unless otherwise noted: **1a** (0.2 mmol), **2a** (0.4 mmol), catalyst, base, oxidant (0.24 mmol), solvent (0.5 mL), 80 °C, 12 h under N<sub>2</sub> atmosphere. <sup>b</sup>No oxidant. <sup>c</sup>No base. <sup>d</sup>No ligand. 1,10-phen = 1,10-phenanthroline, Dppp = 1,3-bis(diphenylphosphanyl)propane.

### 3.2 Typical procedure and characterization of products

To a 25 ml flame-dried Schlenk tube was added *tert*-cyclobutanol **1m** (0.2 mmol, 39.6 mg), 2-methyl-1*H*-indole **2a** (0.4 mmol, 52.4 mg), Ni(PPh<sub>3</sub>)<sub>2</sub>Br<sub>2</sub> (5 mol%, 0.01 mmol, 7.4 mg), **Ox2** (0.24 mmol, 42.4 mg), *t*-BuONa (0.4 mmol, 38.4 mg), and toluene (0.5 mL) sequentially under positive nitrogen atmosphere. The reaction tube was sealed and stirred at 80 °C for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (2.0 mL) and filtered through a short pad silica gel washing with ethyl acetate (10 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the product **3a** in 86% yield.

#### 3-(2-methyl-1*H*-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (**3a**)



Yield: 86% (56.2 mg), yellow solid, mp: 86-88 °C.

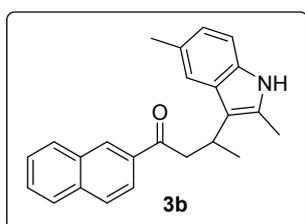
<sup>1</sup>H NMR (500 MHz, DMSO) δ 10.63 (s, 1H), 8.56 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.97-7.88 (m, 3H), 7.70 (d, *J* = 7.3

Hz, 1H), 7.65-7.60 (m, 1H), 7.58 (d,  $J = 7.7$  Hz, 1H), 7.22 (d,  $J = 7.2$  Hz, 1H), 7.02-6.91 (m, 2H), 3.75-3.63 (m, 2H), 3.56-3.46 (m, 1H), 2.28 (s, 3H), 1.47 (d,  $J = 6.7$  Hz, 3H).

**$^{13}\text{C}$  NMR (125 MHz, DMSO)**  $\delta$  200.0, 135.9, 135.3, 134.6, 132.6, 131.1, 130.2, 129.9, 128.9, 128.6, 128.0, 127.2, 127.2, 124.0, 120.1, 119.1, 118.5, 114.3, 111.0, 45.8, 27.8, 21.7, 12.1.

**HRMS (ESI)** Calculated for  $\text{C}_{23}\text{H}_{21}\text{NNaO}^+$  ( $[\text{M}+\text{Na}]^+$ ): 350.15153, found: 350.15154.

### 3-(2,5-dimethyl-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3b)



Yield: 66% (45 mg), yellow solid, mp: 146-148 °C.

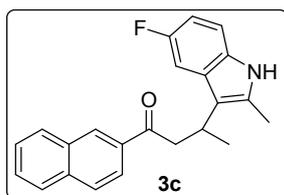
**$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )**  $\delta$  8.32 (s, 1H), 8.00-7.96 (m, 1H), 7.86-7.77 (m, 3H), 7.60-7.49 (m, 4H), 7.14 (d,  $J = 8.2$  Hz, 1H), 7.03-6.89 (m, 1H), 3.82-3.74 (m, 1H), 3.71-3.68

(m, 1H), 3.48-3.42 (m, 1H), 2.51 (s, 3H), 2.36 (s, 3H), 1.57 (d,  $J = 7.0$  Hz, 3H).

**$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )**  $\delta$  200.3, 135.4, 134.6, 133.9, 132.5, 130.5, 129.9, 129.5, 128.23, 128.2, 128.1, 127.6, 127.5, 126.5, 123.9, 122.2, 118.9, 115.1, 110.2, 45.9, 27.9, 21.7, 21.1, 12.1.

**HRMS(ESI)** Calculated for  $\text{C}_{24}\text{H}_{23}\text{NNaO}^+$  ( $[\text{M}+\text{Na}]^+$ ): 364.16718, found: 364.16719.

### 3-(5-fluoro-2-methyl-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3c)



Yield: 65% (44.8 mg), yellow solid, mp: 122-124 °C.

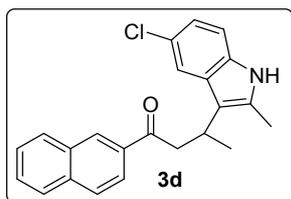
**$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )**  $\delta$  8.31 (s, 1H), 7.98-7.93 (m, 1H), 7.85-7.79 (m, 3H), 7.71 (s, 1H), 7.60-7.50 (m, 2H), 7.44-7.39 (m, 1H), 7.16-7.07 (m, 1H), 6.91-6.81 (m, 1H),

3.82-3.74 (m, 1H), 3.73-3.67 (m, 1H), 3.43-3.37 (m, 1H), 2.36 (s, 3H), 1.56 (d,  $J = 7.1$  Hz, 3H).

**$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )**  $\delta$  200.0, 157.4 (d,  $J_{\text{C-F}} = 231.9$  Hz), 135.4, 134.5, 132.6, 132.4, 132.0, 129.8, 129.5, 128.3, 128.2, 127.6, 127.4 (d,  $J_{\text{C-F}} = 9.4$  Hz), 126.6, 123.8, 115.7 (d,  $J_{\text{C-F}} = 4.5$  Hz), 110.9 (d,  $J_{\text{C-F}} = 9.8$  Hz), 108.6 (d,  $J_{\text{C-F}} = 25.8$  Hz), 104.1 (d,  $J_{\text{C-F}} = 23.5$  Hz), 45.5, 27.7, 20.96, 12.1.

**HRMS(ESI)** Calculated for  $\text{C}_{23}\text{H}_{20}\text{FNNaO}^+$  ( $[\text{M}+\text{Na}]^+$ ): 368.14211, found: 368.14211.

### 3-(5-chloro-2-methyl-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3d)



Yield: 75% (54.1 mg), yellow solid, mp: 180-182 °C.

**<sup>1</sup>H NMR (500 MHz, DMSO)** δ 10.83 (s, 1H), 8.59 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.8 Hz, 2H), 7.91-7.89 (m, 1H), 7.69 (d, *J* = 1.9 Hz, 1H), 7.65-7.62 (m, 1H), 7.61-

7.57 (m, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 6.96-6.94 (m, 1H), 3.67-3.62 (m, 2H), 3.54-3.49 (m, 1H), 2.27 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, DMSO)** δ 199.4, 134.9, 134.1, 133.8, 132.9, 132.1, 129.8, 129.5, 128.4, 128.1, 127.8, 127.6, 126.8, 123.5, 122.6, 119.4, 117.7, 113.9, 111.9, 45.2, 27.0, 21.0, 11.6.

**HRMS(ESI)** Calculated for C<sub>23</sub>H<sub>20</sub>ClNNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 384.11256, found: 384.11256.

### 3-(1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3e)<sup>9</sup>

Yield: 80% (50.1 mg), yellow solid, mp: 120-122 °C

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 8.46 (d, *J* = 1.0 Hz, 1H), 8.09-8.05 (m, 2H), 7.91-7.86 (m, 3H), 7.79-7.77 (m, 1H), 7.63-7.60 (m, 1H), 7.58-7.54 (m, 1H), 7.40-7.37 (m, 1H), 7.27-7.23 (m, 1H), 7.21-7.17 (m, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 3.96-3.91 (m, 1H), 3.68-3.64 (m, 1H), 3.44-3.38 (m, 1H), 1.55 (d, *J* = 6.9 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 199.8, 136.6, 135.5, 134.6, 132.5, 129.8, 129.5, 128.3, 127.67, 126.6, 126.3, 123.9, 121.9, 121.4, 120.3, 119.2, 119.2, 111.3, 46.5, 27.5, 21.0.

### 3-(5-methyl-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3f)

Yield: 61% (39.9 mg), yellow solid, mp: 118-120 °C.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 8.47 (s, 1H), 8.10-8.06 (m, 1H), 7.96-7.85 (m, 4H), 7.64-7.52 (m, 3H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.09-6.99 (m, 2H), 3.94-3.86 (m, 1H), 3.67-3.62 (m, 1H), 3.42-3.35 (m, 1H), 2.51 (s, 3H), 1.54 (d, *J* = 6.9 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 199.9, 135.5, 134.9, 134.7, 132.5, 129.8, 129.5, 128.5, 128.3, 127.7, 126.6, 126.6, 123.9, 123.6, 121.0, 120.4, 118.9, 111.0, 46.6, 27.4, 21.5, 20.9.

**HRMS(ESI)** Calculated for C<sub>23</sub>H<sub>21</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 350.15153, found: 350.15154.

### 3-(7-methyl-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3g)

Yield: 57% (37.3 mg), yellow solid, mp: 105-107 °C.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.44 (d, *J* = 1.1 Hz, 1H), 8.09-8.05 (m, 1H), 7.96 (s, 1H), 7.91-7.87 (m, 3H), 7.64-7.59 (m, 2H), 7.58-7.53 (m, 1H), 7.14-7.08 (m, 1H), 7.08-7.02 (m, 2H), 3.95-3.88 (m, 1H), 3.68-3.63 (m, 1H), 3.43-3.37 (m, 1H), 2.50 (s, 3H), 1.54 (d, *J* = 6.9 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 199.8, 136.2, 135.5, 134.7, 132.5, 129.8, 129.5, 128.3, 127.7, 126.6, 125.9, 123.9, 122.6, 122.1, 120.5, 119.9, 119.5, 116.9, 46.5, 27.6, 20.9, 16.5.

HRMS(ESI) Calculated for C<sub>23</sub>H<sub>21</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 350.15153, found: 350.15154.

### 3-(5-methoxy-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3h)

Yield: 70% (48.0 mg), yellow oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.44 (s, 1H), 8.05 (M, 1H), 7.92-7.86 (m, 4H), 7.62-7.52 (m, 2H), 7.28-7.25 (m, 1H), 7.15 (d, *J* = 2.4 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.89 (M, 1H), 3.89-3.83 (m, 4H, overlap), 3.63-3.58 (m, 1H), 3.41-3.35 (m, 1H), 1.51 (d, *J* = 6.9 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 199.8, 153.9, 135.5, 134.7, 132.5, 131.7, 129.8, 129.5, 128.4, 127.7, 126.8, 126.7, 123.9, 121.4, 121.0, 112.2, 111.9, 101.3, 56.0, 46.5, 27.4, 20.9.

HRMS(ESI) Calculated for C<sub>23</sub>H<sub>21</sub>NNaO<sub>2</sub><sup>+</sup> ([M+Na]<sup>+</sup>): 366.14645, found: 366.14645.

### 3-(5-fluoro-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3i)

Yield: 53% (37.5 mg), yellow oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.43 (s, 1H), 8.07 - 7.92 (m, 2H), 7.92-7.85 (m, 3H), 7.63-7.58 (m, 1H), 7.57-7.53 (m, 1H), 7.41-7.34 (m, 1H), 7.28-7.25 (m, 1H), 7.09 (d, *J* = 2.4 Hz, 1H), 7.00-6.91 (m, 1H), 3.88-3.80 (m, 1H), 3.62-3.56 (m, 1H), 3.40-3.34 (m, 1H), 1.51 (d, *J* = 6.9 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 199.5 (s), 157.6 (d, *J*<sub>C-F</sub> = 234.5 Hz), 135.1 (d, *J*<sub>C-F</sub> = 114.8 Hz), 132.8 (d, *J*<sub>C-F</sub> = 70.6 Hz), 129.6 (d, *J*<sub>C-F</sub> = 30.2 Hz), 128.4 (s), 127.7 (s),

126.7 (s), 123.9 (s), 122.1 (s), 121.6 (d,  $J_{C-F} = 4.7$  Hz), 111.8 (d,  $J_{C-F} = 9.6$  Hz), 110.5 (s), 110.3 (s), 104.2 (d,  $J_{C-F} = 23.4$  Hz), 46.3 (s), 27.4 (s), 21.0 (s).

**HRMS(ESI)** Calculated for  $C_{22}H_{18}FNNaO^+$  ( $[M+Na]^+$ ): 354.12646, found: 354.12646.

### 3-(5-chloro-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3j)

Yield: 50% (34.7 mg), yellow oil.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)**  $\delta$  8.44 (s, 1H), 8.12 (s, 1H), 8.05-8.01 (m, 1H), 7.93-7.86 (m, 3H), 7.70 (d,  $J = 1.9$  Hz, 1H), 7.63-7.53 (m, 2H), 7.27 (d,  $J = 6.3$  Hz, 1H), 7.21-7.09 (m, 1H), 7.05 (d,  $J = 2.3$  Hz, 1H), 3.89-3.80 (m, 1H), 3.61-3.55 (m, 1H), 3.41-3.34 (m, 1H), 1.51 (d,  $J = 6.9$  Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)**  $\delta$  199.6, 135.5, 134.9, 134.5, 132.5, 129.8, 129.5, 128.4, 127.7, 127.4, 126.7, 124.9, 123.8, 122.3, 121.8, 121.2, 118.7, 112.3, 46.3, 27.4, 21.1.

**HRMS(ESI)** Calculated for  $C_{22}H_{18}ClNNaO^+$  ( $[M+Na]^+$ ): 370.09691, found: 370.09691.

### 3-(5-bromo-1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3k)

Yield: 61% (47.7 mg), yellow solid, mp: 85-87 °C.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)**  $\delta$  8.43 (s, 1H), 8.15 (s, 1H), 8.06-8.00 (m, 1H), 7.94-7.90 (m, 3H), 7.90-7.84 (m, 3H), 7.63-7.54 (m, 2H), 7.30-7.26 (m, 1H), 7.20 (d,  $J = 8.6$  Hz, 1H), 7.03 (d,  $J = 2.3$  Hz, 1H), 3.87-3.80 (m, 1H), 3.61-3.55 (m, 1H), 3.40-3.34 (m, 1H), 1.50 (d,  $J = 6.9$  Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)**  $\delta$  199.6, 135.5, 135.1, 134.5, 132.5, 129.8, 129.5, 128.4, 128.1, 127.7, 126.7, 124.8, 123.8, 121.8, 121.6, 121.1, 112.7, 112.5, 46.3, 27.4, 21.1.

**HRMS(ESI)** Calculated for  $C_{22}H_{18}BrNNaO^+$  ( $[M+Na]^+$ ): 414.04640, found: 414.04640.

### 1-(naphthalen-2-yl)-3-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-3-yl)butan-1-one (3l)

Yield: 35% (30.7 mg), yellow solid, mp: 60-62 °C.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)**  $\delta$  8.47 (s, 1H), 8.28 (s, 1H), 8.10-8.03 (m, 2H), 7.95-7.86 (m, 3H), 7.71-7.66 (m, 1H), 7.62-7.52 (m, 2H), 7.37 (d,  $J = 8.2$  Hz, 1H), 7.05 (d,

$J = 2.2$  Hz, 1H), 3.97-3.88 (m, 1H), 3.64-3.68 (m, 1H), 3.32-3.37 (m, 1H), 1.51 (d,  $J = 6.9$  Hz, 3H), 1.39 (d,  $J = 2.2$  Hz, 12H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  199.8, 138.6, 135.5, 134.6, 132.5, 129.9, 129.6, 128.4, 128.3, 128.3, 127.7, 126.9, 126.6, 126.2, 123.9, 122.2, 120.2, 110.7, 83.5, 46.7, 27.6, 24.9, 24.9, 21.0.

HRMS(ESI) Calculated for  $\text{C}_{28}\text{H}_{30}\text{BNNaO}_3^+$  ( $[\text{M}+\text{Na}]^+$ ): 462.22109, found: 462.22110.

### 3-(2-methyl-1H-indol-3-yl)-1-phenylbutan-1-one (3m)<sup>10</sup>

Yield: 59% (32.7 mg), yellow oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.92 (M, 2H), 7.79 (s, 1H), 7.74-7.71 (m, 1H), 7.53 (M, 1H), 7.43-7.39 (m, 2H), 7.28-7.25 (m, 1H), 7.15-7.09 (m, 2H), 3.77-3.81 (m, 1H), 3.54-3.59 (m, 1H), 3.39-3.44 (m, 1H), 2.40 (s, 3H), 1.54 (d,  $J = 7.1$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  200.1, 137.3, 135.5, 132.7, 130.3, 128.4, 128.0, 127.1, 120.58, 118.9, 118.9, 115.4, 110.5, 76.8, 45.6, 27.3, 21.0, 11.9.

### 3-(2-methyl-1H-indol-3-yl)-1-(p-tolyl)butan-1-one (3n)<sup>10</sup>

Yield: 72% (41.9 mg), yellow oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.88-7.82 (m, 3H), 7.77-7.74 (m, 1H), 7.28-7.25 (m, 1H), 7.23 (d,  $J = 8.0$  Hz, 2H), 7.17-7.12 (m, 2H), 3.78-3.83 (m, 1H), 3.54-3.58 (m, 1H), 3.39-3.44 (m, 1H), 2.42 (s, 3H), 2.39 (s, 3H), 1.56 (d,  $J = 7.1$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  199.7, 143.5, 135.5, 134.9, 130.3, 129.1, 128.1, 127.1, 120.5, 118.9, 118.8, 115.4, 110.5, 45.5, 27.4, 21.4, 20.9, 11.9.

### 1-(4-(tert-butyl)phenyl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3o)

Yield: 81% (54 mg), yellow oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (d,  $J = 8.5$  Hz, 2H), 7.87 (s, 1H), 7.76-7.74 (m, 1H), 7.46 (d,  $J = 8.5$  Hz, 2H), 7.28-7.26 (m, 1H), 7.15-7.13 (m, 2H), 3.85-3.80 (m, 1H), 3.59-3.54 (m, 1H), 3.46-3.41 (m, 1H), 2.41 (s, 3H), 1.56 (d,  $J = 7.1$  Hz, 3H), 1.37 (s, 9H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  199.8, 156.4, 135.5, 134.7, 130.3, 127.9, 127.1, 125.3, 120.5, 118.9, 118.8, 115.5, 110.5, 45.5, 34.9, 31.0, 27.3, 20.9, 11.9.

**HRMS(ESI)** Calculated for  $C_{23}H_{27}NNaO^+$  ( $[M+Na]^+$ ): 356.19848, found: 356.19849.

**1-([1,1'-biphenyl]-4-yl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3p)**

Yield: 65% (45.9 mg), yellow oil.

**$^1H$  NMR (500 MHz,  $CDCl_3$ )**  $\delta$  8.00-7.96 (m, 2H), 7.79-7.73 (m, 2H), 7.65-7.61 (m, 4H), 7.52-7.47 (m, 2H), 7.45-7.39 (m, 1H), 7.29-7.26 (m, 1H), 7.17-7.11 (m, 2H), 3.87-3.79 (m, 1H), 3.65-3.59 (m, 1H), 3.47-3.41 (m, 1H), 2.42 (s, 3H), 1.57 (d,  $J = 7.1$  Hz, 3H).

**$^{13}C$  NMR (125 MHz,  $CDCl_3$ )**  $\delta$  199.7, 145.4, 139.9, 135.9, 135.5, 132.9, 130.3, 130.2, 128.9, 128.6, 128.1, 127.2, 127.1, 127.0, 120.6, 118.9, 118.9, 115.4, 110.5, 45.7, 27.5, 21.0, 11.9.

**HRMS(ESI)** Calculated for  $C_{25}H_{23}NNaO^+$  ( $[M+Na]^+$ ): 376.16718, found: 376.16719.

**1-(4-methoxyphenyl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3q)**

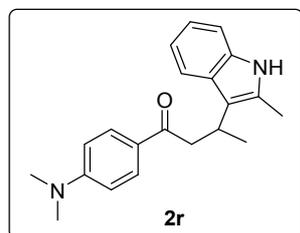
Yield: 70% (43.0 mg), yellow oil.

**$^1H$  NMR (500 MHz,  $CDCl_3$ )**  $\delta$  7.92-7.90 (m, 2H), 7.88 (s, 1H), 7.75-7.73 (m, 1H), 7.27-7.24 (m, 1H), 7.14-7.12 (m, 2H), 6.90-6.87 (m, 2H), 3.85 (s, 3H), 3.81-3.76 (m, 1H), 3.54-3.50 (m, 1H), 3.39-3.35 (m, 1H), 2.37 (s, 3H), 1.54 (d,  $J = 7.1$  Hz, 3H).

**$^{13}C$  NMR (125 MHz,  $CDCl_3$ )**  $\delta$  198.7, 163.2, 135.5, 130.3, 130.3, 130.3, 127.1, 120.5, 118.9, 118.8, 115.4, 113.5, 110.5, 55.3, 45.3, 27.5, 20.9, 11.9.

**HRMS(ESI)** Calculated for  $C_{20}H_{21}NNaO_2^+$  ( $[M+Na]^+$ ): 330.14645, found: 330.14645.

**1-(4-(dimethylamino)phenyl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3r)**



Yield: 62% (39.7 mg), yellow solid, mp: 130-132 °C.

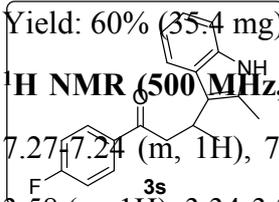
**$^1H$  NMR (500 MHz,  $CDCl_3$ )**  $\delta$  7.88-7.81 (m, 3H), 7.76-7.72 (m, 1H), 7.29-7.25 (m, 1H), 7.13-7.08 (m, 2H), 6.63-6.60 (m, 2H), 3.79-3.74 (m, 1H), 3.46-3.41 (m, 1H), 3.37-3.31 (m, 1H), 3.04 (s, 6H), 2.39 (s, 3H), 1.51 (d,  $J = 7.1$  Hz, 3H).

**$^{13}C$  NMR (125 MHz,  $CDCl_3$ )**  $\delta$  198.2, 153.2, 135.5, 130.3, 130.2, 127.3, 125.4, 120.4, 119.1, 118.8, 115.9, 110.6, 110.4, 44.9, 39.9, 27.8, 20.9, 11.9.

**HRMS(ESI)** Calculated for  $C_{21}H_{24}N_2NaO^+$  ( $[M+Na]^+$ ): 343.17808, found: 343.17808.

**1-(4-fluorophenyl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3s)<sup>10</sup>**

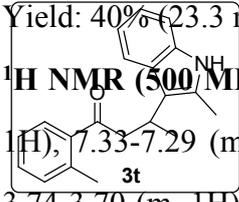
Yield: 60% (35.4 mg), yellow oil.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 7.92-7.89 (m, 2H), 7.80 (s, 1H), 7.73-7.71 (m, 1H), 7.27-7.24 (m, 1H), 7.14-7.12 (m, 2H), 7.08-7.04 (m, 2H), 3.80-3.75 (m, 1H), 3.54-3.58 (m, 1H), 3.34-3.38 (m, 1H), 2.38 (s, 3H), 1.55 (d, *J* = 7.1 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 198.5, 165.5 (d, *J*<sub>C-F</sub> = 254.2 Hz), 135.5, 133.7 (d, *J*<sub>C-F</sub> = 3.0 Hz), 130.6 (d, *J*<sub>C-F</sub> = 9.2 Hz), 130.4, 127.0, 120.6, 118.9 (d, *J*<sub>C-F</sub> = 2.8 Hz), 115.5, 115.3, 115.2, 110.5, 45.5, 27.5, 21.0, 11.9.

### 3-(2-methyl-1H-indol-3-yl)-1-(o-tolyl)butan-1-one (3t)

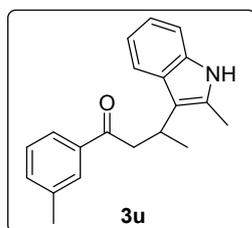
Yield: 40% (23.3 mg), yellow oil

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 7.71 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.49-7.47 (m, 1H), 7.33-7.29 (m, 1H), 7.27-7.25 (m, 1H), 7.20-7.17 (m, 2H), 7.11-7.04 (m, 2H), 3.74-3.70 (m, 1H), 3.48-3.43 (m, 1H), 3.36-3.31 (m, 1H), 2.34 (s, 3H), 2.30 (s, 3H), 1.49 (d, *J* = 7.1 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 204.4, 138.7, 137.6, 135.5, 131.7, 130.8, 130.3, 128.1, 127.1, 125.5, 120.7, 119.0, 118.9, 115.2, 110.4, 48.8, 27.6, 21.0, 20.7, 11.9.

**HRMS(ESI)** Calculated for C<sub>20</sub>H<sub>21</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 314.15153, found: 314.15154.

### 3-(2-methyl-1H-indol-3-yl)-1-(m-tolyl)butan-1-one (3u)



Yield: 75% (43.7 mg), yellow oil

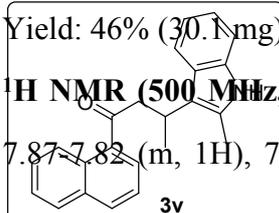
**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 7.80 (s, 1H), 7.76-7.70 (m, 3H), 7.35-7.29 (m, 2H), 7.28-7.25 (m, 1H), 7.15-7.12 (m, 2H), 3.82-3.77 (m, 1H), 3.61-3.56 (m, 1H), 3.41-3.36 (m, 1H), 2.39 (s, 3H), 2.36 (s, 3H), 1.56 (d, *J* = 7.1 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 200.4, 138.1, 137.3, 135.5, 133.5, 130.3, 128.6, 128.3, 127.11, 125.2, 120.6, 118.9, 118.9, 115.4, 110.5, 45.7, 27.5, 21.2, 21.0, 11.9.

**HRMS(ESI)** Calculated for C<sub>20</sub>H<sub>21</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 314.15153, found: 314.15154.

### 3-(2-methyl-1H-indol-3-yl)-1-(naphthalen-1-yl)butan-1-one (3v)

Yield: 46% (30.1 mg), yellow oil.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 8.26 (d, *J* = 8.3 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.87-7.82 (m, 1H), 7.71-7.66 (m, 3H), 7.51-7.45 (m, 2H), 7.42-7.38 (m, 1H), 7.26-

7.22 (m, 1H), 7.14-7.08 (m, 2H), 3.84-3.79 (m, 1H), 3.71-3.65 (m, 1H), 3.48-3.43 (m, 1H), 2.23 (s, 3H), 1.56 (d,  $J = 7.1$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  204.6, 136.8, 135.5, 133.8, 131.9, 130.4, 130.0, 128.2, 127.5, 127.0, 126.9, 126.2, 125.6, 124.3, 120.6, 119.0, 118.9, 114.9, 110.4, 49.4, 27.9, 21.1, 11.8.

HRMS(ESI) Calculated for  $\text{C}_{23}\text{H}_{21}\text{NNaO}^+$  ( $[\text{M}+\text{Na}]^+$ ): 350.15153, found: 350.15154.

### 1-(benzo[d][1,3]dioxol-5-yl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3w)

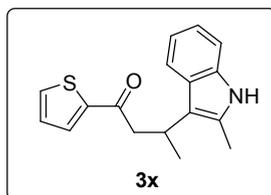
Yield: 51% (32.7 mg), yellow oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.76 (s, 1H), 7.71-7.69 (m, 1H), 7.50-7.48 (m, 1H), 7.40 (d,  $J = 1.7$  Hz, 1H), 7.27-7.24 (m, 1H), 7.12-7.09 (m, 2H), 6.78 (d,  $J = 8.2$  Hz, 1H), 6.01 (s, 2H), 3.77-3.72 (m, 1H), 3.49-3.44 (m, 1H), 3.34-3.29 (m, 1H), 2.40 (s, 3H), 1.51 (d,  $J = 7.1$  Hz, 3H).

$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  198.1, 151.5, 148.0, 135.5, 132.2, 130.3, 127.1, 124.3, 120.6, 118.9, 118.9, 115.5, 110.5, 107.9, 107.7, 101.7, 45.4, 27.6, 21.0, 11.9.

HRMS(ESI) Calculated for  $\text{C}_{20}\text{H}_{19}\text{NNaO}_3^+$  ( $[\text{M}+\text{Na}]^+$ ): 344.12571, found: 344.12571.

### 3-(2-methyl-1H-indol-3-yl)-1-(thiophen-2-yl)butan-1-one (3x)



Yield: 40% (22.6 mg), yellow oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.74-7.69 (m, 2H), 7.60-7.53 (m, 2H), 7.27-7.25 (m, 1H), 7.13-7.08 (m, 2H), 7.04-7.01 (m, 1H), 3.79-3.74 (m, 1H), 3.51-3.46 (m, 1H), 3.33-3.28 (m, 1H),

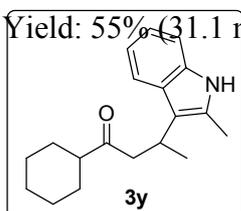
2.40 (s, 3H), 1.54 (d,  $J = 7.1$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  192.9, 144.8, 135.5, 133.3, 131.8, 130.5, 127.9, 127.1, 120.6, 118.9, 118.9, 115.2, 110.5, 46.4, 27.9, 20.9, 11.9.

HRMS(ESI) Calculated for  $\text{C}_{17}\text{H}_{17}\text{NNaOS}^+$  ( $[\text{M}+\text{Na}]^+$ ): 306.09230, found: 306.09231.

### 1-cyclohexyl-3-(2-methyl-1H-indol-3-yl)butan-1-one (3y)

Yield: 55% (31.1 mg), yellow oil.

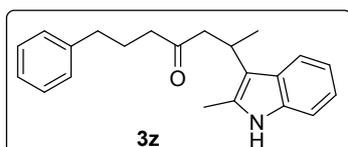


**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 7.77 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.28-7.24 (m, 1H), 7.16-7.03 (m, 2H), 3.66-3.53 (m, 1H), 3.04-2.98 (m, 1H), 2.91-2.85 (m, 1H), 2.41 (s, 3H), 2.23-2.16 (m, 1H), 2.07-1.43 (m, 10H), 1.41 (d, *J* = 7.1 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 213.7, 135.5, 130.2, 127.1, 120.5, 119.0, 118.8, 115.5, 110.4, 51.2, 47.5, 28.4, 27.9, 26.7, 25.8, 25.7, 25.5, 21.0, 11.9.

**HRMS(ESI)** Calculated for C<sub>19</sub>H<sub>25</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 306.18283, found: 306.18284.

### 6-(2-methyl-1H-indol-3-yl)-1-phenylheptan-4-one (3z)



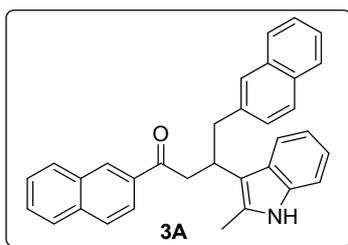
Yield: 40% (25.5 mg), yellow oil.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 7.70 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.28-7.23 (m, 3H), 7.20-7.16 (m, 1H), 7.12-7.03 (m, 4H), 3.55-3.62 (m, 1H), 3.00-3.04 (m, 1H), 2.75-2.79 (m, 1H), 2.49-2.41 (m, 2H), 2.39 (s, 3H), 2.33-2.28 (m, 1H), 2.23-2.17 (m, 1H), 1.78-1.75 (m, 2H), 1.43 (d, *J* = 7.1 Hz, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 210.6, 141.7, 135.5, 130.3, 128.4, 128.3, 127.0, 125.8, 120.7, 118.9, 118.9, 115.1, 110.5, 49.5, 42.7, 34.9, 27.2, 24.9, 21.1, 11.9.

**HRMS(ESI)** Calculated for C<sub>22</sub>H<sub>25</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 342.18283, found: 342.18284.

### 3-(2-methyl-1H-indol-3-yl)-1,5-di(naphthalen-2-yl)pentan-1-one (3A)



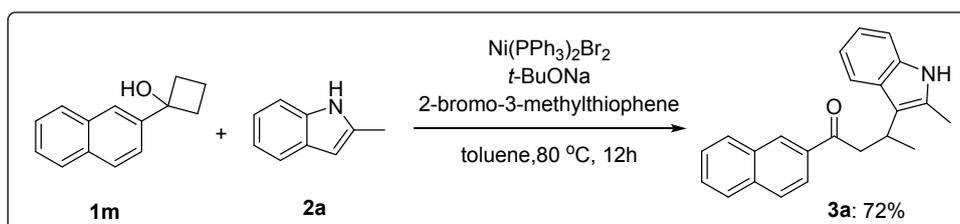
Yield: 13% (12.2 mg), yellow oil.

**<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)** δ 8.27 (s, 1H), 7.96-7.90 (m, 2H), 7.84-7.80 (m, 2H), 7.78-7.74 (m, 2H), 7.69-7.65 (m, 2H), 7.57-7.49 (m, 4H), 7.42-7.38 (m, 2H), 7.26-7.15 (m, 4H), 4.03-3.96 (m, 1H), 3.90-3.84 (m, 1H), 3.67-3.61 (m, 1H), 3.46-3.36 (m, 2H), 1.96 (s, 3H).

**<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)** δ 199.9, 138.6, 135.7, 135.4, 134.6, 133.5, 132.4, 132.0, 131.9, 129.8, 129.5, 128.2, 128.2, 127.8, 127.6, 127.5, 127.4, 127.3, 127.2, 126.5, 125.6, 125.0, 123.8, 120.7, 119.1, 119.0, 112.7, 110.7, 43.6, 41.5, 35.7, 11.6.

**HRMS(ESI)** Calculated for C<sub>34</sub>H<sub>29</sub>NNaO<sup>+</sup> ([M+Na]<sup>+</sup>): 490.21414, found: 490.21414.

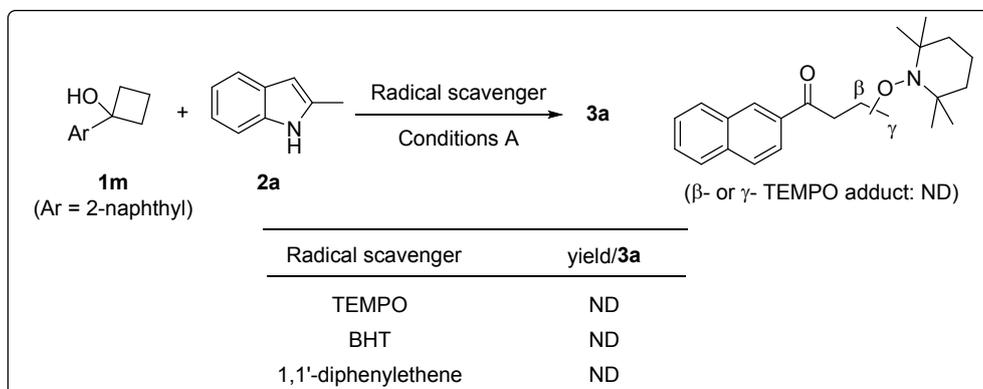
### 3.3 Gram-scale reaction



Following the general procedure: **1m** (5 mmol, 980 mg), **2a** (10 mmol, 1.31g, 2 equiv),  $\text{Ni}(\text{PPh}_3)_2\text{Br}_2$  (0.25 mmol, 197.5 mg, 5 mol%), toluene (12.5 ml),  $t\text{-BuONa}$  (10 mmol, 960mg, 2equiv), and 2-bromo-3-methylthiophene **Ox2** (6 mmol, 1.06 g, 1.2 equiv) were added sequentially to the 100 ml Schlenk tube under nitrogen atmosphere. The reaction was sealed and heated at 80°C for 12 h. After the completion, the solvent was quenched with  $\text{H}_2\text{O}$  and extracted with ethyl acetate (3×30 ml). The combined organic phase was further washed with brine (20 ml) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and purified by a silica gel column to give **3a** in 72% yield (1.17g).

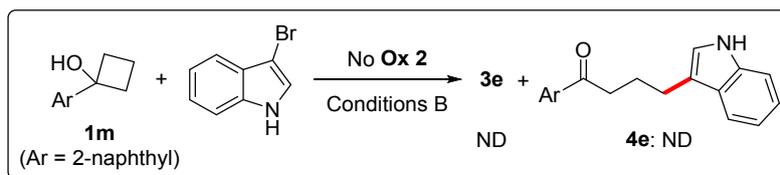
## 4. Mechanistic Studies

### 4.1 Radical-trapping experiment

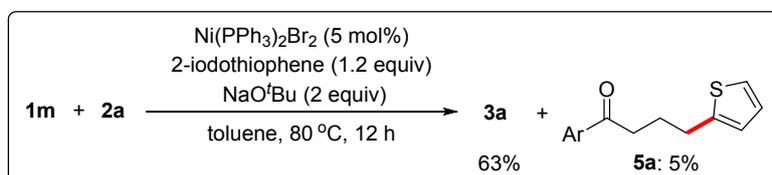


Under the positive nitrogen atmosphere, **1m** (0.2 mmol, 39.6 mg), **2a** (0.4 mmol, 52.4 mg, 2 equiv),  $t\text{-BuONa}$  (0.4 mmol, 38.4 mg, 2 equiv),  $\text{Ni}(\text{PPh}_3)_2\text{Br}_2$  (0.01 mmol, 7.43 mg, 5 mol%), radical scavenger (1 equiv), toluene (0.5 ml), and 2-bromo-3-methylthiophene (0.24 mmol, 42.5 mg, 1.2 equiv) were added sequentially to the 25 ml Schlenk tube. The reaction was conducted at 80°C for 12 hours. After the completion, the resulting mixture was monitored by TLC and crude  $^1\text{H}$  NMR analysis. As a result, both the product **3a** and TEMPO adduct could not be detected.

### 4.2 Reaction intermediate investigation

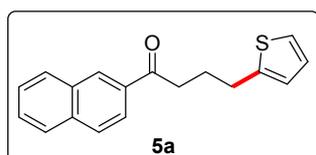


To a 25 ml flame-dried Schlenk tube was added *tert*-cyclobutanol **1m** (0.2 mmol, 39.6 mg), 3-bromo-1*H*-indole (0.4 mmol, 78 mg), *t*-BuONa (0.4 mmol, 38.4 mg) NiBr<sub>2</sub> (20 mol%, 0.04 mmol, 8.76 mg), **L3** (20 mol%, 0.04 mmol, 17 mg), and toluene (0.5 mL) sequentially under nitrogen. The tube was sealed and stirred at 80 °C for 12 h. After completion, the reaction mixture was monitored by TLC and crude <sup>1</sup>H NMR analysis. Unfortunately, both the product **3e** and **4e** failed to be detected.



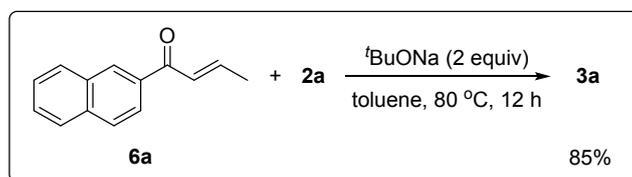
To a 25 ml flame-dried Schlenk tube was added cyclobutanol **1m** (0.5 mmol, 99 mg), 2-methyl-1*H*-indole **2a** (1.0 mmol, 131 mg), Ni(PPh<sub>3</sub>)<sub>2</sub>Br<sub>2</sub> (5 mol%, 0.025 mmol, 18.5 mg), 2-iodothiophene **Ox5** (0.6 mmol, 126 mg), *t*-BuONa (1.0 mmol, 96 mg), and toluene (1.2 mL) sequentially under nitrogen. The tube was sealed and stirred at 80 °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 (30 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the product **3a** in 63% yield. Surprisingly, the side product **5a** was also isolated in 5% yield, the structure of which was characterized by <sup>1</sup>H/<sup>13</sup>C NMR and HRMS analysis.

### 1-(naphthalen-2-yl)-4-(thiophen-2-yl)butan-1-one (**5a**)

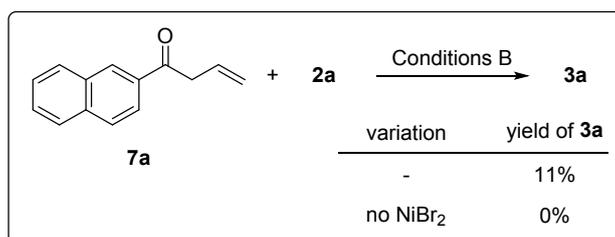


<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.45 (s, 1H), 8.05 (dd, *J*<sub>1</sub> = 10.5 Hz, *J*<sub>2</sub> = 2.5 Hz, 1H), 7.98 (d, *J* = 10 Hz, 1H), 7.93-7.89 (m, 2H), 7.65-7.55 (m, 2H), 7.18 (dd, *J*<sub>1</sub> = 6.0 Hz, *J*<sub>2</sub> = 1.0 Hz, 1H), 6.99-6.95 (m, 1H), 6.88-6.86 (m, 1H), 3.12 (t, *J* = 9.0 Hz, 2H), 3.02 (t, *J* = 9.0 Hz, 2H), 2.27-2.19 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 199.8, 144.5, 135.6, 134.3, 132.5, 129.7, 129.5, 128.4, 128.3, 127.8, 126.8, 126.7, 124.6, 123.8,

123.2, 37.4, 29.2, 26.2; **HRMS(+p ESI)** Calculated for C<sub>18</sub>H<sub>17</sub>OS<sup>+</sup> ([M+H]<sup>+</sup>): 281.10056, found: 281.10013.



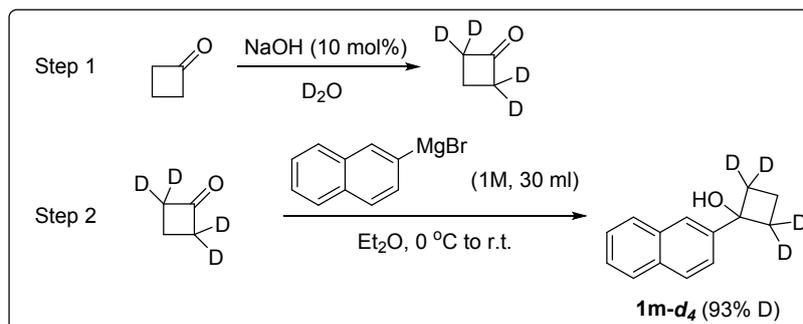
To a 25 ml flame-dried Schlenk tube was added (*E*)-1-(naphthalen-2-yl)but-2-en-1-one **6a** (0.2 mmol, 39.2 mg), **2a** (0.4 mmol, 52.4 mg), *t*-BuONa (0.4 mmol, 38.4 mg), and toluene (0.5 mL) sequentially under nitrogen. The tube was sealed and stirred at 80 °C for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (2.0 mL) and filtered through a short pad silica gel washing with ethyl acetate (10 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the product **3a** in 85% yield.



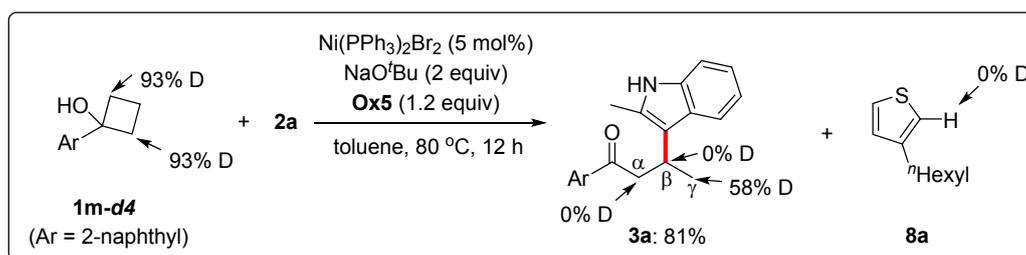
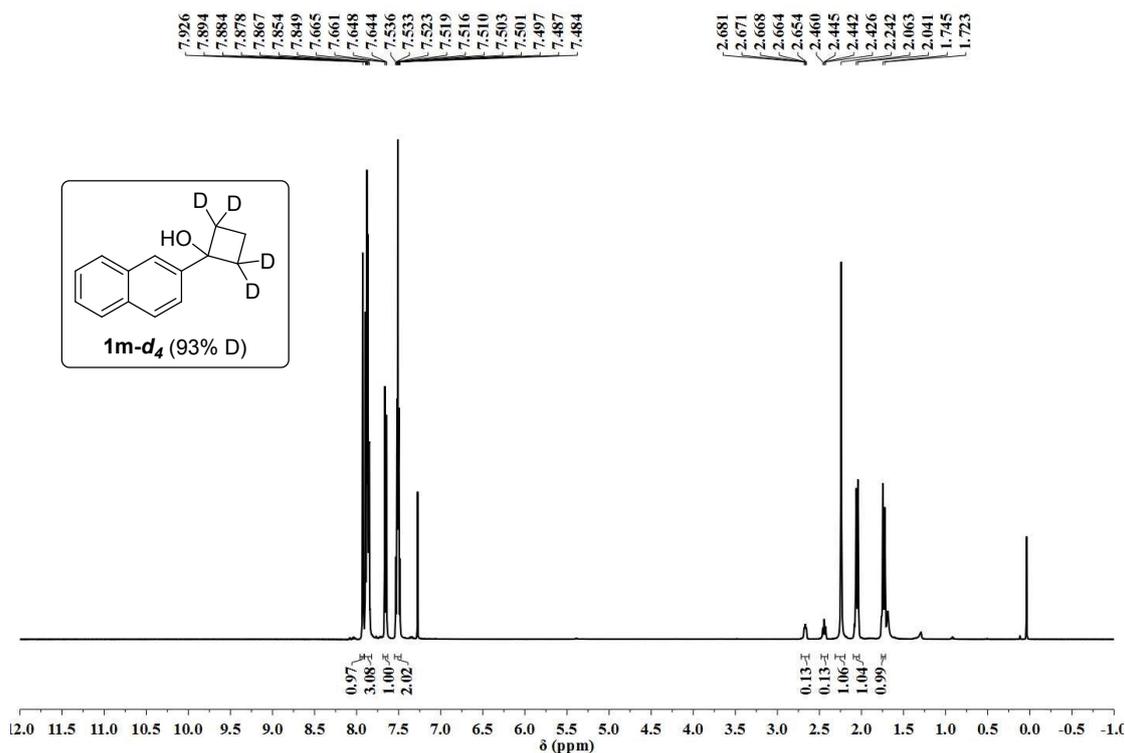
To a 25 ml flame-dried Schlenk tube was added 1-(naphthalen-2-yl)but-3-en-1-one **7a** (0.2 mmol, 39.2 mg), **2a** (0.4 mmol, 52.4 mg), NiBr<sub>2</sub> (20 mol%, 0.04 mmol, 8.76 mg), **L3** (20 mol%, 0.04 mmol, 17 mg), *t*-BuONa (0.4 mmol, 38.4 mg), and toluene (0.5 mL) sequentially under nitrogen. The tube was sealed and stirred at 80 °C for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (2.0 mL) and filtered through a short pad silica gel washing with ethyl acetate (10 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the product **3a** in 11% yield. A control experiment by removal of NiBr<sub>2</sub> was also conducted while no product **3a** was detected.

### 4.3 Deuterium-labeling experiments

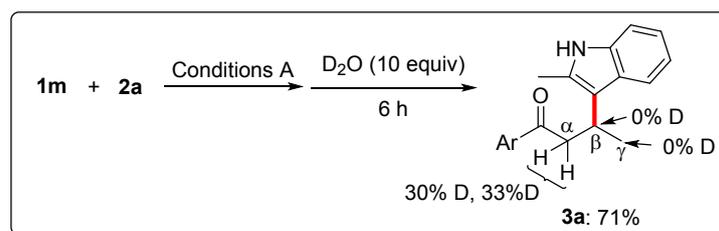
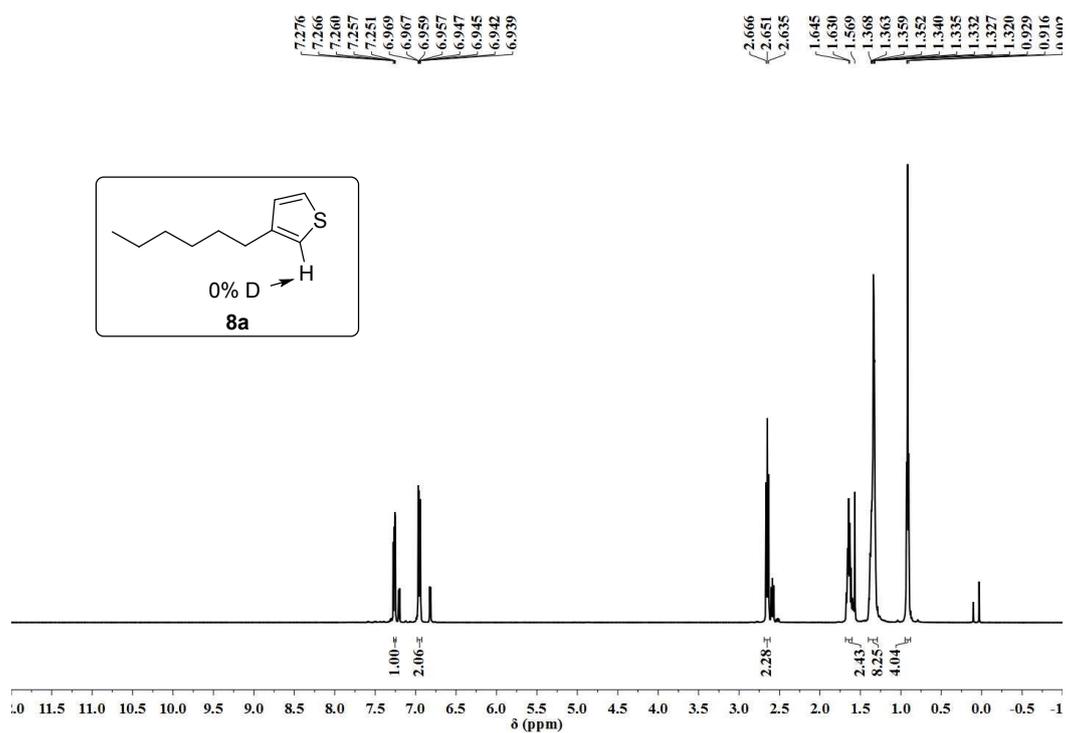
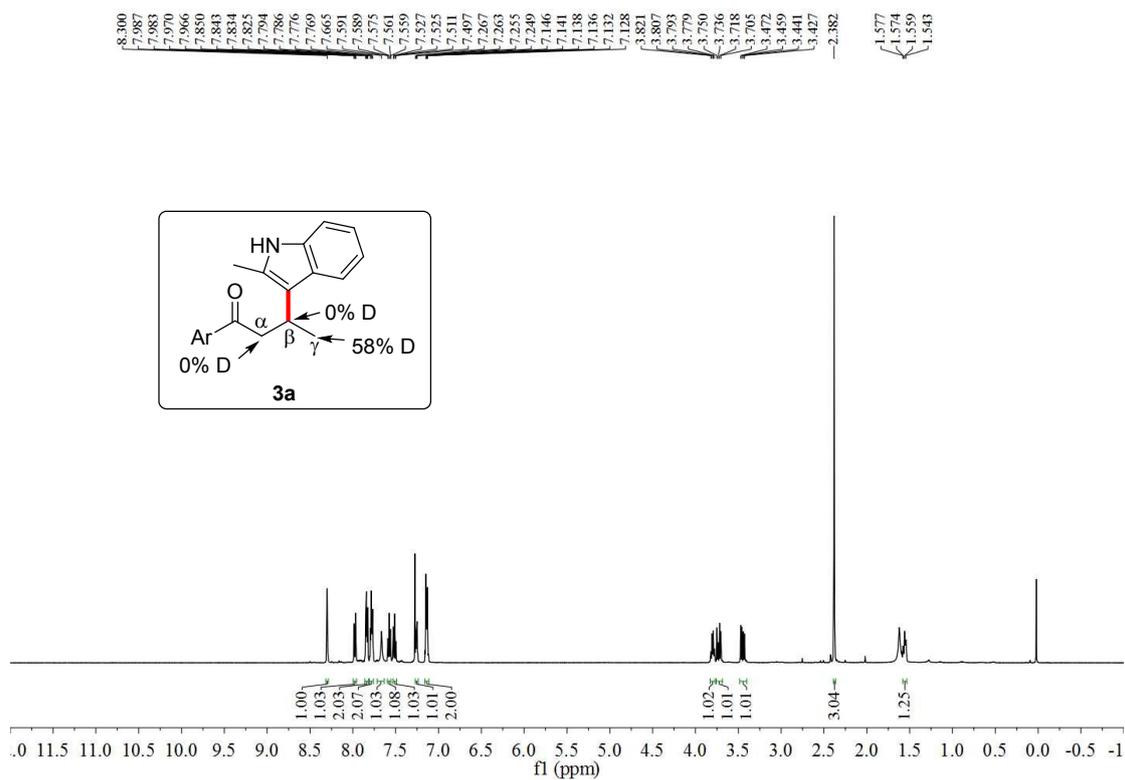
Preparation of deuterated *tert*-cyclobutanol **1m-d<sub>4</sub>**



To a 50 ml Schlenk tube was added cyclobutanone (20 mmol, 1.4 g), D<sub>2</sub>O (12.8 ml), and NaOH (2 mmol, 80 mg). The reaction mixture was stirred at rt for 12 h and the aqueous solution was extracted with Et<sub>2</sub>O (2×5 ml). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and used directly without further purification. Naphthalen-2-ylmagnesium bromide (1M in 30 ml THF) was freshly prepared in a 100 ml Schlenk tube and the deuterated cyclobutanone in Et<sub>2</sub>O was injected slowly via a syringe under N<sub>2</sub> at 0 °C. The reaction was allowed to warm to rt and stirred for another 6 h. After completion, the reaction was quenched with H<sub>2</sub>O (20 ml) and the organic solvent was removed under reduced pressure and refilled with ethyl acetate (20 ml). The organic layer was separated and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the crude product was purified by silica gel column chromatography providing the product **1m-d<sub>4</sub>** in 18% yield.

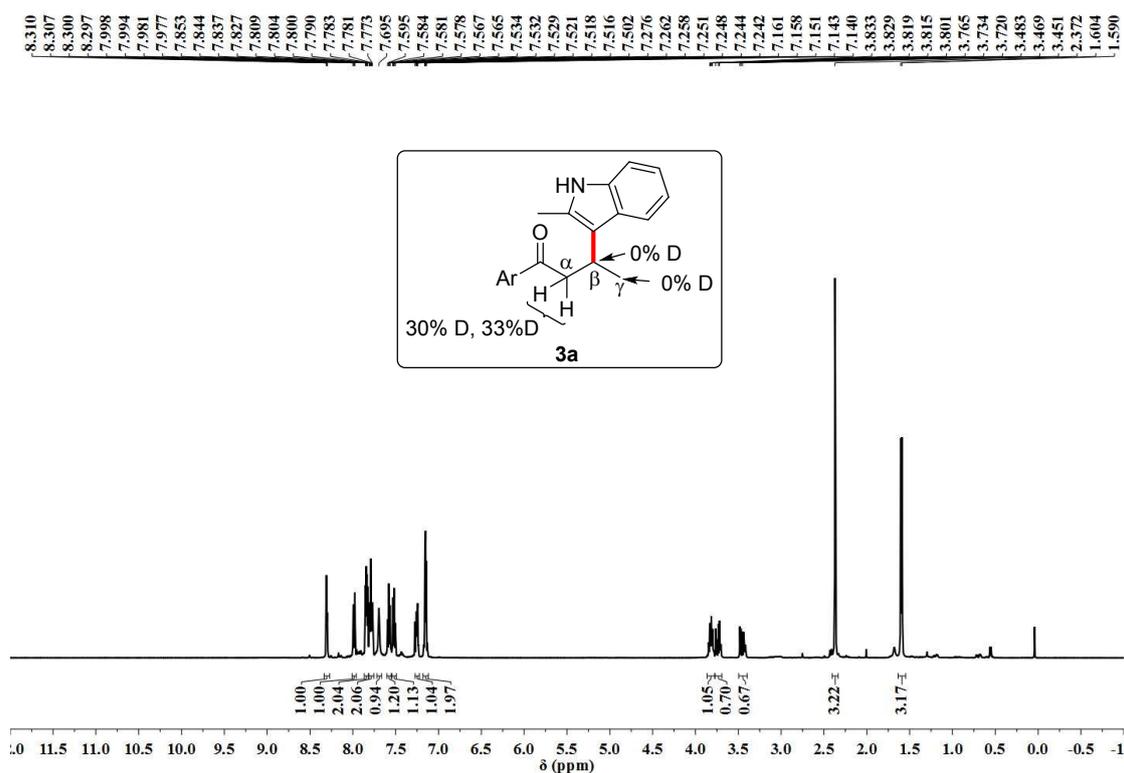


To a 25 ml flame-dried Schlenk tube was added deuterated *tert*-cyclobutanol **1m-d<sub>4</sub>** (0.2 mmol, 40.4 mg), 3-methyl indole **2a** (0.4 mmol, 52.4 mg), *t*-BuONa (0.4 mmol, 38.4 mg) Ni(PPh<sub>3</sub>)<sub>2</sub>Br<sub>2</sub> (0.01 mmol, 7.4 mg), **Ox5** (0.24 mmol, 59 mg), and toluene (0.5 mL) sequentially under nitrogen. The tube was sealed and stirred at 80 °C for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (2.0 mL) and filtered through a short pad silica gel washing with ethyl acetate (10 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the product **3a** in 62% yield. However, the reductant **8a**<sup>11</sup> could not be purified and it was isolated as a mixture.



To a 25 ml flame-dried Schlenk tube was added cyclobutanol **1m** (0.2 mmol, 39.6

mg), 3-methyl indole **2a** (0.4 mmol, 52.4 mg), Ni(PPh<sub>3</sub>)<sub>2</sub>Br<sub>2</sub> (5 mol%, 0.01 mmol, 7.4 mg), **Ox2** (0.24 mmol, 42.4 mg), *t*-BuONa (0.4 mmol, 38.4 mg), and toluene (0.5 mL) sequentially under nitrogen. The tube was sealed and stirred at 80 °C for 12 h. After cooling, D<sub>2</sub>O (2 mmol, 40 mg) was added to the reaction mixture and stirred for further 6 h. The mixture was filtered through a short pad silica gel washing with ethyl acetate (20 mL). The filtrate was concentrated and purified by silica gel column chromatography to provide the **3a** in 71% yield.



## 5. References

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## 6. $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra

