Benzylic Aroylation of Toluenes Mediated by a $LiN(SiMe_3)_2/Cs^+$ System

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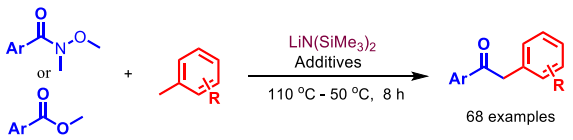
Supporting Information Placeholder



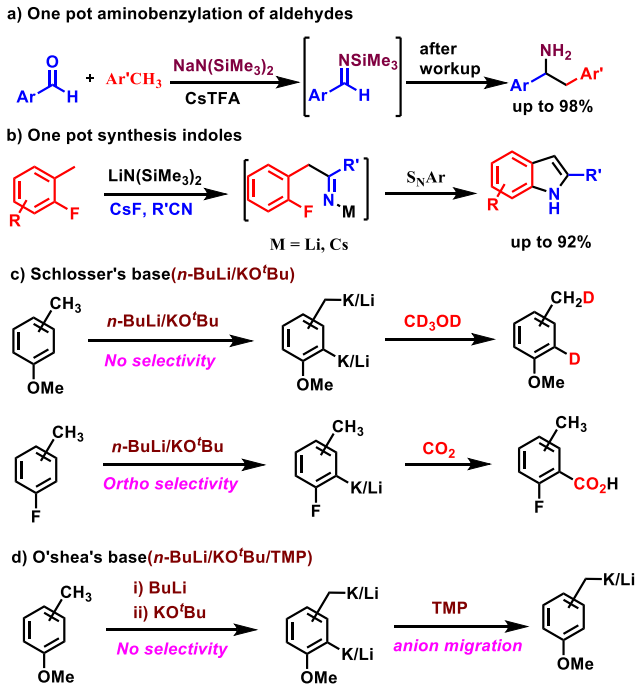
ABSTRACT: Chemoselective deprotonative functionalization of benzylic C–H bonds is challenging, because the arene ring contains multiple aromatic C(sp^2) – H bonds, which can be competitively deprotonated and lead to selectivity issues. Recently it was found that bimetallic [$MN(SiMe_3)_2$ M = Li, Na] / Cs^+ combinations exhibit excellent benzylic selectivity. Herein, is reported the first deprotonative addition of toluenes to Weinreb amides mediated by $LiN(SiMe_3)_2$/CsF for the synthesis of a diverse array of 2-arylacetophenones. Surprisingly, simple methyl benzoates also react with toluenes under similar conditions to form 2-arylacetophenones without double addition to give tertiary alcohol products. This finding greatly increases the practicality and impact of this chemistry. Some challenging substrates with respect to benzylic deprotonations, such as fluoro and methoxy substituted toluenes, are selectively transformed to 2-aryl acetophenones. The value of benzylic deprotonation of 3-fluorotoluene is demonstrated by the synthesis of a key intermediate in the preparation of Polmacoxib.

INTRODUCTION

The introduction of straightforward and economical methods for the formation of C–C bonds by the functionalization of C–H bonds is of great importance in industry and academics. Petroleum feedstocks,[1] such as toluene derivatives, are ideal sources for C–H functionalizations due to their ready availability and low costs. The benzylic derivatization of alkylarenes is generally performed under oxidative conditions.[2] Recent studies, however, have highlighted an alternative route that involves reversible deprotonation of the benzylic C–H bonds ($pK_a \approx 43$ in DMSO) and with relatively mild bases [$MN(SiMe_3)_2$, M = Li, Na, K, Cs, $pK_a \approx 26$ for $HN(SiMe_3)_2$ in THF].[3] The resulting transient organometallic, MCH_2Ar, can be elaborated for a net benzylic C–H functionalization. It has been proposed that the deprotonation is facilitated by the formation of cation-π interactions between group(I) metals and arenes.[4, 3a] Some recent examples from our work include the aminobenzylation of toluenes (Scheme 1a)[3b] and an efficient indole synthesis from 2-fluorotoluene (Scheme 1b),[3e] both using $MN(SiMe_3)_2$ bases with Cs^+ additives. Others have used stronger bases to deprotonate toluene derivatives, including mixed bases [*n*-BuLi, *t*-BuOK and TMP (TMP = 2,2,6,6,-tetramethylpiperidine) by O'Shea,[5] *t*-BuOK and LiTMP[6] or KCH_2TMS and $KN(SiMe_3)_2$ by Kobayashi,[7] $KZn(N(SiMe_3)_2)_3$ by Mulvey[8] and LDA by Guan].[9] For deprotonation of substituted toluenes, Schlosser's super base (*n*-BuLi / *t*-BuOK) exhibits a high degree of substrate dependency. For example, *n*-BuLi / *t*-BuOK exhibited no selectivity in the deprotonation of methoxy substituted toluenes (Scheme 1c top).[5a] Furthermore, *n*-BuLi / *t*-BuOK preferentially metallates halogen substituted toluenes at aromatic C(sp^2)–H bonds adjacent to the halogens (Scheme 1c bottom).[10, 5a] The site selectivity issue was overcome by O'Shea and coworkers' base-promoted anion migration strategy, although few examples were demonstrated (Scheme 1d).[5a] These issues highlight the central challenge of successful benzylic deprotonation of toluenes. It is noteworthy that classical approaches to such benzylic organometallic reagents involve 1) halogenation of the benzylic C–H bonds under strongly oxidizing conditions and 2) conversion of the resulting benzyl halide to the organometallic

reagent, such as $ClMgCH_2Ar$ or $LiCH_2Ar$, by treatment with the appropriate main group metal. Based on our previous efforts, we sought to employ our toluene functionalization strategy from Scheme 1a and b to the synthesis of 2-arylacetophenones.

Scheme 1. Routes for Toluene Deprotonation

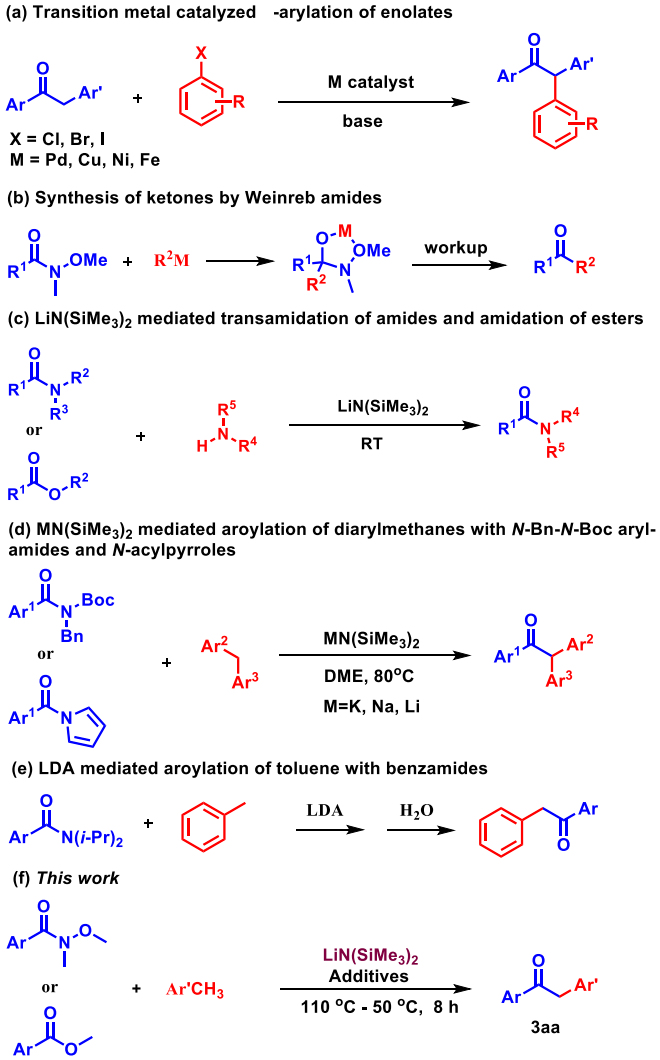


2-Arylacetophenones are an important class of pharmaceutical, flavor and fragrance intermediates, and have wide applications in the fields of medicinal chemistry and organic synthesis.[11] For example, marketed Tamoxifen, Daidzein and Oxcarbazepine either contain the 2-arylacetophenone motif or can be prepared through intermediates that possess this common building block.[12] Despite the simplicity of 2-aryl acetophenones, step efficient syntheses remain in demand.

An elegant approach to the synthesis of 2-aryl acetophenones is the transition metal catalyzed α-arylation of ketone enolates. This chemistry can be traced back to the 1997 discoveries by Miura, Buchwald, Hartwig and their co-workers on the palladium catalyzed α-arylation of ketone enolates with aryl halides (Scheme 2a).[13] Since the initial breakthrough with Pd-based catalysts, copper, nickel, iron and other transition metals have been used in this class of transformations.[14] In addition, Fu and co-workers developed an arylation strategy using α-halo carbonyl compounds with organometallic reagents.[15] These approaches, while attractive, rely on transition metals that can be costly and must be removed after the transformation to limit carryover of trace transition metal contaminants. Kürti and his team introduced a transition metal-free arylation reaction using nitro arenes as the aryl electrophiles.[16]

A complementary strategy for the synthesis of 2-arylacetophenones to the α-arylation of ketones is the addition of organometallic reagents to carbonyl compounds. As taught in most sophomore organic chemistry classes worldwide, however, the reactions of polar organometallic reagents (RLi, RMgBr) in ethereal solvents with esters takes place rapidly at low temperature (sometimes –78 °C) and affords tertiary alcohols via addition of two equiv of the organometallic reagent to the ester.[17] To circumvent this problem, Weinreb and Nahm introduced the so called Weinreb amides.[18] In the Weinreb ketone synthesis (Scheme 2b) the unique structure of the tetrahedral intermediate formed on addition of strong nucleophiles to the Weinreb amide is stabilized at low temperature until workup, preventing formation of the ketone carbonyl group and over addition of the nucleophile. In an effort to diversify tactics for the synthesis of carbonyl compounds, chemists have aimed to use amides with different reactivity to complement the reactivity of Weinreb amides. In the realm of transamidation and amidation of esters, Szostak and co-workers developed transition-metal-free methods to form new C–N bonds. For example, in the transamidation of tertiary amides, aniline derivatives were successfully

Scheme 2. Reactions of carbonyl compounds



employed in the presence of $LiN(SiMe)_2$ base (Scheme 2c).[19] Recently, some of our team members reported a method to synthesize 1,2,2-triarylethanones by acylation of 2-arylmethanes using *N*-acyl pyrroles or *N*-benzyl *N*-Boc amides without the involvement of transition metals (Scheme 2d).[20] In these cases, the reactions gave better yields when one of the aryl groups of the pro-nucleophile was a heteroaryl group (I.e., $Ar–CH_2–Ar_{Hetero}$), lowering the p*Ka* of the benzylic C–H bonds. Toluene can also be used with 2,5-dimethyl *N*-acyl pyrroles to furnish 2-arylacetophenones.[21] This year, Guan and co-workers nicely demonstrated that toluene could be deprotonated in the presence of LDA (H–N*i*Pr$_2$ pK_a 36 in THF)[22] at 60 °C in the presence of benzamides, ArCON*i*Pr$_2$, to give 2-aryl acetophenones in good

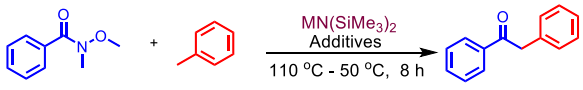
yields (Scheme 2e).[9b] Concurrently with the Guan study, we explored the use of silyl amides to deprotonate toluene in the presence of Weinreb amides (Scheme 2f). Silyl amide bases are significantly less aggressive and basic than LDA and expected to exhibit greater functional group tolerance. Remarkably, we were also able to introduce conditions for the use of simple methyl benzoates as precursors, greatly increasing the practicality and impact of this chemistry.

RESULTS AND DISCUSSION

We began our study by using *N*-methoxy-*N*-methylbenzamide (**1a**) and toluene (**2a**) as model substrates (Table 1). We initially tested three different silylamide bases, ($LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, and $KN(SiMe_3)_2$), and their combinations with various cesium salts at different temperatures, because it is well known that the nature of the main group metal can have a dramatic impact on reactivity of main group organometallics.[23] Unfortunately, these bases could not give acceptable results (see the Supporting Information for details). We speculated that Weinreb amides decomposed under the basic conditions, because they could not be recovered from the crude reaction mixtures. Therefore, we changed the experimental operation by adding the silylamide bases to toluene first and stirring at 110 °C for 4 h. Next, the reaction mixture was cooled to room temperature and the *N*-methoxy-*N*-methylbenzamide was added. After the addition, the reaction mixture was placed in an oil bath at 50 °C for 4 h. Using this procedure, we rescreened three different silylamide bases [$LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, and $KN(SiMe_3)_2$] and found that $KN(SiMe_3)_2$ gave the desired product in 33% AY (Table 1, entry 1–3, AY = assay yield determined by GC integration of the unpurified reaction mixture against an internal standard).

In our previous reports (Scheme 1a and 1b) we demonstrated the beneficial impact of cesium salts on the toluene deprotonation process. In the present case, we found that when the combination of $LiN(SiMe_3)_2$ (3 equiv) and CsF (3 equiv) was used, the yield of the target product reached 92% (Table 1, entry 4). The yields with other combinations of $LiN(SiMe_3)_2$ and Cs^+ salts were lower (entries 5–9). Next, we screened the ratio of $LiN(SiMe_3)_2$ to CsF and found that the amount of CsF could be reduced from 3 equiv to 2 equiv without affecting the yield (Table 1, entries 11–13). Ultimately, the optimized conditions employed 3 equiv of $LiN(SiMe_3)_2$, 0.6 mL toluene, and 2 equiv of CsF at 110 °C for 4 h, cooling the reaction mixture to room temperature, adding 1 equiv *N*-methoxy-*N*-methylbenzamide (**1a**), and then heating to 50 °C for 4 h (Table 1, entry 10). The exact reason that pre-heating the solution of $LiN(SiMe_3)_2$, CsF and toluene is necessary for high yields is unclear. We speculate that the CsF salt will be more soluble at the higher temperature and more readily interact, possibly through establishment of an equilibrium between $LiN(SiMe_3)_2$ and $CsN(SiMe_3)_2$ via metathesis.[24]

Table 1.Optimization of Reaction Conditions[a]



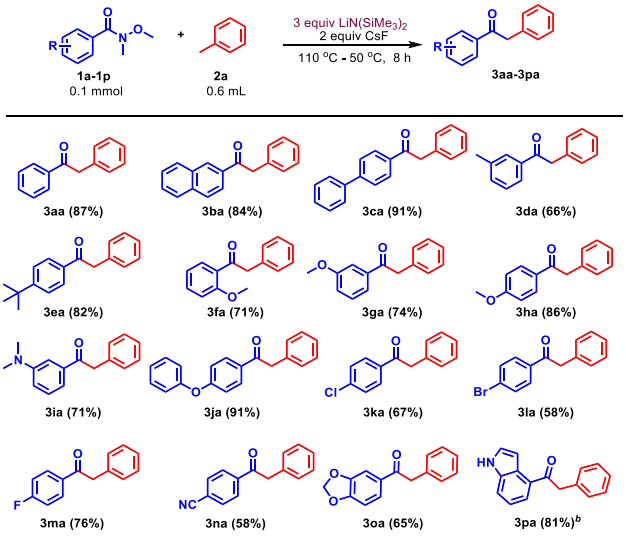
1a, 0.1 mmol **2a**, 0.6 mL **3aa**

entry	base	additives	base/additive	AY[b](%)
1	$LiN(SiMe_3)_2$		3:0	0
2	$NaN(SiMe_3)_2$		3:0	trace
3	$KN(SiMe_3)_2$		3:0	33
4	$LiN(SiMe_3)_2$	CsF	3:3	92
5	$LiN(SiMe_3)_2$	CsCl	3:3	trace
6	$LiN(SiMe_3)_2$	CsBr	3:3	trace
7	$LiN(SiMe_3)_2$	Cs_2SO_4	3:3	trace
8	$LiN(SiMe_3)_2$	Cs_2CO_3	3:3	61
9	$LiN(SiMe_3)_2$	CF_3CO_2Cs	3:3	0
10	**$LiN(SiMe_3)_2$**	**CsF**	**3:2**	**93**
11	$LiN(SiMe_3)_2$	CsF	3:1	59
12	$LiN(SiMe_3)_2$	CsF	2:2	78
13	$LiN(SiMe_3)_2$	CsF	2:1	31

[a]Reactions conducted under argon on 0.1 mmol scale, 0.6 mL toluene, 3 equiv $LiN(SiMe_3)_2$, 2 equiv CsF, 110 °C, and 4 h, then add **1a** (0.1 mmol), 50 °C, and 4 h. [b]Assay yield determined by GC integration with *n*-tetradecane as an internal standard.

With the optimized conditions in hand, we evaluated the scope of *N*-methoxy-*N*-methylbenzamide derivatives with toluene (Scheme 3). In general, under our optimized conditions, various aryl Weinreb amides with different substituents on the aryl group were compatible. The parent *N*-methoxy-*N*-methylbenzamide was successfully converted to **3aa** in 87% isolated yield. *N*-Methoxy-*N*-methyl-2-naphthamide (**1b**) and aryl Weinreb amides with 4-Ph substituents were good substrates. The target products **3ba** and **3ca** were obtained in 84% and 91% yields, respectively. The yields of products from alkyl substituted benzamides, such as **3da** (3-Me) and **3ea** (4-^{t}Bu), were 66% and 82%, respectively. Aryl Weinreb amides bearing electron-donating substituents, such as 2-OMe, 4-OMe, and 4-OPh gave **3fa**, **3ha** and **3ja** in 86%, 74% and 91% yields, respectively. Aryl Weinreb amides bearing electron-withdrawing groups, such as 3-OMe and 3-NMe_2, were also suitable substrates giving the substitution products in good yields (**3ga** and **3ia**, 71–74%). For aryl Weinreb amides containing halogen substituents, such as 4-Cl, 4-Br and 4-F, the target products **3ka**, **3la** and **3ma** were obtained in 67%, 58% and 76% yields, respectively. These substrates could be further functionalized using cross-coupling strategies. Nitriles are known to undergo nucleophilic addition reactions with organometallic reagents. Surprisingly, aryl Weinreb amides containing 4-CN provided the target product **3na** in 58% yield under the standard reaction conditions. Weinreb amides containing heterocycles, including 1,3-dioxolan groups and indole with a free NH, provided addition products **3oa**-**3pa** in 65–81% yields. The indole derivative required additional base compared to the standard conditions, most likely to deprotonate the N–H.

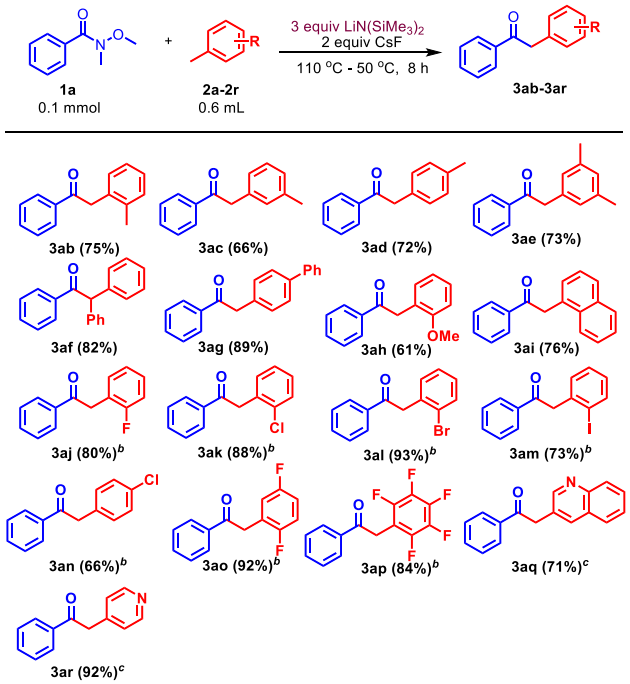
Scheme 3. Substrate Scope of Weinreb amide[a]



[a] Reactions conducted under argon on 0.1 mmol scale, 0.6mL toluene, 3 equiv $LiN(SiMe_3)_2$, 2 equiv CsF, 110 °C for 4 h, then addition of **1** (0.1 mmol), 50 °C for 4 h. Yield is that of the isolated product. [b] 6 equiv $LiN(SiMe_3)_2$.

Next, we used *N*-methoxy-*N*-methylbenzamide to explore the scope of toluene derivatives. As shown in Scheme 4. For polymethyl-substituted toluene derivatives, such as ortho-, meta-, or para-xylene and mesitylene, the target products **3ab**–**3ae** could be obtained in 66–75% yields. Toluene derivatives with multiple aromatic rings, such as diphenylmethane and 4-methylbiphenyl, proved to be suitable substrates giving the target products in 82% (**3af**) and 89% (**3ag**) isolated yields, respectively. It is worth noting that 1-methoxy-2-methylbenzene and 1-methyl naphthalene, which have increase steric profiles around the reactive methyl group, generated target products **3ah** and **3ai** in 61% and 76% yields, respectively. For toluene derivatives with halogen substituents, conversions to the target products were poor under the standard conditions. We, therefore, re-optimized the method. The modified conditions involved 3 equiv of $LiN(SiMe_3)_2$, 2 equiv of CsF and 0.5 mL 2-MeTHF at 110 °C for 4 h, cooling the reaction mixture to room temperature, adding 1 equiv *N*-methoxy-*N*-methylbenzamide and 0.3 mL of the halogenated toluene, and then heating to 50 °C for 4 h. Using the revised conditions, the yields of target halogenated ketones **3aj**–**3ap** were 66–93%. Compared with super base systems, our method exhibited high benzylic selectivity for these halogen containing substrates. For 3-methylquinoline and 4-methylpyridine, which contain nitrogen heterocycles that acidify their methyl groups, only 3 equiv of the heterocycle (see Scheme 4 for details) were used to obtain the target products in 71% and 92% yield, respectively.

Scheme 4. Substrate Scope of Toluene Derivatives[a]

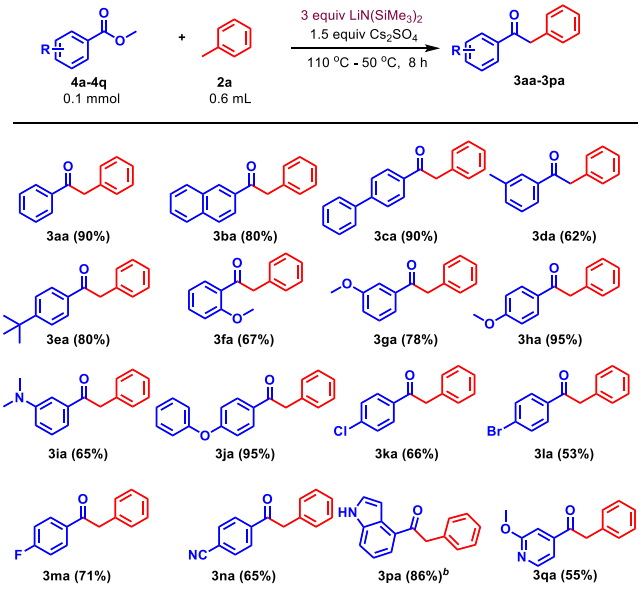


[a]Reactions conducted under argon on 0.1 mmol scale 0.6mL toluene derivatives, 3 equiv $LiN(SiMe_3)_2$, 2 equiv CsF, 110 °C for 4 h, then addition of **1a** (0.1 mmol), 50 °C for 4 h. Yield is that of the isolated product. [b]0.5 mL 2-MeTHF, 3 equiv $LiN(SiMe_3)_2$, 2 equiv CsF, 110 °C for 4 h, then add **2** (0.3 mL), **1a** (0.1 mmol), 50 °C for 4 h. [c]**2** (3 equiv), 0.5 mL 2-MeTHF, 3 equiv $LiN(SiMe_3)_2$, 2 equiv CsF, 110 °C for 4 h, then add **1a** (0.1 mmol), 50 °C for 4 h.

Methyl benzoates are readily available from commercial sources, making them ideal starting materials for laboratory and large scale applications. With this in mind, and cognizant of potential problems of direct reaction of the silyl amides with the esters, we set out to determine if esters were potentially useful electrophiles in the toluene functionalization chemistry. Surprisingly, the aroylation of toluene was successfully extended to methyl benzoates (see Supporting Information for reaction optimization). The important difference was the use of Cs_2SO_4 as the Cs^+ source (1.5 equiv).

With the optimized conditions in hand, we next conducted an examination of the scope of the reaction using toluene with a wide range of methyl benzoate derivatives (Scheme 5). Toluene reacted with methyl 2-naphthoate and methyl benzoate substituted by 4-Ph, 3-Me, 4-^{t}Bu, 3-NMe_2, 4-OMe, 3-OMe and 4-OPh to provide the products in 61–95% yields. Methyl 2-methoxybenzoate, with a higher steric profile, provided the ketone product in 67% yield. Similarly, for methyl benzoates containing halogen substituents, such as 4-Cl, 4-Br and 4-F, the target products **3ka**, **3la** and **3ma** were obtained in 66%, 53% and 71% yields, respectively. The methyl benzoate bearing a reactive 4-CN substituent generated the target product **3na** in 65% yield under the standard conditions. The indole-based methyl benzoate derivative was also a good substrate, providing 86% yield of the product **3pa** (with 5 equiv $LiN(SiMe_3)_2$).

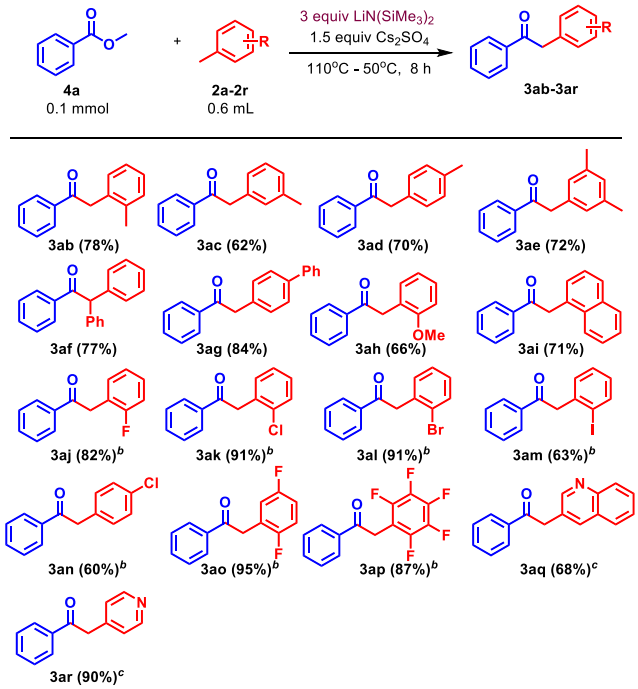
Scheme 5. Substrate Scope of Methyl benzoates[a]



[a] Reactions conducted under argon on 0.1 mmol scale with 0.6mL toluene, 3 equiv $LiN(SiMe_3)_2$, 1.5 equiv Cs_2SO_4, 110 °C for 4 h, then addition of **4** (0.1 mmol), 50 °C for 4 h. Yield is that of the isolated product. [b] with 5 equiv $LiN(SiMe_3)_2$.

We next used the parent methyl benzoate to explore the scope of toluene derivatives (Scheme 6). We were pleased to find that a wide range of toluene derivatives could be easily converted into the expected ketone products. Toluene derivatives with various substituents (2-Me, 3-Me, 4-Me, and mesitylene) were employed to obtain the target products **3ab–3ae** in 62–78% yields. Diphenylmethane, 4-methylbiphenyl, 2-methylanisole and 1-methylnaphthalene were also compatible with the standard method. The products **3af**, **3ag**, **3ah** and **3ai** were obtained in 77%, 84%, 66% and 71% yields, respectively. Similar to the previous results with Weinreb amides, for toluene derivatives containing halogens, we reoptimized the conditions. We used 3 equiv of $LiN(SiMe_3)_2$, 1.5 equiv Cs_2SO_4, and 0.5 mL of 2-MeTHF and heated the solution at 110 °C for 4 h. After cooling to room temperature, 0.3 mL of halogenated toluene and 0.1 mmol of methyl benzoate were added at the same time. The resulting solution was heated at 50 °C for 4 h to obtain the target products **3aj–3ap** in 60–95% yields. Heterocyclic substrates, such as 3-methylquinoline and 4-methylpyridine, were also compatible with our method, providing the ketone products **3aq** and **3ar** in 68% and 90% yields.

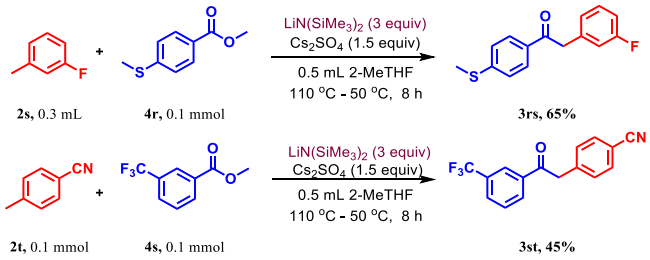
Scheme 6. Substrate Scope of Toluene Derivatives[a]



[a]Reactions conducted under argon on 0.1 mmol scale. Yield is that of the isolated product. [b]0.5mL 2-MeTHF, 3 equiv $LiN(SiMe_3)_2$, 1.5 equiv Cs_2SO_4, 110 °C for 4 h, then addition of **2** (0.3 mL), **4a** (0.1 mmol), 50 °C for 4 h. [c]**2** (3 equiv), 0.5 mL 2-MeTHF, 3 equiv $LiN(SiMe_3)_2$, 1.5 equiv Cs_2SO_4, 110 °C for 4 h, then addition of **4a** (0.1 mmol), 50 °C for 4 h.

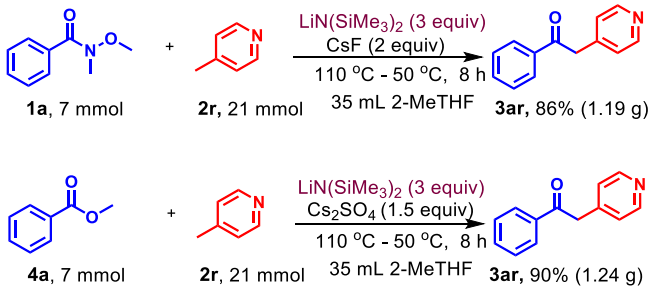
As noted earlier, 2-aryl acetophenone derivatives are common building-blocks in the pharmaceutical and agricultural industries. As a pharmaceutical intermediate, 2-(3-fluorophenyl)-1-(4-(methylthio)phenyl)ethanone **(3rs)** was used in the synthesis of Polmacoxib.[25] By using 3-fluorotoluene (**2s**) and methyl 4-(methylthio)benzoate (**4r**), we successfully obtained the target product **3rs** in 65% yield using the $LiN(SiMe_3)_2$ / Cs_2SO_4 system. It is noteworthy that either *n*-BuLi or super base (*n*-BuLi, *t*-BuOK) preferentially metallated next to the fluoro substituent.[5a, c] Examples with related benzylic deprotonation of fluoro substituted toluene derivatives are rare and noticeably absent from the scope with other bases.[26, 10, 5a, 9a, 9b] Similarly, in this system, we successfully synthesized 2-(4-cyanophenyl)-3'-trifluoromethylacetophenone (**3st**) in 45% yield (Scheme 7). The reduced yield in this transformation may be due to the stabilization of the benzylic carbanion by the cyano group. Compound **3st** is an important intermediate of metaflumizone (a highly selective insecticide).[27] The corresponding Weinreb amide could also be successfully converted to the target products **3rs** and **3st** under the $LiN(SiMe_3)_2$ / CsF system. In these cases, the yields were 55% and 40%, respectively (see Experimental Section).

Scheme 7. Synthesis of Intermediates toward Polmacoxib and Metaflumizone



To test the scalability of this transformation, 7 mmol of *N*-methoxy-*N*-methylbenzamide (**1a**) and 7 mmol methyl benzoate (**4a**) were employed to react with 4-methylpyridine (**2r**) with the $LiN(SiMe_3)_2$/cesium salts system, respectively (Scheme 8). The desired product **3ar** was isolated in 86% yield and 90% yields, respectively (for additional screening of conditions, see the Experimental Section). These results suggest that the reactions can be easily scaled.

Scheme 8. Scale-up of the Transformation on 7.0 mmol Scale



In summary, 2-aryl acetophenones are common building-blocks in the pharmaceutical and agricultural industries. We have presented s simple, convenient, and economical method to make a wide range of derivatives (68 examples, 45–95% yields) of these valuable compounds through the C–H functionalization of toluene in the presence of Weinreb amide or methyl benzoate electrophiles. This method compares well with the traditional approach, which entails conversion of toluenes to the corresponding benzyl halide followed by metallation with Mg or Li metal. The resulting organometallic reagent could be used in an addition reaction with a Weinreb amide at low temperature. Use of methyl benzoate would likely result in over addition and contamination of the product with the tertiary alcohol. We propose that the key to avoidance of the over addition product in our system is the fast rate of deprotonation of the 2-aryl acetophenones by the silyl amide base.[21] Once the enolate is formed, it is inert to over addition. Our method also has advantages over α-arylation of acetophenones in that it does not require transition metals or specialized ligands. Given the benefits of this toluene functionalization, we envision that it will be of use in the pharmaceutical and agricultural industries.

■ EXPERIMENTAL SECTION

General information. All reactions were carried out under an atmosphere of dry argon. Unless otherwise stated, reagents were commercially available and used as purchased. Chemicals were obtained from Sigma-Aldrich, Acros, Innochem, Energy Chemical, TCI China or Alfa Aesar. The progress of the reactions was monitored by thin-layer chromatography using TLC plates and visualized by short-wave ultraviolet light. Flash chromatography was performed with Qingdao Haiyang flash silica gel (200–300 mesh). The NMR spectra were obtained using a Brüker 400 MHz Fourier-transform NMR spectrometer. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz. The infrared spectra were obtained with KBr plates by using IS10 FT-IR Spectrometer (ThermoFisher Corporation). High resolution mass spectrometry (HRMS) data were obtained on Waters LC-TOF mass spectrometer (Xevo G2-XS QTof) using electrospray ionization (ESI) in positive or negative mode. Melting points were measured using a WRS-1C Melt-Temp apparatus and were uncorrected. In cases where the same product was prepared by the two methods developed herein, the higher yielding procedure is given first and the method to prepare the compound in lower yield is given with the corresponding yield.

Sources of toluene derivatives (2a-2r): toluene derivatives were obtained from Sigma-Aldrich, Acros, Innochem, Energy Chemical, TCI China or Alfa Aesar.

Preparation of *N*-methoxy-*N*-methylarylamides: *N*-methoxy-*N*-methylarylamides were prepared according to the literature procedures.[28]

Preparation of Methyl benzoates: Methyl benzoates were prepared according to the literature procedures.[29]

Scale-up the transformation to 7.0 mmol for the synthesis of 3ar. ***Procedure A*:** To an oven-dried round bottom flask (100.0 mL) equipped with a fusiform stir bar (30× 10 mm) under an argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (3.51 g, 21.0 mmol), CsF (2.13 g, 14.0 mmol), 4-methylpyridine (21 mmol) and dry 2-MeTHF (35.0 mL). The round bottom flask was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, the *N*-methoxy-*N*-methylbenzamide (**1a**) (7.0 mmol) were added via pipette, and then heated to 50 °C for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 1.5 mL of water was added. The reaction mixture was passed through a short pad of silica, washed with an additional 30.0 mL of ethyl acetate (3×10 mL), and the combined solutions were concentrated under reduced pressure. The crude material was loaded onto a column of silica gel (petroleum ether: EtOAc = 15:1) to give **3ar** (1.19 g, 86%) as a white solid.

***Procedure B*:** To an oven-dried round bottom flask (100.0 mL) equipped with a fusiform stir bar (30× 10 mm) under an argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (3.51 g, 21.0 mmol), Cs_2SO_4 (3.80 g, 10.5 mmol) 4-methylpyridine (21 mmol) and dry 2-MeTHF (35.0 mL). The round bottom flask was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, the methyl benzoate (**4a**) (7.0 mmol) were added via pipette and then heated to 50 °C for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 1.5 mL of water was added. The reaction mixture was passed through a short pad of silica, washed with an additional 30.0 mL of ethyl acetate (3×10 mL), and the combined solutions were concentrated under reduced pressure. The crude material was loaded onto a column of silica gel (petroleum ether: EtOAc = 15:1) to give 3aa (1.24 g, 90%) as a white solid.

Synthesis of Intermediates toward Polmacoxib. ***Procedure C*:** To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), CsF (30.4 mg, 0.2 mmol) and dry 2-MeTHF (0.5 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, 3-fluorotoluene (**2s**, 0.3 mL) and *N*-methoxy-*N*-methyl-4-(methylthio)benzamide (**1r**, 0.1 mmol) were added via syringe, and then heating to 50 °C for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined

solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification (petroleum ether: EtOAc = 15:1) to give **3rs** (15.3 mg, 59% yield) as a white solid.

***Procedure D*:** To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and dry 2-MeTHF (0.5 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, 3-fluorotoluene (**2s**, 0.3 mL) and methyl 4-(methylthio)benzoate (**4r**, 0.1 mmol) were added via syringe, and then heating to 50 ºC for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification (petroleum ether: EtOAc = 15:1) to give **3rs** (17.2 mg, 65% yield) as a white solid.

Synthesis of Intermediates toward Metaflumizone. ***Procedure E*:** To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and dry 2-MeTHF (0.5 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, *p*-tolunitrile (**2t**, 0.12 mmol) and *N*-methoxy-*N*-methyl-*3*-(trifluoromethyl)benzamide (**1s**, 0.10 mmol) were added via syringe, and then heating to 50 ºC for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification (petroleum ether: EtOAc = 15:1) to give **3st** (11.3 mg, 39% yield) as a light yellow solid.

***Procedure F*:** To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and dry 2-MeTHF (0.5 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, *p*-tolunitrile (**2t**, 0.10 mmol) and methyl 3-(trifluoromethyl)benzoate (**4s**, 0.10 mmol) were added via syringe, and then heating to 50 ºC for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification (petroleum ether: EtOAc = 15:1) to give **3rs** (13.0 mg, 45% yield) as a light yellow solid.

Synthesis of 2-phenylacetophenones. General Procedure G: To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and dry toluene (0.6 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 ºC in an oil bath and stirred for 4 h. After cooling to room temperature, the corresponding Weinreb amide (0.10 mmol) was added via syringe, and then heating to 50 ºC for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated in *vacuo*. The crude material was loaded onto a column of silica gel for purification.

General Procedure H: To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and dry 2-MeTHF (0.5 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, the toluene derivative (0.3 mL) and the corresponding Weinreb amide (0.10 mmol) were added via syringe, and then heating to 50 ºC for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification.

General Procedure I: To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol), dry 2-MeTHF (0.5 mL) and the corresponding toluene derivative (0.30 mmol) was added. Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, the corresponding Weinreb amide (0.10 mmol) were added via syringe. Then the reaction was continued at 50 °C for 4 hours. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification.

General Procedure J: To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and dry toluene (0.6 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 ºC in an oil bath and stirred for 4 h. After cooling to room temperature, the corresponding methyl benzoate (0.10 mmol) was added via syringe, and then heating to 50 ºC for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated in *vacuo*. The crude material was loaded onto a column of silica gel for purification.

General Procedure K: To an oven-dried microwave vial equipped with a stir bar under argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and dry 2-MeTHF (0.5 mL). Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, the toluene derivative (0.3 mL) and the corresponding methyl

benzoate (0.10 mmol) were added via syringe, and then heating to 50 °C for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification.

General Procedure L: To an oven-dried microwave vial equipped with a stir bar under an argon atmosphere inside a glove box was added $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol), dry 2-MeTHF (0.5 mL) and the corresponding toluene derivative (0.30 mmol) was added. Then the microwave vial was sealed with a cap and removed from the glove box. The reaction mixture was heated to 110 °C in an oil bath and stirred for 4 h. After cooling to room temperature, the corresponding methyl benzoate (0.10 mmol) were added via syringe. Then the reaction was continued at 50 °C for 4 h. The sealed vial was cooled to room temperature, opened to air, and then 3 drops of water were added. The reaction mixture was passed through a short pad of silica, washed with an additional 6 mL of ethyl acetate (3 × 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a column of silica gel for purification.

2-Phenyl acetophenone ***(3aa).*** The reaction was performed following the General Procedure J with methyl benzoate (**4a**) (12.5 μL, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (17.6 mg, 90% yield) as a white solid. 87% yield was obtained from amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, *J*=7.4, 2H), 7.63 – 7.55 (m, 1H), 7.49 (dd, *J*=8.4, 6.9, 2H), 7.41 – 7.33 (m, 2H), 7.30 (d, *J*=10.2, 3H), 4.32 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 197.6, 136.6, 134.5, 133.2, 129.5, 128.69, 128.66, 128.63, 126.9, 45.5. The spectroscopic data for this product match the literature data.[30]

2-(Naphthalen-2-yl)-1-phenylethanone ***(3ba).*** The reaction was performed following the General Procedure G with **1b** (21.5 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (20.7 mg, 84% yield) as a white solid. 80% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.55 (s, 1H), 8.07 (dd, *J*=8.6, 1.8 HZ, 1H), 7.97 (d, *J*=7.5, 1H), 7.93 – 7.82 (m, 2H), 7.62 – 7.53 (m, 2H), 7.38 – 7.31 (m, 4H), 7.28 – 7.24 (m, 1H), 4.42 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 197.8, 135.7, 134.8, 134.0, 132.6, 130.6, 129.7, 129.6 128.8, 128.70, 128.65, 127.9, 127.0, 126.9, 124.4, 45.7. The spectroscopic data for this product match the literature data.[31]

1-(Biphenyl-4-yl)-2-phenylethanone ***(3ca).*** The reaction was performed following the General Procedure G with **1c** (24.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (24.8 mg, 91% yield) as a white solid. 90% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 – 8.05 (m, 2H), 7.71 – 7.60 (m, 4H), 7.51 – 7.44 (m, 2H), 7.43 – 7.25 (m, 6H), 4.32 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 197.4, 145.9, 139.9, 135.3, 134.7, 129.6, 129.4, 129.1, 128.8, 128.4, 127.41, 127.38, 127.0, 45.7. The spectroscopic data for this product match the literature data.[31]

1-(3-Methylphenyl)-2-phenylethanone ***(3da).*** The reaction was performed following the General Procedure G with **1d** (17.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (14.0 mg, 66% yield) as a white solid. 62% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 – 7.79 (m, 2H), 7.41 – 7.31 (m, 5H), 7.28 – 7.25 (m, 2H), 4.28 (s, 2H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 198.0, 138.6, 136.7, 134.7, 134.1, 129.6, 129.2, 128.8, 128.6, 127.0, 126.0, 45.6, 21.5. The spectroscopic data for this product match the literature data.[32]

1-[4-(1,1-Dimethylethyl)phenyl]-2-phenylethanone ***(3ea).*** The reaction was performed following the General Procedure G with **1e** (22.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (20.7 mg, 82% yield) as a white solid. 80% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 – 7.94 (m, 2H), 7.49 – 7.45 (m, 2H), 7.35 – 7.22 (m, 5H), 4.27 (s, 2H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 197.4, 157.0, 134.9, 134.1, 129.6, 128.8, 128.7, 126.9, 125.7, 45.6, 35.2, 31.2. One resonance were not observed due to overlapping resonances. The spectroscopic data for this product match the literature data.[33]

1-(2-Methoxyphenyl)-2-phenylethanone ***(3fa).*** The reaction was performed following the General Procedure G with **1f** (19.5 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (16.1 mg, 71% yield) as a colorless oil. 67% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72 – 7.62 (m, 1H), 7.50 – 7.39 (m, 1H), 7.31 – 7.21 (m, 5H), 7.01 – 6.92 (m, 2H), 4.30 (s, 2H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 200.3, 158.5, 135.3, 133.7, 130.8, 129.8, 128.5, 128.2, 126.7, 120.8, 111.5, 55.6, 50.3. The spectroscopic data for this product match the literature data.[30]

1-(3-Methoxyphenyl)-2-phenylethanone ***(3ga).*** The reaction was performed following the General Procedure J with **4g** (16.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (17.6 mg, 78% yield) as a white solid. 74% yield was obtained from the amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 – 7.59 (m, 1H), 7.52 (dd, *J*=2.7, 1.6 HZ, 1H), 7.39 – 7.31 (m, 3H), 7.28 – 7.25 (m, 3H), 7.10 (ddd, *J*=8.2, 2.7, 0.9 HZ, 1H), 4.27 (s, 2H), 3.83 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 197.6, 159.9, 138.0, 134.6, 129.7, 129.6, 128.8, 127.0, 121.4, 119.8, 112.9, 55.5, 45.7. The spectroscopic data for this product match the literature data.[34]

1-(4-Methoxyphenyl)-2-phenylethanone ***(3ha).*** The reaction was performed following the General Procedure J with **4h** (16.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (21.5 mg, 95% yield) as a white solid. 86% yield was obtained from the

amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 – 7.97 (m, 2H), 7.36 – 7.20 (m, 5H), 6.94 – 6.89 (m, 2H), 4.23 (s, 2H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.4, 163.6, 135.1, 131.1, 129.6, 129.5, 128.8, 126.9, 113.9, 55.6, 45.4. The spectroscopic data for this product match the literature data.[30]

1-[3-(Dimethylamino)phenyl]-2-phenylethanone ***(3ia).*** The reaction was performed following the General Procedure G with **1i** (20.8 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 10:1) to give the product (17.0 mg, 71% yield) as a white solid. 65% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 – 7.27 (m, 8H), 6.90 (d, *J*=6.5Hz, 1H), 4.27 (s, 2H), 2.97 (s, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 198.5, 150.7, 137.4, 135.1, 129.6, 129.3, 128.7, 126.9, 117.2, 117.1, 111.8, 45.8, 40.6. The spectroscopic data for this product match the literature data.[35]

1-(4-Phenoxyphenyl)-2-phenylethanone ***(3ja).*** The reaction was performed following the General Procedure J with **4j** (22.8 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (27.4 mg, 95% yield) as a white solid. 91% yield was obtained from the amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 – 7.98 (m, 2H), 7.43 – 7.25 (m, 7H), 7.22 – 7.17 (m, 1H), 7.09 – 7.05 (m, 2H), 7.00 – 6.97 (m, 2H), 4.24 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.4, 162.2, 155.4, 134.8, 131.2, 131.1，130.2, 129.5, 128.8, 127.0, 124.8, 120.4, 117.3, 45.5. The spectroscopic data for this product match the literature data.[36]

1-(4-Chlorophenyl)-2-phenylethanone ***(3ka).*** The reaction was performed following the General Procedure G with **1k** (19.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (15.5 mg, 67% yield) as a white solid. 66% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 – 7.93 (m, 2H), 7.43 – 7.40 (m, 2H), 7.34 – 7.31 (m, 2H), 7.31 – 7.19 (m, 4H), 4.25 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.5, 139.7, 134.9, 134.2, 130.2, 129.5, 129.1, 128.9, 127.2, 45.6. The spectroscopic data for this product match the literature data.[37]

1-(4-Bromophenyl)-2-phenylethanone ***(3la).*** The reaction was performed following the General Procedure G with **1l** (24.3 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (16.0 mg, 58% yield) as a yellow solid. 53% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87 – 7.84 (m, 2H), 7.60 – 7.57 (m, 2H), 7.38 – 7.27 (m, 3H), 7.29 – 7.25 (m, 1H), 7.23 (s, 2H), 4.24 (s, 2H).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.7, 135.3, 134.2, 132.1, 130.3, 129.5, 128.9, 128.5, 127.2, 45.6. The spectroscopic data for this product match the literature data.[37]

1-(4-Fluorophenyl)-2-phenylethanone ***(3ma).*** The reaction was performed following the General Procedure G with **1m** (18.3 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (16.3 mg, 76% yield) as a white solid. 71% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 – 8.01 (m, 2H), 7.35 – 7.30 (m, 2H), 7.28 – 7.25 (m, 2H), 7.25 – 7.23 (m, 1H), 7.15 – 7.08 (m, 2H), 4.26 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.2, 165.9 (d, $J^1_{C\text{-}F}$ = 255.5 Hz), 134.4, 133.0 (d, $J^4_{C\text{-}F}$ = 3.0 Hz), 131.4 (d, $J^3_{C\text{-}F}$ = 9.5 Hz), 129.5, 128.9, 127.1, 115.9 (d, $J^2_{C\text{-}F}$ = 21.2 Hz), 45.6. ^{19}F NMR (377MHz, $CDCl_3$): -104.8. The spectroscopic data for this product match the literature data.[37]

4-(2-Phenylacetyl)benzonitrile ***(3na).*** The reaction was performed following the General Procedure J with **4n** (16.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 10:1) to give the product (14.3 mg, 65% yield) as a white solid. 58% yield was obtained from the amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 – 8.06 (m, 2H), 7.78 – 7.71 (m, 2H), 7.36 – 7.31 (m, 2H), 7.30 – 7.25 (m, 1H), 7.25 – 7.21 (m, 2H), 4.29 (s, 2H).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.4, 139.5, 133.5, 132.7, 129.5, 129.1, 129.0, 127.4, 118.1, 116.5, 45.9. The spectroscopic data for this product match the literature data.[37]

1-(1,3-Benzodioxol-5-yl)-2-phenylethanone ***(3oa).*** The reaction was performed following the General Procedure G with **1o** (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (15.6 mg, 65% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (dd, *J*=8.2, 1.8, 1H), 7.47 (d, *J*=1.7, 1H), 7.37 – 7.29 (m, 2H), 7.27 – 7.21 (m, 3H), 6.83 (d, *J*=8.1, 1H), 6.01 (s, 2H), 4.20 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 195.9, 151.9, 148.3, 134.9, 131.4, 129.5, 128.8, 127.0, 125.2, 108.4, 108.0, 102.0, 45.5. The spectroscopic data for this product match the literature data.[32]

1-(1H-indol-4-yl)-2-phenylethan-1-one ***(3pa).*** The reaction was performed following the General Procedure J with **4p** (17.5 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (83.7 mg, 0.50 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 10:1) to give the product (20.3 mg, 86% yield) as a pale yellow solid. 81% yield was obtained from amide following procedure G. Mp 111.0 –111.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.45 (s, 1H), 7.88 (dd, *J*=7.5, 0.8, 1H), 7.65 – 7.56 (m, 1H), 7.42 – 7.32 (m, 5H), 7.31 – 7.17 (m, 3H), 4.43 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 199.1, 136.9, 135.5, 129.7, 128.7, 128.5, 127.3, 126.8, 126.7, 123.5, 121.1, 116.7, 104.6, 46.3. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{13}NaNO$ 258.0895; Found 258.0899. IR (neat):3062, 3028, 1655, 1567, 1496, 1346, 1274, 1123, 1052, 760, 717, 649.

1-(2-methoxypyridin-4-yl)-2-phenylethan-1-one ***(3qa).*** The reaction was performed following the General Procedure J with **4q** (16.7 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and toluene (**2a**) (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 10:1) to give the product (12.5 mg, 55% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.85 (dd, *J*=2.5 HZ, 1H), 8.15 (dd, *J*=8.8, 2.5 HZ, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.21 (m, 3H), 6.76 (d, *J*=8.7,

1H), 4.21 (s, 2H), 3.98 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 194.1, 166.3, 150.5, 138.0, 133.6, 129.4, 128.9, 127.1, 124.9, 111.4, 55.3, 45.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}NO_2$ 228.1025; Found 228.1022. IR (neat):1654, 1602, 1496, 1372, 1292, 1263, 1216, 1118, 1014, 650, 622.

2-(2-Methylphenyl)acetophenone ***(3ab).*** The reaction was performed following the General Procedure J with methyl benzoate (**4a)** (13.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and **2b** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (16.4 mg, 78% yield) as a white solid. 75% yield was obtained from the amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (dd, *J*=8.4, 1.3 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.51 – 7.46 (m, 2H), 7.23 – 7.11 (m, 4H), 4.32 (s, 2H), 2.26 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 197.6, 137.0, 136.9, 133.5, 133.3, 130.5, 130.4, 128.8, 128.5, 127.4, 126.2, 43.6, 20.0. The spectroscopic data for this product match the literature data.[38]

2-(3-Methylphenyl)acetophenone ***(3ac).*** The reaction was performed following the General Procedure G with *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2c** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (13.9 mg, 66% yield) as a yellow oil. 62% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 – 7.99 (m, 2H), 7.58 – 7.53 (m, 1H), 7.48 – 7.43 (m, 2H), 7.22 (t, *J*=7.5, 1H), 7.11 – 7.04 (m, 3H), 4.25 (s, 2H), 2.33 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 197.9, 138.4, 136.6, 134.5, 133.3, 130.3, 128.76, 128.69 127.8, 126.6, 45.6, 21.6. One resonance were not observed due to overlapping resonances. The spectroscopic data for this product match the literature data.[39]

2-(4-Methylphenyl)-1-phenylethanone ***(3ad).*** The reaction was performed following the General Procedure G with *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2d** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (15.1 mg, 72% yield) as a white solid. 70% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (dd, *J*=8.4 Hz, 1.3, 2H), 7.57 – 7.52 (m, 1H), 7.48 – 7.41 (m, 2H), 7.18 – 7.10 (m, 4H), 4.25 (s, 2H), 2.31 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 198.0, 136.6, 133.6, 131.5, 129.5, 129.4, 128.76, 128.74, 128.72 45.2, 21.2. The spectroscopic data for this product match the literature data.[31]

2-(3,5-Dimethylphenyl)-1-phenylethanone ***(3ae).*** The reaction was performed following the General Procedure G with *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2e** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (16.4 mg, 73% yield) as a white solid. 72% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 – 8.00 (m, 2H), 7.58 – 7.53 (m, 1H), 7.48 – 7.43 (m, 2H), 6.89 (s, 3H), 4.21 (s, 2H), 2.29 (s, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 198.0, 138.3, 136.7, 134.4, 133.3, 128.8, 128.74, 128.73, 127.3, 45.5, 21.4. The spectroscopic data for this product match the literature data.[31]

2,2-Diphenylacetophenone ***(3af).*** The reaction was performed following the General Procedure G with *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2f** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (22.3 mg. 82% yield) as a white solid. 77% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (m, 2H), 7.52 (m, 1H), 7.42 (m, 2H), 7.38 – 7.31 (m, 4H), 7.32 – 7.23 (m, 6H), 6.07 (s, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 198.3, 139.2, 136.8, 133.2, 129.3, 129.1, 128.9, 128.8, 127.3, 59.5. The spectroscopic data for this product match the literature data.[20]

2-(Biphenyl-4-yl)-1-phenylethanone ***(3ag).*** The reaction was performed following the General Procedure G with *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2g** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (24.2 mg, 89% yield) as a white solid. 84% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 – 7.98 (m, 2H), 7.61 – 7.54 (m, 5H), 7.50 – 7.40 (m, 4H), 7.38 – 7.30 (m, 3H), 4.34 (s, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 197.8, 140.9, 139.9, 136.6, 133.6, 133.4, 130.1, 128.9, 128.88, 128.82, 127.6, 127.4, 127.2, 45.2. The spectroscopic data for this product match the literature data.[39]

2-(2-Methoxyphenyl)acetophenone ***(3ah).*** The reaction was performed following the General Procedure J with methyl benzoate (**4a)** (13.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and **2h** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (14.9 mg, 66% yield) as a colorless oil. 61% yield was obtained from the amide following procedure G. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 – 8.02 (m, 2H), 7.58 – 7.52 (m, 1H), 7.48 – 7.43 (m, 2H), 7.29 – 7.21 (m, 1H), 7.17 (dd, *J*=7.4, 1.8, 1H), 6.94 – 6.87 (m, 2H), 4.28 (s, 2H), 3.78 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 198.1, 157.3, 137.0, 133.0, 131.1, 128.6, 128.5, 128.5, 123.7, 120.7, 110.6, 55.5, 40.1. The spectroscopic data for this product match the literature data.[40]

α-(1-Naphthalenyl)acetophenone ***(3ai).*** The reaction was performed following the General Procedure G with *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2i** (0.6 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (18.7 mg,76% yield) as a white solid. 71% yield was obtained from the ester following procedure J. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 – 8.06 (m, 2H), 7.90 – 7.84 (m, 2H), 7.80 (d, *J*=8.2 Hz, 1H), 7.62 – 7.57(m, 1H), 7.51 – 7.41 (m, 5H), 7.36 (d, *J*=6.3 Hz, 1H), 4.74 (s, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 197.8, 136.7, 134.0, 133.5, 132.3, 131.4, 129.0, 128.9, 128.6, 128.2, 128.0, 126.5, 125.9, 125.6, 124.0, 43.3. The spectroscopic data for this product match the literature data.[31]

2-(2-Fluorophenyl)acetophenone ***(3aj).*** The reaction was performed following the General Procedure K with 2-MeTHF (0.5 mL), methyl benzoate (**4a)** (13.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and **2j** (0.3 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (17.5 mg, 82% yield) as a white solid. 80% yield was obtained from the amide following procedure H. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 – 7.98 (m, 2H), 7.63 – 7.55 (m, 1H),

7.51 – 7.44 (m, 2H), 7.30 – 7.25 (m, 1H), 7.25 – 7.17 (m, 1H), 7.15 – 7.01 (m, 2H), 4.33 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.4, 161.1 (d, J^1_{C-F} = 246.2 Hz), 136.4, 133.5, 131.8 (d, J^5_{C-F} = 4.9 Hz), 129.0 (d, J^4_{C-F} = 8.3 Hz), 128.8, 128.5, 124.3 (d, J^6_{C-F} = 3.7 Hz), 121.9 (d, J^3_{C-F} = 16.0 Hz), 115.5 (d, J^2_{C-F} = 22 Hz), 38.8. ^{19}F NMR (377MHz, $CDCl_3$): -117.0. The spectroscopic data for this product match the literature data.[32]

2-(2-Chlorophenyl)acetophenone ***(3ak).*** The reaction was performed following the General Procedure K with 2-MeTHF (0.5 mL), methyl benzoate (**4a)** (13.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and **2k** (0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (21.0 mg, 91% yield) as a white solid. 88% yield was obtained from the amide following procedure H. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.07 – 8.03 (m, 2H), 7.62 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 7.45 – 7.37 (m, 1H), 7.26 – 7.23 (m, 3H), 4.44 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.5, 136.6, 134.6, 133.5, 133.2, 131.8, 129.6, 128.8, 128.7, 128.5, 127.0, 43.4. The spectroscopic data for this product match the literature data.[37]

2-(2-Bromophenyl)acetophenone ***(3al).*** The reaction was performed following the General Procedure H with 2-MeTHF (0.5 mL), *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2l** (0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (25.6 mg, 93% yield) as a yellow oil. 91% yield was obtained from the ester following procedure K. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.08 – 8.04 (m, 2H), 7.62 – 7.57 (m, 2H), 7.52 – 7.46 (m, 2H), 7.31 – 7.23 (m, 2H), 7.18 – 7.13 (m, 1H), 4.46 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.5, 136.7, 135.1, 133.5, 132.9, 131.9, 128.9, 128.8, 128.5, 127.7, 125.2, 45.9. The spectroscopic data for this product match the literature data.[41]

2-(o-Iodophenyl)acetophenone ***(3am).*** The reaction was performed following the General Procedure H with 2-MeTHF (0.5 mL), *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2m** (0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (23.5 mg, 73% yield) as a white solid. 63% yield was obtained from the ester following procedure K. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.07 – 8.04 (m, 2H), 7.87 (dd, *J*=7.9, 1.2, 1H), 7.63 – 7.58 (m, 1H), 7.52 – 7.47 (m, 2H), 7.32 (td, *J*=7.5, 1.3, 1H), 7.23 (dd, *J*=7.6, 1.7, 1H), 6.98 (td, *J*=7.6, 1.8, 1H), 4.47 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.5, 139.6, 138.7, 136.8, 133.5, 131.0, 128.92, 128.86, 128.6, 128.5, 101.6, 50.6. The spectroscopic data for this product match the literature data.[42]

2-(p-Chlorophenyl)acetophenone ***(3an).*** The reaction was performed following the General Procedure H with 2-MeTHF (0.5 mL), *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2n** (0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (15.2 mg, 66% yield) as a white solid. 60% yield was obtained from the ester following procedure K. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.07 – 7.96 (m, 2H), 7.67 – 7.56 (m, 1H), 7.54 – 7.46 (m, 2H), 7.41 – 7.31 (m, 2H), 7.25 – 7.19 (m, 2H), 4.29 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 197.2, 136.4, 133.5, 132.98, 132.95, 131.0, 128.9, 128.8, 128.6, 44.8. The spectroscopic data for this product match the literature data.[37]

2-(2,5-Difluorophenyl)-1-phenylethanone ***(3ao).*** The reaction was performed following the General Procedure K with 2-MeTHF (0.5 mL), methyl benzoate (**4a)** (13.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and **2o** (0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (22.0 mg, 95% yield) as a white solid. 92% yield was obtained from the amide following procedure H. Mp 75.2–75.9°C. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.04 – 8.01 (m, 2H), 7.62 – 7.57 (m, 1H), 7.51 – 7.47 (m, 2H), 7.08 – 7.00 (m, 1H), 7.00 – 6.89 (m, 2H), 4.30 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 195.7, 158.6 (dd, J^4_{C-F} = 2.5 Hz, J^1_{C-F} = 242.4 Hz), 157.1 (dd, J^4_{C-F} = 2.7 Hz, J^1_{C-F} = 242.0 Hz), 136.2, 133.7, 128.9, 128.5, 123.5 (dd, J^2_{C-F} = 18.9 Hz, J^3_{C-F} =8.2 Hz), 118.2 (dd, J^2_{C-F} = 24.3 Hz, J^3_{C-F} = 4.6 Hz), 116.4 (dd, J^2_{C-F} = 25.1 Hz, J^3_{C-F} = 8.8 Hz), 115.4 (dd, J^2_{C-F} = 24.1 Hz, J^3_{C-F} = 8.6 Hz), 38.7. ^{19}F NMR (377MHz, $CDCl_3$): -119.0 (d, *J* = 26.9 Hz), -123.2 (d, *J* = 27.9 Hz). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{10}F_2NaO$ 255.0597; Found 255.0593. IR (neat):3083, 2918, 1691, 1496, 1334, 1206, 1094, 997, 834, 755, 687, 571.

Ethanone, 2-(pentafluorophenyl)-1-phenyl- (9CI) ***(3ap).*** The reaction was performed following the General Procedure K with 2-MeTHF (0.5 mL), methyl benzoate (**4a)** (13.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and **2p** (0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (24.9 mg, 87% yield) as a white solid. 84% yield was obtained from the amide following procedure H. Mp 114.0–114.9°C. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.08 – 7.99 (m, 2H), 7.69 – 7.59 (m, 1H), 7.56 – 7.49 (m, 2H), 4.40 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 192.9, 146.6 (m), 144.4 (m), 141.8 (m), 139.0 (m), 136.3 (m), 135.7, 133.9, 128.9, 128.3, 108.5 (m), 32.6. ^{19}F NMR (377MHz, $CDCl_3$): -142.1 (d, *J* = 23.9 Hz), -155.3, -162.4. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_7F_5NaO$ 309.0315; Found 309.0311. IR (neat):2962, 2922, 1689, 1505, 1451, 1342, 1205, 1001, 938, 763, 687, 563.

1-Phenyl-2-(3-quinolinyl)ethenone ***(3aq).*** The reaction was performed following the General Procedure I with 2-MeTHF (0.5 mL), *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2q** (42.9 mg, 0.30 mmol). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (17.5 mg, 71%) as brown oil. 68% yield was obtained from the amide following procedure L. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.83 (d, J=2.2, 1H), 8.10 – 8.03 (m, 4H), 7.79 – 7.76 (m, 1H), 7.70 – 7.66 (m, 1H), 7.62 – 7.57 (m, 1H), 7.55 – 7.47 (m, 3H), 4.48 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.7, 152.1, 147.3, 136.4, 136.3, 133.7, 129.4, 129.3, 129.0, 128.6, 128.1, 127.7, 127.5, 126.9, 42.6. The spectroscopic data for this product match the literature data.[43]

1-Phenyl-2-(pyridin-4-yl)ethenone ***(3ar).*** The reaction was performed following the General Procedure I with 2-MeTHF (0.5 mL), *N*-methoxy-*N*-methylbenzamide (**1a**) (20.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), CsF (30.4 mg, 0.20 mmol) and **2q** (27.9 mg, 0.3 mmol). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 6:1) to give the product (18.1 mg, 92% yield) as yellow solid. 90% yield was obtained from the amide following procedure L. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.57 –

8.52 (m, 2H), 8.02 – 7.95 (m, 2H), 7.64 – 7.52 (m, 1H), 7.50 – 7.43 (m, 2H), 7.22 – 7.13 (m, 2H), 4.28 (s, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 196.0, 150.1, 143.5, 136.2, 133.8, 129.0, 128.6, 125.1, 44.7. The spectroscopic data for this product match the literature data.[44]

2-(3-Fluorophenyl)-1-[4-(methylthio)phenyl]ethanone ***(3rs)*****.** The reaction was performed following the General Procedure D with 2-MeTHF (0.5 mL), methyl 4-(methylthio)benzoate (**4r**) (18.2 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and 3-fluorotoluene (**2s**, 0.30 mL). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (17.2 mg, 66% yield) as a white solid. 59% yield was obtained from the amide following procedure C. Mp 97.2–97.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91 – 7.87 (m, 2H), 7.30 – 7.26 (m, 1H), 7.26 – 7.23 (m, 2H), 7.05 – 6.89 (m, 3H), 4.22 (s, 2H), 2.50 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 194.5, 163.0 (d, $J^{1}_{C\text{-}F}$ = 246.7 Hz), 147.4, 137.1(d, $J^{5}_{C\text{-}F}$ = 7.7 Hz), 132.7, 130.2(d, $J^{4}_{C\text{-}F}$ = 8.3 Hz), 128.7, 125.2(d, $J^{6}_{C\text{-}F}$ =2.9 Hz), 125.1, 116.6 (d, $J^{2}_{C\text{-}F}$ = 21.7 Hz) 114.0, (d, $J^{3}_{C\text{-}F}$ = 21.1 Hz) 43.3, 14.8. ^{19}F NMR (377MHz, $CDCl_3$): -112.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}FOS$ 261.0749; Found 261.0753. IR (neat):3061, 1678, 1588, 1490, 1449, 1331, 1257, 1216, 1005, 815, 777, 569.

2-(4-Cyanophenyl)-3′-trifluoromethylacetophenone ***(3st)*****.** The reaction was performed following the General Procedure F with 2-MeTHF (0.5 mL), Methyl 3-(trifluoroMethyl)benzoate (**4s**) (20.4 mg, 0.1 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), Cs_2SO_4 (54.3 mg, 0.15 mmol) and 3-fluorotoluene (**2s**, 0.10 mmol). The crude material was purified by flash chromatography on silica gel (Eluent: Petroleum ether: EtOAc = 15:1) to give the product (13.0 mg, 45% yield) as a faint yellow solid. 39% yield was obtained from the amide following procedure E. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.24 (s, 1H), 8.17 (d, *J*=7.8, 1H), 7.85 (d, *J*=9.1, 1H), 7.67 – 7.61 (m, 3H), 7.36 (d, *J*=8.2, 2H), 4.39 (s, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ: 194.92, 138.0(q, $J^{1}_{C\text{-}F}$ = 251.1 Hz), 132.56, 131.5(q, $J^{2}_{C\text{-}F}$ = 18.8 Hz), 130.6, 130.2(q, $J^{4}_{C\text{-}F}$ = 7.1 Hz), 128.9, 125.3(q, $J^{3}_{C\text{-}F}$ = 7.5 Hz), 124.8, 122.1, 118.8, 111.4, 41.8. ^{19}F NMR (377MHz, $CDCl_3$): -63.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{10}F_3NaNO$ 312.0612; Found 312.0620. IR (neat):2227, 1636, 1414, 1325, 1122, 1070, 998, 773, 692, 652, 549.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. ^{1}H and ^{13}C NMR spectra for all pure products

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