Exploration of Aryl Phosphates in Palladium-catalyzed Mono-α-arylation of Aryl and Heteroaryl Ketones

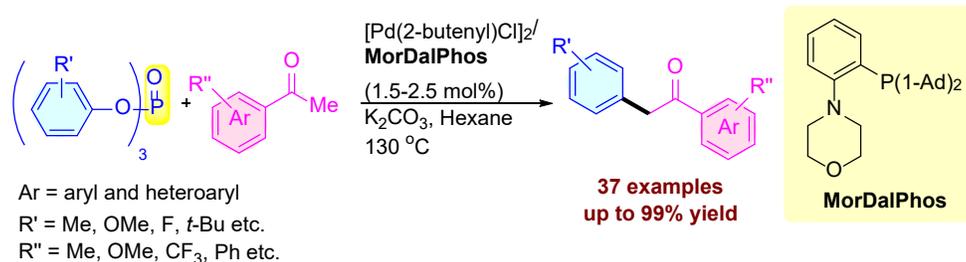Xiangmeng Chen,[†] Zicong Chen[†] and Chau Ming So,*[,†,‡]

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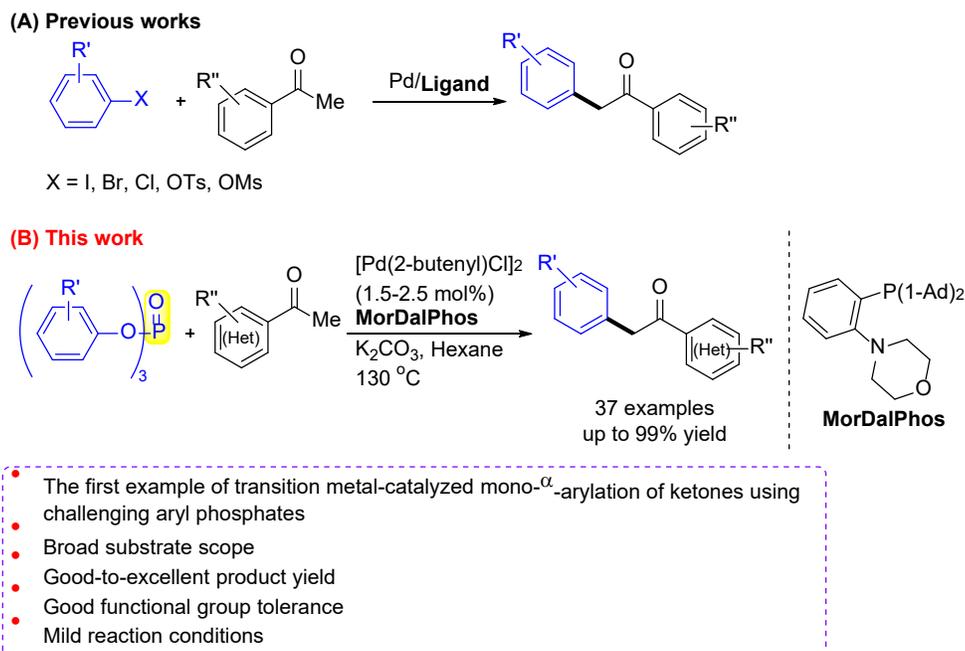
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ABSTRACT. This paper presents the first general examples of selective palladium-catalyzed mono-α-arylation of aryl and heteroaryl ketones with aryl phosphates. The catalyst system, consisting of [Pd(2-butenyl)Cl]$_2$ and MorDalPhos, exhibited high catalytic reactivity towards this reaction. A wide range of aryl phosphates were efficiently coupled with aryl and heteroaryl ketones with good selectivity. Excellent-to-good product yields were afforded. The gram-scale reaction was conducted smoothly. Reductive elimination or transmetalation might be a rate-determining step in this reaction.

Introduction

α-Arylated carbonyl motifs are commonly found in natural products and pharmaceutically active molecules.[1] Palladium-catalyzed α-arylation of carbonyl compounds is one of the most powerful and attractive methodologies for the construction of $C(sp^3)$-$C(sp^2)$ bonds to access these valuable products.[2] Since the research groups of Miura,[3] Buchwald,[4] and Hartwig[5] independently disclosed their findings on palladium-catalyzed α-arylation of ketones, substantial effort has been made to advance this technology, including fine-tuning ligands, precatalysts, and other reaction parameters.[2,6]
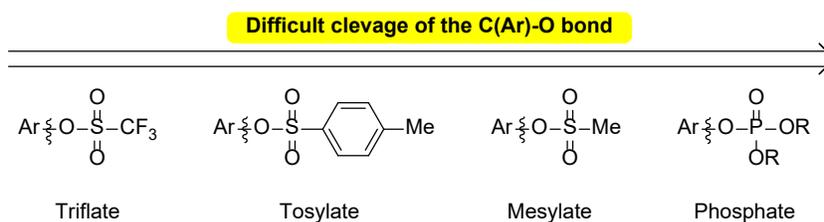
Aryl halides are commonly employed as electrophiles in palladium-catalyzed α-arylation of ketone derivatives due to their easy oxidative addition (Scheme 1A).[6] However, halogenated compounds are not readily available in the field of medicinal chemistry. Additional steps are required to synthesize aryl halides from naturally occurring aromatic compounds. Indeed, aryl electrophiles generated from phenolic compounds are highly desirable complements because they are easier to prepare from commercially available phenols, they have a higher stability towards air and moisture, are more cost-effective, have larger substitution patterns that are not easily accessible with their halide counterparts, and exhibit higher crystallinity allowing for simpler isolation and purification.[7] In the past few years, aryl sulfonates, such as triflates, tosylates, and mesylates, were found to be successful substrates for palladium-catalyzed α-arylation of ketone derivatives (Scheme 1A).[8] Moreover, aryl phosphates derived from phenols also have similar advantages; and in general, they are a biologically important functional group. To the best of our knowledge, no previous study has investigated the transition metal-catalyzed α-arylation of ketone derivatives using aryl phosphates as electrophilic partners.[9]

The application of aryl phosphates on palladium catalysis is limited by their inherently high stability, indicating that it is difficult for them to undergo oxidative addition with Pd (0) species (Scheme 2A). Additionally, several challenges are associated with the reaction: 1) further arylation would occur due to the increased acidity of the remaining α-C-H bonds after the first step of arylation of the ketones, resulting in undesired α,α-diarylated products; 2) the complete hydrolysis would occur under harsh reaction conditions; and 3) the demanding balance between the oxidative addition of the aryl phosphates and the reductive elimination of the aryl-Pd-ketone enolate species must be tackled by effective supporting ligands (Scheme 2B).
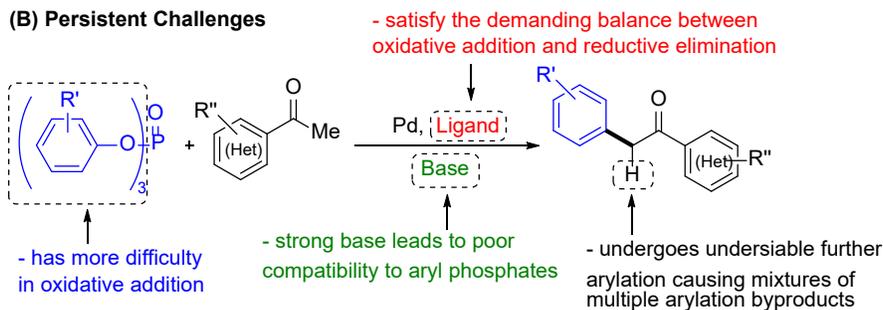
(A) Previous works

X = I, Br, Cl, OTs, OMs

(B) This work

[Pd(2-butenyl)Cl]₂
(1.5-2.5 mol%)
MorDalPhos
K₂CO₃, Hexane
130 °C

37 examples
up to 99% yield

MorDalPhos

- The first example of transition metal-catalyzed mono-α-arylation of ketones using challenging aryl phosphates
- Broad substrate scope
- Good-to-excellent product yield
- Good functional group tolerance
- Mild reaction conditions

Scheme 1. Palladium-catalyzed mono-α-arylation

(A) Comparison of phenol derivatives

Difficult clevage of the C(Ar)-O bond

Triflate Tosylate Mesylate Phosphate

(B) Persistent Challenges

- satisfy the demanding balance between oxidative addition and reductive elimination

- has more difficulty in oxidative addition

- strong base leads to poor compatibility to aryl phosphates

- undergoes undersiable further arylation causing mixtures of multiple arylation byproducts

Scheme 2. Persistent challenges in palladium-catalyzed mono-α-arylation

To address this challenging circumstance, it is important to develop a general and active catalyst system. In the past decade, state-of-the-art ligands have been developed and selected for tackling the electrophiles that are considered to be extremely difficult, such as aryl chlorides, tosylates, and mesylates in palladium-catalyzed α-arylation of ketones.[2,6,8] As a continuation of our research interest in the development of phosphine ligands [10] and their application in α-arylation using challenging

electrophiles,[6q,8d,11] this paper presents the first palladium-catalyzed α-arylation of aryl and heteroaryl ketones with aryl phosphates (Scheme 1B).

Results and Discussion

To address the challenges in palladium-catalyzed α-arylation of aryl ketones with aryl phosphates, we first investigated the catalytic efficacy of a library of electronically and sterically diverse phosphine ligands using triphenyl phosphate and acetophenone as model substrates (See Supporting Information, Table S1). A total of 20 state-of-the-art ligands with diverse scaffolds, which are commercially available and/or effective in C-O bond activation reactions, were tested. PPh$_3$ and PCy$_3$ showed no product yields. Biphosphine ligands, such as dppf, XantPhos, NiXantPhos, and BINAP, were found to be inactive towards this reaction. The reaction results for Buchwald-type ligands, such as Cy-JohnPhos, DavePhos, SPhos, RuPhos, XPhos, BrettPhos, and tBuXPhos, were also poor. Moreover, CM-Phos and PhMezole-Phos ligands failed in this reaction. No conversion occurred with the Beller group ligands, such as cataCXium®A and cataCXium®ABn. To our delight, Stradiotto's *P,N*-type phosphine ligand MorDalPhos was outstanding in this survey. According to previous reports, MorDalPhos has an excellent performance in α-arylation of carbonyl compounds via C(sp^2)-O bond cleavage.[8c,8d] With our preliminary reaction condition, we found that MorDalPhos produced a monoarylated product yield of 43%. Yet, PPh$_2$-MorDalPhos and PCy$_2$-MorDalPhos failed to afford the desired product. We believe that the superior performance of MorDalPhos is attributed to the electron-richness and steric hindrance provided by the -P(1-Ad)$_2$ group and the aryl-amine scaffold, respectively.

Encouraged by the initial ligand screening results, we conducted a series of investigations to optimize the reaction conditions (Table 1). Commonly used inorganic bases were screened (Table 1, entries 1–7). Mild base K$_2$CO$_3$, which minimized the aryl phosphate hydrolysis, was found to be superior to the other bases that were screened. Among the surveyed organic solvents, hexane provided a better product yield than dioxane, THF, CPME, *t*-BuOH, DMF, and toluene (Table 1, entries 1 and 8–13). We found that the decomposition of aryl phosphate to phenol occurred when polar solvents, such as *t*-BuOH and DMF, were used. After investigating the palladium sources, [Pd(2-butenyl)Cl]$_2$ was found to be the most suitable palladium precursor for this coupling reaction; the desired product yield was 81% (Table 1, entries 1 and 14–19). In our reaction temperature study, decreasing the reaction temperature reduced the desired product yield (Table 1, entries 1 and 20). The best product yield was obtained at a temperature of 130 °C; thus, it was chosen as the reaction temperature for further study. Excellent product yield (96%) was achieved by prolonging the reaction time to 10 h (Table 1, entries 1 and 21). Increasing the ketone equivalents to 5 equiv. was found to be the suitable ratio to preserve this

coupling reaction because of the reduction in the occurrence of the undesired diarylation reaction (Table 1, entries 21–24). After reducing the use of triphenyl phosphate to 0.067 mmol, the product yield decreased to 29%. This result indicates that only one aryl group was utilized in the reaction (Table 1, entry 25).

Table 1. Reaction condition optimization[a]
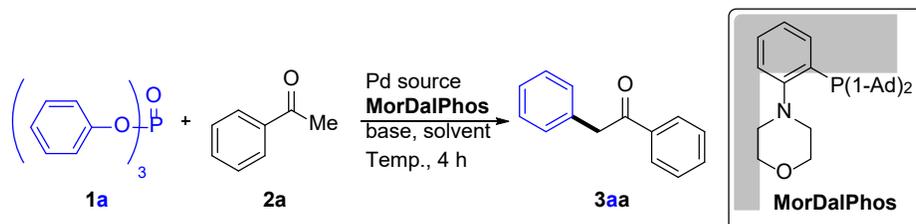
Entry	Pd source (mol%)	base	solvent	%yield[b]
1	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	Dioxane	42
2	Pd(OAc)$_2$ (3)	Na$_2$CO$_3$	Dioxane	28
3	Pd(OAc)$_2$ (3)	Cs$_2$CO$_3$	Dioxane	30
4	Pd(OAc)$_2$ (3)	K$_3$PO$_4$	Dioxane	23
5	Pd(OAc)$_2$ (3)	KOAc	Dioxane	32
6	Pd(OAc)$_2$ (3)	KF	Dioxane	26
7	Pd(OAc)$_2$ (3)	NaOt-Bu	Dioxane	17
8	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	THF	12
9	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	CPME	0
10	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	t-BuOH	10
11	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	DMF	0
12	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	Toluene	0
13	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	Hexane	54
14	Pd(TFA)$_2$ (3)	K$_2$CO$_3$	Dioxane	29
15	Pd(acac)$_2$ (3)	K$_2$CO$_3$	Dioxane	41
16	PdCl$_2$(CH$_3$CN)$_2$ (3)	K$_2$CO$_3$	Dioxane	41
17	[Pd(π-cinamyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Dioxane	64
18	[Pd(2-butenyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Dioxane	81
19	Pd$_2$dba$_3$ (1.5)	K$_2$CO$_3$	Dioxane	7

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20	Pd(OAc)$_2$ (3)	K$_2$CO$_3$	Hexane	28[c]
21	[Pd(2-butenyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Hexane	96[d]
22	[Pd(2-butenyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Hexane	73[d, e]
23	[Pd(2-butenyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Hexane	95[d, f]
24	[Pd(2-butenyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Hexane	98 (90)[d, g]
25	[Pd(2-butenyl)Cl]$_2$ (1.5)	K$_2$CO$_3$	Hexane	29[h]

[a]Reaction condition: triphenyl phosphate (0.2 mmol), acetophenone (0.3 mmol), Pd/MorDalPhos = 1:1.5, base (0.6 mmol) and solvent (1.0 ml) were stirred at 130 °C under N$_2$ for 4 h. [b]Calibrated GC yields were reported using dodecane as the internal standard. Isolated yield is shown in parentheses. [c]The reaction was performed at 120 °C. [d]The reaction time was 10 h. [e]acetophenone (0.2 mmol) was used. [f]acetophenone (0.4 mmol) was used. [g]acetophenone (1.0 mmol) was used. [h]triphenylphosphate (0.067mmol) and acetophenone (0.2 mmol) were used and the reaction time was 12 h.

With the optimized reactions in hand, we then probed the substrate scope using the newly developed [Pd(2-butenyl)Cl]$_2$/MorDalPhos catalyst system. We examined a wide range of non-activated and activated aryl phosphates, and the results are shown in Table 2. Electron-neutral (4-H, 4-Me, 3,5-diMe, 3,4,5-triMe, and 4-*t*-Bu) and -rich (3-OMe and 4-OMe) aryl phosphates were converted to the corresponding products in good-to-excellent yields (Table 2, compounds **3aa**, **3ba**, **3cf**, **3ea**, **3fa**, **3ga**, and **3ha**). Aryl phosphate bearing slightly electron-withdrawing substituent (4-F) also worked well in this reaction condition (Table 2, compound **3ia** and **3id**). Other aryl phosphates with functional groups, such as 4-CF$_3$, 4-CN, 4-COOMe and 4-NO$_2$ were attempted. However, poor or even no product yields were obtained. Sterically hindered tris(1-naphthyl)phosphate and tris(2-tolyl)phosphate were found to be applicable substrates and afforded the desired products in good yields (Table 2, compounds **3ja** and **3ka**). A diverse library of aryl methyl ketones was investigated as cross-coupling partners. Electron-poor (4-CF$_3$), -neutral (4-Me, 4-Ph and 3-Me), and -rich (4-OMe) aryl methyl ketones were effective substrates, and α-arylated smoothly in good-to-excellent product yields (Table 2, compounds **3ab**, **3ac**, **3ad**, **3ae**, **3af**, **3bc**, **3bd**, **3bf**, **3cf**, **3cd**, **3dd**, **3fd**, **3hd**, and **3jd**). 2-Acetonapthone derivatives also proceeded successfully (Table 2, compounds **3ag** and **3ah**). Sterically hindered aryl methyl ketones were able to couple with aryl phosphates and give good product yields. (Table 2, compounds **3ai**, **3aj**, **3ak**, **3al**, **3an**, **3bi** and **3ci**). Heteroaryl ketones, such as 3-acetyl-2,5-dimethylfuran and 2-acetylthiophenone were monoarylated smoothly and the heterocyclic substituents were well tolerated under this reaction condition (Table 2, compound **3ao**, **3bo** and 3**cq**). Moreover, α-Tetralone was found

to be a feasible cross-coupling partner (Table 2, compound **3ap**). Propiophenone was also coupled with tris(3-methoxyphenyl) phosphate smoothly and afforded excellent product yield (Table 2, compound **3cr**).

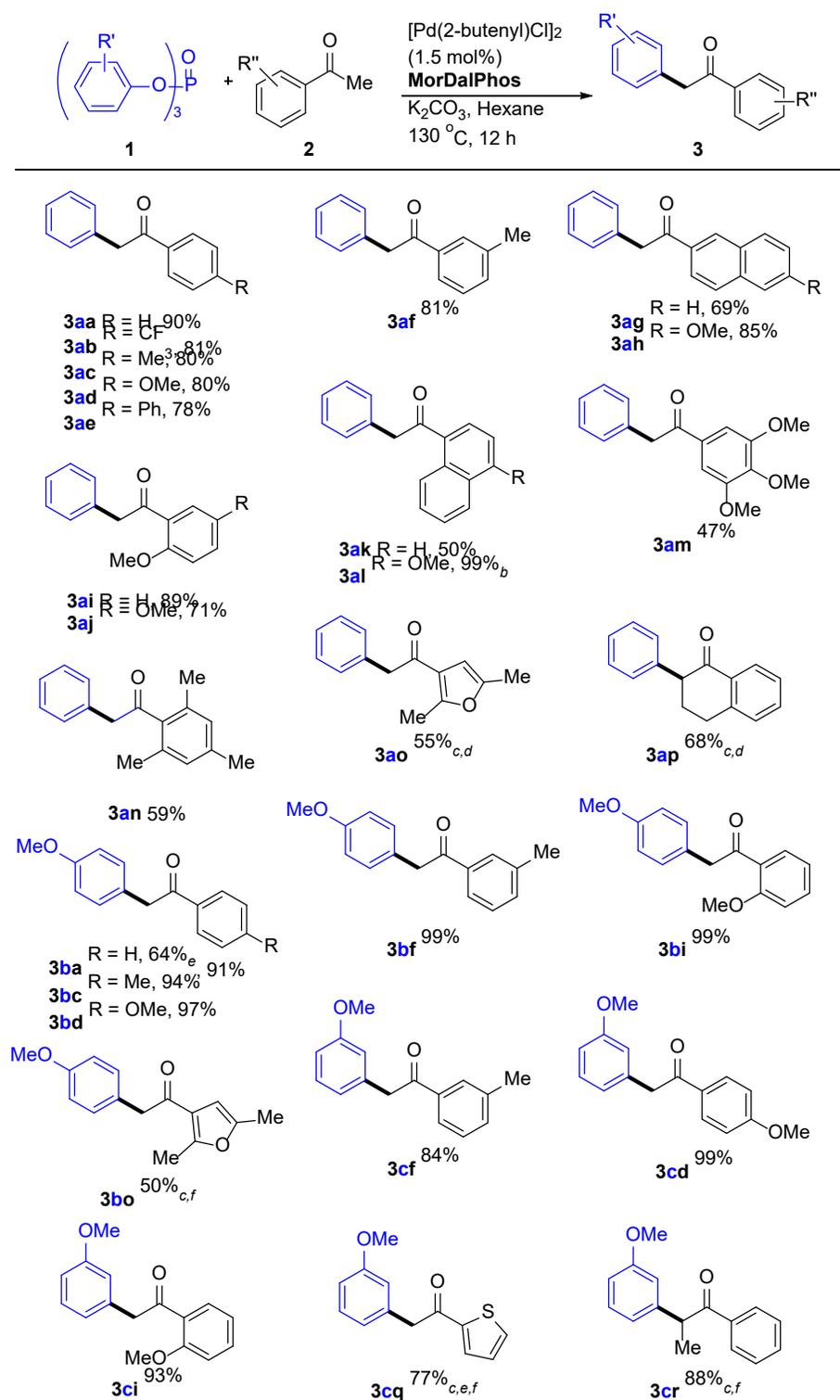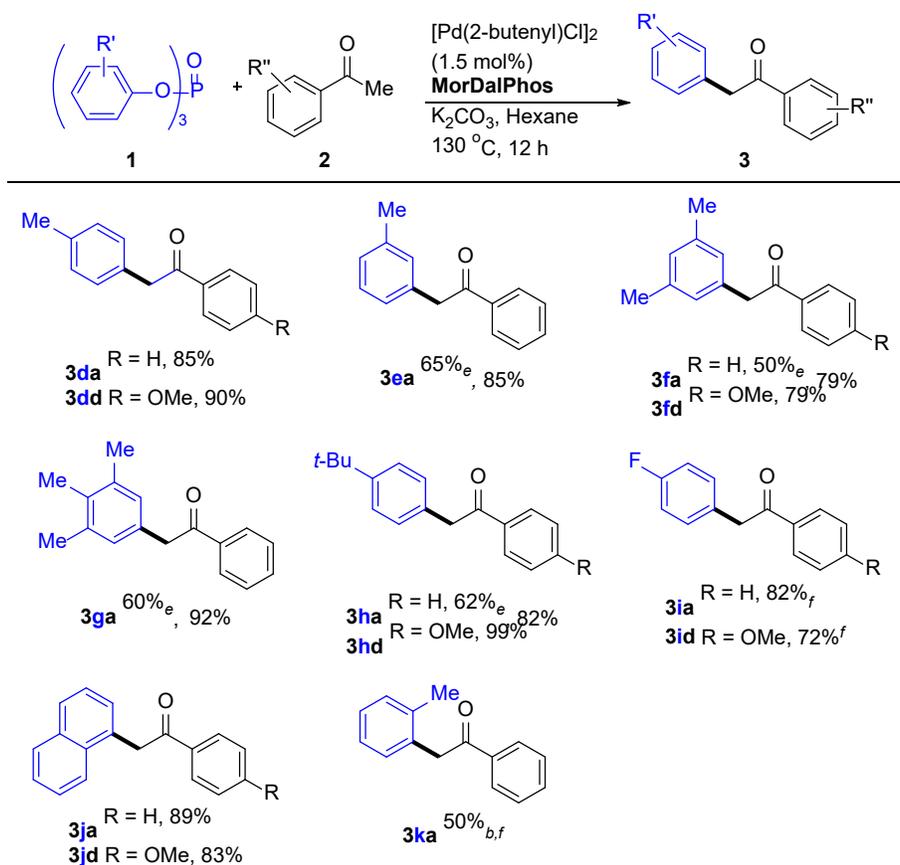***Table 2.*** Palladium-catalyzed α-arylation of aryl and heteroaryl ketones with aryl phosphates[a]

3aa R = H, 90%
3ab R = CF₃, 81%
3ac R = Me, 80%
3ad R = OMe, 80%
3ae R = Ph, 78%

3af 81%

3ag R = H, 69%
3ah R = OMe, 85%

3ai R = H, 89%
3aj R = OMe, 71%

3ak R = H, 50%
3al R = OMe, 99%[b]

3am 47%

3an 59%

3ao 55%[c,d]

3ap 68%[c,d]

3ba R = H, 64%[e]
3bc R = Me, 94%
3bd R = OMe, 97%

91%

3bf 99%

3bi 99%

3bo 50%[c,f]

3cf 84%

3cd 99%

3ci 93%

3cq 77%[c,e,f]

3cr 88%[c,f]

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Table 2. (Continued)

3da R = H, 85%	**3ea** 65%[e], 85%	**3fa** R = H, 50%[e] 79%
3dd R = OMe, 90%		**3fd** R = OMe, 79%

3ga 60%[e], 92%	**3ha** R = H, 62%[e] 82%	**3ia** R = H, 82%[f]
	3hd R = OMe, 99%	**3id** R = OMe, 72%[f]

3ja R = H, 89%	**3ka** 50%[b,f]
3jd R = OMe, 83%	

[a]Reaction condition: aryl phosphate (0.2 mmol), aryl ketone (1.0 mmol), [Pd(2-butenyl)Cl]₂ (1.5 mol%), MorDalPhos (4.5 mol%), K₂CO₃ (0.6 mmol), and hexane (1.0 ml) were stirred at 130 °C under N₂ for 12 h. Isolated yields were reported. [b][Pd(2-butenyl)Cl]₂ (2.0 mol%) was used. [c]Pd(2-butenyl)Cl]₂ (2.5 mol%) was used. [d]36 h was conducted. [e]aryl ketone (0.3 mmol) was used. [f]24 h was conducted.

To test the feasibility of scaling up the current reaction conditions, a gram-scale α-arylation of aryl ketone with aryl phosphate was conducted (Scheme 3). Triphenyl phosphate and acetophenone was directly scaled up 50 times to give the coupling product in 80% yield.
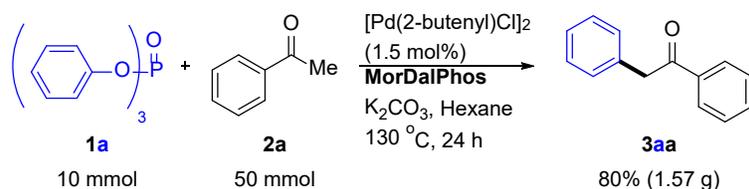

Scheme 3. Gram-scale α-arylation of aryl ketone with aryl phosphate (Reaction condition: triphenyl phosphate (10 mmol), acetophenone (50 mmol), [Pd(2-butenyl)Cl]₂ (1.5 mol%), MorDalPhos (4.5 mol%), K₂CO₃ (30 mmol), and hexane (50 ml) were stirred at 130 °C under N₂ for 24 h. Isolated yields

were reported.)
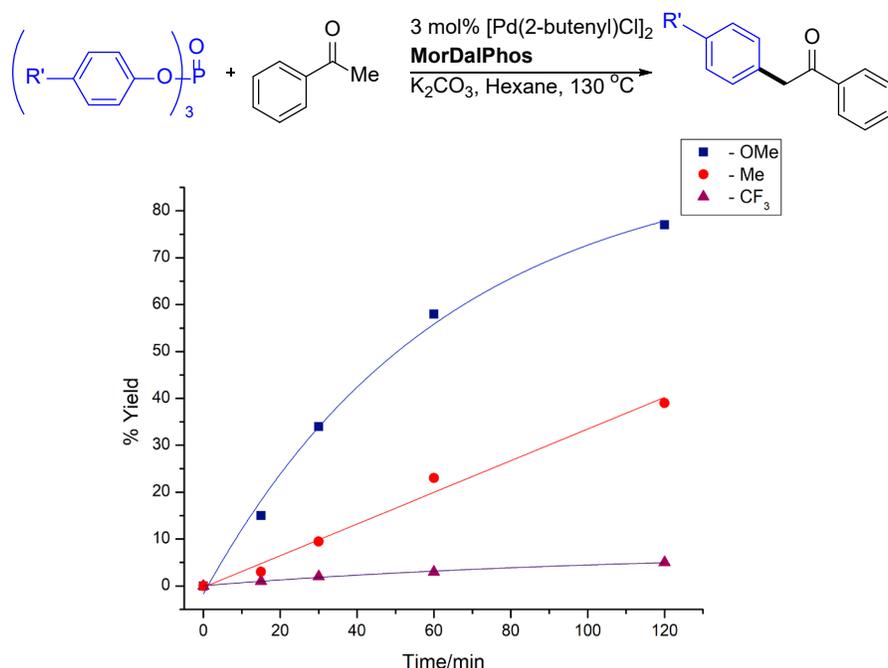
Scheme 4. Reaction rate study of electronically different aryl phosphate in α-arylation of aryl ketones

Table 3. Competition experiment of different aryl phosphates[a]
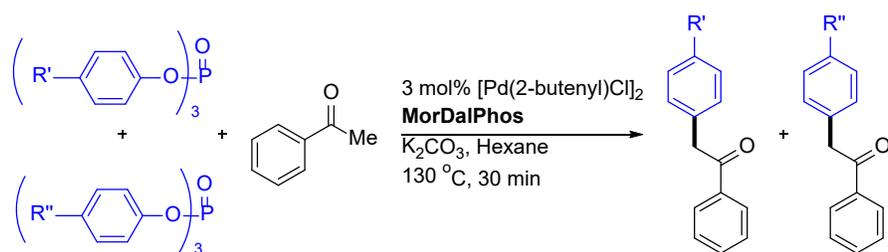
Entry	substrate 1	%yield[b]	substrate 2	%yield[b]
1	R' = OMe	24	R'' = Me	31
2	R' = CF$_3$	7	R'' = Me	0

[a]Reaction condition: (^{1}ArO)$_3$P(O) (0.1 mmol), (^{2}ArO)$_3$P(O) (0.1 mmol), acetophenone (1.0 mmol), Pd/MorDalPhos = 1:1.5, K$_2$CO$_3$ (0.6 mmol) and hexane (1.0 ml) were stirred at 130 °C under N$_2$ for 30 min. [b]Calibrated GC yields were reported using dodecane as the internal standard. Maximum yield for each substrate in the reaction mixture is 50%.

To obtain a more mechanistic insight into this α-arylation of aryl phosphate reaction under a

[Pd(2-butenyl)Cl]₂ and MorDalPhos catalyst system, competition experiments were conducted in combination with studies of initial reaction rates for a series of aryl phosphates. Tris(4-anisyl)phosphate, tris(4-tolyl)phosphate, and tris(4-trifluorophenyl)phosphate were selected to study the electronic effect with respect to the initial rates of the reaction (Scheme 4). We found that electron-rich tris(4-anisyl)phosphate proceeded at the fastest rate, while electron-deficient tris(4-trifluorophenyl)phosphate proceeded at the slowest rate. We have also used a combination of different aryl phosphates in the competition reactions. The mixtures of more electron-rich aryl phosphates proceeded at an overall higher conversion (Table 3, entry 1) than those of electron-poor substrates (Table 3, entry 2). Moreover, although the electron-rich substrate showed a faster reaction rate in the individual rate studies, the favored product in each competition experiment came from the more electron-deficient aryl phosphates. Furthermore, the presence of electron-poor aryl phosphate inhibited the α-arylation of more electron-rich substrates. More rapid oxidative addition of the electron-poor aryl phosphate followed by a slow reductive elimination may inhibit the catalyst from reacting with electron-rich aryl phosphate. These results suggest that either the transmetalation or reductive elimination may be the rate-limiting step for the [Pd(2-butenyl)Cl]₂ and MorDalPhos catalyst system using aryl phosphate as the electrophile.

Conclusion

In summary, we demonstrated the first palladium-catalyzed mono-α-arylation of aryl and heteroaryl ketones using aryl phosphates. The combination of [Pd(2-butenyl)Cl]₂ and MorDalPhos as the catalyst system exhibited excellent chemo- and monoselectivity towards this reaction. A wide range of aryl phosphates bearing electron-rich, -neutral, and -poor substituents were well coupled with the aryl ketones, and they afforded the corresponding products in good-to-excellent yields. Moreover, sterically hindered aryl phosphates were smoothly monoarylated. Heteroaryl ketones were shown to be applicable substrates using this approach. The gram-scale reaction was also conducted smoothly. Further investigation of the development of phosphine ligands for challenging aryl phosphate coupling is now underway in our laboratory.

Experimental Section

General Information. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All arylation reactions were performed in resealable screw-capped Schlenk flask (approx. 20 mL volume) in the presence of Teflon-coated magnetic stirrer bar (5 mm × 10 mm). Dioxane, tetrahydrofuran (THF), cyclopentyl methyl ether (CPME) and toluene were freshly distilled from sodium and sodium benzophenone ketyl under nitrogen.[12] Anhydrous *N, N*-

dimethylacetamide (DMF) in Sure/Seal bottles was purchased from Aldrich and used directly. Hexane and *tert*-butanol (*t*-BuOH) was freshly distilled from anhydrous CaH_2 under nitrogen. K_3PO_4, Na_2CO_3, K_2CO_3, Cs_2CO_3, KOAc, KF and NaO*t*-Bu were purchased from commercial suppliers and used as received. $Pd(OAc)_2$, $PdCl_2(CH_3CN)_2$, [Pd(π-cinamyl)Cl]$_2$ and $Pd_2(dba)_3$ were purchased from Strem. $Pd(TFA)_2$, $Pd(acac)_2$ and [Pd(2-butenyl)Cl]$_2$ was purchased from Aldrich. Indolyl phosphine ligand CM-Phos was prepared according to the reported literature.[10a] PhMezole-Phos was prepared according to the reported literature.[10b] PPh$_2$-MorDalPhos and PCy$_2$-MorDalPhos were prepared according to the reported literature.[8b] PCy$_3$, PPh$_3$, dppf, XantPhos, NiXantPhos, BINAP, Cy-JohnPhos, DavePhos, SPhos, RuPhos, XPhos, BrettPhos, *t*-BuXPhos, cataCXium®A, cataCXium®ABn and MorDalPhos, were purchased from commercial suppliers. Known aryl phosphates (triphenyl phosphate, tris(4-methoxyphenyl) phosphate, tris(3-methoxyphenyl) phosphate, tri-*m*-tolyl phosphate, tri-*p*-tolyl phosphate, tris(3,5-dimethylphenyl) phosphate, tris(4-(*tert*-butyl)phenyl) phosphate, tris(4-fluorophenyl) phosphate, tri-*o*-tolyl phosphate, and tri(naphthalen-1-yl) phosphate) were prepared according to the reported procedure.[13] Thin layer chromatography was conducted on Merck pre-coated silica gel 60 F254 plates. Silica gel (Merck, 230-400 mesh) was used for column chromatography. Melting points were measured on an uncorrected Büchi Melting Point B-545 instrument. NMR spectra were obtained on a Brüker spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C, 376 MHz for ^{19}F, 162 MHz for ^{31}P). Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) acted as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. ^{31}P NMR spectra were referenced to 85% H3PO4 externally. Coupling constants (J) were reported in Hertz (Hz). Mass spectra (EI-MS and ESI-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FTICR mass spectrometer (ESI-MS). GC-MS analysis was performed on a HP 5977A GCD system using a HP5MS column (30 m × 0.25 mm). The products reported in GC yield were referred to the authentic samples/dodecane calibration standard from HP 78990B GC-FID system. All isolated yield of compounds were estimated to be greater than 95% purity according to capillary gas chromatography (GC) or ^1H NMR measurement. Compounds described in the literature were characterized by comparison of their ^1H, ^{13}C and/or ^{19}F NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reports in tables.

General procedure for initial ligand screenings: A stock solution of $Pd(OAc)_2$ (0.06 mmol) in freshly

distilled 10 mL dioxane (3.0 mol% Pd per 1.0 mL stock solution) was first prepared under N_2. Ligands (6.0 mol% without specific notice), triphenyl phosphate (0.20 mmol) and K_2CO_3 (0.60 mmol) were added into an array of Schlenk tubes that charged with Teflon-coated magnetic stir bar (5 mm × 10 mm), and equipped with screw cap. The tubes were carefully evacuated and flushed with nitrogen (3 cycles). Acetophenone (0.30 mmol) was then added via syringe. The corresponding volume of stock solution of $Pd(OAc)_2$ were finally added to the array of Schlenk tubes via syringe. The reaction mixture was stirred for 1 min at room temperature. The batch of Schlenk tubes were sealed and magnetically stirred in a preheated 130 °C oil bath for 4 h. The reactions were then allowed to reach room temperature. Ethyl acetate (~8 mL), dodecane (45.2 µL, internal standard) and water (~4 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

General procedure for reaction condition screening: Palladium sources (3 mol%), MorDalPhos (4.5 mol%), triphenyl phosphate (0.20 mmol) and base (0.60 mmol) were added into an array of Schlenk tubes that charged with Teflon-coated magnetic stir bar (5 mm × 10 mm), and equipped with screw cap. The tubes were carefully evacuated and flushed with nitrogen (3 cycles). Acetophenone (0.30-1.0 mmol) and solvent (1.0 mL) were added via syringes. The reaction mixtures were stirred for 1 min at room temperature. The batch of Schlenk tubes were sealed and magnetically stirred in a preheated 120-130 °C oil bath for 4-10 h. The reactions were then allowed to reach room temperature. Ethyl acetate (~8 mL), dodecane (45.2 µL, internal standard) and water (~4 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

General procedure for α-arylation of aryl and heteroaryl ketones with aryl phosphates: [Pd(2-butenyl)Cl]$_2$ (1.5-2.5 mol%), MorDalPhos (4.5-7.5 mol%), aryl phosphate (0.20 mmol, if solid), aryl or heteroaryl ketone (0.3-1.0 mmol, if solid) and K_2CO_3 (0.60 mmol) were added into the Schlenk tube that charged with Teflon-coated magnetic stir bar (5 mm × 10 mm), and equipped with screw cap. The tube was carefully evacuated and flushed with nitrogen (3 cycles). Aryl phosphate (0.2 mmol, if liquid), aryl or heteroaryl ketone (0.30-1.0 mmol, if liquid), and hexane (1.0 mL) were added via syringes to the tube. The reaction mixture was stirred for 1 min at room temperature. The Schlenk tube was sealed and magnetically stirred in a preheated 130 °C oil bath for 12-36 h. After the completion of the reaction, the Schlenk tube was allowed to reach room temperature. Ethyl acetate (~8 mL) and water (~4 mL) were added. The organic layer was subjected to GC analysis. The organic layer was then separated and the aqueous layer was washed with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

General procedure for gram-scale α-arylation of acetophenone with triphenyl phosphate: [Pd(2-butenyl)Cl]$_2$ (1.5 mol%), MorDalPhos (4.5 mol%), triphenyl phosphate (10 mmol), and K$_2$CO$_3$ (30 mmol) were added into the 250 mL Schlenk flask that charged with Teflon-coated magnetic stir bar (8 mm × 30 mm), and equipped with screw cap. The tube was carefully evacuated and flushed with nitrogen (3 cycles). Acetophenone (50 mmol), and hexane (50 mL) were added via syringes to the flask. The reaction mixture was stirred for 1 min at room temperature. The Schlenk flask was sealed and magnetically stirred in a preheated 130 °C oil bath for 24 h. After the completion of the reaction, the Schlenk tube was allowed to reach room temperature. Ethyl acetate and water were added. The organic layer was subjected to GC analysis. The organic layer was then separated and the aqueous layer was washed with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was subjected to vacuum distillation and further purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

Tris(3,4,5-trimethylphenyl) phosphate

Tris(3,4,5-trimethylphenyl) phosphate, was synthesized according to general procedure.[13] To 3,4,5-trimethylphenol (30.0 mmol) and Et$_3$N (or NaH) (100.0 mmol) in toluene (50 mL) was slowly added POCl$_3$ (11.0 mmol) at 0 °C under vigorous stirring. Then reaction mixture was stirred at room temperature for 3 h. A solution of NaOH (10.0 g) in water (30 mL) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with toluene (5 × 50 mL). The combined organic layers were washed with saturated brine (3 × 15 mL), and dried over anhydrous Na$_2$SO$_4$. Solvent was removed under the reduced pressure, and the final product was recrystallized from methanol affording tris(3,4,5-trimethylphenyl) phosphate as a white solid 4.08 g (82%). m.p.= 114.8–115.3 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.12 (s, 3H), 2.25 (s, 6H), 6.89 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 14.8, 20.6, 118.9 (d, J = 5.2 Hz), 132.1, 137.9, 147.8 (d, J = 7.3 Hz); ^{31}P NMR (162 MHz, CDCl$_3$) δ -16.70; MS (EI): m/z (relative intensity) 452.3 (M$^+$, 100), 221.2 (14), 135.1 (13), 91.1 (14); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_{27}$H$_{34}$O$_4$P: 453.2181; Found 453.2189.

1,2-Diphenylethan-1-one (Table 2, compound 3aa)[14]

Yield: 90% (35.3 mg). Eluents (Toluene, R$_f$= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.32 (s, 2H), 7.27-7.38 (m, 5H), 7.49 (t, J= 7.4 Hz, 2H), 7.59 (t, J= 7.4 Hz, 1H), 8.05 (d, J= 7.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.5, 126.8, 128.57, 128.60, 128.63, 129.4, 133.1, 134.5, 136.6, 197.6; MS (EI): m/z (relative intensity) 196.1 (M$^+$, 6), 165.1 (3), 105.1 (100), 91.1 (7), 77.1 (33).

2-Phenyl-1-(4-(trifluoromethyl)phenyl)ethan-1-one (Table 2, compound 3ab)[14]

Yield: 81% (42.2 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.31 (s, 2H), 7.25-7.29 (m, 3H), 7.33-7.36 (m, 2H), 7.72 (d, J= 8.2 Hz, 2H), 8.11 (d, J= 8.1 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.8, 123.5 (q, J= 274 Hz), 125.7 (q, J= 3.7 Hz), 127.2, 128.8, 128.9, 129.4, 133.8, 134.4 (q, J= 36.2 Hz), 139.2, 196.6; ^{19}F NMR (376 MHz, CDCl$_3$) δ -63.1; MS (EI): m/z (relative intensity) 264.0 (M$^+$, 7), 173.0 (100), 145.0 (33), 91.1 (12).

2-Phenyl-1-(*p*-tolyl)ethan-1-one (Table 2, compound 3ac)[15]

Yield: 80% (33.6 mg). Eluents (Toluene, R_f= 0.60) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.44 (s, 3H), 4.29 (s, 2H), 7.26-7.37 (m, 7H), 7.95 (d, J= 8.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.6, 45.4, 126.8, 128.6, 128.7, 129.3, 129.4, 134.1, 134.7, 143.9, 197.2; MS (EI): m/z (relative intensity) 210.1 (M$^+$, 3), 119.1 (100), 91.1 (34), 65.0 (12).

1-(4-Methoxyphenyl)-2-phenylethan-1-one (Table 2, compound 3ad)[14]

Yield: 80% (36.2 mg). Eluents (Toluene, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.86 (s, 3H), 4.24 (s, 2H), 6.93 (d, J= 8.8 Hz, 2H), 7.24-7.34 (m, 5H), 8.00 (d, J= 8.9 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.2, 55.4, 113.8, 126.7, 128.6, 129.4, 129.6, 130.9, 134.9, 163.5, 196.2; MS (EI): m/z (relative intensity) 226.1 (M$^+$, 3), 135.0 (100), 107.0 (7), 92.0 (8), 77.0 (9)

1-([1,1'-Biphenyl]-4-yl)-2-phenylethan-1-one (Table 2, compound 3ae)[16]

Yield: 78% (42.4 mg). Eluents (Toluene, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.33 (s, 2H), 7.26-7.43 (m, 6H), 7.46-7.50 (m, 2H), 7.63 (d, J= 6.8 Hz, 2H), 7.69 (d, J= 8.4 Hz, 2H), 8.10 (d, J= 8.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.5, 126.9, 127.22, 127.24, 128.2, 128.7, 128.9, 129.2, 129.4, 134.6, 135.2, 139.8, 145.8, 197.2; MS (EI): m/z (relative intensity) 272.1 (M$^+$, 2), 181.1 (100), 152.1 (37), 91.1 (5).

2-Phenyl-1-(*m*-tolyl)ethan-1-one (Table 2, compound 3af)[16]

Yield: 81% (34.0 mg). Eluents (Toluene, R_f= 0.60) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.41 (s, 3H), 4.28 (s, 2H), 7.26-7.27 (m, 3H), 7.31-7.38 (m, 4H), 7.80-7.82 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.4, 45.5, 125.8, 126.8, 128.5, 128.6, 129.1, 129.4, 133.9, 134.6, 136.6, 138.4, 197.8; MS (EI): m/z (relative intensity) 210.1 (M$^+$, 2), 119.0 (100), 91.0 (32), 65.1 (9).

1-(Naphthalen-2-yl)-2-phenylethan-1-one (Table 2, compound 3ag)[14]

Yield: 69% (33.9 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column

chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.42 (s, 2H), 7.25-7.28 (m, 1H), 7.31-7.37 (m, 4H), 7.54-7.62 (m, 2H), 7.87-7.90 (m, 2H), 7.97 (d, *J*= 8.0 Hz, 1H), 8.07 (d, *J*= 8.6 Hz, 1H), 8.55 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.5, 124.2, 126.8, 126.9, 127.7, 128.49, 128.52, 128.7, 129.5, 129.6, 130.4, 132.5, 133.9, 134.6, 135.6, 197.6; MS (EI): m/z (relative intensity) 246.1 (M$^+$, 7), 155.0 (100), 127.0 (54), 91.1 (4), 77.1 (5).

1-(6-Methoxynaphthalen-2-yl)-2-phenylethan-1-one (Table 2, compound 3ah)[17]

Yield: 85% (46.9 mg). Eluents (Toluene, R$_f$= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.94 (s, 3H), 4.39 (s, 2H), 7.14 (d, *J*= 2.2 Hz, 1H), 7.21 (dd, *J*= 9.1 Hz, 2.4 Hz, 1H), 7.24-7.28 (m, 1H), 7.32-7.37 (m, 4H), 7.76 (d, *J*= 8.6 Hz, 1H), 7.85 (d, *J*= 9.0 Hz, 1H), 8.05 (dd, *J*= 8.5 Hz, 1.6 Hz, 1H), 8.48 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.3, 55.4, 105.7, 119.7, 125.0, 126.8, 127.1, 127.8, 128.6, 129.4, 130.2, 131.1, 132.0, 134.9, 137.3, 159.8, 197.3; MS (EI): m/z (relative intensity) 276.1 (M$^+$, 7), 185.0 (100), 157.0 (23), 142.0 (10), 114.0 (10).

1-(2-Methoxyphenyl)-2-phenylethan-1-one (Table 2, compound 3ai)[18]

Yield: 89% (40.2 mg). Eluents (EA: Hexane = 1: 20, R$_f$= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.92 (s, 3H), 4.31 (s, 2H), 6.95-7.01 (m, 2H), 7.23-7.26 (m, 3H), 7.29-7.33 (m, 2H), 7.46 (t, *J*= 7.8 Hz, 1H), 7.68 (d, *J*= 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 50.1, 55.4, 111.4, 120.7, 126.5, 128.2, 128.3, 129.6, 130.6, 133.4, 135.2, 158.3, 200.1; MS (EI): m/z (relative intensity) 226.1 (M$^+$, 1), 135.0 (100), 92.0 (10), 77 (19).

1-(2,5-Dimethoxyphenyl)-2-phenylethan-1-one (Table 2, compound 3aj)[19]

Yield: 71% (36.4 mg). Eluents (Toluene, R$_f$= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.77 (s, 3H), 3.87 (s, 3H), 4.32 (s, 2H), 6.90 (d, *J*= 9.0 Hz, 1H), 7.00-7.03 (m, 1H), 7.22-7.26 (m, 4H), 7.29-7.32 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 50.1, 55.7, 55.9, 113.0, 114.2, 120.1, 126.5, 128.3, 129.6, 135.2, 152.9, 153.4, 199.7; MS (EI): m/z (relative intensity) 256.1 (M$^+$, 9), 165.0 (100), 150.0 (5), 122.0 (6), 107.0 (8).

1-(Naphthalen-1-yl)-2-phenylethan-1-one (Table 2, compound 3ak)[20]

Yield: 50% (24.6 mg). Eluents (Toluene, R$_f$= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.38 (s, 2H), 7.24-7.27 (m, 1H), 7.29-7.35 (m, 4H), 7.45-7.59 (m, 3H), 7.86 (d, *J*= 7.6 Hz, 1H), 7.97 (t, *J*= 7.5 Hz, 2H), 8.6 (d, *J*= 8.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 48.9, 124.3, 125.8, 126.5, 126.9, 127.9, 128.0, 128.4, 128.7, 129.5, 130.4, 132.7, 134.0, 134.5, 135.6, 201.5; MS (EI): m/z (relative intensity) 246.1 (M$^+$, 6), 155.1 (100), 127.1 (51).

1-(4-Methoxynaphthalen-1-yl)-2-phenylethan-1-one (Table 2, compound 3al)[21]

Yield: 99% (54.7 mg). Eluents (Toluene, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.05 (s, 3H), 4.37 (s, 2H), 6.78 (d, J= 8.2 Hz, 1H), 7.22-7.28 (m, 1H), 7.32-7.35 (m, 4H), 7.51 (t, J= 8.0 Hz, 1H), 7.61 (t, J= 7.6 Hz, 1H), 8.09 (d, J= 8.2 Hz, 1H), 8.31 (d, J= 8.6 Hz, 1H), 8.93 (d, J= 8.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 48.0, 55.7, 102.0, 122.0, 125.8, 126.1, 126.7, 127.0, 128.6, 128.7, 129.3, 131.4, 132.3, 135.4, 143.3, 159.1, 199.6; MS (EI): m/z (relative intensity) 276.1 (M$^+$, 3), 185.1 (100), 157.0 (12), 142.0 (7), 114.0 (15).

2-Phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-one (Table 2, compound 3am)[22]

Yield: 47% (26.9 mg). Eluents (Toluene, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.88 (s, 6H), 3.90 (s, 3H), 4.24 (s, 2H), 7.25-7.28 (m, 5H), 7.30-7.35 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.6, 56.2, 60.9, 106.2, 126.9, 128.7, 129.2, 131.6, 134.8, 142.5, 153.0, 196.4; MS (EI): m/z (relative intensity) 286.1 (M$^+$, 9), 195.1 (100), 152.0 (7), 137.0 (5), 91.1 (7).

1-Mesityl-2-phenylethan-1-one (Table 2, compound 3an)[23]

Yield: 59% (28.1 mg). Eluents (Toluene, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.14 (s, 6H), 2.30 (s, 3H), 4.01 (s, 2H), 6.84 (s, 2H), 7.22 (d, J= 6.8 Hz, 2H), 7.27-7.35 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 19.2, 21.0, 51.8, 127.1, 128.45, 128.52, 129.8, 132.7, 133.3, 138.5, 139.1, 207.5; MS (EI): m/z (relative intensity) 238.1 (M$^+$, 1), 147.1 (100), 119.1 (25), 91.1 (15), 77.0 (5).

1-(2,5-Dimethylfuran-3-yl)-2-phenylethan-1-one (Table 2, compound 3ao)

Yield: 55% (23.5 mg). Eluents (Toluene, R_f= 0.50) was used for flash column chromatography. Yellow liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.25 (s, 3H), 2.53 (s, 3H), 3.97 (s, 2H), 6.24 (s, 1H), 7.23-7.27 (m, 3H), 7.31-7.34 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 13.2, 14.3, 48.0, 105.8, 121.2, 126.8, 128.6, 129.4, 134.6, 149.9, 158.0, 193.9; MS (EI): m/z (relative intensity) 214.1 (M$^+$, 10), 123.1 (100), 91.1 (6), 81.0 (8); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd. for C$_{14}$H$_{15}$O$_2$: 215.1067, found 215.1063.

2-Phenyl-3,4-dihydronaphthalen-1(2H)-one (Table 2, compound 3ap)[24]

Yield: 68% (30.2 mg). Eluents (Toluene, R_f= 0.60) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.42-2.47 (m, 2H), 3.02-3.17 (m, 2H), 3.81 (t, J= 7.8 Hz, 1H), 7.20 (d, J= 7.1 Hz, 2H), 2.29 (d, J= 8.2 Hz, 2H), 7.33-7.37 (m, 3H), 7.51 (t, J= 7.4 Hz, 1H), 8.11 (d, J= 7.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 28.7, 31.2, 54.4, 126.7, 126.9, 127.8, 128.4, 128.5, 128.7, 132.9, 133.4, 139.7, 144.0, 198.2; MS (EI): m/z (relative intensity) 222.1 (M$^+$, 96), 131.1 (44), 118.1 (100), 103.1 (58), 90.1 (45).

2-(4-Methoxyphenyl)-1-phenylethan-1-one (Table 2, compound 3ba)[18]

Yield: 91% (41.1 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.76 (s, 3H), 4.20 (s, 2H), 6.85 (d, J= 8.6 Hz, 2H), 7.16 (d, J= 8.6 Hz, 2H), 7.43 (t, J= 7.4 Hz, 2H), 7.53 (t, J= 7.4 Hz, 1H), 7.99 (d, J= 7.3 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 44.5, 55.2, 114.1, 126.4, 128.5, 128.6, 130.4, 133.0, 136.5, 158.5, 197.9; MS (EI): m/z (relative intensity) 226.1 (M$^+$, 16), 121.0 (100), 105.0 (90), 91.1 (5), 77.0 (38).

2-(4-Methoxyphenyl)-1-(p-tolyl)ethan-1-one (Table 2, compound 3bc)[25]

Yield: 94% (45.1 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.40 (s, 3H), 3.78 (s, 3H), 4.20 (s, 2H), 6.86 (d, J= 8.6 Hz, 2H), 7.18 (d, J= 8.6 Hz, 2H), 7.25 (d, J= 8.6 Hz, 2H), 7.91 (d, J= 8.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.6, 44.5, 55.2, 114.1, 126.7, 128.7, 129.3, 130.4, 134.1, 143.9, 158.5, 197.6; MS (EI): m/z (relative intensity) 240.1 (M$^+$, 15), 119.0 (100), 91.1 (24), 78.1 (5).

1,2-Bis(4-methoxyphenyl)ethan-1-one (Table 2, compound 3bd)[26]

Yield: 97% (50.5 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.78 (s, 3H), 3.86 (s, 3H), 4.17 (s, 2H), 6.86 (d, J= 8.4 Hz, 2H), 6.92 (d, J= 8.7 Hz, 2H), 7.18 (d, J= 8.3 Hz, 2H), 7.99 (d, J= 8.7 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 44.3, 55.2, 55.4, 113.7, 114.1, 126.9, 129.6, 130.3, 130.9, 158.4, 163.4, 196.5; MS (EI): m/z (relative intensity) 256.1 (M$^+$, 7), 135.0 (100), 121.1 (8), 107.0 (5), 77.0 (11).

2-(4-Methoxyphenyl)-1-(m-tolyl)ethan-1-one (Table 2, compound 3bf)[27]

Yield: 99% (47.5 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.41 (s, 3H), 3.79 (s, 3H), 4.22 (s, 2H), 6.85-6.89 (m, 2H), 7.18 (d, J= 8.6 Hz, 2H), 7.32-7.38 (m, 2H), 7.80-7.82 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.3, 44.6, 55.2, 114.1, 125.8, 126.6, 128.4, 129.0, 130.4, 133.8, 136.6, 138.4, 158.5, 198.1; MS (EI): m/z (relative intensity) 240.1 (M$^+$, 29), 119.0 (100), 91.1 (26), 78.1 (4), 65.1 (7).

1-(2-Methoxyphenyl)-2-(4-methoxyphenyl)ethan-1-one (Table 2, compound 3bi)

Yield: 99% (50.7 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. Yellow liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.78 (s, 3H), 3.92 (s, 3H), 4.24 (s, 2H), 6.83-6.86 (m, 2H), 6.95-7.00 (m, 2H), 7.14 (d, J= 8.6 Hz, 2H), 7.42-7.47 (m, 1H), 7.67 (dd, J= 7.6 Hz, 1.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 49.2, 55.1, 55.4, 111.4, 113.7, 120.6, 127.2, 128.2, 130.5, 130.6, 131.7, 133.4, 158.2, 200.5; MS (EI): m/z (relative intensity) 256.1 (M$^+$, 9), 135.0 (100), 121.1 (15), 92.0 (87), 77.1 (12); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_{16}$H$_{17}$O$_3$: 257.1172, found

257.1170.

1-(2,5-Dimethylfuran-3-yl)-2-(4-methoxyphenyl)ethanone (Table 2, compound 3bo)

Yield: 50% (24.4 mg). Eluents (Toluene, R_f= 0.50) was used for flash column chromatography. Yellow liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.24 (s, 3H), 2.53 (s, 3H), 3.79 (s, 3H), 3.90 (s, 2H), 6.22 (s, 1H), 6.86 (d, J= 8.6 Hz, 2H), 7.15 (d, J= 8.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 13.2, 14.3, 47.1, 55.2, 105.8, 114.0, 121.1, 126.6, 130.4, 149.9, 157.9, 158.4, 194.3; MS (EI): m/z (relative intensity) 244.1 (M$^+$, 20), 123.1 (100), 91.1 (10), 78.0 (4); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_{15}$H$_{17}$O$_3$: 245.1172 found 245.1169.

2-(3-Methoxyphenyl)-1-(*m*-tolyl)ethan-1-one (Table 2, compound 3cf)

Yield: 84% (40.3 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. Yellow liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.41 (s, 3H), 3.79 (s, 3H), 4.25 (s, 2H), 6.79-6.83 (m, 2H), 6.86 (d, J= 7.6 Hz, 1H), 7.24 (t, J= 7.8 Hz, 1H), 7.32-7.38 (m, 2H), 7.81-7.83 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.3, 45.5, 55.1, 112.3, 115.0, 121.8, 125.8, 128.4, 129.0, 129.5, 133.9, 136.1, 136.6, 138.4, 159.7, 197.7; MS (EI): m/z (relative intensity) 240.1 (M$^+$, 20), 119.0 (100), 91.0 (29), 78.1 (3), 65.1 (7); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_{16}$H$_{17}$O$_2$: 241.1223, found 241.1221.

2-(3-Methoxyphenyl)-1-(4-Methoxyphenyl)ethan-1-one (Table 2, compound 3cd)[28]

Yield: 99% (50.7 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.80 (s, 3H), 3.87 (s, 3H), 4.22 (s, 2H), 6.80-6.85 (m, 2H), 6.88 (d, J= 7.7 Hz, 1H), 6.93-6.96 (m, 2H), 7.23-2.28 (m, 1H), 8.00-8.03 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.3, 55.1, 55.4, 112.2, 113.7, 114.9, 121.7, 129.5, 130.9, 136.4, 159.7, 163.5, 196.0; MS (EI): m/z (relative intensity) 256.1 (M$^+$, 3), 135.0 (100), 107.0 (6), 92.0 (8), 77.1 (12).

1-(2-Methoxyphenyl)-2-(3-methoxyphenyl)ethan-1-one (Table 2, compound 3ci)

Yield: 93% (47.8 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. Colorless liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.78 (s, 3H), 3.92 (s, 3H), 4.28 (s, 2H), 6.77-6.83 (m, 3H), 6.95-7.00 (m, 2H), 7.21 (t, J= 7.5 Hz, 1H), 7.45 (t, J= 7.9 Hz, 1H), 7.67 (dd, J= 7.6 Hz, 1.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 50.1, 55.1, 55.4, 111.4, 112.1, 115.2, 120.7, 122.1, 128.1, 129.2, 130.6, 133.5, 136.6, 158.3, 159.5, 199.9; MS (EI): m/z (relative intensity) 256.1 (M$^+$, 7), 135.0 (100), 92.0 (7), 77.0 (11); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for C$_{16}$H$_{17}$O$_3$$^+$: 257.1172, found 257.1169.

2-(3-Methoxyphenyl)-1-(thiophen-2-yl)ethan-1-one (Table 2, compound 3cq)[29]

Yield: 77% (35.8 mg). Eluents (EA: Hexane = 1: 9, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.79 (s, 3H), 4.16 (s, 2H), 6.80 (d, J= 8.4 Hz, 1H), 6.86-6.91 (m, 2H), 7.11 (t, J= 4.5 Hz, 1H), 7.24 (t, J= 7.9 Hz, 1H), 7.63 (d, J= 4.8 Hz, 1H), 7.77 (d, J= 3.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 46.4, 55.1, 112.5, 114.9, 121.7, 128.1, 129.6, 132.7, 134.0, 135.7, 143.8, 159.7, 190.3; MS (EI): m/z (relative intensity) 232.1 (M$^+$, 29), 111.0 (100), 91.1 (7), 78.1 (7).

2-(3-Methoxyphenyl)-1-phenylpropan-1-one (Table 2, compound 3cr)[30]

Yield: 88% (42.2 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.52 (d, J= 6.8 Hz, 3H), 3.76 (s, 3H), 4.65 (q, J= 14.6 Hz, 1H), 6.74 (d, J= 8.2 Hz. 1H), 6.82 (s, 1H), 6.87 (d, J= Hz, 1H), 7.21 (t, J= 7.9 Hz, 1H), 7.36-7.40 (m, 2H), 7.48 (t, J= 7.4 Hz, 1H), 7.95 (d, J= 7.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 19.3, 47.8, 55.0, 112.0, 113.3, 120.0, 128.3, 128.6, 129.8, 132.6, 136.3, 142.9, 159.8, 200.0; MS (EI): m/z (relative intensity) 240.1 (M$^+$, 16), 135.1 (12), 105.0 (100), 77.0 (27).

1-Phenyl-2-(p-tolyl)ethan-1-one (Table 2, compound 3da)[16]

Yield: 85% (35.7 mg). Eluents (Toluene, R_f= 0.60) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.35 (s, 3H), 4.28 (s, 2H), 7.16-7.21 (m, 4H), 7.48 (t, J= 7.4 Hz, 2H), 7.58 (t, J= 7.4 Hz, 1H), 8.05 (d, J= 7.3 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.0, 45.1, 128.6, 129.3, 129.4, 131.4, 133.0, 136.4, 136.6, 197.8; MS (EI): m/z (relative intensity) 210.1 (M$^+$, 10), 105.1 (100), 77.1 (26), 51.0 (6).

1-(4-Methoxyphenyl)-2-(p-tolyl)ethan-1-one (Table 2, compound 3dd)[6n]

Yield: 90% (43.2 mg). Eluents (EA: Hexane = 1: 9, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.32 (s, 3H), 3.86 (s, 3H), 4.19 (s, 2H), 6.92 (d, J= 8.9 Hz, 2H), 7.11-7.17 (m, 4H), 8.00 (d, J= 8.9 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.0, 44.9, 55.4, 113.7, 129.2, 129.3, 129.6, 130.9, 131.8, 136.3, 163.4, 196.4; MS (EI): m/z (relative intensity) 240.1 (M$^+$, 3), 135.1 (100), 107.0 (6), 92.0 (8), 77.1 (13).

1-Phenyl-2-(m-tolyl)ethan-1-one (Table 2, compound 3ea)[16]

Yield: 85% (35.7 mg). Eluents (Toluene, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.34 (s, 3H), 4.26 (s, 2H), 7.07-7,10 (m, 3H), 7.21-7.26 (m, 1H), 7.47 (t, J= 7.4 Hz, 2H), 7.56 (t, J= 7.4 Hz, 1H), 8.03 (d, J= 7.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.3, 45.4, 126.4, 127.6, 128.5, 128.6, 130.1, 133.1, 134.4, 136.6, 138.3, 197.7; MS (EI): m/z (relative intensity) 210.1 (M$^+$, 4), 105.0 (100), 77.0 (33), 51.0 (6).

2-(3,5-Dimethylphenyl)-1-phenylethan-1-one (Table 2, compound 3fa)[8d]

Yield: 79% (35.4 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.30 (s, 6H), 4.22 (s, 2H), 6.90 (s, 3H), 7.47 (t, *J*= 7.4 Hz, 2H), 7.56 (t, *J*= 7.4 Hz, 1H), 8.03 (d, *J*= 8.0 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.2, 45.3, 127.2, 128.56, 128.59, 133.0, 134.3, 136.6, 138.1, 197.8; MS (EI): m/z (relative intensity) 224.1 (M[+], 8), 105.0 (100), 91.1 (5), 77.0 (28).

2-(3,5-Dimethylphenyl)-1-(4-methoxyphenyl)ethan-1-one (Table 2, compound 3fd)

Yield: 79% (40.1 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. Colorless liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.29 (s, 6H), 3.86 (s, 3H), 4.16 (s, 2H), 6.89-6.90 (m, 3H), 6.93 (d, *J*= 8.8 Hz, 2H), 8.01 (d, *J*= 8.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 21.2, 45.1, 55.4, 113.7, 127.1, 128.4, 129.6, 130.9, 134.7, 138.1, 163.4, 196.4; MS (EI): m/z (relative intensity) 254.1 (M[+], 3), 135.0 (100), 119.1 (3), 107.0 (5), 92.0 (6); HRMS (ESI-TOF) m/z: [M + H][+] Calcd for C$_{17}$H$_{19}$O$_2$: 255.1380, found 255.1378.

1-Phenyl-2-(3,4,5-trimethylphenyl)ethan-1-one (Table 2, compound 3ga)

Yield: 92% (43.8 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.40) was used for flash column chromatography. Yellow liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.15 (s, 3H), 2.28 (s, 6H), 4.20 (s, 2H), 6.94 (s, 2H), 7.47 (t, *J*= 7.4 Hz, 2H), 7.56 (t, *J*= 7.3 Hz, 1H), 8.05 (d, *J*= 7.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ15.0, 20.5, 45.0, 128.1, 128.5, 128.6, 131.1, 133.0, 133.6, 136.6, 136.7, 198.0; MS (EI): m/z (relative intensity) 238.1 (M[+], 25), 133.1 (28), 105.0 (100), 91.0 (5), 77.0 (20); HRMS (ESI-TOF) m/z: [M + H][+] Calcd for C$_{17}$H$_{19}$O: 239.1430, found 239.1427.

2-(4-(*tert*-Butyl)phenyl)-1-phenylethan-1-one (Table 2, compound 3ha)[8d]

Yield: 82% (41.3 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ1.32 (s, 9H), 4.27 (s, 2H), 7.22 (d, *J*= 8.2 Hz, 2H), 7.37 (d, *J*= 8.3 Hz, 2H), 7.47 (t, *J*= 7.3 Hz, 2H), 7.57 (t, *J*= 7.4 Hz, 1H), 8.04 (d, *J*= 7.7 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 31.3, 34.4, 44.9, 125.6, 128.6, 129.1, 129.9, 131.3, 133.1, 136.6, 149.6, 197.8; MS (EI): m/z (relative intensity) 252.1 (M[+], 9), 207.0 (3), 105.0 (100), 77.1 (18).

2-(4-(*tert*-Butyl)phenyl)-1-(4-methoxyphenyl)ethan-1-one (Table 2, compound 3hd)[31]

Yield: 99% (55.9 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.31 (s, 9H), 3.86 (s, 3H), 4.21 (s, 2H), 6.93 (d, J= 8.9 Hz, 2H), 7.22 (d, *J*= 8.2 Hz, 2H), 7.35 (d, *J*= 8.2 Hz, 2H), 8.02 (d, *J*= 8.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 31.3, 34.4, 44.7, 55.4, 113.7, 125.5, 129.0, 129.7, 130.9, 131.8, 149.5, 163.4, 196.4; MS (EI): m/z (relative intensity) 282.1 (M[+], 2), 135.0 (100), 107.0 (4), 92.0 (4), 77.1 (6).

2-(4-Fluorophenyl)-1-phenylethan-1-one (Table 2, compound 3ia)[18]

Yield: 82% (35.1 mg). Eluents (Toluene, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.27 (s, 2H), 7.00-7.04 (m, 2H), 7.21-7.24 (m, 2H), 7.47 (t, J= 7.8 Hz, 2H), 7.58 (t, J= 7.3 Hz, 1H), 8.00 (t, J= 7.3 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 44.5, 115.5 (d, J= 21.3 Hz), 128.5, 128.7, 130.1 (d, J= 3.4 Hz), 131.0 (d, J= 31.6 Hz), 133.3, 136.4, 161.9 (d, J= 243.7 Hz), 197.4; ^{19}F NMR (376 MHz, CDCl$_3$) δ -116.0; MS (EI): m/z (relative intensity) 214.1 (M$^+$, 2), 105.1 (100), 215.1 (42), 83.1 (6), 77.1 (37).

2-(4-Fluorophenyl)-1-(4-methoxyphenyl)ethan-1-one (Table 2, compound 3id)[32]

Yield: 72% (35.3 mg). Eluents (Toluene, R_f= 0.35) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.86 (s, 3H), 4.21 (s, 2H), 6.94 (d, J= 8.8 Hz, 2H), 7.00 (t, J= 8.6 Hz, 2H), 7.20-7.24 (m, 2H), 7.99 (d, J= 8.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 44.2, 55.4, 113.8, 115.4 (d, J= 21.4 Hz), 129.4, 130.5 (d, J= 3.4 Hz), 130.8, 130.9 (d, J= 7.9 Hz), 161.8 (d, J= 243.4Hz), 163.6, 195.9; ^{19}F NMR (376 MHz, CDCl$_3$) δ -116.2; MS (EI): m/z (relative intensity) 244.1 (M$^+$, 2), 135.1 (100), 107.1 (15), 92.1 (17), 77.1 (19).

2-(Naphthalen-1-yl)-1-phenylethan-1-one (Table 2, compound 3ja)[8d]

Yield: 89% (43.8 mg). Eluents (EA: Hexane = 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.75 (s, 2H), 7.37 (d, J= 6.8 Hz, 1H), 7.42-7.51 (m, 5H), 7.60 (t, J= 7.4 Hz, 1H), 7.81 (d, J= 8.1 Hz, 1H), 7.87-7.90 (m, 2H), 8.10 (d, J= 7.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 43.1, 123.8, 125.5, 125.7, 126.3, 127.9, 128.0, 128.5, 128.7, 128.8, 131.3, 132.2, 133.2, 133.9, 136.7, 197.6; MS (EI): m/z (relative intensity) 246.1 (M$^+$, 26), 141.0 (16), 105.0 (100), 77.0 (23).

1-(4-Methoxyphenyl)-2-(naphthalen-1-yl)ethan-1-one (Table 2, compound 3jd)[31]

Yield: 83% (45.8 mg). Eluents (Toluene, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.87 (s, 3H), 4.69 (s, 2H), 6.95 (d, J= 8.8 Hz, 2H), 7.35 (d, J= 6.9 Hz, 1H), 7.42 (t, J= 8.0 Hz, 1H), 7.46-7.51 (m, 2H), 7.79 (d, J= 8.1 Hz, 1H), 7.86-7.91 (m, 2H), 8.06 (d, J= 8.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 42.8, 55.4, 113.8, 123.9, 125.4, 125.6, 126.2, 127.7, 127.9, 128.7, 129.7, 130.8, 131.7, 132.2, 133.8, 163.5, 196.2; MS (EI): m/z (relative intensity) 276.1 (M$^+$, 7), 135.0 (100), 115.1 (7), 92.0 (7), 77.1 (10).

1-Phenyl-2-(o-tolyl)ethan-1-one (Table 2, compound 3ka)[24]

Yield: 50% (21.0 mg). Eluents (Toluene, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.28 (s, 3H), 4.32 (s, 2H), 7.13-7.24 (m, 4H), 7.47-7.51 (m, 2H), 7.59 (t, J= 7.4 Hz, 1H), 8.03 (d, J= 7.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 19.8, 43.4, 126.1, 126.5, 127.2, 128.3, 128.6, 130.2, 130.3, 133.1, 133.4, 136.8, 197.4; MS (EI): m/z (relative intensity) 210.1

(M[+], 11), 105.1 (100), 77.1 (29).

1,2-Diphenylethan-1-one (Scheme 3, compound 3aa)[14]

Yield: 80% (1.57 g). Eluents (Toluene, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.30 (s, 2H), 7.25-7.36 (m, 5H), 7.47 (t, *J*= 7.8 Hz, 2H), 7.56 (t, *J*= 7.4 Hz, 1H), 8.03 (d, *J*= 7.3 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 45.5, 126.8, 128.57, 128.60, 128.63, 129.4, 133.1, 134.5, 136.5, 197.6; MS (EI): m/z (relative intensity) 196.1 (M[+], 4), 165.0 (3), 105.0 (100), 91.0 (8), 77.1 (37).

Supporting Information Available: Copies of ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, ^{31}P NMR and HRMS spectra of synthesized compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

Acknowledgments

References

(1) (a) Naresh, K.; George, I. Lactams, Processes for Preparing Them, Pharmaceutical Compositions Containing Them, and Their Use as Antibacterial Agents. PCT Int. Appl. WO2007085042A1, 2007. (b) Prasada Rao, L. V. S.; Abraham, T.; Neelima, K.-J.; Vidya Ganapati, K. Preparation of Styrene Derivatives as TRPV3 Antagonists for the Treatment of Pain. Indian Pat. Appl. IN2009MU01140, 2010. (c) Vitale, P.; Tacconelli, S.; Perrone, M. G.; Malerba, P.; Simone, L.; Scilimati, A.; Lavecchia, A.; Dovizio, M.; Marcantoni, E.; Bruno, A.; Patrignani, P. Synthesis, Pharmacological Characterization, and Docking Analysis of a Novel Family of Diarylisoxazoles as Highly Selective Cyclooxygenase-1 (COX-1) Inhibitors. *J. Med. Chem.* **2013**, *56*, 4277-4299. (d) Parry, N. J.; O'Keeffe, J. C.; Smith, C. F. Antimicrobial Composition Comprising a Lactam and A Hydrotrope. PCT Int. Appl. WO 2014118240A1, 2014. (e) Singh, F. V.; Vatsyayan, R.; Roy, U.; Goel, A. Arylanthranilodinitriles: A New Biaryl Class of Antileishmanial Agents. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2734-2737. (f) Singh, F. V.; Parihar, A.; Chaurasia, S.; Singh, A. B.; Singh, S. P.; Tamrakar, A. K.; Srivastava, A. K.; Goel, A. 5,6-Diarylanthranilo-1,3-dinitriles as A New Class of Antihyperglycemic Agents. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2158-2161.

(2) For reviews, see: (a) Culkin, D. A.; Hartwig, J. F. Palladium-Catalyzed α-Arylation of Carbonyl Compounds and Nitriles. *Acc. Chem. Res.* **2003**, *36*, 234-245. (b) Bellina, F.; Rossi, R. Transition Metal-Catalyzed Direct Arylation of Substrates with Activated sp^3-Hybridized C-H Bonds and Some of Their Synthetic Equivalents with Aryl Halides and Pseudohalides. *Chem. Rev.* **2010**, *110*, 1082-1146. (b) Johansson, C. C. C.; Colacot, T. J. Metal-Catalyzed α-Arylation of Carbonyl and Related Molecules: Novel Trends in C-C Bond Formation by C-H Bond Functionalization. *Angew. Chem. Int. Ed.* **2010**, *49*, 676-707. (c) Sivanandan, S. T.; Shaji, A.; Ibnusaud, I.; Johansson Seechurn, C. C. C.; Colacot, T. J. Palladium-Catalyzed α-Arylation Reactions in Total Synthesis. *Eur. J. Org. Chem.* **2015**, 38-49. (d) Potukuchi, H. K.; Spork, A. P.; Donohoe, T. J. Palladium-Catalyzed α-Arylation of Carbonyls in the *de novo* Synthesis of Aromatic Heterocycles. *Org. Biomol. Chem.* **2015**, *13*, 4367-4373. (e) Novak, P.; Martin, R. Pd-catalyzed α-Arylation of Carbonyl and Related Compounds: Recent Developments and Perspectives. *Curr. Org. Chem.* **2011**, *15*, 3233-3262. (f) Schranck, J.; Rotzler, J. Valorization of the Primary Building Blocks Ammonia and Acetone Featuring Pd- and Ni-Catalyzed Monoarylations. *Org. Process Res. Dev.* **2015**, *19*, 1936-1943.

(3) Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. Palladium-Catalyzed Regioselective Mono- and Diarylation Reactions of 2-Phenylphenols and Naphthols with Aryl Halides. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1740-1742.

(4) Palucki, M.; Buchwald, S. L. Palladium-Catalyzed α-Arylation of Ketones. *J. Am. Chem. Soc.* **1997**, *119*, 11108-11109.

(5) Hamann, B. C.; Hartwig, J. F. Palladium-Catalyzed Direct α-Arylation of Ketones. Rate Acceleration by Sterically Hindered Chelating Ligands and Reductive Elimination from a Transition Metal Enolate Complex. *J. Am. Chem. Soc.* **1997**, *119*, 12382-12383.

(6) For selected references, see: (a) Åhman, J. Wolfe, J. P.; Troutman, M. V.; Palucki, M.; Buchwald, S. L. Asymmetric Arylation of Ketone Enolates. *J. Am. Chem. Soc.* **1998**, *120*, 1918-1919. (b) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. Highly Active and Selective Catalysts for the Formation of α-Aryl Ketones. *J. Am. Chem. Soc.* **2000**, *122*, 1360-1370. (c) Ehrentraut, A.; Zapf, A.; Beller, M. Progress in the Palladium-Catalyzed α-Arylation of Ketones with Chloroarenes. *Adv. Synth. Catal.* **2002**, *344*, 209-217. (d) Viciu, M. S.; Germaneau, R. F.; Nolan, S. P. Well-Defined, Air-Stable (NHC)Pd(Allyl)Cl (NHC = N-Heterocyclic Carbene) Catalysts for the Arylation of Ketones. *Org. Lett.* **2002**, *4*, 4053-4056. (e) Hamada, T.; Chieffi, A.; Åhman, J.; Buchwald, S. L. An Improved Catalyst for the Asymmetric Arylation of Ketone Enolates. *J. Am. Chem. Soc.* **2002**, *124*, 1261-1268. (f) Rutherford, J. L.; Rainka, M. P.; Buchwald, S. L. An Annulative Approach to Highly Substituted Indoles: Unusual Effect of Phenolic Additives on the Success of the Arylation of Ketone Enolates. *J. Am. Chem. Soc.* **2002**, *124*, 15168-15169. (g) Adjabeng, G.; Brenstrum, T.; Frampton, C. S.; Robertson, A. J.; Hillhouse, J.; McNulty, J.; Capreta, A. Palladium Complexes of 1,3,5,7-Tetramethyl-2,4,8-trioxa-6-phenyl-6-phosphaadamantane: Synthesis, Crystal Structure and Use in the Suzuki and Sonogashira Reactions and the α-Arylation of Ketones. *J. Org. Chem.* **2004**, *69*, 5082-5086. (h) Culkin, D. A.; Hartwig, J. F. Carbon−Carbon Bond-Forming Reductive Elimination from Arylpalladium Complexes Containing Functionalized Alkyl Groups. Influence of Ligand Steric and Electronic Properties on Structure, Stability, and Reactivity. *Organometallics* **2004**, *23*, 3398-3416. (i) Grasa, G. A.; Colacot, T. J. α-Arylation of Ketones Using Highly Active, Air-Stable (DtBPF)PdX$_2$ (X = Cl, Br) Catalysts. *Org. Lett.* **2007**, *9*, 5489-5492. (j) Grasa, G. A.; Colacot, T. J. A Highly Practical and General Route for α-Arylations of Ketones Using Bis-phosphinoferrocene-Based Palladium Catalysts. *Org. Process Res. Dev.* **2008**, *12*, 522-529. (k) Biscoe, M. R.; Buchwald, S. L. Selective Monoarylation of Acetate Esters and Aryl Methyl Ketones Using Aryl Chlorides. *Org. Lett.* **2009**, *11*, 1773-1775. (l) Crawford, S. M.; Alsabeh, P. G.; Stradiotto, M. Palladium-Catalyzed Mono-α-arylation of Carbonyl-Containing Compounds with Aryl Halides using DalPhos Ligands. *Eur. J. Org. Chem.* **2012**, 6042-6050. (m) Ackermann, L.; Mehta, V. P. Palladium-Catalyzed Mono-α-Arylation of Acetone with Aryl Imidazolylsulfonates. *Chem. Eur. J.* **2012**, *18*, 10230-10233. (n) Marelli, E.; Corpet, M.; Davies, S. R.; Nolan, S. P. Palladium-Catalyzed α-Arylation of Arylketones at Low Catalyst Loadings. *Chem. Eur. J.*

2014, *20*, 17272-17276. (o) Li, P.; Lü, B.; Fu, C.; Ma, S. Zheda-Phos for General α-Monoarylation of Acetone with Aryl Chlorides. *Adv. Synth. Catal.* **2013**, *355*, 1255-1259. (p) Gäbler, C.; Korb, M.; Schaarschmidt, D.; Hildebrandt, A.; Lang, H. Ferrocenyl-Based P,N Catalysts for the Mono-α-Arylation of Acetone. *Adv. Synth. Catal.* **2014**, *356*, 2979-2983. (q) Fu, W. C.; So, C. M.; Chow, W. K.; Yuen, O. Y.; Kwong, F. Y. Design of an Indolylphosphine Ligand for Reductive Elimination-Demanding Monoarylation of Acetone Using Aryl Chlorides. *Org. Lett.* **2015**, *17*, 4612-4614. (r) MacQueen, P. M.; Chisholm, A. J. Hargreaves, B. K. V.; Stradiotto, M. Palladium-Catalyzed Mono-α-arylation of Acetone at Room Temperature. *Chem. Eur. J.* **2015**, *21*, 11006-11009. (s) Xu, Y.; Su, T.; Huang, Z.; Dong, G. Practical Direct α-Arylation of Cyclopentanones by Palladium/Enamine Cooperative Catalysis. *Angew. Chem. Int. Ed.* **2016**, *55*, 2559-2563. (t) Fu, W. C.; Zhou, Z.; Kwong, F. Y. Preparation of a Highly Congested Carbazoyl-Derived P,N-Type Phosphine Ligand for Acetone Monoarylations. *Organometallics* **2016**, *35*, 1553-1558.

(7) (a) Yu, D. -G.; Li, B. -J.; Shi, Z. -J. Exploration of New C−O Electrophiles in Cross-Coupling Reactions. *Acc. Chem. Res.* **2010**, *43*, 1486-1495. (b) Li, B. -J.; Yu, D. -G.; Sun, C. -L.; Shi, Z. -J. Activation of "Inert" Alkenyl/Aryl C-O Bond and Its Application in Cross-Coupling Reactions. *Chem. Eur. J.* **2011**, *17*, 1728-1759. (c) Zeng, H.; Qiu, Z.; Domínguez-Huerta, A.; Hearne, Z.; Chen. Z.; Li, C. -J. An Adventure in Sustainable Cross-Coupling of Phenols and Derivatives via Carbon–Oxygen Bond Cleavage. *ACS Catal.* **2017**, *7*, 510-519.

(8) (a) Nguyen, H. N.; Huang, X.; Buchwald, S. L. The First General Palladium Catalyst for the Suzuki-Miyaura and Carbonyl Enolate Coupling of Aryl Arenesulfonates. *J. Am. Chem. Soc.* **2003**, *125*, 11818-11819. (b) Liao, X.; Weng, Z.; Hartwig, J. F. Enantioselective α-Arylation of Ketones with Aryl Triflates Catalyzed by Difluorphos Complexes of Palladium and Nickel. *J. Am. Chem. Soc.* **2008**, *130*, 195-200. (c) Hesp, K. D.; Lundgren, R. J.; Stradiotto, M. Palladium-Catalyzed Mono-α-arylation of Acetone with Aryl Halides and Tosylates. *J. Am. Chem. Soc.* **2011**, *133*, 5194-5197. (d) Alsabeh, P. G.; Stradiotto, M. Addressing Challenges in Palladium-Catalyzed Cross-Couplings of Aryl Mesylates: Monoarylation of Ketones and Primary Alkyl Amines. *Angew. Chem. Int. Ed.* **2013**, *52*, 7242-7246. (d) Fu, W. C.; So, C. M.; Yuen, O. Y.; Lee, I. T. C.; Kwong, F. Y. Exploiting Aryl Mesylates and Tosylates in Catalytic Mono-α-arylation of Aryl- and Heteroarylketones. *Org. Lett.* **2016**, *18*, 1872-1875.

(9) For selected references of nickel-catalyzed other coupling reactions of aryl phosphates, see: (a) Hayashi, T.; Katsuro, Y.; Okamoto, Y.; Kumada, M. Nickel-Catalyzed Cross-Coupling of Aryl Phosphates with Grignard and Organoaluminium Reagents. Synthesis of Alkyl-, Alkenyl-, and Arylbenzenes form Phenols. *Tetrahedron Lett.* **1981**, *22*, 4449-1981. (b) Huang, J. -H.; Yang, L. -M. Nickel-Catalyzed Amination of Aryl Phosphates through Cleaving Aryl C-O Bond. *Org. Lett.* **2011**, *13*,

3750-3753. (c) Chen, H.; Huang, Z.; Hu, X.; Tang, G.; Xu, P.; Zhao, Y.; Cheng, C. -H. Nickel-Catalyzed Cross-Coupling of Aryl Phosphates with Arylboronic Acids. *J. Org. Chem.* **2011**, *76*, 2338-2344.

(10) (a) So, C. M.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. Palladium-Catalyzed Amination of Aryl Mesylates. *Angew. Chem. Int. Ed.* **2008**, *47*, 6402-6406. (b) Chung, K. H.; So, C. M; Wong, S. M.; Luk, C. H.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. An Efficient Palladium-Benzimidazolyl Phosphine Complex for the Suzuki-Miyaura Coupling of Aryl Mesylates: Facile Ligand Synthesis and Metal Complex Characterization. *Chem. Commun.* **2012**, *48*, 1967-1969.

(11) So, C. M.; Kwong, F. Y. Palladium-Catalyzed Cross-Coupling Reactions of Aryl Mesylates. *Chem. Soc. Rev*. **2011**, *40*, 4963-4972.

(12) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals.*, 4th ed.; Butterworth-Heinemann: Oxford, UK, 1996.

(13) Gong, D. R.; Dong, W. M.; Hu, Y. M.; Bi, J. F.; Zhang, X. Q.; Jiang, L. S. Syndiotactically Enriched 1,2-Selective Polymerization of 1,3-Butadiene Initiated by Iron Catalysts Based on A New Class of Donors. *Polymer*, **2009**, *50*, 5980-5986.

(14) Simmons, B. J.; Weires, N. A.; Dander, J. E.; Garg, N. K. Nickel-Catalyzed Alkylation of Amide Derivatives. *ACS Catal.* **2016**, *6*, 3176-3179.

(15) Wong, Y. -C; Parthasarathy, K.; Cheng, C. -H. Direct Synthesis of Arylketones by Nickel-Catalyzed Addition of Arylboronic Acids to Nitriles. *Org. Lett.* **2010**, *12*, 1736-1739.

(16) Gao, K.; Yorimitsu, H.; Osuka, A. α-Arylation of Ketimines with Aryl Sulfides at a Low Palladium Catalyst Loading. *Angew. Chem. Int. Ed.* **2016**, *55*, 4573-4576.

(17) Fernández-Salas, J. A.; Marelli, E.; Cordes, D. B.; Slawin, A. M. Z.; Nolan, S. P. General and Mild Ni^0-Catalyzed α-Arylation of Ketones Using Aryl Chlorides. *Chem. Eur. J.* **2015**, *21*, 3906-3909.

(18) Ding, Y.; Zhang, W.; Li, H.; Meng, Y.; Zhang, T.; Chen, Q. -Y.; Zhu. C. Metal-Free Synthesis of Ketones by Visible-Light Induced Aerobic Oxidative Radical Addition of Aryl Hydrazines to Alkenes. *Green. Chem.* **2017**, *19*, 2941-2944.

(19) Sarvari, M. H.; Sharghi, H. Reactions on a Solid Surface. A Simple, Economical and Efficient Friedel−Crafts Acylation Reaction over Zinc Oxide (ZnO) as a New Catalyst. *J. Org. Chem.* **2004**, *69*, 6953-6956.

(20) Miao, T.; Wang, G. -W. Synthesis of Ketones by Palladium-Catalysed Desulfitative Reaction of Arylsulfinic Acids with Nitriles. *Chem. Commun.* **2011**, *47*, 9501-9503.

(21) Veverková, E.; Meciarová, M.; Gotov, B.; Toma, Š. Microwave Assisted Acylation of Methoxy-arenes Xatalyzed by EPZG® Catalyst. *Green. Chem.* **2002**, *4*, 361-365.

(22) Liu, M.; Hyder, Z.; Sun, Y.; Tang, W.; Xu, L.; Xiao, J. Efficient Synthesis of Alkyl Aryl Ketones & Ketals via Palladium-Catalyzed Regioselective Arylation of Vinyl Ethers. *Org. Biomol. Chem.* **2010**, *8*, 2012-2015.

(23) Majhi, B.; Kundu, D.; Ranu, B. C. Ascorbic Acid Promoted Oxidative Arylation of Vinyl Arenes to 2-Aryl Acetophenones without Irradiation at Room Temperature under Aerobic Conditions. *J. Org. Chem.* **2015**, *80*, 7739-7745.

(24) Marion, N.; Ecarnot, E. C.; Navarro, O.; Amoroso, D.; Bell, A.; Nolan, S. P. (IPr)Pd(acac)Cl: An Easily Synthesized, Efficient, and Versatile Precatalyst for C−N and C−C Bond Formation. *J. Org. Chem.* **2006**, *71*, 3816-3821.

(25) Liu, J.; Zhou, X.; Rao, H.; Xiao, F.; Li, C. -J.; Deng, G. -J. Direct Synthesis of Aryl Ketones by Palladium-Catalyzed Desulfinative Addition of Sodium Sulfinates to Nitriles. *Chem. Eur. J.* **2011**, *17*, 7996-7999.

(26) Cutulic, S. P. Y.; Findlay, N. J.; Zhou, S. -Z.; Chrystal, E. J. T.; Murphy, J. A. Metal-Free Reductive Cleavage of C−O σ-bonds in Acyloin Derivatives by an Organic Neutral Super-Electron-Donor. *J. Org. Chem.* **2009**, *74*, 8713-8718.

(27) Ma, S.; Bo, L.; Fu, C. 2-Alkoxy-6-Aminophenyl Dialkylphosphine and Synthesis and Use Thereof. PCT Int. Appl. WO 2013166770, 2013.

(28) Adams, H.; Gilmore, N. J.; Jones, S.; Muldowney, M. P.; von Reuss, S. H.; Vemula, R. Asymmetric Synthesis of Corsifuran A by an Enantioselective Oxazaborolidine Reduction. *Org. Lett.* **2008**, *10*, 1457-1460.

(29) Astarloa Maseda, I.; San Martin Faces, R.; Herrero Corral, M. T.; Dominguez Perez, E. Process for the Preparation of 1,2-Di(hetero)arylethanones and 1,2,2-Tri(hetero)arylethanones by Regioselective Arylation of Ketones in the Catalyzed by a Palladium Salt and a Phosphorous Ligand in the Presence of a metal Base and a Quaternary Ammonium Salt in Water. Span. 28pp. Patent. ES2636091, 2018.

(30) Liu, F.; Hu, Y. -Y.; Li, D.; Zhou, Q.; Lu, J. -M. *N*-Heterocyclic Carbene-Palladacyclic Complexes: Synthesis, Characterization and Their Applications in the C-N Coupling and α-Arylation of Ketones Using Aryl Chlorides. *Tetrahedron* **2018**, *74*, 5683-5690.

(31) Wang, X.; Chen, R. -X.; Wei, Z. -F.; Zhang, C. -Y.; Tu, H. -Y.; Zhang. A. -D. Chemoselective Transformation of Diarylethanones to Arylmethanoic Acids and Diarylmethanones and Mechanistic Insights. *J. Org. Chem.* **2016**, *81*, 238-249.

(32) Chen, T.; Li, Y. -F.; An, Y.; Zhang, F. -M. Iron-Catalyzed α-Arylation of Deoxybenzoins with Arenes through an Oxidative Dehydrogenative Approach. *Org. Lett.* **2016**, *18*, 4754-5457.