JOC The Journal of Organic Chemistry

Article

Iron-Catalyzed Ligand Free #-Alkylation of Methylene Ketones and #-Alkylation of Secondary Alcohols Using Primary Alcohols

Anitha Alanthadka, Sourajit Bera, and Debasis Banerjee

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01600 • Publication Date (Web): 09 Aug 2019

Iron-Catalyzed Ligand Free α-Alkylation of Methylene Ketones and β-Alkylation of Secondary Alcohols Using Primary Alcohols

Anitha Alanthadka,[†] Sourajit Bera,[†] and Debasis Banerjee*

Department of Chemistry, Laboratory of Catalysis and Organic Synthesis, Indian Institute of Technology Roorkee, Roorkee 247667, Uttarakhand, India. E-mail: dbane.fcy@iitr.ac.in

ABSTRACT: Herein, we demonstrated a general and broadly applicable catalytic cross coupling of methylene ketones and secondary alcohols with a series of primary alcohols to di-substituted branched ketones. A simple and non-precious $Fe_2(CO)_9$ catalyst enables one-pot oxidations of both primary and secondary alcohols to a range of branched gem-bis(alkyl) ketones. A number of bond activation and formation selectively happened in one pot to provide the ketone products. Coupling reactions could be performed in gram scale and successfully applied in the synthesis of Alzehimer's drug. Alkylation of steroid hormone could be achieve. A single catalyst enables sequential one-pot double alkylation to bis-hetero aryl ketones using two different alcohols. Preliminary mechanistic studies using IR-probe, deuterium labeling and kinetic experiments established the participation of borrowing-hydrogen process using Fe-catalyst and the reaction produces H_2 and H_2O as by products.

KEYWORDS. *Iron • gem-Bis(alkyl) Ketones • α-Alkylation • Hydrogen Borrowing Strategy • Base Metal Catalysis• Renewable alcohols*

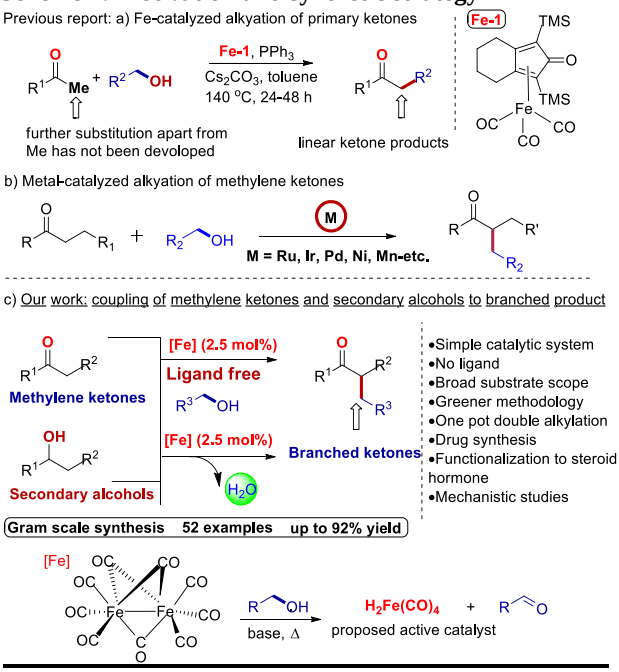
INTRODUCTION

Transition-metal catalyzed C-C bond formation represents one of the most fundamental organic transformations. In this context, enolate alkylation have been utilized as a convenient approach to access branched ketones.[1] Though, several indirect approaches have been established for such α,α-di-substituted branched products, often required multi-step synthesis, expensive alkyl halides in combination with highly acidic or basic conditions and generates stoichiometric halide waste. However, direct utilization of readily available biomass derived renewable alcohols for such alkylation process represents one of the most sustainable approach releasing water as byproduct.[2,3] Nevertheless, to date, often alkylation of ketone enolates using alcohols are limited to the linear ketone products;[4] however direct access to branched ketones utilizing enolate alkylation remains a challenging goal and much less developed (Scheme 1).

α,α-Di-substituted branched ketones are an integral part of many bioactive molecules and used as important building blocks in organic synthesis.[1]

Surprisingly, only a handful examples are known for such geminal di-substituted ketones (Scheme 1b).[5, 13b-c] In this direction, notable breakthrough by Donohoe and co-workers have reported an iridium catalyzed phosphine ligated system, which interrupt the HB process and enables addition of various pro-nucleophiles to the intermediate enone to branched products.[5a] Interestingly, in a recent contribution they have also demonstrated Ir-catalyzed strategy for alkylation of α-substituted methylene ketones. However, use of ortho-substituted phenyl and cyclopropyl ketones in combination with KOH is the key to success.[5b] More recently, Glorius and co-workers have reported an impressive Ru/NHC-catalyzed system for α,α-di-substituted ketones using primary alcohols in presence of lithium base.[5c] Nevertheless, homogeneous Ru-,[5d] and Ir-based catalysts,[5e] as well as reusable Pd-nano-catalysts,[5f-h] and Ag/Mo-oxide,[5i] are known for α,α-di-substituted ketones using primary alcohols. Notably, very recently, we have also demonstrated non-precious Ni-,[13b] and Mn-based catalysts,[13c] for the synthesis of branched ketones using primary alcohols. However, to the best of our knowledge, applications of the first row transition metals, in particular, iron-based catalysts for such applications remain elusive.[6] Surprisingly, till date, another important synthetic route, alkylation of β-substituted secondary alcohols using primary alcohols for the synthesis of α,α-di-substituted branched ketones has not been realized using transition metal catalysts. More specifically, herein for the first time we report a general and broadly applicable Fe-catalyzed alkylation of methylene ketones and β-substituted secondary alcohols using primary alcohols following borrowing hydrogen approach.

Scheme 1: Motivation and synthetic strategy



(a) Iron-catalyzed synthesis of linear ketones. (b) Metal-catalyzed alkylation to methylene ketones. (c) Fe-catalyzed coupling of methylene ketones and secondary alcohols with primary alcohols.

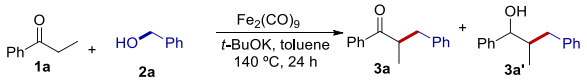
Since, last decades there has been significant drive for the utilization of iron catalysts in cross-coupling reactions,[7] transfer hydrogenations,[8] Lewis acid catalyzed transformations,[9] as well as in kinetic resolutions and for cycloisomerizations.[10] One such

iron-catalyst widely used in catalytic transformations is Knölker-type catalyst (Scheme 1a).[11] Active catalyst, could be generated using trimethylamine N-oxide (Me_3NO) as an activator. Nevertheless, such cyclopentadienyl-based iron-catalysts required multi-step synthesis process and their highly expensive nature are often major concern in comparison to the inexpensive metal-salts. Further, special care are necessary for handling and storing of these catalysts under standard laboratory conditions. In this direction, recent report for enolate alkylation catalyzed by Knölker-type complex Fe-1 is noteworthy (Scheme 1a).[12] However, still there is a need to develop a more general, inexpensive and radially accessible catalytic system and their applications for challenging synthetic strategy to di-substituted branched ketones using Fe-catalyst (Scheme 1c).

RESULTS AND DISCUSSION

Recently, selective alkylation of ketones using primary alcohols have been developed by our laboratory using commercially available manganese and nickel-catalysts in combination with bench stable nitrogen ligands.[13b-d] However, cross-couplings of two different alcohols (secondary and primary alcohols) to geminal-di-substituted ketones remain unknown. The major challenges associated with cross-couplings of secondary alcohols are: i) self-Aldol-coupling to undesire side products and ii) diminishes atom-economy of the process. More importantly, synthesis of α,α-di-substituted branched ketones through cross-couplings of secondary and primary alcohols comprises one pot four steps transformations; dehydrogenation of alcohols to carbonyls, Aldol condensations of carbonyls to enones, hydrogenation of enones and finally dehydrogenation to the desired ketones. Herein, for the first time we demonstrated the catalytic cross coupling of two different alcohols using highly abundant and inexpensive Fe-catalyst. The catalytic process does not need any special ligand and liberated water and dihydrogen as side products.

Table 1. Optimization studies for Fe-catalyzed alkylation[a]

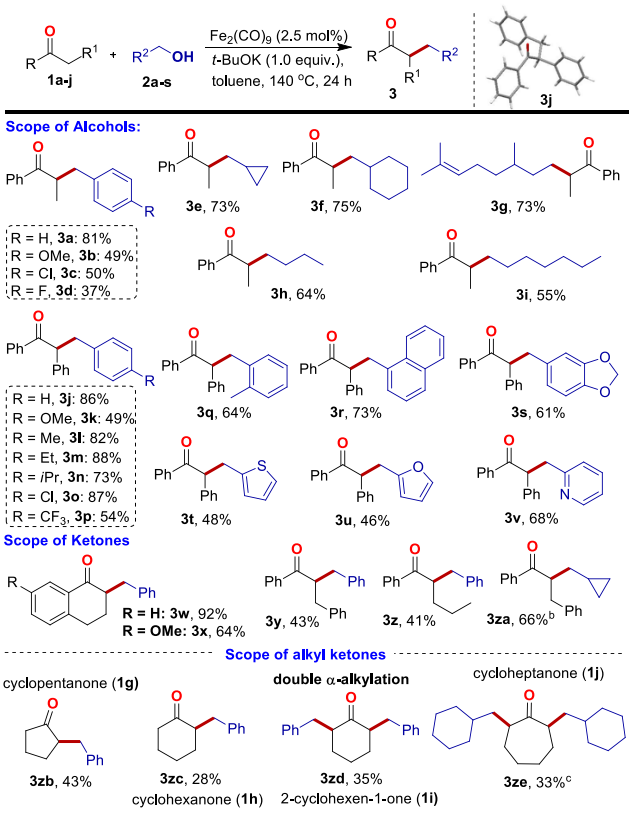


Entry	Deviations from standard conditions	3a (%)	Ratio 3a/3a'
1	None	87 (81)	>18:1
2	$Fe(OAc)_2$ (5)	39	0.9:1
3	$Fe(acac)_3$ (5)	35	0.6:1
4	*t*-BuONa	47	1.7:1
5	Na_2CO_3	6	-
6	K_2CO_3	9	-
7	K_3PO_4	5	-
8	*p*-Xylene	43	1.3:1
9	*t*-Amyl alcohol	62	2.5:1
10	No Base	8	-
11	No Catalyst	24	0.6:1
12	130 °C	67	2.6:1

Reaction conditions: [a]Propiophenone **1a** (0.5 mmol), benzyl alcohol **2a** (0.625 mmol), $Fe_2(CO)_9$ (2.5 mol%), *t*-BuOK (0.5 mmol), toluene (2.0 mL), Schlenk tube under N_2 atmosphere at 140 °C in oil bath for 24 h reaction time. [b]Isolated yield in parenthesis (average of two run). Conversions were determined using GC-MS.

Our initial studies for the α-alkylation were perform using propiophenone **1a** with benzyl alcohol **2a** in combination with iron catalysts having variable oxidation states (0, II or III). Pleasingly, branched ketones **3a** was obtained in 81% isolated yield with >18:1 selectivity (Table 1, entries 1-3). Nevertheless, small amount of reduced alcohol **1a'**, enone **3a"** and trace amount of self-couple product of **1a** was detected in GC-MS analysis of the reaction mixture (Table 1). Under identical conditions, efficiency of different bases such as, *t*-BuONa, Na_2CO_3, K_2CO_3 and K_3PO_4 were examine and resulted only moderate to poor product conversions (Table 1, entries 4-7). Further, influence of different solvents (xylene and *t*-amylalcohol) did not improve any product yields and selectivity to **3a** (Table 1, entries 8-9 and SI Table S1-S5). Notably, control experiments in absence of base and without catalyst as well as lowering reaction temperature to 130 °C drastically diminished the product yields, revealed the potential role of the individual component to achieve higher yield and selectivity (Table 1, entries 10-12 and Supporting Information Table S1-S5). However, in absence of catalyst we observed 24% conversion to product **3a**. At this point, we believe that, in the presence of a base, alkoxide might form with alcohol, followed by the reaction with corresponding ketone or ketone enolate, and resulted the formation of enone-intermediate. Nevertheless, as the reaction was performed in the closed system, at higher temperature base-mediated Meerwein–Ponndorf–Verley reduction might results the formation of 24% conversion to product in absence of catalyst along with others side reactions. However, a more detailed mechanism could be the future scope of the work.

Scheme 2. Catalytic cross-coupling of methylene ketones with primary alcohols.

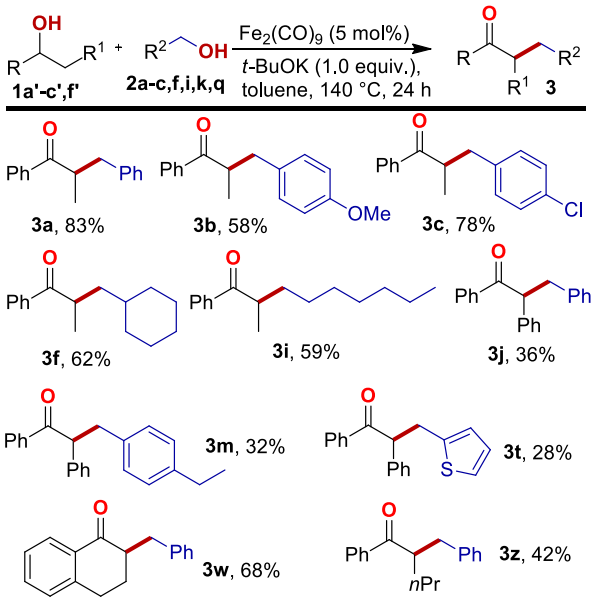


Reaction conditions: [a]Ketone **1** (0.5 mmol), primary alcohol **2** (0.625 mmol), $Fe_2(CO)_9$ (2.5 mol%), *t*-BuOK (0.5 mmol), toluene (2.0 mL), Schlenk tube under N_2 atmosphere, 140 °C oil bath, 24 h reaction time. Isolated yield reported. [b]36 h reaction time. [c]$Fe_2(CO)_9$ (5 mol%), *t*-BuOK (1.0 mmol), 36 h reaction time.

Thereafter, having the optimized conditions, the scope of methylene ketones were tested using a range benzyl, hetero-aryl as well as alkyl primary alcohols and presented in Scheme 2. Primarily, propiophenone **1a** subjected to the alkylation with benzyl alcohols decorated with –OMe, Cl or F-substitution in aryl ring and efficiently transformed to a series of di-substituted ketones **3b-3d** in up to 50% yield. Interestingly, when more challenging cyclopropyl methanol **2e** and cyclohexyl methanol **2f** were employed, the desired α,α-di-alkyl ketones **3e-3f** were obtained in 73-75% yield respectively (Scheme 2). Notably, we studied the performance of readily abundant n-butanol **2h**, n-heptanol **2i** including renewable terpenoid intermediate citronellol **2g** with **1a,** and the di-alkyl branched ketones **3g-3i** were obtained in up to 73% yield without affecting the reducible double bond in **3g**. Next, we investigated the scope of sterically hindered 1,2-diphenylethanone **1b** with benzyl alcohols having electronically different (methoxy, alkyl, chloro as well as trifluoromethyl) substituents at the aryl ring and the desired branched ketones **3j-3p** were isolated in 49-88% yield respectively (Scheme 2). Gratifyingly, sterically demanding 2-methylbenzylalcohol **2n** and 1-naphthyl methanol **2o** effectively participated to provide **3q** and **3r** in 64% and 73% yield respectively. Notably, application of hetero-aryl alcohols, such, as, 1,3-dioxolone substituted benzylalcohol **2p**, 2-thiophenemethanol **2q**, 2-furfurylmethanol **2r** as well as 2-pyridinemethanol **2s** resulted the desired hetero-aryl substituted ketones **3s-3v** in moderate yields. It is to be noted that, tetralone **1c**, 6-methoxytetralone **1d**, 1,3-diphenylpropiophenone **1e** as well as valerophenone **1f** showed promising activity and converted to the desired branched products **3w-3z** and **3za** in moderate to excellent isolated yields (Scheme 2). Further, to establish the general applicability, alkyl ketones, such as, cyclopentanone **1g** and cyclohexanone **1h** were reacted with benzylalcohol **1a** and the desired 2-benzylketones **3zb** and **3zc** were obtain in up to 43% yield (Scheme 2). When using 2-cyclohene-1-one **1i** as coupling partner with **1a**, 2,6-bis-alkylated ketone **3zd** was obtained in 35% yield (Scheme 2). Remarkably, cycloheptanone **1j** could efficiently couple with cyclohexyl methanol **2f** to the desire product **3ze**. These examples, using alkyl ketones with aryl as well as alkyl alcohols highlights the potential applications of the present methodology beyond aryl-methyl or aryl-alkyl ketones reported till date.

Further, we turned our attention to establish the general applicability of the catalytic protocol towards cross coupling between secondary and primary alcohols. A one-pot four-step process demonstrated the synthesis of α,α-di-substituted ketones in moderate to excellent yields (Scheme 3). The alkylation worked well when 1-phenyl-1-propanol **1a'** employed with electronically different benzyl alcohols and resulted **3a-3c** in 58-83% isolated yields (Scheme 3). Next, applications of aliphatic primary alcohols, such as, cyclohexylmethanol **2f** and *n*-heptanol **2i** proceeded equally well, giving 59-62% yield of **3f** and **3i**. Again, the reaction of 1,2-diphenylethanol **1b'**, resulted moderate product yields due to strong steric interaction (Scheme 3, **3j**, **3m**, and **3t**). 1-Tetralol **1c'** and 1-phenyl-1-pentanol **1f'** were also employed with benzyl alcohol and resulted **3w** and **3z** in 68% and 42% yield respectively (Scheme 3).

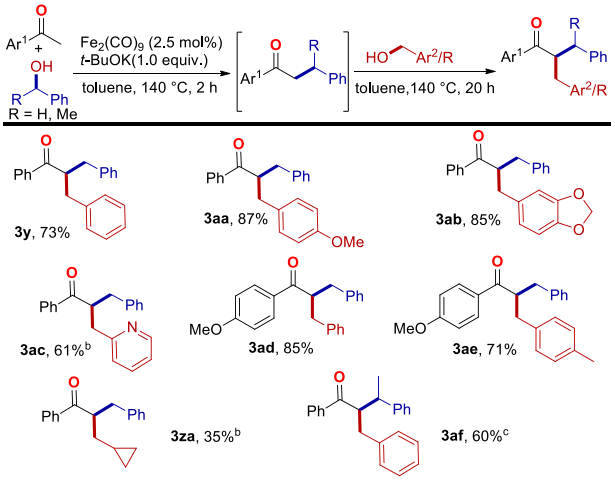
Scheme 3. Catalytic cross coupling of secondary alcohols with primary alcohols.



Reaction conditions: [a]Secondary alcohol **1'** (0.5 mmol), primary alcohol **2** (0.625 mmol), $Fe_2(CO)_9$ (5 mol%), *t*-BuOK (0.5 mmol), toluene (2.0 mL), Schlenk tube under N_2 atmosphere, 140 °C in an oil bath for 24 h reaction time. Isolated yield reported.

Thereafter, we focused our studies for the one-pot sequential double alkylation of acetophenone derivatives using primary and secondary alcohols (Scheme 4). Initially, acetophenone and 4-methoxyphenyl acetophenone were examine using a range of aryl, heteroaryl including alkyl primary alcohols to the linear ketones products. Remarkably, our optimized catalytic protocol was highly selective for mono-alkylation in the first step, followed by in situ addition of another alcohol furnished the desired di-substituted ketones in up to 87% yield (**3y** and **3aa-3ae)** (Scheme 4). Notably, cyclopropyl methanol **1e** as well as 1-phenylethanol, proceeded smoothly to the desired ketones **3za** and **3af** (Scheme 4).

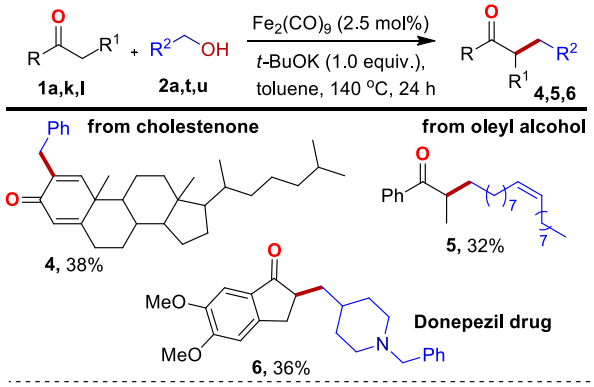
Scheme 4. Sequential one-pot double alkylation.



Reaction conditions: [a]Acetophenone (0.5 mmol), alcohol **2** (0.5 mmol), $Fe_2(CO)_9$ (2.5 mol%), *t*-BuOK (0.5 mmol), toluene (2.0 mL), Schlenk tube under N_2 atmosphere, 140 °C oil bath. After 2 h another alcohol **2** (0.5 mmol) was added under N_2 atmosphere, 140 °C oil bath, 20 h, [b]Second step reaction was carried out for 24 h, [c]First step reaction was carried out for 4 h and second step for 24 h. Isolated yield reported.

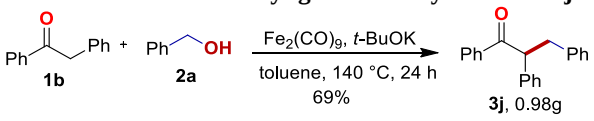
After witnessing the excellent efficiency, we focused to the potential synthetic applications for the present Fe-catalyzed process. For instance, alkylation of 4-cholesten-3-one **1k** with benzyl alcohol **2a** resulted the alkylated product **4** in 38% yield (Scheme 6). It is anticipated that, the condensation product was not reduced under the reaction conditions, instead a double bond isomerization took place. The resulted double bond isomerization product is more stable due to substituted quinone framework and resist the reduction process, hence product **4** is dominated. Notably, we have also observed trace amount of another unidentified products. Again, when using fatty acid derived oleyl alcohol as coupling partner with propiophenone **1a**, chain elongated di-alkylated ketone **5** was obtained in moderate yield. Nevertheless, the catalytic process worked well for one-pot synthesis of donepezil **6,** extensively used for the treatment of Alzheimer's disease.[14] These interesting chemo-selective applications represent the synthetic potential of the catalytic process and sustained well without much affecting the reducible cholestenone as well as fatty acid framework (Scheme 5). In all these complex products (**4**-**6**) low yields were observe due to the presence of unreacted starting materials (25-30%) along with the undesired side products (20-30%).

Scheme 5. Synthetic utility.



Reaction conditions: [a]Ketone **1** (0.25 mmol), primary alcohol **2** (0.3125 mmol), $Fe_2(CO)_9$ (2.5 mol%), *t*-BuOK (0.25 mmol), toluene (2.0 mL), Schlenk tube under N_2 atmosphere, 140 °C oil bath, 36 h reaction time. Isolated yield reported.

Scheme 6. Practical utility: gram scale synthesis of 3j.



Reaction condition: [a]Deoxybenzoin **1b** (1 g, 5.1 mmol), benzyl alcohol **2a** (0.69 g, 6.38 mmol), $Fe_2(CO)_9$ (47 mg, 2.5 mol%), *t*-BuOK (572 mg, 5.1 mmol), toluene (10 mL) in a Schlenk tube under N_2 atmosphere at 140 °C in an oil bath for 24 h.

Notably, herein we established a general catalytic protocol proceeded well in the presence of benzyl alcohols decorated with halides (F and Cl), methoxy, alkyl, trifluoromethyl and 1,3-dioxolone moiety. Heteroaryl alcohols, such as, thiophene, furan and pyridine groups is tolerated. Interestingly, more challenging, long chain, C4-C10 alkyl alcohols efficiently utilized for the alkylation process. Similarly, a variety of methylene ketones, having aryl-alkyl framework, secondary alcohols as well as alkyl ketones efficiently participated under the optimized protocol. Importantly, cholestenone and oleyl alcohol having reducible functional group (steroid framework and terminal alkene) represents the potential of the present catalytic protocol. For a practical utility the present Fe-catalyzed protocol worked efficiently when a gram scale reaction was performed using deoxybenzoin **1b** with benzylalcohol **2a**. Gratifyingly, **3j** was obtain in 69% yield (Scheme 6). However, applications of benzyl alcohols bearing nitro and cyano groups, cinnamyl alcohol, propagyl alcohol, diols as well as amino alcohols were not successful and we observed only trace or no product conversion to the desired products (SI, Scheme S12). Again, in case of 2-indanone, isophorone as well as other linear ketones we observed albeit with poor product conversions (SI, Scheme S12).

Further, to interrogate the reaction mechanism and to gain insight about the active Fe-species for the alkylation process, initially we investigated the reaction using IR probe to analyze the actual changes associated with CO ligand frequency during the progress of the reactions. The pre-catalyst $Fe_2(CO)_9$ was identified by two characteristic signals at 2015 cm^{-1} and 1823 cm^{-1} respectively, which could be attributed as terminal CO and bridged CO ligand frequency.[11a] However, the CO ligand frequency at 1823 cm^{-1} was disappeared when the pre-catalyst $Fe_2(CO)_9$ was heated at 140 ^{0}C for 1 h using benzyl alcohol **2a** and *t*-BuOK in toluene. Nevertheless, one signal at 1635 cm^{-1}, characteristic peak for benzaldehyde, was detected using IR probe (SI, Scheme S10). We anticipated that, under thermal reaction pre-catalyst $Fe_2(CO)_9$ converted to a transient 16-electron species $Fe(CO)_4$ with a vacant coordination site, which thereafter bind with benzyl alcohol **2a** and resulted the intermediate iron-alkoxy species **Fe-2**.[8a] Subsequently, base mediated β-hydride elimination of species **Fe-2** resulted the formation of benzaldehyde and $H_2Fe(CO)_4$, responsible for hydrogenation process (Figure 1).[11f]

Figure 1: IR-probe studies for the detection of intermediate Fe-species.

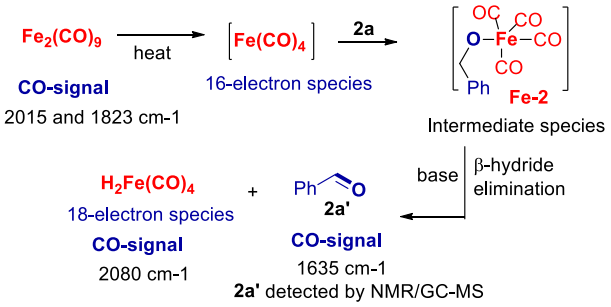
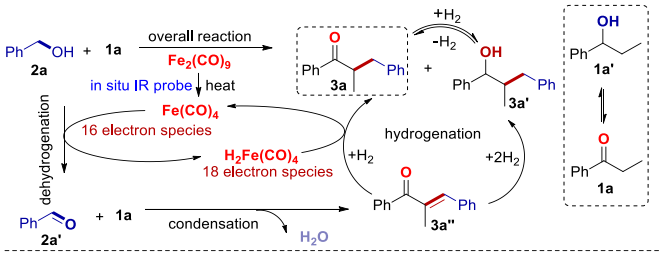
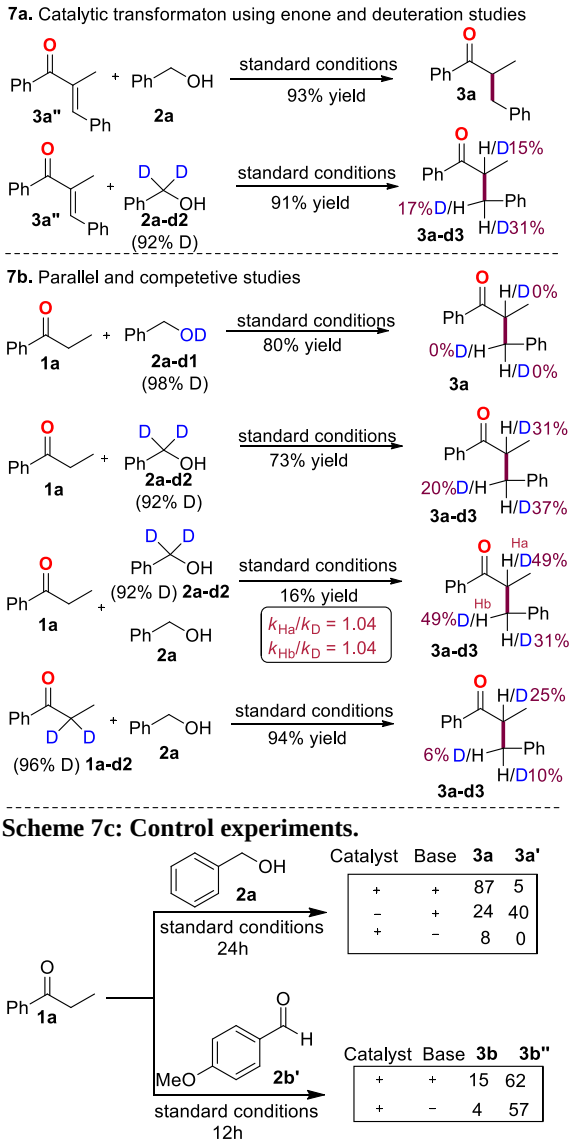


Figure 2: Plausible mechanism for the Fe-catalyzed synthesis of branched ketones and alcohols.



Scheme 7. Catalytic and mechanistic studies.



Scheme 7c: Control experiments.

Reaction condition: All mechanistic studies were performed using **1a** or **3a"** with (0.1 mmol).

Based on the initial findings through IR probe, NMR including GC-MS studies (Figure 1) and related literature reports,[8-9, 11f, 12] herein we proposed a plausible reaction mechanism for the synthesis of branched ketones using Fe-catalyst (Figure 2). Primarily, Fe-catalyzed dehydrogenation of primary alcohols **2a** resulted benzaldehyde **2a'**. Next, base mediated condensation with propiophenone **1a** gave α,β-unsaturated ketone **3a"**. Thereafter, selective hydrogenation of enone **3a"** by *in situ* generated $H_2Fe(CO)_4$ species resulted the desired α,α-di-substituted ketones **3a**. However, **3a** could also be produced *via* a reversible process from alcohol intermediate **3a'**. Additionally, when using secondary alcohol **1a'**, Fe-catalyzed dehydrogenation resulted propiophenone **1a** and continued the general mechanism to access various functionalized branched ketones (Figure 2). Notably, during the progress of the reactions, hydrogen gas was generated and we have experimentally detected the gaseous hydrogen using gas chromatography analysis (SI Scheme S14). Additionally, to establish the hydrogen-borrowing process and bi-functional nature of the Fe-catalyst, a series of deuterium-labelling experiments were performed (Scheme 7). Enone **3a"** was independently prepared and employed with **2a** and **2a-d2** (92% D) under standard conditions of Table 1. As expected, **3a** and **3a-d3** were obtained in up to 91-93% yield respectively and in case of **3a-d3** we observed 14-18% deuterium incorporation (Scheme 7a and SI Scheme S1). However, when benzyl alcohol **2a-d1** reacted with **1a**, no deuterium incorporation observed in the desired α-alkylated product (Scheme 7b and SI Scheme S4). When using 1:1 mixture of **2a** and **2a-d2**, we witnessed the formation of H/D-scrambled products **3a-d3** using ^{1}H-NMR and GC-MS analysis (Scheme 7b and SI Scheme S2-S3). Interestingly, α-alkylation of **1a-d2** (96% D) with **2a** evident the participation of the benzylic C-H bond of the ketones (Scheme 7b and SI Scheme S4). Furthermore, a series of control experiments using **1a** with benzylalcohol **2a** in presence and absence of Fe-catalyst were perform (Scheme 7c). Nevertheless, when 4-methoxybenzaldehyde was use for the alkylation with **1a** under standard conditions of Table 1, **3b** was obtain in 15% product yield. However, in absence of catalyst resulted albeit with poor product conversion (Scheme 7c). Thereafter, deuterium labelling experiments also strongly supports our present findings for D/H exchange involving hydrogen auto-transfer strategy (Scheme 7 and SI Schemes S1-S5).[15]

A time conversion plot for α-alkylation of propiophenone **1a** with benzylalcohol **2a** was monitored using GC. It was observed that, after a certain periods of time, intermediate product alcohol **3a'** gradually dehydrogenated to the ketone product **3a** and at this point, selective control to alcohol is quite challenging (SI Scheme S8 and Figure 2). Notably, concentration of aldehyde **2a'** remained constant during the process. Finally, kinetics studies to determine the rate and order of the alkylation process were perform and observed first order kinetics (SI Schemes S6-S7).

CONCLUSIONS

In summary, herein we demonstrated an unprecedented and general $Fe_2(CO)_9$ catalyzed,[16] synthesis of functionalized branched ketones. A simple catalytic system used for a series of alkyl ketones, symmetrical, and unsymmetrical methylene ketones and secondary alcohols to couple with aromatic as well as C4-C10 alkyl alcohols. A single catalyst successfully employed for dehydrogenation of both primary and secondary alcohols, broaden the scope of this catalytic protocol. We established a sequential one pot double alkylation to hetero bis-alkylated ketones using a single catalyst with two different alcohols. Successful synthetic application to one-step synthesis of Alzheimer's drug and alkylation of steroid hormone highlight the potential of this process. Initial mechanistic studies involving a series of kinetic and deuterium labelling experiments revealed the involvement of hydrogen auto-transfer principle for C-C bond formation. We established that, our protocol could be applied to a complex steroid derivative irrespective to the nature of the ketones and alcohols.

EXPERIMENTAL SECTION

General Experimental Details: All solvents and reagents were used, as received from the suppliers. TLC was performed on Merck Kiesel gel 60, F_{254} plates with the layer thickness of 0.25 mm. Column chromatography was performed on silica gel (100-200 mesh) using a gradient of ethyl acetate and hexane as mobile phase. ^{1}H-NMR spectral data were collected at, 400 MHz (JEOL), and ^{13}C-NMR were recorded at 100 MHz. ^{1}H NMR spectral data are given as chemical shifts in ppm followed

by multiplicity (s- singlet; d- doublet; t- triplet; q- quartet; m- multiplet), number of protons and coupling constants. $^{13}C\{H\}$ NMR chemical shifts are expressed in ppm. HRMS (ESI) spectral data were collected using Bruker High Resolution Mass Spectrometer. GC and GC-MS were recorded using Agilent Gas Chromatography Mass Spectrometry. Elemental analysis data were recorded using Vario Micro Cube elemental analyser. All the reactions were performed in a closed system using Schlenk tube. All Iron salts were purchased from Alfa Aesar. $Fe_2(CO)_9$ (Assay- ≥94.0 to ≤106.0% by Fe, CAS Number 14024-58-9; MDL number: MFCD00000022). Potassium *tert*-butoxide was purchased from Avra Synthesis Pvt. Ltd., India. (Purity-98%, CAS No: 865-47-4, Catalog No- ASP2012).

General procedures for Fe-catalyzed synthesis of branched ketones and alcohols:

Procedure [A]: For the synthesis of 2-methyl-1,3-diphenylpropan-1-one (**3a**): In a 15 mL oven dried Schlenk tube, propiophenone **1a** (0.5 mmol, 67 mg), *t*-BuOK (0.5 mmol, 56.1 mg), $Fe_2(CO)_9$ (2.5 mol%, 4.5 mg) and benzyl alcohol **2a** (0.625 mmol, 1.25 equiv., 67.5 mg) were added followed by toluene 2.0 mL under an atmosphere of N_2 and the reaction mixture was refluxed in an oil bath at 140 °C for 24 h in closed system. The reaction mixture was cooled to room temperature and 3.0 mL of ethyl acetate was added and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product **3a**. This procedure was used as general procedure A.

Procedure [B]: In a 15 mL oven dried Schlenk tube, acetophenone (0.5 mmol, 60.2 mg), *t*-BuOK (0.5 mmol, 56.1 mg), $Fe_2(CO)_9$ (2.5 mol%, 4.54 mg) and alcohols **2** (0.5 mmol, 1.0 equiv.) were added followed by toluene 2.0 mL under an atmosphere of N_2 and the reaction mixture was refluxed in an oil bath at 140 °C for 2 h in closed system. After 2 h another alcohol **2** (0.5 mmol) was added under N_2 atmosphere and the reaction mixture was heated at 140 °C in an oil bath for 20 h, The reaction mixture was cooled to room temperature and 3.0 mL of ethyl acetate was added and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product.

Procedure [C]: In a 15 mL oven dried Schlenk tube, secondary ketones **1** (0.25 mmol), *t*-BuOK (0.25 mmol, 28 mg), $Fe_2(CO)_9$ (2.5 mol%, 2.27 mg) and primary alcohols **2** (0.3125 mmol, 1.25 equiv.) were added followed by toluene 2.0 mL under an atmosphere of N_2 and the reaction mixture was refluxed at 140 °C in an oil bath for 24 h in closed system. The reaction mixture was cooled to room temperature and 3.0 mL of ethyl acetate was added and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product.

Procedure [D]: In a 15 mL oven dried Schlenk tube, secondary alcohols **1a'** (0.5 mmol), *t*-BuOK (0.5 mmol, 56.1 mg), $Fe_2(CO)_9$ (2.5 mol%, 4.54 mg) and primary alcohols **2** (0.625 mmol, 1.25 equiv.) were added followed by toluene 2.0 mL under an atmosphere of N_2 and the reaction mixture was refluxed in an oil bath at 140 °C for 24 h in closed system. The reaction mixture was cooled to room temperature and 3.0 mL of ethyl acetate was added and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product.

Procedure for gram scale reaction: Gram Scale reaction was performed using deoxybenzoin **1b** (1.0 g, 5.1 mmol), benzyl alcohol **2a** (0.69 g, 6.38 mmol), $Fe_2(CO)_9$ (47 mg, 2.5 mol%), *t*-BuOK (572 mg, 5.1 mmol), toluene (10.0 mL) in a 100 mL pressure tube under N_2 atmosphere at 140 °C in oil bath for 24 h. The reaction mixture was cooled to room temperature and 15.0 mL of ethyl acetate was added and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product **3j** (0.98 g, 69% yield).

Preparation of α,α-dideuteriobenzyl alcohol ($PhCD_2OH$) 2a-d2: In a 50 mL round-bottom flask $LiAlD_4$ (150 mg, 3.6 mmol) was taken in THF (20 mL) at 0°C and then, a solution of methyl benzoate (5 mmol, 680 mg) was taken in THF (10 mL). The mixture was stirred for 2 hours at 0 °C. The resulting solution was quenched with HCl 1N and extracted with ether (3×20 mL), followed by concentrating in vacuum and the residue was purified by flash chromatography on a short silica gel to afford 100 mg (92% of D) of $PhCD_2OH$.

Preparation of benzyl alcohol-OD ($PhCH_2OD$) 2a-d1: In a 50 mL round-bottom flask benzyl alcohol **2a** (4.63 mmol, 500 mg) was taken in 5 ml D_2O. The mixture was stirred for 48 hours under room temperature. After concentrating in vacuum, the residue was purified by flash chromatography on a short silica gel to afford 420 mg (98% of D) of $PhCH_2OD$.

Preparation of ($PhC(O)CD_2CH_3$) 1a-d2: In a 100 mL round-bottom flask 805 mg (6.0 mmol) of propiophenone was taken and added 30 mL of CH_3OD. Sodium methoxide (9.5 mmol) was added slowly. The mixture was stirred for 48-60 hours at ambient temperature and monitored the progress of the reaction. Subsequently quenched with cold water (10 mL), and the organics were extracted with Et_2O (3 × 40 mL). And then, concentrating in vacuum and the residue was purified by flash chromatography on a short silica gel to afford 200 mg (97% of D) of $PhC(O)CD_2CH_3$.

2-Methyl-1,3-diphenylpropan-1-one (3a):[13b] Following the general procedure A and D, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 90 mg, 81% yield (Procedure A), 83% yield (Procedure D); ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.7, 1.4 Hz, 2H), 7.56-7.52 (m, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.28-7.24 (m, 2H), 7.21-7.13 (m, 3H), 3.75 (dq, J = 13.9, 7.0 Hz, 1H), 3.16 (dd, J = 14.0, 6.5 Hz, 1H), 2.69 (dd, J = 14.0, 8.0 Hz, 1H), 1.20 (d, J = 7.1 Hz, 3H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.7, 139.9, 136.4, 132.9, 129.1, 128.6, 128.3, 128.2, 126.2, 42.7, 39.3, 17.4.

3-(4-Methoxyphenyl)-2-methyl-1-phenylpropan-1-one (3b):[13b] Following the general procedure A and D, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 5% ethyl acetate in hexane. Yield: 62 mg, 49% yield (Procedure A), 58% yield (Procedure D); ^1H NMR (400 MHz, (100 MHz, $CDCl_3$) δ 7.91 (d, J = 7.3 Hz, 2H), 7.55-7.51 (m, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 3.76 (s, 3H), 3.72-3.66 (m, 1H), 3.09 (dd, J = 13.8, 6.4 Hz, 1H), 2.62 (dd, J = 13.8, 7.7 Hz, 1H), 1.17 (d, J = 6.9 Hz, 3H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.8, 157.9, 136.4, 132.9, 130.1, 129.8, 128.2, 113.6, 109.4, 55.1, 42.9, 38.6, 17.3.

3-(4-Chlorophenyl)-2-methyl-1-phenylpropan-1-one (3c):[13b] Following the general procedure A and D, the title product was obtained as a colorless liquid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield:

64 mg, 50% yield (Procedure A), 78% yield (Procedure D); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.7 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 8.3 Hz, 2H), 7.24 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.9 Hz, 2H), 3.76-3.72 (m, 1H), 3.17 (dd, J = 14.4, 7.2 Hz, 1H), 2.71 (dd, J = 14.4, 7.6 Hz, 1H), 1.23 (d, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 203.3, 138.4, 133.0, 132.0, 130.4, 128.7, 128.6, 128.5, 128.2, 42.7, 38.7, 17.6.

3-(4-Fluorophenyl)-2-methyl-1-phenylpropan-1-one (3d):[13b] Following the general procedure A, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 44 mg, 37% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.9 Hz, 2H), 7.13 (dd, J = 9.0, 5.6 Hz, 2H), 6.92 (t, J = 8.9 Hz, 2H), 3.70 (dd, J = 14.2, 7.1 Hz, 1H), 3.12 (dd, J = 14.1, 7.0 Hz, 1H), 2.67 (dd, J = 14.0, 7.5 Hz, 1H), 1.19 (d, J = 7.1 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.0, 160.2 (d, $J_{C\text{-}F}$ = 242.7 Hz), 136.9, 136.8, 133.1, 130.4 (d, $J_{C\text{-}F}$ = 8 Hz), 128.6, 128.0, 115.2 (d, $J_{C\text{-}F}$ = 20.8 Hz), 40.4, 37.5, 29.2.

3-cyclopropyl-2-methyl-1-phenylpropan-1-one (3e): Following the general procedure A, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 68 mg, 73% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 5.3, 3.3 Hz, 2H), 7.58-7.54 (m, 1H), 7.49-7.45 (m, 2H), 3.62 (h, J = 6.8 Hz, 1H), 1.70 (dd, J = 13.8, 6.9 Hz, 1H), 1.43-1.34 (m, 1H), 1.24 (d, J = 6.9 Hz, 3H), 0.72-0.67 (m, 1H), 0.44-0.35 (m, 2H), 0.04 (dd, J = 4.9, 1.6 Hz, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 204.7, 136.8, 132.8, 128.6, 128.3, 41.1, 38.9, 17.3, 9.2, 4.9, 4.5. Elemental Analysis: $C_{13}H_{16}O$: C, 82.94; H, 8.57; O, 8.50. Found: C, 82.81; H, 8.39; O, 8.38. HRMS (ESI-TOF) m/z $[M+Na]^+$ Calcd for $C_{13}H_{16}O$ 211.1093, Found 211.1076.

3-cyclohexyl-2-methyl-1-phenylpropan-1-one (3f):[17] Following the general procedure A and D, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 86 mg, 75% yield (Procedure A), 62% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.93 (m, 2H), 7.56-7.52 (m, 1H), 7.45 (dd, J = 8.0, 7.0 Hz, 2H), 3.58 (h, J = 6.8 Hz, 1H), 1.73-1.63 (m, 6H), 1.27 (dd, J = 12.4, 6.6 Hz, 2H), 1.16 (d, J = 6.8 Hz, 3H), 1.14-1.06 (m, 3H), 0.89-0.86 (m, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 204.6, 136.6, 132.8, 128.6, 128.2, 41.2, 37.6, 35.3, 33.8, 33.0, 26.5, 26.2, 26.2, 17.5.

2,5,9-Trimethyl-1-phenyldec-8-en-1-one (3g):[13b] Following the general procedure A, the title product was obtained as a pale yellow oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 99 mg, 73% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.9 Hz, 2H), 7.54 (dd, J = 8.2, 6.5 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 5.06-5.04 (m, 1H), 3.42-3.40 (m, 1H), 1.97-1.73 (m, 3H), 1.65 (d, J = 4.2 Hz, 3H), 1.57 (d, J = 5.0 Hz, 2H), 1.35-1.24 (m, 5H), 1.18 (d, J = 6.9 Hz, 3H), 1.15-1.04 (m, 2H), 0.84 (t, J = 6.5 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 204.4, 136.7, 132.7, 131.0, 128.5, 128.1, 124.7, 40.9, 36.9, 36.7, 34.5, 32.4, 31.1, 25.4, 19.5, 17.4.

2-methyl-1-phenylhexan-1-one (3h):[8e] Following the general procedure A, the title product was obtained as a pale yellow oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 60 mg, 64% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 5.2, 3.4 Hz, 2H), 7.56-7.53 (m, 1H), 7.45 (t, J = 7.5 Hz, 2H), 3.45 (h, J = 6.8 Hz, 1H), 1.81-1.77 (m, 1H), 1.42 (dd, J = 12.9, 6.3 Hz, 1H), 1.30-1.28 (m, 4H), 1.18 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 204.6, 136.7 132.8, 128.6, 128.2, 40.5, 33.4, 29.6, 22.8, 17.2, 14.0.

2-methyl-1-phenylnonan-1-one (3i):[13b] Following the general procedure A, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 63 mg, 55% yield (Procedure A), 59% yield (Procedure D); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.3 Hz, 2H), 7.61-7.57 (m, 1H), 7.49 (t, J = 6.8 Hz, 2H), 3.49-3.47 (m, 1H), 1.84-1.80 (m, 1H), 1.51-1.40 (m, 1H), 1.27-1.21 (s, 10H), 1.22 (d, J = 6.6 Hz, 3H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 204.6, 136.8, 132.8, 128.6, 128.2, 40.6, 33.7, 31.8, 29.7, 29.1, 27.4, 22.6, 17.2, 14.1.

1,2,3-Triphenylpropan-1-one (3j):[13b] Following the general procedure A and D, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 122 mg, 86% yield (Procedure A), 36% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, J = 8.3, 1.2 Hz, 2H), 7.44-7.42 (m, 1H), 7.33 (dd, J = 8.0, 7.3 Hz, 2H), 7.25-7.21 (m, 4H), 7.20-7.17 (m, 3H), 7.14-7.12 (m, 1H), 7.08-7.06 (m, 2H), 4.80 (t, J = 7.3 Hz, 1H), 3.56 (dd, J = 13.7, 7.5 Hz, 1H), 3.06 (dd, J = 13.7, 7.0 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.2, 139.8, 139.1, 136.8, 132.8, 129.1, 128.9, 128.7, 128.5, 128.3, 128.2, 127.1, 126.1, 55.9, 40.1.

3-(4-methoxyphenyl)-1,2-diphenylpropan-1-one (3k):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 3% ethyl acetate in hexane. Yield: 77 mg, 49% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.2 Hz, 2H), 7.37 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.6 Hz, 2H), 7.21-7.13 (m, 5H), 6.92 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 8.7 Hz, 2H), 4.70 (t, J = 7.3 Hz, 1H), 3.67 (s, 3H), 3.43 (dd, J = 13.8, 7.5 Hz, 1H), 2.93 (dd, J = 13.8, 7.0 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.4, 158.0, 139.2, 136.8, 132.8, 131.9, 130.0, 128.9, 128.6, 128.4, 128.3, 127.1, 113.2, 56.2, 55.2, 39.3.

1,2-diphenyl-3-(*p*-tolyl)propan-1-one (3l):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 123 mg, 82% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.6 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.6 Hz, 2H), 7.20-7.16 (m, 5H), 6.94-6.89 (m, 4H), 4.72 (t, J = 7.2 Hz, 1H), 3.46 (dd, J = 13.8, 7.6 Hz, 1H), 2.95 (dd, J = 13.8, 6.9 Hz, 1H), 2.19 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.3, 139.2, 136.7, 136.6, 135.5, 132.8, 129.0, 129.0, 128.9, 128.7, 128.4, 128.3, 127.1, 55.9, 39.7, 21.0.

3-(4-ethylphenyl)-1,2-diphenylpropan-1-one (3m):[13c] Following the general procedure A and D, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 138 mg, 88% yield (Procedure A), 32% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.0 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.6 Hz, 2H), 7.20-7.17 (m, 5H), 6.97-6.92 (m, 4H), 4.76-4.72 (m, 1H), 3.47 (dd, J = 13.8, 7.7 Hz, 1H), 2.95 (dd, J = 13.8, 6.7 Hz, 1H), 2.50 (q, J = 7.6 Hz, 2H), 1.11 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.3, 142.0, 139.3, 137.0, 136.8, 132.8, 129.0, 128.9, 128.7, 128.4, 128.3, 127.7, 127.1, 56.1, 39.6, 28.1, 15.4.

3-(4-isopropylphenyl)-1,2-diphenylpropan-1-one (3n):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 119 mg, 73% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.1 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.27 (t, J = 7.6 Hz, 2H), 7.20-7.17 (m, 5H), 6.97 (q, J = 8.2 Hz, 4H), 4.75 (t, J = 7.2 Hz, 1H), 3.49 (dd, J = 13.9, 7.9 Hz, 1H), 2.95 (dd, J = 13.8, 6.5 Hz, 1H), 2.80-2.71 (m, 1H), 1.12 (d, J = 7.1 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.3, 146.6, 139.3, 137.1, 136.7, 132.8, 129.0, 128.9, 128.7, 128.4, 128.3, 127.1, 126.3, 55.8, 39.7, 33.6, 24.0.

3-(4-chlorophenyl)-1,2-diphenylpropan-1-one (3o):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 139 mg, 87% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.1 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 7.6 Hz, 2H), 7.26 (t, J = 7.3 Hz, 3H), 7.21 (d, J = 7.3 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 7.00-6.98 (m, 2H), 4.75 (t, J = 7.3 Hz, 1H), 3.50 (dd, J = 13.8, 7.4 Hz, 1H), 3.03 (dd, J = 13.7, 7.2 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 198.9, 138.7, 138.2, 136.6, 132.9, 131.9, 130.5, 129.0, 128.7, 128.5, 128.3, 128.2, 127.3, 55.7, 39.3.

1,2-diphenyl-3-(4-(trifluoromethyl)phenyl)propan-1-one (3p):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 95 mg, 54% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.4 Hz, 2H), 7.45 (t, J = 8.9 Hz, 3H), 7.34 (t, J = 7.7 Hz, 2H), 7.28-7.25 (m, 2H), 7.19 (dd, J = 12.8, 7.6 Hz, 5H), 4.78 (t, J = 7.3 Hz, 1H), 3.59 (dd, J = 13.7, 7.5 Hz, 1H), 3.11 (dd, J = 13.8, 7.1 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 198.6, 143.9, 143.9, 138.5, 136.3, 133.0, 129.5, 129.1, 128.7, 128.5 (q, J_{F-C} = 32 Hz), 128.2, 127.4, 125.1 (q, J_{F-C} = 8 Hz), 124.2 (d, J_{F-C} = 271 Hz), 55.6, 39.8.

1,2-diphenyl-3-(*o*-tolyl)propan-1-one (3q): Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 96 mg, 64% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.87 (m, 2H), 7.46-7.42 (m, 1H), 7.35-7.32 (m, 2H), 7.27-7.17 (m, 6H), 7.08-6.96 (m, 3H), 4.81-4.78 (m, 1H), 3.58-3.52 (m, 1H), 3.06 (dd, J = 14.1, 7.0 Hz, 1H), 2.21 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.3, 139.2, 137.8, 136.3, 132.8, 130.1, 129.7, 129.1, 128.9, 128.7, 128.5, 128.2, 127.1, 126.2, 125.7, 54.5, 37.1, 19.5. Elemental Analysis: $C_{22}H_{20}O$: C, 87.96; H, 6.71; O, 5.33. Found: C, 87.84; H, 6.59; O, 5.50; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{20}O$ 323.1514, Found 323.1528.

3-(naphthalen-1-yl)-1,2-diphenylpropan-1-one (3r):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 122 mg, 73% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.85-7.82 (m, 3H), 7.66 (d, J = 8.2 Hz, 1H), 7.53-7.47 (m, 2H), 7.41 (t, J = 7.4 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.25-7.20 (m, 6H), 7.10 (d, J = 6.8 Hz, 1H), 4.99 (t, J = 7.0 Hz, 1H), 4.09 (dd, J = 14.1, 7.3 Hz, 1H), 3.47 (dd, J = 14.1, 6.6 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.2, 139.4, 136.6, 135.5, 133.8, 132.8, 131.8, 129.0, 128.9, 128.7, 128.4, 128.3, 128.1, 127.6, 127.2, 127.0, 126.0, 125.3, 123.4, 54.5, 36.9.

3-(1,3-dihydroisobenzofuran-5-yl)-1,2-diphenylpropan-1-one (3s):[13c] Following the general procedure A, the title product was obtained as a colorless solid using silica-gel column chromatography eluting with 5% ethyl acetate in hexane. Yield: 100 mg, 61% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 8.4, 1.3 Hz, 2H), 7.39 (t, J = 7.4 Hz, 1H), 7.29 (t, J = 7.6 Hz, 2H), 7.21-7.13 (m, 5H), 6.58-6.46 (m, 3H), 5.81 (s, 2H), 4.69 (t, J = 7.2 Hz, 1H), 3.41 (dd, J = 13.8, 7.6 Hz, 1H), 2.91 (dd, J = 13.8, 6.9 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.1, 147.0, 145.6, 139.1, 136.6, 133.5, 132.9, 128.9, 128.7, 128.5, 128.2, 127.2, 122.0, 109.5, 108.0, 100.7, 55.9, 39.7.

1,2-diphenyl-3-(thiophen-2-yl)propan-1-one (3t):[13c] Following the general procedure A and D, the title product was obtained as a pale yellow solid using silica-gel column chromatography eluting with 5% ethyl acetate in hexane. Yield: 70 mg, 48% yield (Procedure A), 28% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.6 Hz, 2H), 7.48-7.43 (m, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.27 (dd, J = 3.8, 3.3 Hz, 4H), 7.23-7.10 (m, 1H), 7.05 (d, J = 5.1 Hz, 1H), 6.82 (dd, J = 5.1, 3.4 Hz, 1H), 6.68 (d, J = 3.4 Hz, 1H), 4.84 (dd, J = 7.9, 6.6 Hz, 1H), 3.78 (dd, J = 14.5, 7.5 Hz, 1H), 3.27 (dd, J = 14.8, 6.6 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 198.8, 142.1, 138.6, 133.0, 133.0, 129.0, 128.7, 128.5, 128.2, 127.4, 126.6, 125.7, 123.6, 56.3, 34.1.

3-(furan-2-yl)-1,2-diphenylpropan-1-one (3u):[5c] Following the general procedure A, the title product was obtained as a pale yellow solid using silica-gel column chromatography eluting with 5% ethyl acetate in hexane. Yield: 63 mg, 46% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 8.3, 1.2 Hz, 2H), 7.49-7.44 (m, 1H), 7.39-7.33 (m, 2H), 7.27-7.23 (m, 5H), 7.19 (ddd, J = 9.6, 5.1, 2.9 Hz, 1H), 6.17 (dd, J = 3.1, 1.9 Hz, 1H), 5.86 (dd, J = 3.1, 0.5 Hz, 1H), 4.98 (dd, J = 7.7, 6.9 Hz, 1H), 3.60-3.53 (m, 1H), 3.09 (dd, J = 15.1, 6.8 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 198.7, 153.3, 141.1, 138.7, 136.4, 132.9, 128.9, 128.7, 128.5, 128.0, 127.2, 110.2, 106.5, 52.5, 32.4.

1,2-diphenyl-3-(pyridin-2-yl)propan-1-one (3v):[13c] Following the general procedure A, the title product was obtained as a yellow oil using silica-gel column chromatography eluting with 7% ethyl acetate in hexane. Yield: 97 mg, 68% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45-8.43 (m, 1H), 7.92-7.90 (m, 2H), 7.44-7.41 (m, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.26-7.21 (m, 4H), 7.16-7.11 (m, 1H), 7.01 (t, J = 6.2 Hz, 2H), 5.30 (dd, J = 8.5, 6.3 Hz, 1H), 3.69 (dd, J = 14.1, 8.5 Hz, 1H), 3.18 (dd, J = 14.1, 6.3 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.4, 159.4, 149.1, 139.1, 136.7, 136.1, 132.7, 128.9, 128.8, 128.4, 128.3, 127.1, 124.1, 121.2, 53.2, 42.2.

2-Benzyl-3,4-dihydronaphthalen-1(2*H*)-one (3w):[13c] Following the general procedure A and D, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 108 mg, 92% yield (Procedure A), 68% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, J = 7.9, 1.0 Hz, 1H), 7.48-7.43 (m, 1H), 7.33-7.28 (m, 3H), 7.25-7.19 (m, 4H), 3.49 (dd, J = 13.6, 3.9 Hz, 1H), 2.95-2.90 (m, 2H), 2.77-2.67 (m, 1H), 2.64 (dd, J = 13.6, 9.6 Hz, 1H), 2.12-2.07 (m, 1H), 1.83-1.76 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.4, 144.0, 140.0, 133.3, 132.4, 129.2, 128.7, 128.4, 127.5, 126.6, 126.1, 49.4, 35.6, 28.6, 27.6.

2-Benzyl-7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (3x):[13c] Following the general procedure A, the title product was

obtained as a pale yellow oil using silica-gel column chromatography eluting with 2% ethyl acetate in hexane. Yield: 85 mg, 64% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 2.8 Hz, 1H), 7.32-7.28 (m, 2H), 7.25-7.19 (m, 3H), 7.12 (d, J = 8.4 Hz, 1H), 7.04 (dd, J = 8.4, 2.8 Hz, 1H), 3.83 (s, 3H), 3.47 (dd, J = 13.4, 3.8 Hz, 1H), 2.88-2.86 (m, 2H), 2.66-2.63 (m, 2H), 2.10-2.05 (m, 1H), 1.79-1.73 (m, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.4, 158.3, 140.0, 136.6, 133.2, 129.9, 129.2, 128.4, 126.1, 121.7, 109.4, 55.5, 55.5, 49.3, 35.7, 27.7.

2-benzyl-1,3-diphenylpropan-1-one (3y):[13c] Following the general procedure A and B, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 64 mg, 43% yield (Procedure A), 73% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.34-7.30 (m, 2H), 7.22 (dd, J = 15.4, 7.1 Hz, 4H), 7.19-7.11 (m, 6H), 4.05 – 3.98 (m, 1H), 3.13 (dd, J = 14.2, 8.1 Hz, 2H), 2.80 (dd, J = 14.1, 6.5 Hz, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 203.3, 139.5, 137.3, 132.8, 129.0, 128.4, 128.4, 128.1, 126.2, 50.4, 38.2.

2-benzyl-1-phenylpentan-1-one (3z):[13c] Following the general procedure A, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 51 mg, 41% yield (Procedure A); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.84 (m, 2H), 7.53-7.49 (m, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.24-7.14 (m, 5H), 3.75-3.70 (m, 1H), 3.10 (dd, J = 13.5, 7.7 Hz, 1H), 2.77 (dd, J = 13.6, 6.5 Hz, 1H), 1.79-1.73 (m, 1H), 1.55-1.48 (m, 1H), 1.33-1.23 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 204.0, 140.0, 137.5, 132.8, 129.0, 128.5, 128.3, 128.1, 126.1, 48.1, 38.2, 34.6, 20.6, 14.2.

2-Benzyl-3-(4-methoxyphenyl)-1-phenylpropan-1-one (3aa):[13c] Following the general procedure B, the title product was obtained as a colorless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 143 mg, 87% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.5 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.32 (t, J = 7.7 Hz, 2H), 7.21-7.18 (m, 2H), 7.13-7.11 (m, 3H), 7.04 (d, J = 8.6 Hz, 2H), 6.74 (d, J = 8.6 Hz, 2H), 3.98-3.94 (m, 1H), 3.73 (s, 3H), 3.12-3.03 (m, 2H), 2.80-2.71 (m, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 203.5, 158.0, 139.6, 137.4, 132.7, 131.5, 130.0, 129.0, 128.4, 128.4, 128.1, 126.2, 113.8, 55.2, 50.7, 38.1, 37.4.

3-(Benzo[*d*][1,3]dioxol-5-yl)-2-benzyl-1-phenylpropan-1-one (3ab):[13c] Following the general procedure B, the title product was obtained as a colorless liquid using silica-gel column chromatography eluting with 5% ethyl acetate in hexane. Yield: 146 mg, 85% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.0 Hz, 2H), 7.46 (dd, J = 11.9, 4.4 Hz, 1H), 7.34 (t, J = 7.9 Hz, 2H), 7.22-7.18 (m, 2H), 7.14-7.10 (m, 3H), 6.65-6.58 (m, 3H), 5.86 (dd, J = 3.3, 1.5 Hz, 2H), 3.98-3.91 (m, 1H), 3.12-3.01 (m, 2H), 2.80-2.68 (m, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 203.3, 147.5, 145.9, 139.4, 137.5, 137.3, 133.2, 132.8, 129.0, 128.5, 128.4, 128.1, 126.3, 122.0, 109.4, 108.1, 100.8, 50.7, 38.2, 37.9.

2-Benzyl-1-phenyl-3-(pyridin-2-yl)propan-1-one (3ac):[13c] Following the general procedure B, the title product was obtained as a pale yellow oil using silica-gel column chromatography eluting with 5% ethyl acetate in hexane. Yield: 53.4 mg, 61% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 4.0 Hz, 1H), 7.78 (dd, J = 8.1, 0.9 Hz, 2H), 7.40-7.36 (m, 2H), 7.27 (t, J = 7.6 Hz, 2H), 7.13-7.00 (m, 6H), 6.94 (dd, J = 6.9, 5.2 Hz, 1H), 4.43-4.36 (m, 1H), 3.23 (dd, J = 14.1, 8.5 Hz, 1H), 3.08 (dd, J = 13.6, 7.6 Hz, 1H), 2.90 (dd, J = 14.1, 5.8 Hz, 1H), 2.74 (dd, J = 13.6, 6.6 Hz, 1H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 203.5, 159.3, 149.2, 139.2, 137.3, 136.1, 136.1, 132.7, 129.1, 128.4, 128.3, 126.2, 123.9, 121.2, 47.9, 40.1, 38.4.

2-Benzyl-1-(4-methoxyphenyl)-3-phenylpropan-1-one (3ad):[13c] Following the general procedure B, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 3% ethyl acetate in hexane. Yield: 140 mg, 85% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 9.2 Hz, 2H), 7.39-7.38 (m, 1H), 7.25-7.19 (m, 4H), 7.14-7.11 (m, 5H), 6.80 (d, J = 9.1 Hz, 2H), 4.00-3.93 (m, 1H), 3.80 (s, 3H), 3.12 (dd, J = 14.2, 8.1 Hz, 2H), 2.79 (dd, J = 14.1, 6.5 Hz, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 201.6, 163.2, 139.7, 130.4, 130.3, 129.0, 128.3, 126.2, 113.6, 55.4, 49.9, 38.3.

2-Benzyl-1-(4-methoxyphenyl)-3-(*p*-tolyl)propan-1-one (3ae): [13c] Following the general procedure B, the title product was obtained as a colourless liquid using silica-gel column chromatography eluting with 3% ethyl acetate in hexane. Yield: 122 mg, 71% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.72 (m, 2H), 7.25-7.17 (m, 3H), 7.13-7.11 (m, 3H), 7.01 (d, J = 3.0 Hz, 3H), 6.80 (d, J = 8.9 Hz, 2H), 3.96-3.91 (m, 1H), 3.80 (s, 3H), 3.10-3.04 (m, 2H), 2.79-2.74 (m, 2H), 2.25 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 201.7, 163.2, 139.8, 136.5, 135.6, 130.5, 130.4, 129.0, 128.9, 128.3, 127.6, 126.1, 113.6, 55.5, 50.0, 38.2, 37.9, 21.0.

2-benzyl-3-cyclopropyl-1-phenylpropan-1-one (3ee): Following the general procedure A and B, the title product was obtained as a colourless liquid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 87 mg, 66% yield (Procedure A); 35% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ δ 7.90-7.87 (m, 2H), 7.54-7.50 (m, 1H), 7.43-7.39 (m, 2H), 7.26-7.11 (m, 5H), 3.93-3.82 (m, 1H), 3.12 (dd, J = 14.0, 7.9 Hz, 1H), 2.83 (dd, J = 13.9, 6.7 Hz, 1H), 1.80-1.70 (m, 1H), 1.46-1.42 (m, 1H), 0.72-0.57 (m, 1H), 0.42-0.23 (m, 2H), 0.11-0.01 (m, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 204.3, 140.0, 137.7, 132.8, 129.0, 128.5, 128.3, 128.2, 126.1, 48.8, 38.3, 37.7, 9.3, 5.1, 4.8. Elemental Analysis: $C_{19}H_{20}O$: C, 86.32; H, 7.63; O, 6.05. Found: C, 86.14; H, 7.49; O, 5.90. HRMS (ESI-TOF) *m/z* $[M+Na]^+$ Calcd for $C_{19}H_{20}O$ 287.1406; Found 287.1423.

2-Benzyl-1,3-diphenylbutan-1-one (3ag):[13c] Following the general procedure B, the title product was obtained as a colourless liquid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 94 mg, 60% yield (Procedure B); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.90 (m, 2H), 7.53-7.52 (m, 1H), 7.43 (t, J = 7.6 Hz, 3H), 7.31-7.25 (m, 6H), 7.20-7.14 (m, 3H), 3.54-3.46 (m, 1H), 3.32-3.14 (m, 3H), 1.33 (d, J = 6.9 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 199.1, 146.6, 137.2, 133.0, 129.0, 128.5, 128.5, 128.4, 128.2, 128.0, 128.0, 126.9, 126.3, 47.0, 35.6, 29.7, 21.8.

2-benzylcyclopentanone (3ga):[13b] Following the general procedure A, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 37 mg, 43% yield Procedure A), 33% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.25 (m, 3H), 7.20 (d, J = 7.4 Hz, 1H), 7.14-7.11 (m, 1H), 3.41 (dd, J = 14.0, 3.8 Hz, 1H), 3.22 (t, J = 7.4 Hz, 1H), 3.04-2.97 (m, 1H), 2.88-2.79 (m, 3H), 2.68-2.59 (m, 1H), 2.16-2.12 (m, 2H).

2-benzylcyclohexanone (3ha):[13b] Following the general procedure A, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate

in hexane. Yield: 26 mg, 28% yield Procedure A), 33% yield (Procedure D); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.20 (m, 3H), 7.11-7.06 (m, 2H), 2.94 (d, J = 13.4 Hz, 1H), 2.77 (d, J = 13.4 Hz, 1H), 1.98-1.92 (m, 1H), 1.72-1.67 (m, 1H), 1.60-1.41 (m, 5H), 1.34-1.19 (m, 2H).

2,6-dibenzylcyclohexanone (3iaa):[18] Following the general procedure A, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 48 mg, 35% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 7.21-7.18 (m, 3H), 7.09 (d, J = 7.5 Hz, 2H), 2.81-2.74 (m, 2H), 2.51-2.48 (m, 2H), 1.89-1.82 (m, 2H), 1.83-1.78 (m, 2H), 1.40-1.31 (m, 2H), 1.28-1.14 (m, 2H). ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 216.9, 139.5, 129.2, 128.3, 126.2, 53.5, 38.4, 31.0, 28.5.

2,7-bis(cyclohexylmethyl)cycloheptanone (3jff): Following the general procedure A, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 50 mg, 33% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68-2.62 (m, 2H), 1.82-1.72 (m, 4H), 1.68-1.60 (m, 10H), 1.24-1.09 (m, 16H), 0.88-0.79 (m, 4H); ^{13}C{1H} NMR (101 MHz, $CDCl_3$) δ 218.8 48.1, 40.6, 35.0, 33.8, 33.1, 32.6, 28.5, 26.3. HRMS (ESI-TOF) m/z $[M+Na]^+$ Calcd for $C_{21}H_{36}O$ 327.2658; Found 327.2653.

2-Benzyl-10,13-dimethyl-17-(6-methylheptan-2-yl)-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (4):[13b] Following the general procedure C, the title product was obtained as a yellow oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 44 mg, 38% yield (Procedure C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.18 (t, J = 6.6 Hz, 3H), 6.59 (s, 1H), 6.05 (s, 1H), 3.63 (s, 2H), 2.44-2.30 (m, 2H), 2.16 (s, 1H), 2.02-1.89 (m, 3H), 1.85-1.77 (m, 1H), 1.56-1.48 (m, 4H), 1.33-1.24 (m, 4H), 1.14-1.04 (m, 9H), 0.99-0.92 (m, 4H), 0.85 (dd, J = 6.4, 4.6 Hz, 9H), 0.68 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 186.0, 168.9, 152.4, 139.6, 137.1, 129.1, 128.3, 126.0, 123.6, 56.1, 55.4, 52.7, 43.5, 42.6, 39.5, 36.1, 35.7, 35.5, 35.2, 32.6, 32.5, 28.1, 28.1, 28.0, 24.4, 23.8, 22.9, 22.8, 22.5, 18.7, 18.7, 11.9.

2-methyl-1-phenylicos-11-en-1-one (5):[13b] Following the general procedure C, the title product was obtained as a pale yellow oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield: 17 mg, 32% yield (Procedure C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 5.38 (t, J = 3.7 Hz, 2H), 3.59-3.52 (m, 1H), 2.09-2.04 (m, 4H), 1.89-1.70 (m, 2H), 1.35-1.30 (m, 24H), 0.95-0.77 (m, 6H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 207.1, 143.9, 129.9, 128.1, 127.4, 126.7, 126.3, 115.0, 40.2, 33.1, 32.2, 31.9, 31.0, 30.0, 29.8, 29.6, 29.5, 29.3, 27.2, 27.0, 22.7, 15.7, 14.1.

2-((1-Benzylpiperidin-4-yl)methyl)-5,6-dimethoxy-2,3-dihydro-1*H*-inden-1-one (6):[13b] Following the general procedure C, the title product was obtained as a yellow oil using silica-gel column chromatography eluting with 50 % ethyl acetate in hexane. Yield: 34 mg, 36% yield (Procedure C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 7.2 Hz, 2H), 7.43-7.36 (m, 3H), 7.12 (s, 1H), 6.84 (s, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.64 (s, 2H), 3.34-3.25 (m, 1H), 2.71-2.51 (m, 4H), 1.97-1.85 (m, 5H), 1.50-1.27 (m, 4H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 207.0, 155.6, 149.4, 148.6, 137.4, 131.0, 129.3, 128.9, 127.0, 107.3, 104.2, 70.4, 56.2, 56.0, 52.1, 44.5, 33.6, 31.8, 29.6, 22.6, 14.0.

ASSOCIATED CONTENT

Supporting Information. The Supporting Information is available free of charge on the ACS Publications website
X-ray crystallographic data, CIF file and NMR data (PDF)

AUTHOR INFORMATION

Corresponding Author

* E-mail: dbane.fcy@iitr.ac.in

Author Contributions

ǂ These authors contributed equally to this work.

ACKNOWLEDGMENT

The authors thank DAE-BRNS, India (Young Scientist Research Award to D. B., 37(2)/20/33/2016-BRNS). IIT Roorkee (SMILE-32) and FIST-DST are gratefully acknowledge for instrument facilities. A. A. and S. B. thank IIT-R and INSPIRE Fellowship (DST/2017/IF170766) for financial support.

REFERENCES

(1) (a) *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, 2000. (b) Beletskaya, I. P.; Nájera, C.; Yus, M. Stereodivergent Catalysis. *Chem. Rev*. **2018**, *118*, 5080-5200.

(2) (a) Barta, K.; Ford, P. C. Catalytic Conversion of Nonfood Woody Biomass Solids to Organic Liquids. *Acc. Chem. Res.* **2014**, *47*, 1503-1512. (b) Vispute, T. P.; Zhang, H.; Sanna, A.; Xiao, R.; Huber, G. W. Renewable Chemical Commodity Feedstocks from Integrated Catalytic Processing of Pyrolysis Oils. *Science* **2010**, *330*, 1222-1227. (c) Tuck, C. O.; Pérez, E.; Horváth, I. T.; Sheldon, R. A.; Poliakoff, M. Valorization of Biomass: Deriving More Value from Waste. *Science* **2012**, *337*, 695-699.

(3) For recent selected reviews: (a) Irrgang, T.; Kempe, R. 3d-Metal Catalyzed *N*- and C-Alkylation Reactions via Borrowing Hydrogen or Hydrogen Autotransfer. *Chem. Rev.*, 2019, *119*, 2524-2549. (b) Corma, A.; Navas, J.; Sabater, M. J. Advances in One-Pot Synthesis through Borrowing Hydrogen Catalysis. *Chem. Rev*. 2018, *118*, 1410-1459. (c) Kim, S. W.; Zhang, W.; Krische, M. J. Catalytic Enantioselective Carbonyl Allylation and Propargylation via Alcohol-Mediated Hydrogen Transfer: Merging the Chemistry of Grignard and Sabatier. *Acc. Chem. Res*. 2017, *50*, 2371-2380. (d) Chelucci, G. Ruthenium and Osmium Complexes in C-C Bond-Forming Reactions by Borrowing Hydrogen Catalysis. *Coord. Chem. Rev*. 2017, *331*, 1-36. (e) Obora, Y. Recent Advances in α-Alkylation Reactions Using Alcohols with Hydrogen Borrowing Methodologies. *ACS Catal*. 2014, *4*, 3972-3981. (f) Crabtree, R. H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev*. 2017, *117*, 9228-9246. (g) Huang, F.; Liu, Z. Q.; Yu, Z. K. C-Alkylation of Ketones and Related Compounds by Alcohols: Transition-Metal-Catalyzed Dehydrogenation. *Angew. Chem., Int. Ed*. 2016, *55*, 862-875. (h) Yang, Q.; Wang, Q. F.; Yu, Z. K. Substitution of Alcohols by *N*-nucleophiles via Transition Metal-Catalyzed Dehydrogenation. *Chem. Soc. Rev*. 2015, *44*, 2305-2329. (i) Reed-Berendt, B. G.; Polidano, K.; Morrill, L. C. Recent Advances in Homogeneous Borrowing Hydrogen Catalysis using Earth-abundant First Row Transition Metals. *Org. Biomol. Chem.* **2019**, *17*, 1595-1607.

(4) For selected recent examples, see: (a) Peña-López, M.; Piehl, P.; Elangovan, S.; Neumann, H.; Beller, M. Manganese Catalyzed Hydrogen-Autotransfer C−C Bond Formation: α-Alkylation of Ketones with Primary Alcohols. *Angew. Chem., Int. Ed.* **2016**, *55*, 14967-14971. (b) Zhang, G.; Wu, J.; Zeng, H.; Zhang, S.; Yin, Z.; Zheng, S. Cobalt-Catalyzed α-Alkylation of Ketones with Primary Alcohols**.** *Org. Lett.* **2017**, *19*, 1080-1083. (c) Manojveer, S.; Salahi, S.; Wendt, O. F.; Johnson, M. T. Ru-Catalyzed Cross-Dehydrogenative Coupling between Primary Alcohols to Guerbet Alcohol Derivatives: with Relevance for Fragrance Synthesis. *J. Org. Chem*. **2018**, *83*, 10864-10870.

(5) (a) Shen, D.; Poole, D. L.; Shotton, C. C.; Kornahrens, A. F.; Healy, M. P.; Donohoe, T. J. Hydrogen Borrowing and Interrupted Hydrogen Borrowing Reactions of Ketones and Methanol Catalyzed by Iridium. *Angew. Chem., Int. Ed.* **2015**, *54*, 1642-1645. (b) Frost, J. R.; Cheong, C. B.; Akhtar, W. M.; Caputo, D. F. J.; Stevenson, N. G.; Donohoe, T. J. Strategic Application and Transformation of *ortho*-Disubstituted Phenyl and Cyclopropyl Ketones To Expand the Scope of Hydrogen Borrowing Catalysis**.** *J. Am. Chem. Soc.* **2015**, *137*, 15664-15667. (c) Schlepphorst, C.; Maji, B.; Glorius, F. Ruthenium-NHC Catalyzed α-Alkylation of Methylene Ketones Provides Branched Products through Borrowing Hydrogen Strategy. *ACS Catal.* **2016**, *6*, 4184-4188. (d) Yan, F. -X.; Zhang, M.; Wang, X. -T.; Xie, F.; Chen, M. -M.; Jiang, H. Efficient Ruthenium-Catalyzed α-Alkylation of Ketones using Pyridyl Methanols. *Tetrahedron* **2014**, *70*, 1193-1198. (e) Li, F.; Ma, J.; Wang, N. α-Alkylation of Ketones with Primary Alcohols Catalyzed by a Cp*Ir Complex Bearing a Functional Bipyridonate Ligand. *J. Org. Chem.* **2014**, *79*, 10447-10455. (f) Cho, C. S. A Palladium-Catalyzed Route for α-Alkylation of Ketones by Primary Alcohols. *J. Mol. Catal. A.* **2005**, *240*, 55-60. (g) Yamada, Y. M. A.; Uozumi, Y. A Solid-Phase Self-Organized Catalyst of Nanopalladium with Main-Chain Viologen Polymers: α-Alkylation of Ketones with Primary Alcohols. *Org. Lett.* **2006**, *8*, 1375-1378. (h) Kwon, M. S.; Kim, N.; Seo, S. H.; Park, I. S.; Cheedrala, R. K.; Park, J. Recyclable Palladium Catalyst for Highly Selective α Alkylation of Ketones with Alcohols. *Angew. Chem. Int. Ed*. **2005**, *44*, 6913-6915. (i) Cui, X.; Zhang, Y.; Shi, F.; Deng, Y. Organic Ligand-Free Alkylation of Amines, Carboxamides, Sulfonamides, and Ketones by Using Alcohols Catalyzed by Heterogeneous Ag/Mo Oxides. *Chem. Eur. J.* **2011**, *17*, 1021-1028.

(6) (a) Bullock, R. M. *Catalysis Without Precious Metals*, Eds.: Wiley-VCH, Weinheim, **2010**. (b) Albrecht, M.; Bedford, R.; Plietker, B. Catalytic and Organometallic Chemistry of Earth-Abundant Metals. *Organometallics* **2014**, *33*, 5619-5621. (c) Bauer, I.; Knölker, H.-J. Iron Catalysis in Organic Synthesis. *Chem. Rev*., **2015**, *115*, 3170–3387. (d) Su, B.; Cao, Z.-C.; Shi, Z.-J. Exploration of Earth-Abundant Transition Metals (Fe, Co, and Ni) as Catalysts in Unreactive Chemical Bond Activations. *Acc. Chem. Res.*, **2015**, *48*, 886-896. (e) Robinson, S. J. C.; Heinekey, D. M. Hydride & Dihydrogen Complexes of Earth Abundant Metals: Structure, Reactivity, and Applications to Catalysis. *Chem. Commun.* **2017**, *53*, 669-676.

(7) (a) Kessler, S. N.; Bäckvall, J.-E. Iron-Catalyzed Cross-Coupling of Propargyl Carboxylates and Grignard Reagents: Synthesis of Substituted Allenes. *Angew. Chem., Int. Ed*. **2016**, *55*, 3734-3738. (b) Shaikh, N. S.; Enthaler, S.; Junge, K.; Beller, M. Iron-Catalyzed Enantioselective Hydrosilylation of Ketones. *Angew. Chem., Int. Ed*. **2008**, *47*, 2497-2501. (c) Sui-Seng, C.; Freutel, F.; Lough, A. J.; Morris, R. H. Highly Efficient Catalyst Systems Using Iron Complexes with a Tetradentate PNNP Ligand for the Asymmetric Hydrogenation of Polar Bonds. *Angew. Chem., Int. Ed*. **2008**, *47*, 940-943. (d) Zuo, W.; Lough, A. J.; Li, Y. F.; Morris, R. H. Amine(imine)diphosphine Iron Catalysts for Asymmetric Transfer Hydrogenation of Ketones and Imines. *Science* **2013**, *342*, 1080-1083. (e) Kessler, S. N.; Hundemer, F.; Bäckvall, J.-E. A Synthesis of Substituted α-Allenols via Iron-Catalyzed Cross-Coupling of Propargyl Carboxylates with Grignard Reagents. *ACS Catal*. **2016**, *6*, 7448-7451.

(8) For selected recent examples, see: (a) Yan, T.; Feringa, B. L.; Barta, K. Iron Catalysed Direct Alkylation of Amines with Alcohols. *Nat. Commun*. **2014**, *5*, 5602. (b) Facchini, S. V.; Cettolin, M.; Bai, X.; Casamassima, G.; Pignataro, L.; Gennari, C.; Piarulli, U. Efficient Synthesis of Amines by Iron-Catalyzed C=N Transfer Hydrogenation and C=O Reductive Amination. *Adv. Synth. Catal*. **2018**, *360*, 1054-1059. (c) Roudier, M.; Constantieux, T.; Rodriguez, J.; Quintard, A. Recent Achievements in Enantioselective Borrowing Hydrogen by the Combination of Iron and Organocatalysis. *Chimia* **2016**, *70*, 97-101. (d) Funk, T. W.; Mahoney, A. R.; Sponenburg, R. A.; Zimmerman, K. P.; Kim, D. K.; Harrison, E. E. Synthesis and Catalytic Activity of (3,4-Diphenylcyclopentadienone)Iron Tricarbonyl Compounds in Transfer Hydrogenations and Dehydrogenations. *Organometallics* **2018**, *37*, 1133-
1140. (e) Polidano, K.; Allen, B. D. W.; Williams, J. M. J.; Morrill, L. C. Iron- Catalyzed Methylation Using the Borrowing Hydrogen Approach. *ACS Catal*. **2018**, *8*, 6440-6445. (f) Brown, T. J.; Cumbes, M.; Diorazio, L. J.; Clarkson, G. J.; Wills, M. Use of (Cyclopentadienone)iron Tricarbonyl Complexes for C−N Bond Formation Reactions between Amines and Alcohols. *J. Org. Chem*. **2017**, *82*, 10489-10503. (g) Chakraborty, S.; Lagaditis, P. O.; Förster, M.; Bielinski, A. E.; Hazari, N.; Holthausen, M. C.; Jones, W. D.; Schneider, S.; Well-Defined Iron Catalysts for the Acceptorless Reversible Dehydrogenation-Hydrogenation of Alcohols and Ketones. *ACS Catal*. **2014**, *4*, 3994-4003.

(9) (a) Knölker, H.-J.; Baum, E.; Goesmann, H.; Klauss, R. Demetalation of Tricarbonyl(cyclopentadienone)Iron Complexes Initiated by a Ligand Exchange Reaction with NaOH−X-Ray Analysis of a Complex with Nearly Square-Planar Coordinated Sodium. *Angew. Chem., Int. Ed*. **1999**, *38*, 2064-2066. (b) Sherry, B. D.; Fürstner, A. The Promise and Challenge of Iron-Catalyzed Cross Coupling. *Acc. Chem. Res*. **2008**, *41*, 1500-1511. (c) Bauer, E. B. Iron Catalysis: Historic Overview and Current Trends. *In Topics in Organometallic Chemistry: Iron Catalysis II*; Bauer, E. B., Ed.; Springer International: Cham, Switzerland, **2015**; pp 1-18. (d) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. Iron-Catalyzed Reactions in Organic Synthesis. *Chem. Rev*. **2004**, *104*, 6217-6254. (e) Bauer, I.; Knölker, H.-J. Iron Catalysis in Organic Synthesis. *Chem. Rev*. **2015**, *115*, 3170-3387.

(10) For selected recent examples, see: (a) Gustafson, K.; Guðmundsson, A.; Lewis, K.; Bäckvall, J.-E. Chemoenzymatic Dynamic Kinetic Resolution of Secondary Alcohols Using an Air- and Moisture-Stable Iron Racemization Catalyst. *Chem. - Eur. J*. **2017**, *23*, 1048-1051. (b) Guðmundsson, A.; Gustafson, K.; Mai, B. K.; Yang, B.; Himo, F.; Bäckvall, J.-E. Efficient Formation of 2,3-Dihydrofurans via Iron-Catalyzed Cycloisomerization of α-Allenols. *ACS Catal*. **2018**, *8*, 12-16. (c) Guðmundsson, A.; Gustafson, K.; Mai, B. K.; Hobiger, V.; Himo, F.; Bäckvall, J.-E. Diastereoselective Synthesis of N-Protected 2,3-Dihydropyrroles via Iron-Catalyzed Cycloisomerization of α-Allenic
Sulfonamides. *ACS Catal*. **2019**, *9*, 1733-1737.

(11) For examples on the Knölker-type Iron catalyst and applications, see: (a) Knölker, H.-J. Efficient Synthesis of Tricarbonyliron-Diene Complexes-Development of an Asymmetric Catalytic Complexation. *Chem. Rev*. **2000**, *100*, 2941-2961. (b) Casey, C. P.; Guan, H. An Efficient and Chemoselective Iron Catalyst for the Hydrogenation of Ketones. *J. Am. Chem. Soc*. **2007**, *129*, 5816-5817. (c) Quintard, A.; Rodriguez, J. Iron Cyclopentadienone Complexes: Discovery, Properties, and Catalytic Reactivity. *Angew. Chem., Int. Ed*. **2014**, *53*, 4044-4055. (d) Casey, C. P.; Guan, H. Cyclopentadienone Iron Alcohol Complexes: Synthesis, Reactivity, and Implications for the Mechanism of Iron-Catalyzed Hydrogenation of Aldehydes. *J. Am. Chem. Soc*. **2009**, *131*, 2499-2507. (e) Khusnutdinova, R.; Milstein, D. Metal−Ligand Cooperation. *Angew. Chem., Int. Ed*. **2015**, *54*, 12236-12273. (f) Pandey, S.; Raj, K. V.; Shinde, D. R.; Vanka, K.; Kashyap, V.; Kurungot, S.; Vinod, C. P.; Chikkali. S. H. Iron Catalyzed Hydroformylation of Alkenes under Mild Conditions: Evidence of and Fe(II) Catalyzed Process. *J. Am. Chem. Soc*. **2018**, *140*, 4430-4439. (g) Bettoni, L.; Seck, C.; Mbaye, M. D.; Gaillard, S.; Renaud, J.-L. Iron-Catalyzed Tandem Three-Component Alkylation: Access to α-Methylated Substituted Ketones. *Org. Lett*. **2019**, *21*, 3057-3061.

(12) (a) Elangovan, S.; Sortais, J. -B.; Beller, M.; Darcel, C. Iron-Catalyzed α-Alkylation of Ketones with Alcohols**.** *Angew. Chem., Int. Ed.* **2015**, *54*, 14483-14486. (b) Seck, C.; Mbaye, M. D.; Coufourier, S.; Lator, A.; Lohier, J.-F.; Poater, A.; Ward, T. R.; Gaillard, S.; Renaud, J.-L. Alkylation of Ketones Catalyzed by Bifunctional Iron Complexes: From Mechanistic Understanding to Application. *ChemCatChem* **2017**, *9*, 4410-4416.

(13) (a) Vellakkaran, M.; Singh, K.; Banerjee, D. An Efficient and Selective Nickel-Catalyzed Direct *N*-Alkylation of Anilines with Alcohols. *ACS Catal*. **2017**, *7*, 8152-8158. (b) Das, J.; Singh, K.; Vellakkaran, M.; Banerjee, D., Nickel-Catalyzed Hydrogen-Borrowing Strategy for α-Alkylation of Ketones with Alcohols: A New Route to Branched gem-Bis(alkyl) Ketones *Org. Lett*. **2018**, *20*, 5587-5591. (c) Kabadwal, L. M.; Das, J.; Banerjee, D. Mn(II)-Catalysed Alkylation of Methylene Ketones with Alcohols: Direct Access to Functionalised Branched Products. *Chem. Commun.* **2018**, *54*, 14069-14072. (d) Das, J.; Vellakkaran, M.; Banerjee, D. Nickel-Catalyzed Alkylation of Ketone Enolates: Synthesis of Monoselective Linear Ketones. *J. Org. Chem*. **2019**, *84*, 769-779.

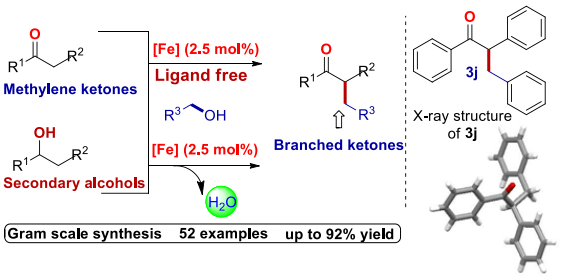
(14) Selected examples for the syntheses of donepezil, see: (a) Dubey, S. K.; Kharbanda, M.; Mathela, C. S. A New Commercially Viable Synthetic Route for Donepezil Hydrochloride: Anti-Alzheimer's Drug. *Chem. Pharm. Bull*. **2010**, *58*, 1157-1160. (b) Elati, C. R.; Kolla, N.; Chalamala, S. R.; Vankawala, P. J.; Sundaram, V.; Vurimidi, H.; Mathad, V. T. New Synthesis of Donepezil Through Palladium-Catalyzed Hydrogenation Approach. *Synth. Commun.* **2006**, *36*, 169-174.

(15) Samec, J. S. M.; Backvall, J. -E.; Andersson, P. G.; Brandt, P. Mechanistic Aspects of Transition metal-Catalyzed Hydrogen Transfer Reactions. *Chem. Soc. Rev.* **2006**, *35*, 237-248.

(16) $Fe_2(CO)_9$ is extremely toxic and contact with skin and eyes are avoided. Proper protection should be taken while use and to circumvent inhale of dust particles from the chemical, wear respiratory mask. $Fe_2(CO)_9$ should be kept in cold place and avoid intact with ignition flames.

(17) Ito, H.; Renaldo, A. F.; Johnson, R. D.; Ueda, M. ^{13}C Chemical Shift Non-equivalence in Methylene Carbons of Monosubstituted Cyclohexanes. *Magn. Reson. Chem.* **1989**, *27*, 273-276.

(18) Kavukcu, S. B.; Günnaz, S.; Şahin, O.; Türkmen, H. Piano-stool Ru (II) Arene Complexes that Contain Ethylenediamine and Application in alpha-Alkylation Reaction of Ketones with Alcohols. *Appl Organometal Chem*. **2019**, *33*, e4888.


Methylene ketones
Secondary alcohols
[Fe] (2.5 mol%)
Ligand free
[Fe] (2.5 mol%)
Branched ketones
3j
X-ray structure of 3j
Gram scale synthesis 52 examples up to 92% yield