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Rhenium(I)-Catalyzed C-Methylation of Ketones, Indoles, and Arylacetonitriles Using Methanol

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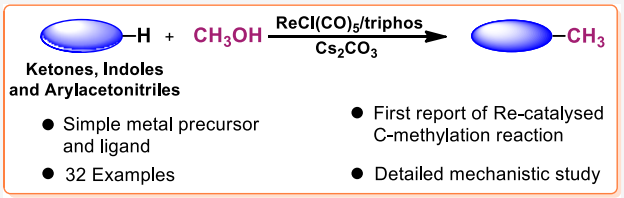
ABSTRACT: A $ReCl(CO)_5$/$MeC(CH_2PPh_2)_3$ (**L2**) system was developed for the C-methylation reactions utilizing methanol and base, following the borrowing hydrogen strategy. Diverse ketones, indoles, and arylacetonitriles underwent mono- and dimethylation selectively up to 99% yield. Remarkably, tandem multiple methylations were also achieved by employing this catalytic system.



The borrowing hydrogen strategy for the direct functionalization of C−H bonds and construction of C−C and C−N bonds using alcohols has become an effective process in modern organic chemistry.[1−5] This process has gained significant attention due to its high atom-economy and a minimum amount of waste generation.[6−8] The utilization of various inexpensive alcohols as alkylating agents is more elegant following this environmentally friendly protocol, which produces H_2O as the sole byproduct.

Although various transition-metal-based complexes have been explored for the borrowing hydrogen strategy, rhenium complexes are relatively less explored. The Zhu group reported a rhenium heptahydride complex $[ReH_7(PCy_3)_2]$-catalyzed amination of alcohols following this methodology.[9] Later on, Beller and co-workers demonstrated a PNP-based rhenium(I) catalyst for the synthesis of α-alkylated ketones, *N*-alkylated sulfonamides as well as the synthesis of pyrroles by the reaction of ketones, diols, and amines.[10] Following the borrowing hydrogen strategy, (PNP)Re(I)-complex-catalyzed *N*-methylation of amines in methanol was conveyed by the Sortais group.[11] Recently, following the acceptorless dehydrogenative coupling tactic, rhenium-catalyzed synthesis of various N-heterocycles such as quinolines, pyrimidines, quinoxalines, pyrroles, etc. was reported by the Kirchner group,[12] whereas Sortais and co-workers demonstrated sustainable synthesis of several substituted quinolines.[13]

Incorporation of a methyl group plays a vital role in changing both the physical and biological properties of molecules.[14,15] Several natural products and drug molecules contain at least one C-, N-, or O-methylated fragment, which displays their characteristic properties. Hence, finding efficient methods for the incorporation of a methyl group into organic molecules has become an attractive research topic.[16] Compared to conventional toxic methylating agents,[17−19] methanol can be utilized as a sustainable greener alternative in this reaction.

Despite the challenges in the dehydrogenation of methanol, recently using both homogeneous and heterogeneous catalysts, several reports have emerged for the C-methylation of ketones and heterocycles.[20−37] However, rhenium-based systems are rare in the literature for similar transformations.[11,12] Employment of an *in situ* generated metal complex from commercially available simple metal precursors and ligand systems is more attractive as it avoids the tedious synthesis and characterization of the metal complex.[38−40] In our continued interest to develop effective protocols for the utilization of methanol via the hydrogen borrowing methodology,[25,41−44] herein, we report a simple and commercially available rhenium precursor/ligand-catalyzed sustainable methylation of ketones, indoles, and arylacetonitriles using methanol as a C1 source (Scheme 1). To the best of our knowledge, similar transformations using rhenium catalysts have not been reported yet.

At first, to commence our study, 4-methoxypropiophenone was selected as a model substrate for the α-methylation of ketone (for detailed optimization, see the Supporting Information, S3−S5). As shown in Table 1, 5 mol % $ReCl(CO)_5$ in the presence of 0.5 equiv of Cs_2CO_3 in methanol in an oil bath temperature of 140 °C produced an 11% yield of 1-(4-methoxyphenyl)-2-methylpropan-1-one (**3**) within 24 h (Table 1, entry 1), indicating that the Re precursor alone was not sufficient to achieve a considerable yield of **3**. To identify the optimal reaction conditions, various phosphine-based ligands in combination with $ReCl(CO)_5$ were screened (Table 1, entries 2−9). Interestingly, 5 mol % 1,1,1-tris(diphenylphosphinomethyl)ethane ligand (**L2**) displayed a

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Scheme 1. Rhenium-Catalyzed Reactions via Borrowing Hydrogen Strategy

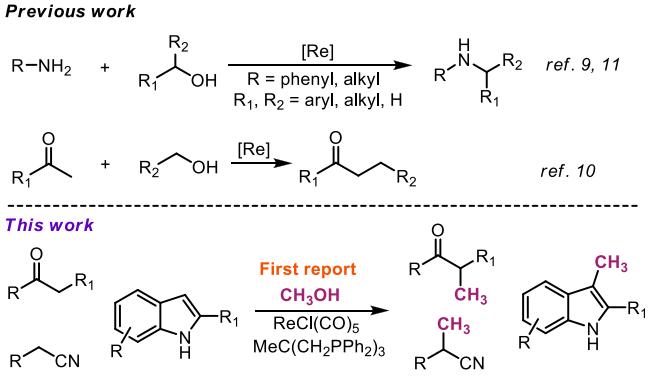
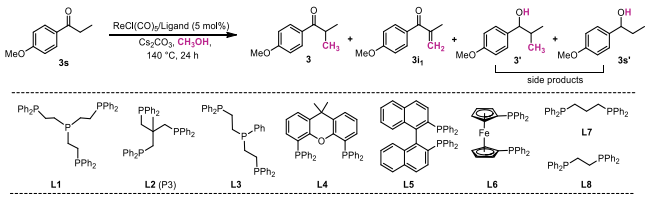


Table 1. Optimization of the Reaction Parameters[a]



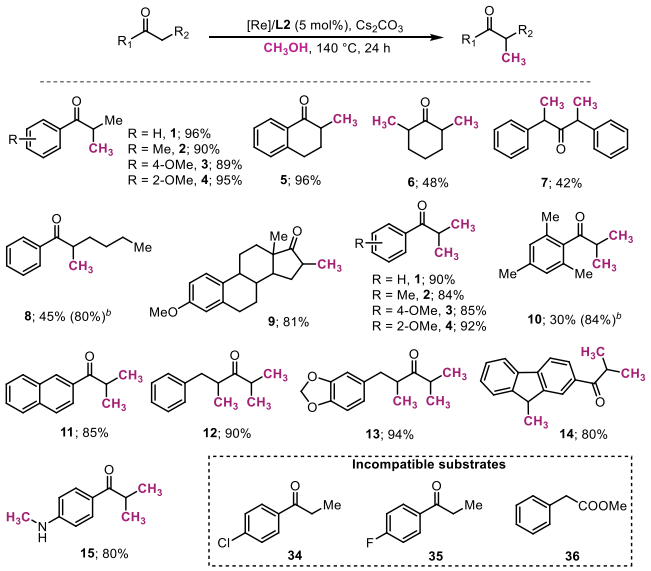
entry	ligand	Cs_2CO_3 (mmol)	conversion (%)	yield (%) 3	$3i_1$	3′	3s′
1		0.2	15	11	4		
2	**L1**	0.2	17	15	<1		2
3	**L2**	0.2	60	58	1	<1	1
4	**L3**	0.2	22	17	4	1	<1
5	**L4**	0.2	24	18	2	2	2
6	**L5**	0.2	38	30	3	1	4
7	**L6**	0.2	13	12			1
8	**L7**	0.2	46	37		1	8
9	**L8**	0.2	34	32		<1	2
10[b]	**L2**	0.2	<1	<1			
11[c]	**L2**			0			
12	**L2**	1.2	99	99	<1		

[a]Reaction conditions: 4-methoxypropiophenone (0.4 mmol), $ReCl(CO)_5$/ligand (0.02 mmol), Cs_2CO_3 (mmol), 140 °C (oil bath temperature), 24 h; GC yield (toluene was used as an internal standard). [b]Without $ReCl(CO)_5$. [c]Without base.

maximum yield of **3** (58%), whereas other ligands yielded ≤37% of the product under similar reaction conditions. In the absence of a ligand (**L2**) and base (Cs_2CO_3), almost no product was observed. These results suggested that both ligand and base were essential for this methylation reaction (Table 1, entries 10 and 11). Among the different bases tested, Cs_2CO_3 provided the best catalytic activity (Table S2). Notably, with an increasing amount of base, the desired product formation improved considerably; 3 equiv of Cs_2CO_3 resulted in 99% yield of **3** (Table 1, entry 12). The use of solvents with higher boiling points, such as toluene and xylene in combination with methanol, exhibited a detrimental effect on product formation (Table S3). The reaction temperature, amount of Cs_2CO_3, and catalyst loading were also screened for this transformation (Table S4). Ultimately, 5 mol % [Re]/**L2** and 3 equiv of Cs_2CO_3 at 140 °C (oil bath temperature) for 24 h were found to be the optimal reaction conditions for the methylation of ketone (Table 1, entry 12).

After identifying the optimized reaction conditions, the general applicability of this protocol was tested for *mono*-methylation of different ketones (Table 2). Electron-donating

Table 2. Substrate Scope of Ketones[a]



[a]Reaction conditions: ketones (0.4 mmol), $ReCl(CO)_5$/**L2** (0.02 mmol), Cs_2CO_3 (1.2 mmol), CH_3OH (3 mL), 140 °C (oil bath temperature), 24 h, isolated yields. [b]Heated for 36 h.

groups at the *ortho*- and *para*-positions of propiophenone derivatives provided excellent isolated yields of the corresponding methylated products (**2**-**4**). 4-Chloro- and 4-fluoro propiophenones (**34**, **35**) were dehalogenated and produced methoxy-substituted corresponding products (Scheme S1). Methyl 2-phenylacetate (**36**) was hydrolyzed under the reaction conditions, and the carboxylate salt of the substrate was detected. Cyclic ketones such as α-tetralone provided an excellent yield of monomethylated product **5**, whereas cyclohexanone furnished a 48% yield of dimethylated product (**6**). 1,3-Diphenyl-2-propanone and 1-phenylhexan-1-one afforded moderate yields probably due to the steric hindrance (**7**, **8**). Estrone 3-methyl ether provided a good yield of the methylated product under the optimized reaction conditions (**9**).

Further, we extended the scope of this protocol for dimethylation of various acetophenone derivatives, and *ortho*/*para*-substituted acetophenone derivatives provided excellent isolated yields of dimethylated products (Table 2, **1**−**4**). For 2,4,6-trimethyl acetophenone, a longer reaction time was essential to obtain a satisfactory yield of dimethylated product (**10**). In addition, 2-acetylnapthalene afforded a double methylated product in 85% yield (**11**), following this strategy. Notably, tandem multiple methylation was achieved following this catalytic system for the aliphatic ketones having both terminal and internal enolizable α-positions around the carbonyl center under the standard reaction conditions. These α-positions were smoothly methylated for 4-phenylbutan-2-one and 4-(3,4-methylenedioxy)phenyl-2-butanone and delivered the desired products in excellent isolated yields (Table 2, **12**, **13**). Employing this protocol, multimethylation of 2-acetylfluorene was also observed, and product **14** was isolated in 80% yield. Following this strategy, utilizing methanol for the

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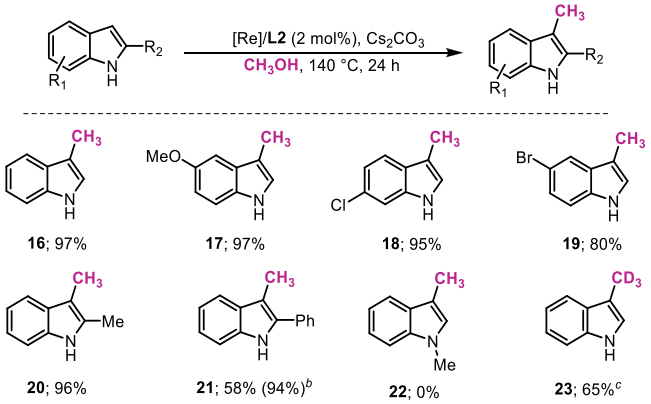
first time, we reported the synthesis of compounds **13** and **14**. Notably, the nitro group of 4-nitroacetophenone was reduced under the optimized reaction conditions, and both N- and C-methylation were observed (**15**).

Next, the C3-methylation of indole was probed utilizing this catalytic system. Notably, this [Re]/**L2** system displayed excellent performance for the methylation of indole; only 2 mol % catalyst and 10 mol % Cs_2CO_3 afforded 3-methylindole (**16**) with 98% yield (Table S5). Indole derivatives having electron-donating and electron-withdrawing groups at the different positions of the aromatic ring were smoothly transformed to the desired methylated products in up to 97% isolated yields (Table 3). A trace amount of

Table 3. Substrate Scope of Indoles[a]



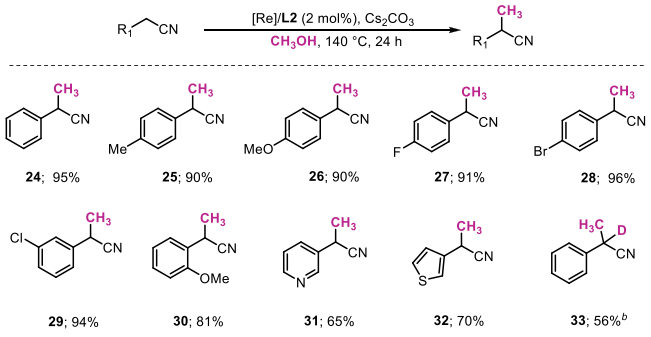
[a]Reaction conditions: indoles (0.4 mmol), $ReCl(CO)_5$/**L2** (0.008 mmol), Cs_2CO_3 (0.04 mmol), CH_3OH (3 mL), 140 °C (oil bath temperature), 24 h, isolated yields. [b]Heated for 32 h. [c]CD_3OD, GC yield (toluene was used as an internal standard).

dehalogenated products was detected for the halogenated substrates (**18**, **19**). The C2-substituted indole, such as 2-methylindole, provided 96% yield of **20**, whereas prolonged heating was required for 2-phenylindole to achieve an excellent yield of the desired product (**21**). However, *N*-methylindole (**22**) did not lead to any product formation, which indicated the importance of the indole N−H proton.[45] Furthermore, d_3-skatole (**23**), which has been used in studying metabolism kinetics, was produced in 65% yield by employing CD_3OD.[46]

To explore the versatility of this catalytic system, C2-methylation of a variety of arylacetonitriles with methanol was next examined. For arylacetonitriles, slightly modified reaction conditions were required to achieve effective α-methylated products (Table S6). A series of differently substituted arylacetonitriles delivered the C2-methylated products in good to excellent isolated yields (Table 4, **24**−**30**). Heterocyclic acetonitrile derivatives, such as 2-(pyridin-3-yl)acetonitrile and 2-(thiophen-3-yl)acetonitrile, also smoothly furnished the corresponding C2-methylated products (**31**, **32**). A moderate yield of deutero-methylated phenylacetonitrile (**33**) was obtained in CD_3OD under the standard reaction conditions. Next, we examined the synthetic applicability of this methodology by the gram-scale synthesis of a few C-methylated products (Scheme S2).

Several control experiments were conducted to acquire mechanistic insight into this process. For this purpose, 4-methoxypropiophenone was selected as a representative substrate. Under the optimized reaction conditions, the

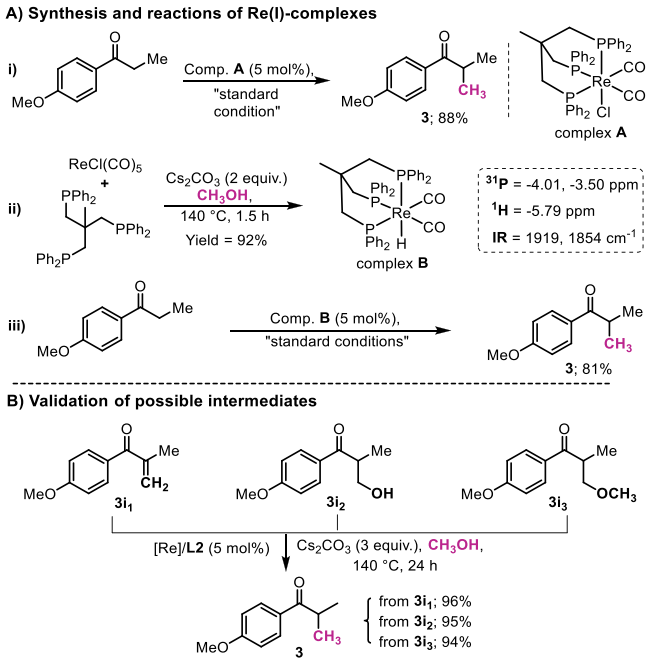
Table 4. Substrate Scope of Arylacetonitriles[a]



[a]Reaction conditions: arylacetonitriles (0.4 mmol), $ReCl(CO)_5$/**L2** (0.008 mmol), Cs_2CO_3 (0.3 mmol), CH_3OH (3 mL), 140 °C (oil bath temperature), 24 h, isolated yields. [b]CD_3OD, GC yield (toluene was used as an internal standard).

isolated (**L2**)$Re(CO)_2Cl$ complex (**A**)[47] (5 mol %) provided 88% yield of **3** (Scheme 2A-i). This result suggested that this

Scheme 2. Mechanistic Investigations



complex may be formed during the reaction. To identify the active rhenium intermediate, a mixture of $ReCl(CO)_5$, **L2**, and Cs_2CO_3 (2 equiv) was heated in methanol for 1.5 h (Scheme 2A-ii). This reaction provided 92% yield of a new rhenium complex (**B**), which was characterized by several spectroscopic techniques. This complex showed peaks at δ = −4.01, −3.50 ppm in the ^{31}P NMR spectrum, and in ^1H NMR spectra, a triplet signal of Re−H was observed at δ = −5.79 ppm (t, J_{HP} = 20.6 Hz); the IR spectra showed two carbonyl frequencies (ν) at 1919 and 1854 cm^{-1}. These data are well-matched with the reported characterization data of the (**L2**)$Re(CO)_2H$ complex.[47] Additionally, independently synthesized complex **B** furnished 81% yield of **3** under the optimized reaction conditions (Scheme 2A-iii). This experiment further confirmed that complex **B** was the active intermediate in this reaction. Interestingly, in most of the α-methylation of the ketone

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reactions, the formation of crystalline Re(I)-H species was observed after the reaction.

The possible intermediates such as 1-(4-methoxyphenyl)-2-methylprop-2-en-1-one ($\mathbf{3i_1}$), 3-hydroxy-1-(4-methoxyphenyl)-2-methylpropan-1-one ($\mathbf{3i_2}$), and 3-methoxy-1-(4-methoxyphenyl)-2-methylpropan-1-one ($\mathbf{3i_3}$) were synthesized following the reported procedures to investigate their involvement in the reaction.[29,48] Next, these intermediates were independently subjected to the optimized reaction conditions (Scheme 2B). All compounds smoothly converted to the desired methylated product **3**, which suggests that they are the plausible intermediates during this transformation. To get more information about the reaction mechanism, reactions of 4-methoxypropiophenone, as well as the probable intermediates ($\mathbf{3i_1}$, $\mathbf{3i_2}$, and $\mathbf{3i_3}$) with CD_3OD, were carried out (Scheme S4). 4-Methoxypropiophenone was converted to the desired product ($\mathbf{3_D}$) in 78% yield, indicating methanol acted as the C1 source. Furthermore, $\mathbf{3i_1}$, $\mathbf{3i_2}$, and $\mathbf{3i_3}$ also provided the corresponding deuterium incorporated products, which conveyed that methanol was the source of the hydrogen molecule.

Next, the time-dependent product distribution study was conducted for 4-methoxypropiophenone under the optimized reaction conditions (Figure 1A). The concentration of the final

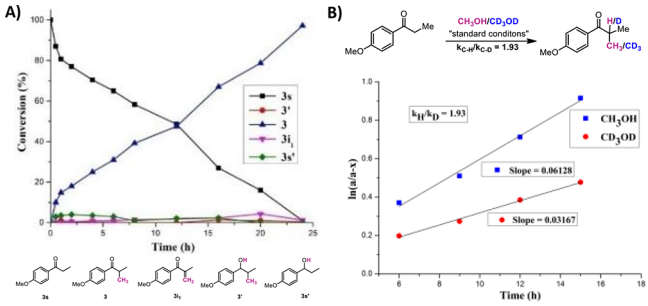


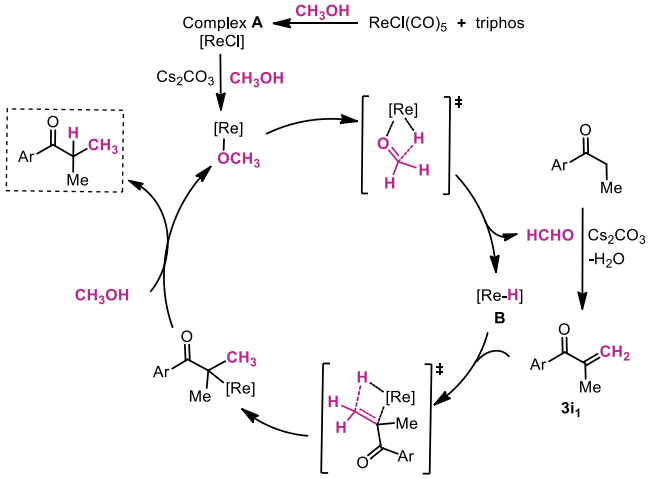
Figure 1. (A) Time-dependent product distribution study and (B) KIE study for C-methylation of 4-methoxypropiophenone.

product **3** gradually increased with time, and throughout the reaction, a small amount of intermediate $\mathbf{3i_1}$ was observed. Along with this, minute amounts of 1-(4-methoxyphenyl)-2-methylpropan-1-ol (**3′**) and 1-(4-methoxyphenyl)propan-1-ol (**3s′**) were detected.

For the C-methylation of 4-methoxypropiophenone, the kinetic isotope effect (KIE) study was carried out using CH_3OH and CD_3OD (Figure 1B). This study revealed a k_{C-H}/k_{C-D} = 1.93, indicating the activation of the C−H bond of methanol is a kinetically important step for this reaction.

Based on the experimental studies and previous literature reports, a plausible mechanism was proposed for the α-methylation of propiophenone derivatives (Scheme 3). In the beginning, the Re(I) complex (**A**) is generated *in situ* by the reaction of $ReCl(CO)_5$ with the **L2** ligand in methanol. Then, complex **A** was transformed into the Re(I)-OMe complex in the presence of Cs_2CO_3 and methanol, which subsequently converts to Re(I)-H species (**B**) via β-hydride elimination, generating a formaldehyde molecule. Next, the base-mediated aldol reaction of ketone with formaldehyde produces intermediate $\mathbf{3i_1}$. After that, insertion of compound $\mathbf{3i_1}$ into the Re(I)-H bond, followed by methanolysis, generates the α-methylated product, regenerating the Re(I)-OMe complex.

Scheme 3. Plausible Mechanism for C-Methylation of Ketones



In conclusion, rhenium-catalyzed C-methylation of various ketones, indoles, and arylacetonitriles using methanol as a greener and sustainable methylating reagent was demonstrated for the first time. Several control experiments and mechanistic investigations were carried out to understand this protocol. Under the optimized reaction conditions, the formation of $(\mathbf{L2})Re(CO)_2H$ was confirmed by several spectroscopic techniques. This Re(I)-H was found to be the plausible active catalyst during the reaction. Experiments with CD_3OD confirmed that methanol acts as both hydrogen and C1 sources in this methylation process.

EXPERIMENTAL SECTION

General Information. All experiments were carried out under an argon atmosphere either inside the argon-filled glovebox or using standard Schlenk line technique unless otherwise stated. The glassware was oven-dried prior to use. Solvents were distilled under an argon atmosphere according to literature procedures and deoxygenated prior to use. All commercial reagents and metal precursors were purchased from Sigma-Aldrich, Alfa-aesar, Spectrochem, Avra, and SD-fine chemical, India. NMR spectra were recorded with a reference to deuterated solvent resonance (δ in ppm and J in Hz) on a JEOL spectrometer (400 and 500 MHz for ^{1}H NMR, 100 and 125 MHz for ^{13}C NMR, and 160 MHz for ^{31}P NMR). ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded with $CDCl_3$, CD_2Cl_2, or DMSO-d_6. For a few kinetic experiments, ^{1}H NMR data were recorded in CD_3OD solvent. All GC analyses were performed using an Agilent 7890 B gas chromatograph, whereas GC−MS was measured using an Agilent 7890 A gas chromatograph equipped with an Agilent 5890 triple-quadruple mass system. High-resolution mass spectra were recorded on a Waters Micromass Quattro Micro triple-quadrupole and Agilent 6230 LC/TOF mass spectrometer. FT-IR spectra were recorded using a PerkinElmer FT-IR spectrometer.

Procedure for the Synthesis of Plausible Intermediates. *1-(4-Methoxyphenyl)-2-methylprop-2-en-1-one ($\mathbf{3i_1}$).* This compound was synthesized according to the literature procedure.[48] A mixture of 4-methoxypropiophenone (2.0 mL, 2.14 g, 13.0 mmol) and DMF (16 mL) was stirred in a 50 mL round-bottomed flask, equipped with a magnetic pallet. To the stirring reaction mixture, paraformaldehyde (2.34 g, 78.0 mmol), piperidine (0.17 mL, 1.7 mmol), and glacial acetic acid (0.17 mL, 2.86 mmol) were added, and the resulting mixture was heated at 100 °C for 24 h. After that, the reaction mixture was cooled down; subsequently, water (30 mL) was added to it. The organic part was extracted with dichloromethane (3 × 25 mL). The combined organic layer was dried with anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude product

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was purified by silica gel chromatography using 5% EtOAc/hexane. The title compound was obtained as a colorless oil in 45% yield (1.03 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, $J_{H,H}$ = 8.92 Hz, 2H), 6.92 (d, $J_{H,H}$ = 8.88 Hz, 2H), 5.79−5.78 (m, 1H), 5.52−5.51 (m, 1H), 3.85 (s, 3H), 2.05 (dd, $J_{H,H}$ = 1.36, 1.00 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.3, 163.2, 144.1, 132.0, 130.2, 124.9, 113.6, 55.6, 19.2. HRMS (APCI-TOF): calcd for $C_{11}H_{13}O_2$ $[M + H]^+$, 177.0910; found, 177.0917.

*3-Hydroxy-1-(4-methoxyphenyl)-2-methylpropan-1-one (**3i$_2$**).* This compound was synthesized according to the literature procedure.[49] 4-Methoxypropiophenone (2.0 mL, 2.14 g, 13.0 mmol), 37% formaldehyde in H_2O (1.95 mL, 26.0 mmol), $NaHCO_3$ (44.0 mg, 0.52 mmol), and methanol (15 mL) were taken into a 100 mL round-bottomed flask, equipped with a magnetic pallet. Then, the reaction mixture was heated at 60 °C for 24 h. After completion, the reaction mixture was cooled and acidified using conc. HCl close to pH 4. Next, dichloromethane solvent was added, and the organic layer was separated by using a separating funnel. This process was repeated three times (3 × 25 mL). The combined organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The title compound was purified by silica gel chromatography using 30% EtOAc/hexane. Colorless oil was obtained in 60% yield (1.51 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, $J_{H,H}$ = 9.00 Hz, 2H), 6.95 (d, $J_{H,H}$ = 8.96 Hz, 2H), 3.91−3.87 (m, 1H), 3.86 (s, 3H), 3.63−3.57 (m, 1H), 2.14 (brs, 1H), 1.23 (d, $J_{H,H}$ = 7.32 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 203.2, 163.8, 130.9, 129.1, 114.0, 64.8, 55.6, 42.5, 14.9. HRMS (APCI-TOF): calcd for $C_{11}H_{15}O_3$ $[M + H]^+$, 195.1016; found, 195.1016.

*3-Methoxy-1-(4-methoxyphenyl)-2-methylpropan-1-one (**3i$_3$**).* This compound was synthesized according to the literature procedure.[49] 4-Methoxypropiophenone (2.0 mL, 2.14 g, 13.0 mmol), 37% formaldehyde in H_2O (1.38 mL, 18.2 mmol), 0.5 N NaOH (36.4 mL, 18.2 mmol), and methanol (8 mL) were taken into a 50 mL round-bottom flask, equipped with a magnetic pallet. Then, the reaction mixture was stirred at room temperature for 24 h. After completion, the reaction mixture was acidified to pH 4 using concentrated HCl. Next, the dichloromethane solvent was added, and the organic layer was separated by using a separating funnel. This process was repeated (3 × 25 mL). The combined organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. By flash silica gel chromatography, 3-methoxy-1-(4-methoxyphenyl)-2-methylpropan-1-one ($3i_3$) was obtained (eluent = 40% EtOAc in hexane) as a colorless oil (1.08 g, 40%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, $J_{H,H}$ = 8.96 Hz, 2H), 6.93 (d, $J_{H,H}$ = 8.80 Hz, 2H), 3.85 (s, 3H), 3.74−3.69 (m, 2H), 3.44−3.39 (m, 1H), 3.30 (s, 3H), 1.18 (d, $J_{H,H}$ = 6.56 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 201.3, 163.6, 130.8, 129.8, 113.9, 75.3, 59.2, 55.6, 40.9, 15.1. HRMS (APCI-TOF): calcd for $C_{12}H_{17}O_3$ $[M + H]^+$, 209.1172; found, 209.1179.

Procedure for Synthesis of Re(I) Complexes. ***(L2)Re(CO)$_2$Cl (A).*** This (**L2**)$Re(CO)_2Cl$ complex (**A**) was prepared following the reported procedure.[47] $ReCl(CO)_5$ (0.181 g, 0.5 mmol), triphos (L2) (0.343 g, 0.55 mmol), and toluene (15 mL) were taken in a 50 mL round-bottomed flask equipped with a magnetic pallet. Then, the resulting mixture refluxed for 7 h. After that, the reaction mixture was cooled to room temperature, and solvent was evaporated under reduced pressure. Then, the crude solid was washed with benzene and ethanol three times (each solvent, 3 × 2 mL). White colored microcrystals of complex **A** were obtained in 75% yield (0.338 g). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.56−7.49 (m, 8H), 7.32−7.13 (m, 10H), 7.07−7.01 (m, 12H), 2.53−2.40 (m, 6H), 1.44 (d, $J_{H,H}$ = 2.48 Hz, 3H). IR (KBr): ν_{CO} 1945, 1883 cm^{-1}. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 160 MHz): 2.40 (t, J = 15.20 Hz), −18.23 (d, J = 14.40 Hz).

(L2)Re(CO)$_2$H (B). $ReCl(CO)_5$ (0.723 g, 0.2 mmol), triphos (L2) (0.125 g, 0.2 mmol), Cs_2CO_3 (0.13 g, 0.4 mmol), and 10 mL of methanol were taken in a pressure tube and heated at 140 °C (oil bath temperature) for 1.5 h. After that, the solvent was evaporated under reduced pressure. Then, the crude solid was dissolved in dichloromethane (20 mL). The solution was filtered through a Celite pad and concentrated to 1 mL. The addition of ethanol (5 mL) to the solution provided the (**L2**)$Re(CO)_2H$ complex (**B**) as an off-white solid in 85% yield (0.147 g). ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.70−7.66 (m, 4H), 7.45−7.41 (m, 4H), 7.20−6.95 (m, 22H), 2.43 (d, $J_{H,H}$ = 7.68 Hz, 2H), 2.30−2.17 (m, 4H), 1.44 (d,, $J_{H,H}$ = 2.52 Hz, 3H), −5.79 (t, J_{HP} = 20.60 Hz, Re−H, 1H). IR (KBr): ν_{CO} 1919, 1854 cm^{-1}. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 160 MHz): −4.01 (d, J = 14.67 Hz.), −3.50 (d, J = 15.88 Hz.).

General Procedures. *α-Methylation of Ketones (General Procedure P).* Ketone (0.4 mmol), $ReCl(CO)_5$ (7.2 mg, 0.02 mmol), triphos (**L2**) (12.5 mg, 0.02 mmol), and Cs_2CO_3 (391.0 mg, 1.2 mmol) were taken inside a pressure tube under an argon atmosphere. Next, 3 mL of dry methanol was added to the reaction mixture. Then, the tube was closed and placed in a preheated oil bath at 140 °C (oil bath temperature) and heated for 24 h. After completion, the reaction mixture was cooled to room temperature and diluted with 3 mL of methanol. Twenty μL of the solution was syringed out for GC analysis (toluene was used as an internal standard). The rest of the reaction mixture was concentrated under reduced pressure. The final products were isolated by column chromatography using hexane and ethyl acetate as an eluent. The products were characterized by NMR, MS, and IR spectroscopic techniques.

C3-Methylation of Indoles (General Procedure Q). Indole (0.4 mmol), $ReCl(CO)_5$ (2.9 mg, 0.008 mmol), triphos (**L2**) (5.0 mg, 0.008 mmol) and Cs_2CO_3 (13.0 mg, 0.04 mmol) were taken inside a pressure tube under an argon atmosphere. After that, 3 mL dry methanol was added to the reaction mixture, and the tube was closed. Then, the tube was placed in a preheated oil bath at 140 °C (oil bath temperature) and heated for 24 h. After cooling at room temperature, the reaction mixture was diluted with 3 mL methanol. Then, 20 μL solution was syringed out for GC analysis (toluene was used as an internal standard). The rest of the reaction mixture was concentrated under reduced pressure. The final products were isolated by column chromatography using hexane and ethyl acetate as eluent. The products were characterized by NMR and MS spectroscopic techniques.

C2-Methylation of Arylacetonitriles (General Procedure R). Arylacetonitrile (0.4 mmol), $ReCl(CO)_5$ (2.9 mg, 0.008 mmol), triphos (**L2**) (5.0 mg, 0.008 mmol), and Cs_2CO_3 (97.7 mg, 0.3 mmol) were taken inside a pressure tube under an argon atmosphere. Next, 3 mL of dry methanol was added to the reaction mixture, and the tube was closed. Then, it was placed in a preheated oil bath at 140 °C (oil bath temperature) and heated for 24 h. After completion of the reaction, the tube was cooled to room temperature, and the reaction mixture was diluted with 3 mL of methanol. Then, 20 μL of solution was syringed out for GC analysis (toluene was used as an internal standard). The rest of the reaction mixture was concentrated under reduced pressure. The final products were isolated by column chromatography using hexane and ethyl acetate as an eluent. The products were characterized by NMR and MS spectroscopic techniques.

*2-Methyl-1-phenylpropan-1-one (**1**).*[21] The compound was prepared from propiophenone (53 mg, 0.4 mmol) and acetophenone (48 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (57 mg, 96% isolated yield from propiophenone; 53 mg, 90% isolated yield from acetophenone). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95−7.93 (m, 2H), 7.55−7.43 (m, 1H), 7.46−7.43 (m, 2H), 3.55 (sept, $J_{H,H}$ = 6.85 Hz, 1H), 1.21 (d, $J_{H,H}$ = 6.80 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 204.6, 136.3, 132.9, 128.7, 128.4, 35.5, 19.3. IR (KBr): ν_{CO} 1683 cm^{-1}. GC−MS (M^+): 148.1.

*2-Methyl-1-p-tolylpropan-1-one (**2**).*[21] The compound was prepared from 1-*p*-tolylpropan-1-one (59 mg, 0.4 mmol) and 1-*p*-tolylethanone (53 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a light-yellow oil (58 mg, 90% isolated yield from 1-*p*-tolylpropan-1-one; 53 mg, 84% isolated yield from 1-*p*-tolylethanone). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, $J_{H,H}$ = 8.28 Hz, 2H), 7.26 (d, $J_{H,H}$ = 8.08 Hz, 1H, including $CDCl_3$ peak), 3.52

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(sept, $J_{H,H}$ = 6.96 Hz, 1H), 2.39 (s, 3H), 1.20 (d, $J_{H,H}$ = 6.96 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 204.3, 143.7, 133.8, 129.4, 128.6, 35.3, 21.7, 19.4. IR (KBr): ν_{CO} 1682 cm^{-1}. GC−MS (M^+): 162.1.

*1-(4-Methoxyphenyl)-2-methylpropan-1-one (**3**).*[21] The compound was prepared from 1-(4-methoxyphenyl)propan-1-one (65 mg, 0.4 mmol) and 1-(4-methoxyphenyl)ethanone (60 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a light yellow oil (63 mg, 89% isolated yield from 1-(4-methoxyphenyl)propan-1-one; 60 mg, 85% isolated yield from 1-(4-methoxyphenyl)ethanone). ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, $J_{H,H}$ = 9.08 Hz, 2H), 6.94 (d, $J_{H,H}$ = 8.96 Hz, 2H), 3.85 (s, 3H), 3.52 (sept, $J_{H,H}$ = 7.00 Hz, 1H), 1.20 (d, $J_{H,H}$ = 7.04 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 203.3, 163.4, 130.7, 129.3, 113.9, 55.6, 35.1, 19.4. IR (KBr): ν_{CO} 1674 cm^{-1}. GC−MS (M^+): 178.1.

*1-(2-Methoxyphenyl)-2-methylpropan-1-one (**4**).*[21] The compound was prepared from 1-(2-methoxyphenyl)-propan-1-one (65 mg, 0.4 mmol) and 1-(2-methoxyphenyl)ethanone (60 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (67 mg, 95% isolated yield from 1-(2-methoxyphenyl)-propan-1-one; 65 mg, 92% from 1-(2-methoxyphenyl)ethanone). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (dd, $J_{H,H}$ = 7.60, 1.68 Hz, 1H), 7.42 (td, $J_{H,H}$ = 8.24, 1.72 Hz, 1H), 6.99 (t, $J_{H,H}$ = 7.36 Hz, 1H), 6.94 (d,, $J_{H,H}$ = 8.32 Hz, 1H), 3.86 (s, 3H), 3.48 (sept, $J_{H,H}$ = 6.80 Hz, 1H), 1.14 (d, $J_{H,H}$ = 6.84 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 208.3, 157.8, 132.7, 130.1, 129.2, 120.8, 111.4, 55.6, 40.2, 18.7. IR (KBr): ν_{CO} 1681 cm^{-1}. GC−MS (M^+): 178.1.

*2-Methyl-3,4-dihydronaphthalen-1(2H)-one (**5**).*[24] The compound was prepared from 3,4-dihydronaphthalen-1(2H)-one (58 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (62 mg, 96% isolated yield). For a 6 mmol scale reaction, the isolated yield was 88% (0.84 g). ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (dd, $J_{H,H}$ = 7.88, 1.00 Hz, 1H), 7.46 (td, $J_{H,H}$ = 7.44, 1.32 Hz, 1H), 7.28 (t, $J_{H,H}$ = 7.64 Hz, 1H), 7.23 (d, $J_{H,H}$ = 7.72 Hz, 1H), 3.03−2.97 (m, 2H), 2.61−2.55 (m, 1H), 2.21−2.16 (m, 1H), 1.92−1.82 (m, 1H), 1.27 (d, $J_{H,H}$ = 6.72 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 201.0, 144.3, 133.2, 132.5, 128.8, 127.5, 126.7, 42.8, 31.5, 29.0, 15.6. IR (KBr): ν_{CO} 1683 cm^{-1}. GC−MS (M^+): 160.1.

*2,6-Dimethylcyclohexanone (**6**).*[24] The compound was prepared from cyclohexanone (39 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (24 mg, 48% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 2.60−2.32 (m, 2H), 2.10−1.88 (m, 2H), 1.82−1.68 (m, 2H), 1.59−1.27 (m, 2H), 1.00 (d, $J_{H,H}$ = 6.36 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 217.5, 214.8, 45.5, 42.8, 37.4, 34.9, 25.7, 20.3, 16.1, 14.7. IR (KBr): ν_{CO} 1710 cm^{-1}. GC−MS (M^+): 126.1.

*2,4-Diphenylpentan-3-one (**7**).*[21] The compound was prepared from 1,3-diphenylpropan-2-one (84 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (40 mg, 42% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.30 (m, 4H), 7.28−7.24 (m, 2H, including $CDCl_3$ peak), 7.17−7.14 (m, 4H), 3.78 (q, $J_{H,H}$ = 6.92 Hz, 2H), 1.25 (d, $J_{H,H}$ = 7.12 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 210.5, 141.1, 129.2, 128.1, 127.3, 51.0, 18.2. IR (KBr): ν_{CO} 1714 cm^{-1}. GC−MS (M^+): 238.1.

*2-Methyl-1-phenylhexan-1-one (**8**).*[25] The compound was prepared from 1-phenylhexan-1-one (70 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (61 mg, 80% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.95−7.93 (m, 2H), 7.56−7.52 (m, 1H), 7.47−7.43 (m, 2H), 3.47 (sext, $J_{H,H}$ = 6.72 Hz, 1H), 1.84−1.75 (m, 1H), 1.46−1.38 (m, 1H), 1.31−1.24 (m, 4H), 1.19 (d, $J_{H,H}$ = 6.76 Hz, 3H), 0.86 (t, $J_{H,H}$ = 7.00 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 204.7, 136.9, 132.9, 128.7, 128.4, 40.7, 33.6, 29.8, 22.9, 17.4, 14.1. IR (KBr): ν_{CO} 1736 cm^{-1}. GC−MS (M^+): 190.2.

*3-Methoxy-13,16-dimethyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta-phenanthren-17-(14H)-one (**9**).*[50] The compound was prepared from estrone methyl ether (114 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless dense liquid (57 mg, 81% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, $J_{H,H}$ = 8.48 Hz, 1H), 6.72 (dd, $J_{H,H}$ = 8.56, 2.68 Hz, 1H), 6.64 (d, $J_{H,H}$ = 2.68 Hz, 1H), 2.91−2.84 (m, 2H), 2.40−2.13 (m, 3H), 2.02−1.89 (m, 2H), 1.68−1.30 (m, 7H), 1.24 (d, $J_{H,H}$ = 7.08 Hz, 3H), 0.86 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 223.3, 222.8, 157.7, 137.9, 132.3, 126.4, 114.0, 111.7, 55.3, 49.2, 48.7, 48.5, 47.8, 44.3, 44.2, 44.2, 43.9, 39.4, 38.4, 38.1, 32.1, 32.0, 30.8, 30.1, 29.8, 26.9, 26.6, 26.0, 17.1, 16.8, 14.6, 14.3. IR (KBr): ν_{CO} 1736 cm^{-1}. GC−MS (M^+): 298.2.

*1-Mesityl-2-methylpropan-1-one (**10**).*[33] The compound was prepared from 1-mesityl-2-methylpropan-1-one (65 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (64 mg, 84% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 6.82 (s, 2H), 2.98 (sept, $J_{H,H}$ = 7.00 Hz, 1H), 2.27 (s, 3H), 2.18 (s, 3H), 1.17 (d, $J_{H,H}$ = 7.12 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 214.5, 139.2, 138.4, 133.3, 128.7, 42.3, 21.1, 19.7, 18.1. IR (KBr): ν_{CO} 1694 cm^{-1}. GC−MS (M^+): 190.2.

*2-Methyl-1-(naphthalen-2-yl)propan-1-one (**11**).*[21] The compound was prepared from 1-(naphthalen-2-yl)ethanone (68 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a white solid (67 mg, 85% isolated yield). For a 6 mmol scale, the reaction isolated yield was 75% (0.89 g). ^1H NMR (500 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.03 (dd, $J_{H,H}$ = 8.60, 1.65 Hz, 1H), 7.96 (d, $J_{H,H}$ = 8.00 Hz, 1H), 7.90−7.86 (m, 2H), 7.60−7.52 (m, 2H), 3.73 (sept, $J_{H,H}$ = 6.85 Hz, 1H), 1.28 (d, $J_{H,H}$ = 6.85 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 204.6, 135.7, 133.7, 132.8, 129.8, 129.7, 128.6, 128.4, 127.9, 126.8, 124.5, 35.6, 19.5. IR (KBr): ν_{CO} 1678 cm^{-1}. GC−MS (M^+): 198.2.

*2,4-Dimethyl-1-phenylpentan-3-one (**12**).*[20] The compound was prepared from 4-phenylbutan-2-one (59 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (68 mg, 90% isolated yield). ^1H NMR (500 MHz, $CDCl_3$): δ 7.26−7.23 (m, 2H), 7.18−7.15 (m, 1H), 7.13 (d, $J_{H,H}$ = 7.05 Hz, 2H), 3.00−2.92 (m, 2H), 2.56−2.48 (m, 2H), 1.08 (d, $J_{H,H}$ = 6.70 Hz, 3H), 1.01 (d, $J_{H,H}$ = 6.95 Hz, 3H), 0.87 (d, $J_{H,H}$ = 6.85 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 217.9, 140.2, 129.2, 128.5, 126.3, 46.7, 40.5, 39.7, 18.2, 17.9, 17.3. IR (KBr): ν_{CO} 1711 cm^{-1}. GC−MS (M^+): 190.2.

*1-Benzo-(1,3)-dioxol-5-yl-2,4-dimethylpentan-3-one (**13**).* The compound was prepared from 4-benzo-(1,3)-dioxol-5-yl-butan-2-one (77 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (88 mg, 94% isolated yield). ^1H NMR (500 MHz, $CDCl_3$): δ 6.69 (d, $J_{H,H}$ = 7.85 Hz, 1H), 6.61 (s, 1H), 6.56 (dd, $J_{H,H}$ = 7.90, 1.25 Hz, 1H), 5.89 (d, $J_{H,H}$ = 0.90 Hz, 2H), 2.95−2.82 (m, 2H), 2.54−2.43 (m, 2H), 1.05 (d, $J_{H,H}$ = 7.85 Hz, 3H), 1.01 (d, $J_{H,H}$ = 0.85 Hz, 3H), 0.89 (d, $J_{H,H}$ = 6.85 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 217.9, 147.6, 146.0, 133.9, 122.0, 109.5, 108.2, 100.9, 46.8, 40.6, 39.4, 18.1, 17.9, 17.2. IR (KBr): ν_{CO} 1709 cm^{-1}. GC−MS (M^+): 234.2. HRMS (ESI-TOF): calcd for $C_{14}H_{19}O_3$ $[M + H]^+$, 235.1329; found, 235.1331.

*2-Methyl-1-(9-methyl-9H-fluoren-2-yl)propan-1-one (**14**).* The compound was prepared from 1-(9*H*-fluoren-2-yl)ethanone (83 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a colorless oil (80 mg, 80% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 8.00 (dd, $J_{H,H}$ = 7.96, 1.28 Hz, 1H), 7.81−7.79 (m, 2H), 7.54−7.53 (m, 1H), 7.41−7.36 (m, 2H), 4.00 (q, $J_{H,H}$ = 7.44 Hz, 1H), 3.65 (sept, $J_{H,H}$ = 6.92 Hz, 1H), 1.56 (d, $J_{H,H}$ = 7.40 Hz, 3H), 1.26 (d, $J_{H,H}$ = 6.76 Hz, 6H). $^{13}C\{^1H\}$ NMR (100

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MHz, $CDCl_3$): δ 204.5, 150.4, 149.3, 145.2, 139.5, 135.0, 128.3, 128.0, 127.4, 124.4, 124.1, 120.9, 119.8, 42.6, 35.5, 19.5, 19.5, 18.1. IR (KBr): ν_{CO} = 1678 cm^{-1}. GC−MS (M^+): 250.2. HRMS (APCI-TOF): calcd for $C_{18}H_{19}O$ $[M + H]^+$, 251.1430; found, 251.1436.

2-Methyl-1-(4-(methylamino)phenyl)propan-1-one (**15**).[51] The compound was prepared from 1-(4-aminophenyl)ethanone (66 mg, 0.4 mmol) following general procedure P. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 9:1) and obtained as a light-yellow oil (56 mg, 80% isolated yield). ^1H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, $J_{H,H}$ = 8.65 Hz, 2H), 6.56 (d, $J_{H,H}$ = 8.75 Hz, 2H), 3.48 (sept, $J_{H,H}$ = 6.70 Hz, 1H), 2.88 (s, 3H), 1.18 (d, $J_{H,H}$ = 6.80 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 202.9, 153.1, 130.9, 125.3, 111.3, 34.5, 30.2, 19.6. IR (KBr): ν_{CO} 1652 cm^{-1}. GC−MS (M^+): 177.1.

3-Methyl-1H-indole (**16**).[52] The compound was prepared from 1*H*-indole (47 mg, 0.4 mmol) following general procedure Q. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 4:1) and obtained as a white solid (51 mg, 97% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (brs, 1H), 7.62 (d, $J_{H,H}$ = 7.76 Hz, 1H), 7.35 (d, $J_{H,H}$ = 8.04 Hz, 1H), 7.22 (td, $J_{H,H}$ = 6.88, 1.00 Hz, 1H), 7.15 (td, $J_{H,H}$ = 7.88, 1.12 Hz, 1H), 6.96 (s, 1H), 2.36 (d, $J_{H,H}$ = 1.04 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.4, 128.4, 122.0, 121.7, 119.2, 119.0, 111.8, 111.1, 9.8. GC−MS (M^+): 131.1.

5-Methoxy-3-methyl-1H-indole (**17**).[52] The compound was prepared from 5-methoxy-1*H*-indole (59 mg, 0.4 mmol) following general procedure Q. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 4:1) and obtained as a white solid (62 mg, 97% isolated yield). For a 6 mmol scale reaction, the isolated yield was 90% (0.87 g). ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (brs, 1H), 7.23 (d, $J_{H,H}$ = 8.68 Hz, 1H), 7.03 (d, $J_{H,H}$ = 2.40 Hz, 1H), 6.94 (s, 1H), 6.88 (dd, $J_{H,H}$ = 8.68, 2.44 Hz, 1H), 3.89 (s, 3H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.0, 131.6, 128.7, 122.6, 112.2, 111.8, 111.5, 100., 56.1, 9.8. GC−MS (M^+): 161.2.

6-Chloro-3-methyl-1H-indole (**18**).[52] The compound was prepared from 6-chloro-1*H*-indole (60 mg, 0.4 mmol) following general procedure Q. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 4:1) and obtained as a white solid (62 mg, 95% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (brs, 1H), 7.48 (d, $J_{H,H}$ = 8.52 Hz, 1H), 7.31 (d, $J_{H,H}$ = 1.48 Hz, 1H), 7.10 (dd, $J_{H,H}$ = 8.52, 1.36 Hz, 1H), 6.94 (s, 1H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.7, 128.0, 127.1, 122.3, 120.0, 119.9, 112.1, 111.0, 9.7. GC−MS (M^+): 165.1.

5-Bromo-3-methyl-1H-indole (**19**).[52] The compound was prepared from 5-bromo-1*H*-indole (78 mg, 0.4 mmol) following general procedure Q. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 4:1) and obtained as a brown solid (67 mg, 80% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (brs, 1H), 7.70 (d, $J_{H,H}$ = 1.68 Hz, 1H), 7.27−7.25 (m, 1H, including $CDCl_3$ peak), 7.20 (d, $J_{H,H}$ = 8.56 Hz, 1H), 6.96 (s, 1H), 2.29 (d, $J_{H,H}$ = 1.08 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 134.9, 130.2, 124.8, 123.0, 121.7, 112.5, 111.6, 9.7. GC−MS (M^+): 210.1.

2,3-Dimethyl-1H-indole (**20**).[52] The compound was prepared from 2-methyl-1*H*-indole (52 mg, 0.4 mmol) following general procedure Q. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 4:1) and obtained as a brown solid (55 mg, 96% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (brs, 1H), 7.51 (d, $J_{H,H}$ = 6.88 Hz, 1H), 7.26−7.24 (m, 1H, including $CDCl_3$ peak), 7.16−7.09 (m, 2H), 2.35 (s, 3H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 135.7, 131.7, 129.5, 120.4, 118.4, 117.8, 110.7, 105.47, 11.7, 8.8. GC−MS (M^+): 145.1.

3-Methyl-2-phenyl-1H-indole (**21**).[52] The compound was prepared from 2-phenyl-1*H*-indole (77 mg, 0.4 mmol) following general procedure Q. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 4:1) and obtained as a white solid (78 mg, 94% isolated yield). ^1H NMR (400 MHz, DMSO- d_6): δ 11.14 (brs, 1H), 7.67 (d, $J_{H,H}$ = 7.84 Hz, 2H), 7.51−7.45 (m, 3H), 7.37−7.30 (m, 2H), 7.11 (t, $J_{H,H}$ = 6.88 Hz, 1H), 7.01 (t, $J_{H,H}$ = 7.36 Hz, 1H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 136.5, 134.3, 133.7, 130.0, 129.2, 128.0, 127.5, 122.1, 119.1, 119.0, 111.6, 107.3, 10.4. GC−MS (M^+): 207.1.

2-Phenylpropanenitrile (**24**).[21] The compound was prepared from 2-phenylacetonitrile (47 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (49 mg, 95% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.40−7.29 (m, 5H), 3.90 (q, $J_{H,H}$ = 7.28 Hz, 1H), 1.64 (d, $J_{H,H}$ = 7.28 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 137.2, 129.2, 128.1, 126.8, 121.7, 31.3, 21.5. GC−MS (M^+): 131.1.

2-p-Tolylpropanenitrile (**25**).[53] The compound was prepared from 2-*p*-tolylacetonitrile (52 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (52 mg, 90% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.24−7.17 (m, 4H), 3.86 (q, $J_{H,H}$ = 7.28 Hz, 1H), 2.34 (s, 3H), 1.62 (d, $J_{H,H}$ = 7.28 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 138.0, 134.2, 129.9, 126.7, 121.9, 31.0, 21.6, 21.2. GC−MS (M^+): 145.1.

2-(4-Methoxyphenyl)propanenitrile (**26**).[21] The compound was prepared from 2-(4-methoxyphenyl)acetonitrile (59 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a light-yellow oil (58 mg, 90% isolated yield). For a 6 mmol scale reaction, the isolated yield was 82% (0.79 g). ^1H NMR (400 MHz, $CDCl_3$): δ 7.27−7.23 (m, 2H, including $CDCl_3$ peak), 6.91−6.87 (m, 2H), 3.85 (q, $J_{H,H}$ = 7.28 Hz, 1H), 3.79 (s, 3H), 1.61 (d, $J_{H,H}$ = 7.32 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.4, 129.2, 127.9, 122.0, 114.6, 55.5, 30.6, 21.6. GC−MS (M^+): 161.1.

2-(4-Fluorophenyl)propanenitrile (**27**).[54] The compound was prepared from 2-(4-fluorophenyl)acetonitrile (54 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a light-yellow oil (54 mg, 91% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33−7.30 (m, 2H), 7.07−7.04 (m, 2H), 3.89 (q, $J_{H,H}$ = 7.25 Hz, 1H), 1.62 (d, $J_{H,H}$ = 7.35 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.4, 161.5, 133.0, 129.8 (d, *J* = 8.7 Hz), 128.6 (d, *J* = 7.5 Hz), 121.5, 116.3 (d, *J* = 20.0 Hz), 30.7, 21.6. GC−MS (M^+): 149.1.

2-(4-Bromophenyl)propanenitrile (**28**).[55] The compound was prepared from 2-(4-bromophenyl)acetonitrile (78 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a light-yellow oil (80 mg, 96% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, $J_{H,H}$ = 8.48 Hz, 2H), 7.23 (d, $J_{H,H}$ = 8.40 Hz, 2H), 3.86 (q, $J_{H,H}$ = 7.28 Hz, 1H), 1.62 (d, $J_{H,H}$ = 7.28 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 136.2, 132.4, 128.5, 122.2, 121.1, 30.9, 21.4. GC−MS (M^+): 209.0.

2-(3-Chlorophenyl)propanenitrile (**29**).[56] The compound was prepared from 2-(3-chlorophenyl)acetonitrile (60 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (62 mg, 94% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34−7.22 (m, 4H, including $CDCl_3$ peak), 3.87 (q, $J_{H,H}$ = 7.28 Hz, 1H), 1.63 (d, $J_{H,H}$ = 7.28 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.0, 135.1, 130.5, 128.4, 127.1, 125.0, 121.0, 31.0, 21.3. GC−MS (M^+): 165.1.

2-(2-Methoxyphenyl)propanenitrile (**30**).[57] The compound was prepared from 2-(2-methoxyphenyl)acetonitrile (59 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 49:1) and obtained as a colorless oil (52 mg, 81% isolated yield). ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (dd, $J_{H,H}$ = 7.68, 1.60 Hz, 1H), 7.29 (td, $J_{H,H}$ = 7.80, 1.64 Hz, 1H), 6.98 (td, $J_{H,H}$ = 7.48, 1.00 Hz, 1H), 6.90 (d, $J_{H,H}$ = 7.96 Hz, 1H), 4.25 (q, $J_{H,H}$ = 7.20 Hz, 1H), 3.85 (s, 3H), 1.58 (d, $J_{H,H}$ = 7.08 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 156.2, 129.4, 127.7, 125.5, 122.1, 121.1, 110.9, 55.6, 25.7, 19.6. GC−MS (M^+): 161.1.

2-(Pyridin-3-yl)propanenitrile (**31**).[58] The compound was prepared from 2-(pyridin-3-yl)acetonitrile (47 mg, 0.4 mmol) following general procedure R. The title product was isolated by column

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chromatography (*n*-hexane/EtOAc: 9:1) and obtained as a yellow oil (34 mg, 65% isolated yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58−8.55 (m, 2H), 7.72 (dt, $J_{H,H}$ = 8.00, 1.92 Hz, 1H), 7.32 (dd, $J_{H,H}$ = 7.92, 4.88 Hz, 1H), 3.94 (q, $J_{H,H}$ = 7.32 Hz, 1H), 1.65 (d, $J_{H,H}$ = 7.32 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.5, 148.2, 134.4, 133.0, 124.0, 120.6, 29.1, 21.3. GC−MS (M^+): 132.1.

*2-(Thiophen-2-yl)propanenitrile (**32**).*[59] The compound was prepared from 2-(thiophen-2-yl)acetonitrile (49 mg, 0.4 mmol) following general procedure R. The title product was isolated by column chromatography (*n*-hexane/EtOAc: 19:1) and obtained as a light-yellow oil (38 mg, 70% isolated yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (dd, $J_{H,H}$ = 5.15, 1.25 Hz, 1H), 7.07 (dt, $J_{H,H}$ = 3.45, 0.95 Hz, 1H), 6.97 (dd, $J_{H,H}$ = 5.15, 3.50 Hz, 1H), 4.17 (q, $J_{H,H}$ = 7.55 Hz, 1H), 1.73 (d, $J_{H,H}$ = 7.35 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 139.4, 127.2, 125.7, 125.5, 120.8, 26.7, 21.6. GC−MS (M^+): 137.1.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00376.

Detail reaction optimization, control experiments, reaction kinetics, and NMR spectra of all compounds (PDF)

FAIR data, including the primary NMR FID files, for compounds **A**, **B**, **1**−**3**, **3i$_1$**, **3i$_2$**, **3i$_3$**, **4**−**21**, and **24**−**32** (ZIP)

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Notes

The authors declare no competing financial interest.

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