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Synthesis of *a*-Alkylated Ketones via Tandem Acceptorless Dehydrogenation/*a*-Alkylation from Secondary and Primary Alcohols Catalyzed by Metal−Ligand Bifunctional Iridium Complex [Cp*Ir(2,2′-bpyO)(H_2O)]

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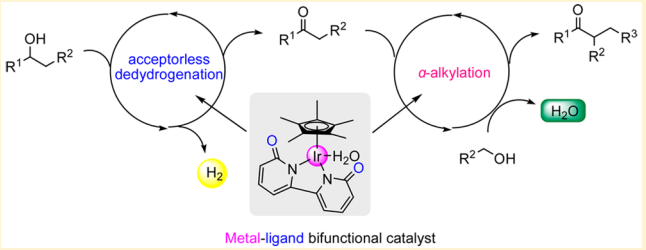
Supporting Information

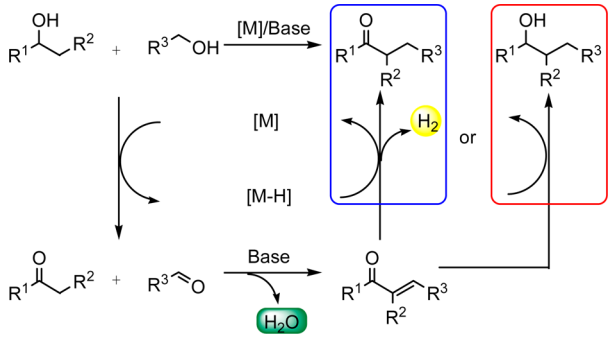
ABSTRACT: A new strategy for the synthesis of α-alkylated ketones via tandem acceptorless dehydrogenation/α-alkylation from secondary and primary alcohols was proposed and accomplished. In the presence of metal−ligand bifunctional iridium complex [Cp*Ir(2,2′-bpyO)(H_2O)], various desirable products were obtained in high yields. Compared with previous methods for the direct dehydrogenative coupling of secondary alcohols with primary alcohols to α-alkylated ketones, this protocol has obvious advantages including complete selectivity for α-alkylated ketones and more environmentally benign conditions. Notably, the study also exhibited the potential to develop tandem reactions catalyzed using a metal−ligand bifunctional iridium complex.



INTRODUCTION

The development of catalytic transformations using readily available starting materials, high atom economy, and high selectivity is one of the most significant goals of modern organic synthesis.[1] α-Alkylated ketones represent a class of compounds possessing a broad spectrum of biological activities and are also used as key synthetic intermediates.[2] These compounds are traditionally synthesized via the α-alkylation of ketones with alkyl halides as alkylating agents in the presence of an inorganic strong base.[3] In recent years, significant efforts have been devoted to the synthesis of α-alkylated ketones via the α-alkylation of ketones with primary alcohols as alkylating agents. These alkylating agents utilize the "hydrogen autotransfer process"[4] and include ruthenium,[5] iridium,[6] palladium,[7] and other transition-metal catalysts.[8] This methodology is very promising because of high atom economy and the generation of water as the sole byproduct. More recently, the direct dehydrogenative coupling of secondary alcohols with primary alcohols to α-alkylated ketones has been developed using a heterogeneous γ-alumina-supported silver subnanocluster,[9] a homogeneous Ir-based PC(sp^3)P pincer complex,[10] and a bis(benzoxazolyl) iridium complex as catalysts.[11,12] In this process, secondary and primary alcohols are initially dehydrogenated to give the corresponding ketones and aldehydes, thus generating a metal hydride species. Furthermore, a base-promoted cross-aldol condensation between the resulting ketones and aldehydes occurs, producing α,β-unsaturated ketones. The C═C bond of these ketones then undergoes selective transfer hydrogenation to afford α-alkylated ketones upon liberation of hydrogen gas (Scheme 1). However, it remains extremely challenging to control reaction selectivity. In the above process, the resulting α,β-unsaturated ketones easily undergo successive hydrogenation of the C═C and C═O bonds via metal hydride species; thus, the β-alkylation of secondary alcohols with primary alcohols inevitably occurs as a side reaction.[13] Moreover, these procedures require a long reaction time (48 h)[9] or a stoichiometric base.[10,11] From a sustainable-chemistry standpoint, it is necessary to develop a new strategy and catalytic system for the preparation of α-

Scheme 1. Direct Coupling of Secondary Alcohols with Primary Alcohols



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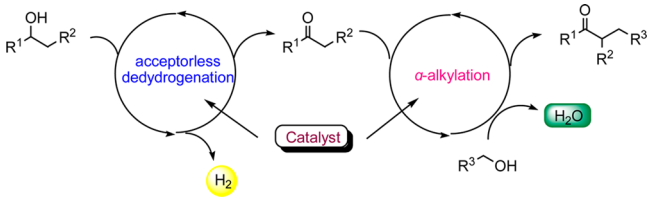
alkylated ketones from secondary and primary alcohols with higher selectivity under more environmentally benign conditions.

Fujita, Yamaguchi, and co-workers recently developed a series of Cp*Ir complexes bearing a hydroxypyridine[14] or bipyridonate ligand,[15] which exhibit high activity for the acceptorless dehydrogenation of alcohols to carbonyl compounds and are based on the concept of "ligand-promoted dehydrogenation". More recently, we have demonstrated that such complexes are highly effective and versatile catalysts for the *N*-alkylation of sulfonamides with alcohols in water[16] and the α-alkylation of ketones with primary alcohols under extremely environment-friendly conditions.[17,18] A mechanistic investigation revealed that such complexes can be used as metal–ligand bifunctional catalysts in the "hydrogen autotransfer process". As a continuing effort to develop catalytic transformations with alcohols as electrophiles,[16,17,19] herein, we explore a new and alternative protocol for synthesizing α-alkylated ketones via iridium-catalyzed tandem acceptorless dehydrogenation/α-alkylation from secondary and primary alcohols. As outlined in Scheme 2, the secondary alcohols

Scheme 2. Proposed Strategy to Synthesize α-Alkylated Ketones



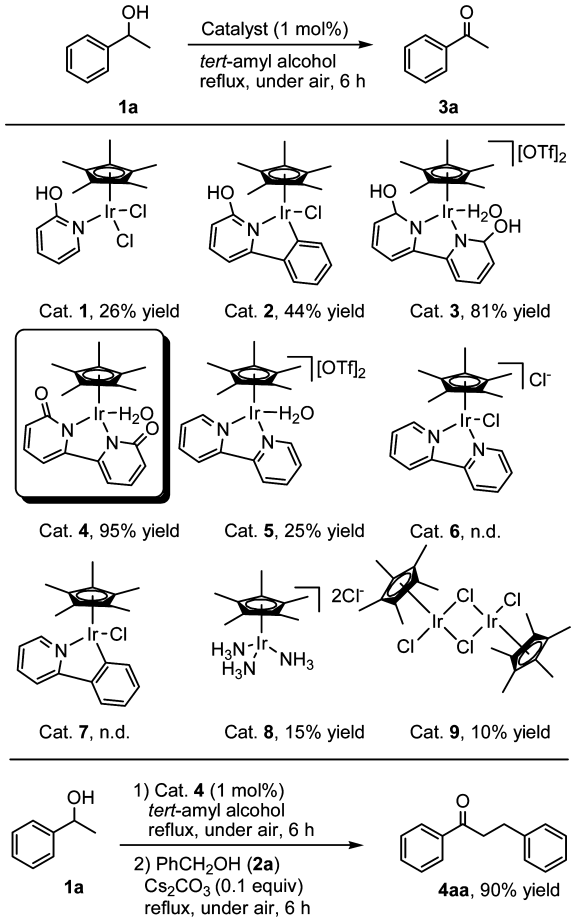
undergo acceptorless dehydrogenation to form ketones, which is followed by conversion of the resulting ketones to α-alkylated ketones via α-alkylation with alcohols.

RESULTS AND DISCUSSION

In the initial experience, the transformation of 1-phenylethanol (**1a**) and benzyl alcohol (**2a**) was selected as the model reaction. As shown in Scheme 3, a range of Cp*Ir complexes bearing a hydroxypyridine (Cat. **1**–**3**) and the Cp*Ir complex bearing a bipyridonate ligand (Cat. **4**), which were originally reported by the group of Fujita and Yamaguchi,[14,15] were initially selected as the catalysts for the acceptorless dehydrogenation of **1a**. In the presence of the catalyst (1 mol %), the reaction of **1a** was performed in *tert*-amyl alcohol at reflux under air for 6 h. The Cp*Ir complex bearing a bipyridonate ligand (Cat. **4**) exhibited higher activity than Cp*Ir complexes bearing a hydroxypyridine ligand (Cat. **1**–**3**), and the corresponding acetophenone (**3a**) was produced in 95% yield. Furthermore, low catalytic activity was observed when other Cp*Ir complexes (Cat. **5**–**9**) were evaluated. It is apparent that the hydroxyl or carbonyl groups on the bpy ligand are critically important for the acceptorless dehydrogenation of **1a**. As a result, Cat. **4** was selected as the catalyst for the proposed tandem reaction. When **1a** was completely converted to intermediate **3a**, benzyl alcohol (**2a**) (1.1 equiv) and Cs_2CO_3 (0.1 equiv) were added, and this reaction mixture continued to reflux under air for another 6 h to produce **4aa** in 90% yield.

With the optimal reaction conditions established, we investigated the reactions with respect to primary alcohols,

Scheme 3. Exploration of the Feasibility of a Model Reaction



and the results are outlined in Table 1. The transformations of **1a** with electron-rich substituted benzyl alcohols (**2b**–**2e**) gave the corresponding products **4ab**–**4ae** in 85–89% yields (Table 1, entries 1–4). When halogenated benzyl alcohols (**2f**–**2i**) were used, the α-alkylated products **4af**–**4ai** were isolated in 85–90% yields (Table 1, entries 5–8). Stronger electron-deficient substituted benzyl alcohols (**2j** and **2k**) were also converted to the desired products **4aj** and **4ak** in 83 and 80% yields, respectively (Table 1, entries 9 and 10). Furthermore, 1-naphthylmethanol (**2l**) and 2-furanmethanol (**2m**) were also demonstrated to be suitable substrates, and the α-alkylated products **4al** and **4am** were obtained in 84 and 83% yields, respectively (Table 1, entries 11–12). The highly catalytic actitivites were also observed in aliphatic primary alcohols, such as 1-hexanol (**2n**), 1-octanol (**2o**), 2-methylbutan-1-ol (**2p**), and cyclohexylmethanol (**2q**), affording the corresponding products **4an** and **4ao** in 79–86% yields, respectively (Table 1, entries 13–16).

To further expand the reaction generality, we evaluated the transformations with respect to secondary alcohols (Table 2). Reactions of electron-rich substituted 1-phenylethanols (**1b**–**1e**) afforded the desired products **4ba**–**4ea** in 82–88% yields (Table 2, entries 1–4). For halogenated 1-phenylethanols (**1f**–**i**) and stronger electron-deficient substituted 1-phenylethanols (**1j**), the corresponding products **4fa**–**4ja** were isolated in 79–89% yields (Table 2, entries 5–9). The desired product **4ka** was also isolated in high yield when 1-(naphthalen-2-yl)ethanol (**1k**) was used as a substrate (Table 2, entry 10). In the case of 1-phenylpropan-1-ol (**1l**), 1-indanol (**1m**), and 1-tetralinol

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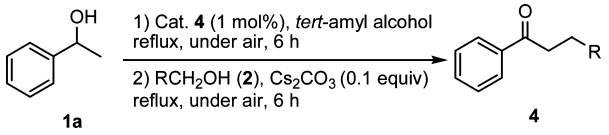
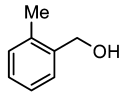
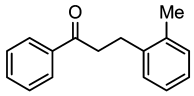
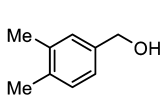
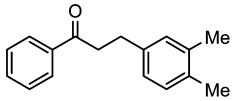
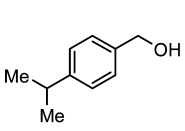
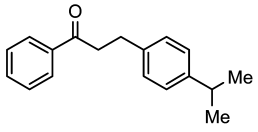
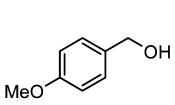
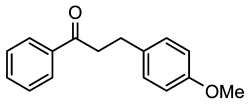
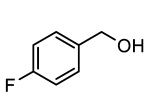
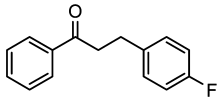
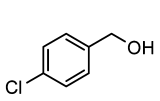
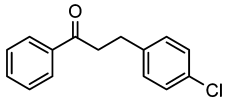
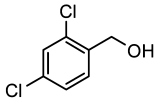
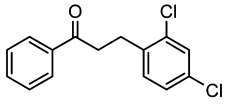
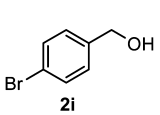
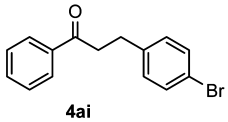
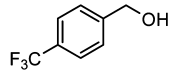
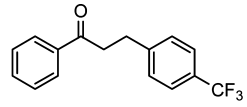
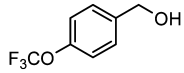
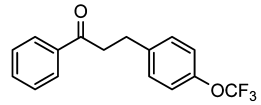
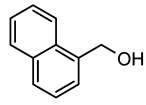
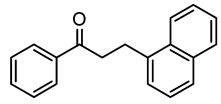
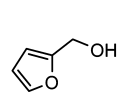
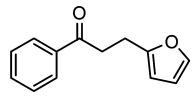
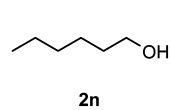
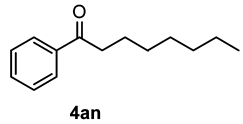
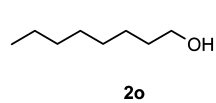
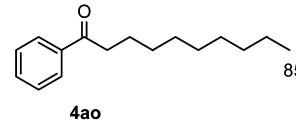
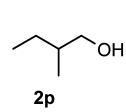
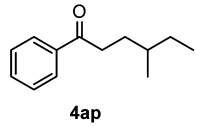
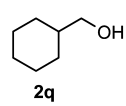
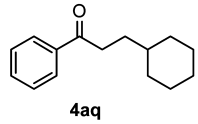
Table 1. Reactions of 1-Phenylethanol (1a) with Various Primary Alcohols (2)[a]



1a 4

Entry	Primary Alcohol	Product	Yield (%)
1	 2b	 4ab	86
2	 2c	 4ac	85
3	 2d	 4ad	87
4	 2e	 4ae	89
5	 2f	 4af	85
6	 2g	 4ag	88
7	 2h	 4ah	90
8	 2i	 4ai	89
9	 2j	 4aj	83
10	 2k	 4ak	80
11	 2l	 4al	84
12	 2m	 4am	83
13	 2n	 4an	79
14	 2o	 4ao	85
15	 2p	 4ap	83
16	 2q	 4aq	86

[a]Reaction conditions: (1) **1a** (1 mmol), Cat. **4** (1 mol %), *tert*-amyl alcohol (1 mL), reflux, under air, 6 h; (2) **2** (1.1 mmol), Cs_2CO_3 (0.1 equiv), reflux, under air, 6 h.

(**1n**), the reactions afforded the corresponding products **4la**–**4na** in 80–82% yields (Table 2, entries 11–13). Aliphatic secondary alcohols, such as 1-cyclopropylethanol (**1o**) and 3-methylbutan-2-ol (**1p**), were converted to the desired products **4na** and **4oa** in 84 and 82% yields, respectively, although 2 equiv of secondary alcohol was required (Table 2, entries 14–15).

A plausible mechanism for this tandem acceptorless dehydrogenation/α-alkylation from secondary and primary alcohols to α-alkylated ketones is shown in Scheme 4. This mechanism is closely related to the proposed mechanism of Fujita and Yamaguchi for the dehydrogenative oxidation of secondary alcohols to ketones[15] and our proposed mechanism for the α-alkylation of ketones with primary alcohols, which is catalyzed by the metal–ligand bifunctional Cp*Ir complex [Cp*Ir(2,2′-bpyO)(H_2O)].[17] In cycle I, the bipyridonate ligand of iridium species **A** accepted a proton from the secondary alcohol to afford alkoxy iridium species **B**, which underwent β-hydrogen elimination to produce iridium hydride species **C** and a ketone. The ligand-promoted hydrogen transfer from the hydride hydroxyl proton on the bpy ligand and the hydride on the iridium then occurred, releasing hydrogen gas and regenerating catalytic species **A**.[20] In the initial stage of cycle II, similar to the case of secondary alcohols, the primary alcohols were initially converted to aldehydes, generating iridium hydride species **C**. A base-promoted cross-aldol condensation between aldehydes and ketones, which were generated in cycle I, afforded α,β-unsaturated ketones. The hydride on the iridium and hydroxy proton on the ligand of species **C** were simultaneously transferred to the C=C bond of

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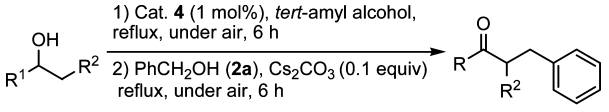
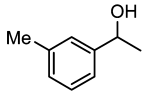
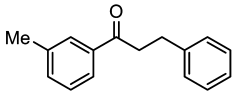
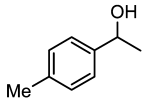
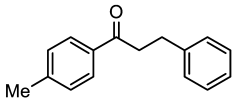
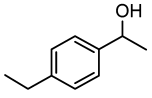
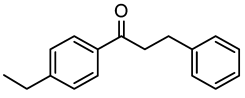
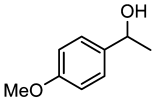
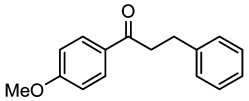
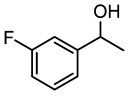
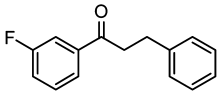
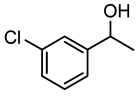
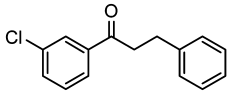
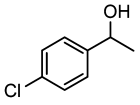
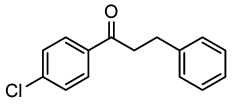
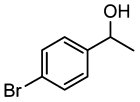
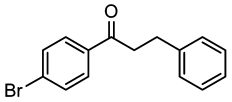
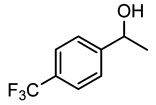
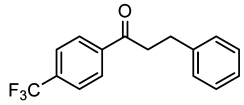
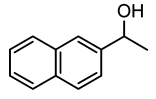
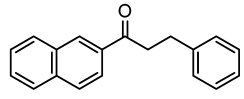
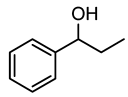
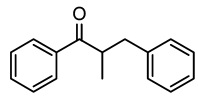
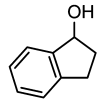
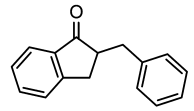
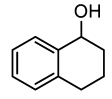
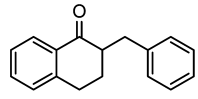
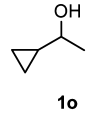
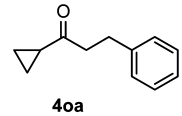
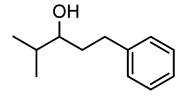
Table 2. Reactions of a Range of Secondary Alcohols (1) with Benzyl Alcohol (2a)[a]



1 4

Entry	Secondary Alcohol	Product	Yield (%)
1	 **1b**	 **4ba**	88
2	 **1c**	 **4ca**	82
3	 **1d**	 **4da**	87
4	 **1e**	 **4ea**	88
5	 **1f**	 **4fa**	79
6	 **1g**	 **4ga**	83
7	 **1h**	 **4ha**	82
8	 **1i**	 **4ia**	89
9	 **1j**	 **4ja**	81
10	 **1k**	 **4ka**	84
11	 **1l**	 **4la**	80[b]
12	 **1m**	 **4ma**	82
13	 **1n**	 **4na**	80
14	 **1o**	 **4oa**	84[c]
15	 **1p**	 **4pa**	82[c]

[a]Reaction conditions: (1) **1** (1 mmol), Cat. **4** (1 mol %), *tert*-amyl alcohol (1 mL), reflux, under air, 6 h; (2) **2a** (1.1 mmol), Cs_2CO_3 (0.1 equiv), reflux, under air, 6 h. [b]Cs_2CO_3 (0.3 equiv), 20 h. [c]With **1** (2.0 mmol) and **2a** (1.0 mmol); the yield is based on the amount of **2a**.

the α,β-unsaturated ketones, resulting in the regeneration of catalytic species **A** and formation of α-alkylated ketones as final products.[21]

Furthermore, the direct coupling of a secondary alcohol and a primary alcohol, which was catalyzed by the present catalytic system, was investigated (Scheme 5). In the presence of Cat. **4**, the reaction of **1a** with **2a** was performed for 12 h to afford a mixture of **4aa** and **5aa** in 69 and 31% yields, respectively. It was apparent that the tandem reaction exhibited advantageous selectivity for α-alkylated ketones compared with the direct coupling reaction when identical starting materials were used.

■ CONCLUSIONS

In summary, we have demonstrated a new strategy to synthesize α-alkylated ketones via the tandem acceptorless dehydrogenation/α-alkylation from secondary and primary alcohols. In the presence of metal−ligand bifunctional iridium complex [Cp*Ir(2,2′-bpyO)(H_2O)], various desirable products were obtained in high yields. Compared with previous methods for the direct dehydrogenative coupling of secondary alcohols with primary alcohols to α-alkylated ketones, this protocol has obvious advantages, including complete selectivity for α-alkylated ketones and more environmentally benign conditions. Notably, the study also exhibited the potential to develop tandem reactions catalyzed by a metal−ligand bifunctional iridium complex.

■ EXPERIMENTAL SECTION

Experimental Details. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 500 MHz. Chemical shifts are

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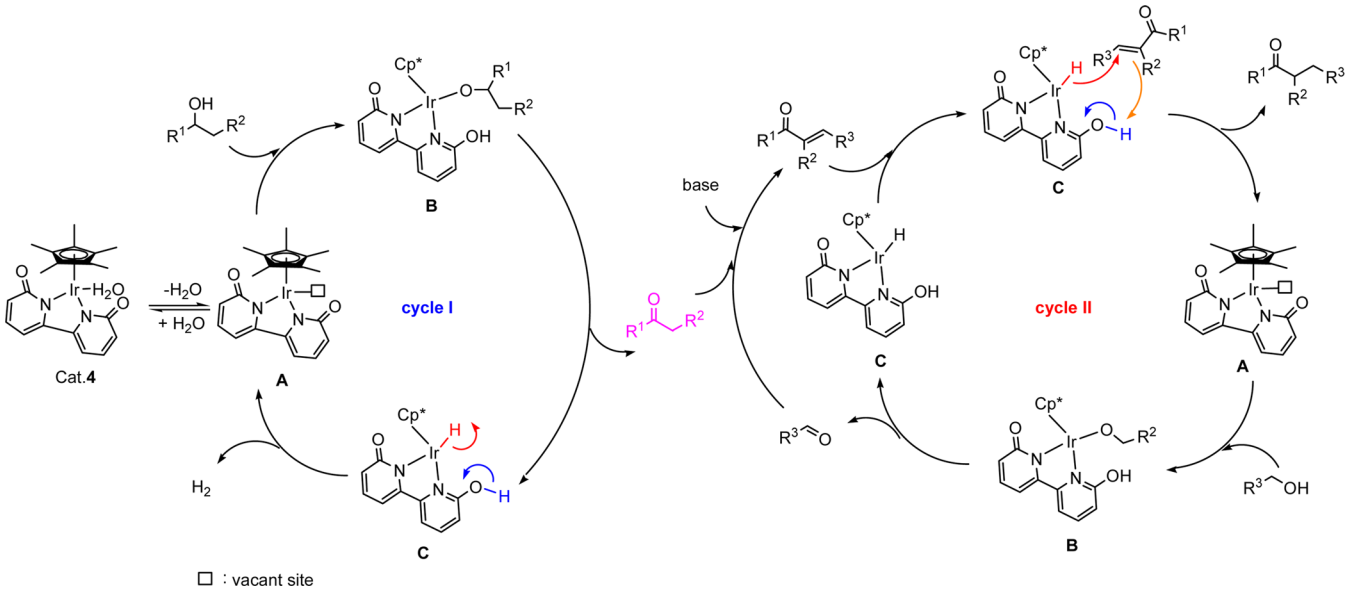
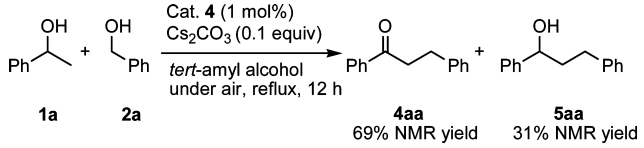
Scheme 4. Proposed Reaction Mechanism



Scheme 5. Direct Coupling of 1a with 2a Catalyzed by Cat. 4



reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for $CDCl_3$. Coupling constants J values are reported in Hertz (Hz), and the splitting patterns were designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; and b, broad. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 125 MHz. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.0 ppm for $CDCl_3$. ^{13}C NMR spectra were routinely run with broadband decoupling.

$[Cp^*(2\text{-}(OH)py)]Cl_2$ (Cat. **1**),[14a] $Cp^*Ir[2\text{-}(2\text{-}(2\text{-}(OH)py)phenyl]\text{-}Cl$ (Cat. **2**),[14b] $[Cp^*(6,6'\text{-}(OH)_2bpy)][OTf]_2$ (Cat. **3**),[14c] $[Cp^*Ir\text{-}(2,2'\text{-}bpyO)(H_2O)]$ (Cat. **4**),[15] $[Cp^*Ir(bpy)(H_2O)][OTf]_2$ (Cat. **5**),[22] $[Cp^*Ir(bpy)Cl)][Cl]$ (Cat. **6**),[23] $[Cp^*Ir(2\text{-}phenylpyridine\text{-}kC,N)]Cl$ (Cat. **7**),[24] $[Cp^*Ir(NH_3)_3][Cl]_2$ (Cat. **8**),[25] and $[Cp^*IrCl_2]_2$ (Cat. **9**)[26] were synthesized according to previous reports.

General Procedure for the Synthesis of α-Alkylated Ketones via Tandem Acceptorless Dehydrogenation/α-Alkylation from Secondary Alcohols and Primary Alcohols Catalyzed by $[Cp^*Ir(2,2'\text{-}bpyO)(H_2O)]$ (Tables 1–2). In a round-bottomed flask with a condenser tube were added secondary alcohol (1 mmol), Cat. **4** (5.3 mg, 0.01 mmol, 1 mol %), and *tert*-amyl alcohol (1 mL) under air atmosphere. The reaction mixture was heated under reflux in an oil bath for 6 h and then cooled to ambient temperature. Primary alcohol (1.1 mmol, 1.1 equiv) and Cs_2CO_3 (33 mg, 0.1 mmol, 0.1 equiv) were added, and the mixture was heated under reflux for 6 h. The reaction mixture was cooled to ambient temperature, concentrated in vacuo, and purified by flash column chromatography with hexane/ethyl acetate to afford the corresponding product.

1,3-Diphenylpropan-1-one (***4aa***).[5e] White solid; 90% yield (188 mg); mp 69–70 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 6.9 Hz, 1H), 7.46 (t, J = 6.9 Hz, 2H), 7.32–7.26 (m, 4H), 7.21 (t, J = 7.2 Hz, 1H), 3.31 (t, J = 7.3 Hz, 2H), 3.07 (t, J = 7.3 Hz, 2H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.2, 141.2, 136.8, 133.0, 128.6, 128.5, 128.4, 128.0, 126.1, 40.4, 30.1.

1-Phenyl-3-o-tolylpropan-1-one (***4ab***).[8d] White solid; 86% yield (193 mg); mp 48–49 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98–7.96 (m, 2H), 7.56 (t, J = 6.8 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.20–7.14 (m, 4H), 3.26 (t, J = 7.9 Hz, 2H), 3.06 (t, J = 7.9 Hz, 2H), 2.35 (s, 3H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.4, 139.4, 136.8, 136.0, 133.1, 130.3, 128.7, 128.6, 128.0, 126.3, 126.2, 39.1, 27.5, 19.3.

3-(3,4-Dimethylphenyl)-1-phenylpropan-1-one (***4ac***)[19j]. White solid; 85% yield (203 mg); mp 59–60 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.8 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.08–6.99 (m, 3H), 3.28 (t, J = 7.8 Hz, 2H), 3.00 (t, J = 7.8 Hz, 2H), 2.25 (s, 3H), 2.23 (s, 3H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.4, 138.7, 136.9, 136.6, 134.3, 133.0, 129.8, 128.6, 128.0, 125.7, 40.7, 29.7, 19.7, 19.3.

3-(4-Isopropylphenyl)-1-phenylpropan-1-one (***4ad***).[27] Pale yellow oil; 87% yield (220 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.20–7.16 (m, 4H), 3.30 (t, J = 7.8 Hz, 2H), 3.04 (t, J = 7.8 Hz, 2H), 2.91–2.86 (m, 1H), 1.25 (d, J = 6.9 Hz, 6H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.4, 146.7, 138.5, 136.9, 133.0, 128.6, 128.3, 128.0, 126.5, 40.5, 33.7, 29.7, 24.0.

3-(4-Methoxyphenyl)-1-phenylpropan-1-one (***4ae***).[5e] White solid; 89% yield (213 mg); mp 64–65 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 3.79 (s, 3H), 3.27 (t, J = 7.4 Hz, 2H), 3.01 (t, J = 7.4 Hz, 2H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.3, 158.0, 136.9, 133.3, 133.0, 129.3, 128.6, 128.0, 113.9, 55.2, 40.7, 29.3.

3-(4-Fluorophenyl)-1-phenylpropan-1-one (***4af***).[28] White solid; 85% yield (193 mg); mp 65–66 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.22–7.19 (m, 2H), 6.98 (t, J = 8.7 Hz, 2H), 3.28 (t, J = 7.5 Hz, 2H), 3.05 (t, J = 7.5 Hz, 2H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.0, 162.3, 160.4, 136.9, 133.1, 129.8 (d, J_{C-F} = 6.4 Hz), 128.6, 128.0, 115.3 (d, J_{C-F} = 19.9 Hz), 40.4, 29.2.

3-(4-Chlorophenyl)-1-phenylpropan-1-one (***4ag***).[29] White solid; 88% yield (215 mg); mp 53–54 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.26 (d, J = 4.2 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 3.28 (t, J = 7.5 Hz, 2H), 3.04 (t, J = 7.5 Hz, 2H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 198.8, 139.7, 136.7, 133.1, 131.8, 129.8, 128.6, 128.6, 127.8, 40.1, 29.3.

3-(2,4-Dichlorophenyl)-1-phenylpropan-1-one (***4ah***).[28] White solid; 90% yield (252 mg); mp 64–65 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.37 (d, J = 2.1 Hz, 1H), 7.26 (d, J = 8.2 Hz, 1H), 7.18 (dd, J = 8.2 and 2.1 Hz, 1H), 3.31 (t, J = 7.6 Hz, 2H), 3.15 (t, J = 7.5 Hz, 2H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 198.6, 137.4, 136.6, 134.5, 133.2, 132.6, 131.6, 129.3, 128.6, 128.0, 127.2, 38.1, 27.6.

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3-(4-Bromophenyl)-1-phenylpropan-1-one (**4ai**).[30] White solid; 89% yield (258 mg); mp 63−64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.42 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 3.28 (t, J = 7.5 Hz, 2H), 3.03 (t, J = 7.5 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.8, 140.2, 136.7, 133.2, 131.2, 130.2, 128.6, 128.0, 119.9, 40.0, 29.4.

1-Phenyl-3-(4-(trifluoromethyl)phenyl)propan-1-one (**4aj**).[28] White solid; 83% yield (231 mg); mp 47−48 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.58−7.54 (m, 3H), 7.46 (t, J = 7.7 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 3.32 (t, J = 7.5 Hz, 2H), 3.13 (t, J = 7.5 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.5, 145.5, 136.7, 133.2, 128.8, 128.7, 128.2 (q, J_{C-F} = 31.6 Hz), 128.0, 125.4 (q, J_{C-F} = 2.7 Hz), 123.2 (q, J_{C-F} = 270.9 Hz), 39.8, 29.8.

1-Phenyl-3-(4-(trifluoromethoxy)phenyl)propan-1-one (**4ak**).[31] Pale yellow oil; 80% yield (234 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.2 Hz, 2H), 3.29 (t, J = 7.5 Hz, 2H), 3.07 (t, J = 7.5 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.7, 147.6, 140.1, 136.7, 133.2, 130.0, 128.6, 128.0, 121.1, 119.5 (q, J_{C-F} = 255.3 Hz), 40.1, 29.3.

3-(Naphthalen-1-yl)-1-phenylpropan-1-one (**4al**).[5e] White solid; 84% yield (219 mg); mp 51−52 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 7.1 Hz, 2H), 7.89 (d, J = 7.7 Hz, 1H), 7.75 (t, J = 4.4 Hz, 1H), 7.57−7.48 (m, 3H), 7.46−7.41 (m, 4H), 3.55 (t, J = 7.4 Hz, 2H), 3.43 (t, J = 7.4 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 199.3, 137.4, 136.8, 133.9, 133.1, 131.7, 128.9, 128.6, 128.0, 127.0, 126.1, 126.1, 125.6, 125.6, 123.5, 39.7, 27.2.

2-Furfuryl alcohol (**4am**).[32] Brown oil; 83% yield (166 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.31 (s, 1H), 6.28−6.27 (m, 1H), 6.05−6.04 (m, 1H), 3.33 (t, J = 7.2 Hz, 2H), 3.09 (t, J = 7.2 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.6, 154.7, 141.1, 136.7, 133.1, 128.6, 128.0, 110.2, 105.3, 36.9, 22.5.

1-Phenyloctan-1-one (**4an**).[33] Pale yellow oil; 79% yield (162 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.1 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 2.96 (t, J = 7.4 Hz, 2H), 1.77−1.71 (m, 2H), 1.36−1.25 (m, 8H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 200.6, 137.1, 132.8, 128.5, 128.0, 38.6, 31.7, 29.3, 29.1, 24.4, 22.6, 14.0.

1-Phenyldecan-1-one (**4ao**).[34] Pale yellow oil; 85% yield (197 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.4 Hz, 2H), 7.55−7.52 (m, 1H), 7.46−7.43 (m, 2H), 2.95 (t, J = 7.4 Hz, 2H), 1.76−1.70 (m, 2H), 1.36−1.27 (m, 12H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C{1H} NMR (125 MHz, CDCl3) δ 200.5, 137.1, 132.8, 128.5, 128.0, 38.6, 31.9, 29.5, 29.5, 29.4, 29.3, 24.4, 22.7.

4-Methyl-1-phenylhexan-1-one (**4ap**).[5e] Pale yellow oil; 83% yield (158 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 7.3 Hz, 2H), 7.6 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 3.03−2.98 (m, 2H), 1.84−1.80 (m, 1H), 1.62−1.59 (m, 2H), 1.49−1.43 (m, 2H), 1.29−1.21 (m, 1H), 0.98−0.93 (m, 6H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 200.8, 137.1, 132.8, 128.5, 128.0, 36.4, 34.2, 31.0, 29.3, 19.0, 11.3.

3-Cyclohexyl-1-phenylpropan-1-one (**4aq**).[5e] White solid; 86% yield (186 mg); mp 39−40 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 2.98 (t, J = 7.7 Hz, 2H), 1.78−1.69 (m, 4H), 1.65−1.61 (m, 3H), 1.32−1.27 (m, 1H), 1.25−1.14 (m, 3H), 0.98−0.91 (m, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 200.9, 137.1, 132.8, 128.5, 128.0, 37.4, 36.1, 33.2, 31.8, 26.5, 26.3.

3-Phenyl-1-m-tolylpropan-1-one (**4ba**).[35] Pale yellow oil; 88% yield (196 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77−7.74 (m, 2H), 7.36−7.33 (m, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.26−7.24 (m, 2H), 7.20 (t, J = 7.1 Hz, 1H), 3.28 (t, J = 7.8 Hz, 2H), 3.06 (t, J = 7.8 Hz, 2H), 2.39 (s, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 199.4, 141.3, 138.4, 136.9, 133.8, 128.6, 128.5, 128.4, 128.4, 126.1, 125.2, 40.5, 30.2, 21.3.

3-Phenyl-1-p-tolylpropan-1-one (**4ca**).[35] White solid; 82% yield (184 mg); mp 68−69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.2 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.26−7.24 (m, 4H), 7.20 (t, J = 7.1 Hz, 1H), 3.28 (t, J = 7.8 Hz, 2H), 3.06 (t, J = 7.8 Hz, 2H), 2.40 (s, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.9, 143.8, 141.4, 134.4, 129.3, 128.5, 128.4, 128.1, 126.1, 40.3, 30.2, 21.6.

1-(4-Ethylphenyl)-3-phenylpropan-1-one (**4da**).[31] White solid; 87% yield (208 mg); mp 64−65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 2H), 7.32−7.25 (m, 6H), 7.21 (t, J = 7.1 Hz, 1H), 3.28 (t, J = 7.7 Hz, 2H), 3.06 (t, J = 7.7 Hz, 2H), 2.71 (q, J = 7.6 Hz, 2H), 1.25 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.9, 150.0, 141.4, 134.6, 128.5, 128.4, 128.2, 128.1, 126.1, 40.3, 30.2, 28.9, 15.2.

1-(4-Methoxyphenyl)-3-phenylpropan-1-one (**4ea**).[36] White solid; 88% yield (212 mg); mp 95−96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 8.9 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.26 (d, J = 6.8 Hz, 2H), 7.21 (t, J = 7.1 Hz, 1H), 6.93 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H), 3.25 (t, J = 7.8 Hz, 2H), 3.06 (t, J = 7.8 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 197.8, 163.4, 141.4, 130.2, 129.9, 128.5, 128.4, 126.1, 113.7, 55.4, 40.1, 30.3.

1-(3-Fluorophenyl)-3-phenylpropan-1-one (**4fa**).[37] Pale yellow oil; 79% yield (179 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 7.8 Hz, 1H), 7.64−7.61 (m, 1H), 7.43−7.39 (m, 1H), 7.31 (t, J = 7.5 Hz, 2H), 7.26−7.19 (m, 4H), 3.28 (t, J = 7.6 Hz, 2H), 3.08 (t, J = 7.6 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 197.9 (d, J_{C-F} = 1.6 Hz), 163.8 (d, J_{C-F} = 246.6 Hz), 141.0, 139.0 (d, J_{C-F} = 5.9 Hz), 130.0 (d, J_{C-F} = 6.9 Hz), 128.6, 128.4, 126.2, 123.8 (d, J_{C-F} = 2.0 Hz), 120.1(d, J_{C-F} = 21.1 Hz), 114.8 (d, J_{C-F} = 21.8 Hz), 40.6, 30.0.

1-(3-Chlorophenyl)-3-phenylpropan-1-one (**4ga**).[38] Pale yellow oil; 83% yield (203 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91−7.90 (m, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.51−7.49 (m, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.29 (t, J = 7.5 Hz, 2H), 7.24−7.19 (m, 3H), 3.26 (t, J = 7.7 Hz, 2H), 3.05 (t, J = 7.7 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 197.8, 141.0, 138.4, 134.9, 133.0, 129.9, 128.6, 128.4, 128.2, 126.2, 126.1, 40.5, 29.9.

1-(4-Chlorophenyl)-3-phenylpropan-1-one (**4ha**).[29] White solid; 82% yield (201 mg); mp 73−74 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.26−7.20 (m, 3H), 3.27 (t, J = 7.7 Hz, 2H), 3.06 (t, J = 7.7 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 197.9, 141.0, 139.5, 135.1, 129.4, 128.9, 128.5, 128.4, 126.2, 40.4, 30.0.

1-(4-Bromophenyl)-3-phenylpropan-1-one (**4ia**).[39] White solid; 89% yield (257 mg); mp 98−99 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.6 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 7.31−7.19 (m, 5H), 3.26 (t, J = 7.7 Hz, 2H), 3.06 (t, J = 7.7 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 192.8, 141.0, 135.6, 131.9, 129.6, 128.6, 128.4, 128.2, 126.2, 40.4, 30.0.

3-Phenyl-1-(4-(trifluoromethyl)phenyl)propan-1-one (**4ja**).[37] White solid; 81% yield (226 mg); mp 46 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.24 (m, 3H), 3.33 (t, J = 7.6 Hz, 2H), 3.08 (t, J = 7.6 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 198.2, 140.8, 139.5, 134.7 (q, J_{C-F} = 32.5 Hz), 128.6, 128.4, 128.3, 126.3, 125.7, 125.6, 40.7, 29.9.

1-(Naphthalen-2-yl)-3-phenylpropan-1-one (**4ka**).[40] White solid; 84% yield (219 mg); mp 93−94 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.05 (dd, J = 8.6 and 1.7 Hz, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.88 (t, J = 8.9 Hz, 2H), 7.60 (t, J = 6.8 Hz, 1H), 7.55 (t, J = 6.9 Hz, 1H), 7.34−7.29 (m, 4H), 7.22 (t, J = 5.8 Hz, 1H), 3.45 (t, J = 7.8 Hz, 2H), 3.13 (t, J = 7.8 Hz, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 199.1, 141.4, 135.6, 134.2, 132.5, 129.7, 129.5, 128.6, 128.5, 127.8, 126.8, 126.2, 123.8, 40.6, 30.3.

2-Methyl-1,3-diphenylpropan-1-one (**4la**).[41] Pale yellow oil; 80% yield (179 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.3 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 7.25 (t, J = 7.5 Hz, 2H), 7.20−7.15 (m, 3H), 3.75 (sextet, J = 7.0 Hz, 1H), 3.17 (dd, J = 13.7 and 6.3 Hz, 1H), 2.69 (dd, J = 13.7 and 7.9 Hz, 1H), 1.2 (d, J = 7.0 Hz, 3H); ^{13}C{1H} NMR (125 MHz, CDCl3) δ 203.7, 140.0, 136.5, 132.9, 129.1, 128.6, 128.4, 128.3, 126.2, 42.8, 39.4, 17.4.

2-Benzyl-2,3-dihydroinden-1-one (**4ma**).[42] Yellow oil; 82% yield (183 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.6 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 6.1 Hz, 1H), 7.36 (d, J = 7.4 Hz, 1H), 7.29 (t, J = 7.4 Hz, 2H), 7.24−7.19 (m, 3H), 3.40 (dd, J = 14.0

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and 4.3 Hz, 1H), 3.16 (dd, J = 17.2 and 7.8 Hz, 1H), 3.01−2.97 (m, 1H), 2.86 (dd, J = 17.2 and 4.0 Hz, 1H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 207.8, 153.6, 139.6, 136.5, 134.8, 128.9, 128.5, 127.4, 126.6, 126.3, 124.0, 48.9, 37.0, 32.2.

*2-Benzyl-3,4-dihydronaphthalen-1-one (**4na**).*[43] Pale yellow oil; 80% yield (189 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 7.8 Hz, 1H), 7.48−7.45 (m, 1H), 7.33−7.29 (m, 3H), 7.24−7.21 (m, 4H), 3.50 (dd, J = 4.0 and 4.0 Hz, 1H), 2.95−2.91 (m, 2H), 2.77−2.72 (m, 1H), 2.67−2.62 (m, 1H), 2.13−2.09 (m, 1H), 1.83−1.76 (m, 1H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 199.4, 144.0, 140.0, 133.2, 132.5, 129.2, 128.7, 128.4, 127.5, 126.6, 126.1, 49.4, 35.6, 28.6, 27.6.

*1-Cyclopropyl-3-phenylpropan-1-one (**4oa**).*[44] Pale yellow oil; 84% yield (147 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.29−7.24 (m, 2H), 7.20−7.17 (m, 3H), 2.92−2.87 (m, 4H), 1.91−1.88 (m, 1H), 1.02−1.00 (m, 2H), 0.86−0.83 (m, 2H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 209.9, 141.2, 128.4, 128.3, 126.0, 44.9, 29.9, 20.5, 10.7.

*4-Methyl-1-phenylpentan-3-one (**4pa**).*[34] Pale yellow oil; 82% yield (145 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.29−7.25 (m, 2H), 7.19−7.17 (m, 3H), 2.89 (t, J = 7.6 Hz, 2H), 2.76 (t, J = 7.6 Hz, 2H), 2.57−2.55 (m, 1H), 1.07 (d, J = 7.0 Hz, 6H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 213.7, 141.3, 128.4, 128.3, 126.0, 41.9, 41.0, 29.8, 18.1.

Procedure for the Direct Coupling of a Secondary Alcohol with a Primary Alcohol Catalyzed by [Cp*Ir(2,2′-bpyO)(H_2O)] (Scheme 5). In a round-bottomed flask with a condenser tube, **1a** (1 mmol), **2a** (1.1 mmol, 1.1 equiv), Cat. **4** (5.3 mg, 0.01 mmol, 1 mol %), Cs_2CO_3 (33 mg, 0.1 mmol, 0.1 equiv), and *tert*-amyl alcohol (1 mL) were placed under air atmosphere. The reaction mixture was heated under reflux in an oil bath for 12 h and was then cooled to ambient temperature. Yields of **4aa** and **5aa** were determined by ^1H NMR of the crude reaction mixture.

*1,3-Diphenylpropan-1-ol (**5aa**).*[13b] Pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.33 (d, J = 4.1 Hz, 4H), 7.28−7.25 (m, 3Hs), 7.19−7.16 (m, 3H), 4.67−4.65 (m, 1H), 2.75−2.62 (m, 2H), 2.14−1.98 (m, 2H), 1.96 (s, 1H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.6, 141.8, 128.5, 128.5, 128.4, 127.6, 125.9, 125.9, 73.9, 40.5, 32.1.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01975.

^1H NMR and ^{13}C NMR spectra of the products (PDF)

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Notes

The authors declare no competing financial interest.

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