One-Pot, Fast and Modular Approach to Alkyl- and Aryl Ketones via Sequential 1,2-Addition/Cross-Coupling of Organolithium Reagents with Weinreb Amides.

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# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table of Contents</td>
<td>S2</td>
</tr>
<tr>
<td>General Methods</td>
<td>S3</td>
</tr>
<tr>
<td>Synthesis of the Weinreb amides</td>
<td>S3</td>
</tr>
<tr>
<td>General Procedures for the one-pot 1,2 addition /cross-coupling procedure</td>
<td>S3</td>
</tr>
<tr>
<td>Preparation of Organolithium Reagents</td>
<td>S4</td>
</tr>
<tr>
<td>Additional experimental data</td>
<td>S4</td>
</tr>
<tr>
<td>Experimental Details and Spectral Data of Compounds</td>
<td>S6</td>
</tr>
<tr>
<td>$^1$H and $^{13}$C NMR of isolated compounds</td>
<td>S14</td>
</tr>
</tbody>
</table>
General methods:

All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. THF and toluene were dried and distilled over sodium. Chromatography: Merck silica gel type 9385 230-400 mesh, TLC: Merck silica gel 60, 0.25 mm. Components were visualized by UV and cerium/molybdenum or potassium permanganate staining. Progress and conversion of the reaction were determined by GC-MS (GC, HP6890: MS HP5973) with an HP1 or HP5 column (Agilent Technologies, Palo Alto, CA). Mass spectra were recorded on an AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). $^1$H- and $^{13}$C-NMR were recorded on a Varian AMX400 (400 and 100.59 MHz, respectively) using CDCl$_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl$_3$: $\delta$ 7.26 for $^1$H, $\delta$ 77.0 for $^{13}$C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Carbon assignments are based on APT $^{13}$C-NMR experiments. Melting points were measured using a Büchi Melting Point B-545. Pd$_2$(dba)$_3$, P(tBu)$_3$, XPhos, SPhos and Pd-PEPPSI-IPent were purchased from Aldrich and used without further purification. $^t$BuLi (1.6 M solution in hexane) was purchased from Acros. $^t$BuLi (1.7 M in pentane), PhLi (1.8 M solution in dibutylether), 2-Thienyllithium (1.0 M solution in THF/hexane) and the compounds used as precursor for the preparation of lithium reagents, namely, 1,3-dimethoxybenzene, 1-bromo-4-methybenzene, 3-bromoanisole, cyclopropylbromide and furane were purchased from Aldrich. The Acyl/chlorides and carboxylic acids and the reagents used for the preparation of the Weinreb amides as well as N,O-dimethylhydroxylamine hydrochloride were purchased from Aldrich. Organolithium reagents other than the aforementioned were prepared according to described procedures (see below).

Synthesis of the Weinreb amides:

A. 4-Bromo-N-methoxy-N-methyl-benzamide (1a), 3-bromo-N-methoxy-N-methylbenzamide (1d):
Weinreb amides 1a and 1d were synthetized according to a reported procedure.$^1$

B. 3-(4-Bromophenyl)-N-methoxy-N-methylpropanamide (1b), 3-(2-Bromophenyl)-N-methoxy-N-methylpropanamide (1c):
Weinreb amides 1b and 1c were synthetized according to a reported procedure.$^2$

General Procedures for the one-pot 1,2 addition /cross-coupling procedure:

In a dry Schlenk flask the substrate (0.3 mmol) was dissolved in 0.7 mL of dry toluene at room temperature. The corresponding lithium reagent (1.0 equiv. diluted from the original solution to 0.8 ml with toluene) was slowly added over 1 h by syringe pump. When the addition was completed a previously stirred mixture of Pd$_2$(dba)$_3$ (2.5 mol%,$^{1}$ C. W. Muir, A. R. Kennedy, J. M. Redmond and A. J. R. Watson, Org. Biomol. Chem. 2013, 11, 3337.
$^2$ E. F. Kleinman, WO 00/09504.
0.0075 mmol, 6.87 mg) and XPhos (10 mol%, 0.03 mmol, 14.3 mg) in 0.5 ml of toluene was added to the reaction medium and the vessel was heated with a preheated oil bath to 40°C (unless otherwise noted) followed by the slow addition (1.5 hours unless otherwise specified) of the corresponding organolithium reagent (1.5 equiv. diluted from the original solution to 1 ml with toluene). At addition completed the reaction was stopped and a saturated aqueous solution of NH₄Cl was added whereupon the mixture was extracted with ether (3 x 5mL). The organic phases were combined and evaporation of the solvent under reduced pressure afforded the crude product that was then purified by column chromatography.

Preparation of organolithium reagents:

A. 3-Methoxyphenyllithium, 4-methyl-phenyllithium and 3-trifluoromethyl-phenyllithium.
In a dry Schlenk flask the corresponding bromide (1.8 mmol) was dissolved in dry THF (0.9 mL) and the solution was cooled down to -78 ºC. tBuLi (2 equiv) was added slowly and the solution was stirred for 1 h. Then the solution was allowed to reach room temperature.

B. 2,6-Dimethoxyphenyllithium.
In a dry Schlenk flask 2,6-dimethoxybenzene (1.8 mmol, 230.26 µL) was dissolved in dry THF (0.9 mL) and the solution was cooled down to -10 ºC. nBuLi (1.6 M in hexane, 1 equiv, 1.125 mL) was added slowly and the solution was stirred for 30 min. Then the solution was allowed to reach room temperature. The resulting solution of the lithium reagent was diluted with 1 mL of toluene.

C. Cyclopropyllithium.
In a dry Schlenk flask, lithium shot (91 mg) was suspended in dry ether (2 mL) at room temperature. Then bromocyclopropane (7.2 mmol, 0.871 g, 0.577 mL) was dissolved in ether (2 mL) and added slowly over 30 min using a syringe pump. After the addition the mixture was stirring for 15 min.

D. 2-Furyllithium.
Furan (9.0 mmol, 612.6 mg, 654.5 µl) was dissolved in THF (4.5 mL) and the solution was cooled down to -40 ºC. nBuLi (8.5 mmol) was added slowly. Then the solution was allowed to reach room temperature, stirred for 3 h and diluted with 4.4 mL of THF to reach a final concentration of 0.6M.³

Additional experimental data:

-Evaluation of the 1,2 addition to amides in the reaction conditions.

The choice of the Weinreb amide as the model substrate was done in virtue of the higher selectivity shown during the optimization in comparison with the corresponding \(N,N\)-dimethylamide, especially the low levels of dehalogenation observed during the cross-coupling (see Table 1 in main text). Another pivotal factor taken in account was the higher reliability in the 1,2-addition step when compared with \(N,N\)-dimethylamides in the

chosen conditions. When the meta-substituted \(N,N\)-dimethyl-3-bromo-benzoic amide was used, formation of the tertiary alcohol generated by overaddition of \(n\)BuLi was observed (Table S1, entry 1) while the Weinreb amides performed reliably independently from the position of the bromine atom (Table S1, entry 2 and 3) and of the amide moiety (also alkylamide underwent smoothly 1,2-addition under the tested conditions see Table S1, entry 5). The only limitation encountered with Weinreb amides was the intramolecular elimination of formaldehyde to form the amide \(S1\) (1:1 ratio with the expected ketone product, Table S1, entry 4) when using a homobenzylic Weinreb amide. This notorious elimination of the methoxy substituent of the amide is probably induced by a rapid deprotonation of the acidic \(\alpha\) proton and subsequent intramolecular elimination. This complication was observed only when the \(\alpha\) proton was on a more activated benzylic position. Already moving the \(\alpha\) position to the homobenzylic position completely suppressed this side reaction (Table S1, entry 5), proving that this side reaction affects only very specific substrates and doesn’t represent a limitation for the methodology. Nevertheless methods have been reported to suppress this elimination.

Table S1. Screening of substrates for the 1,2-addition step.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Br</th>
<th>(n)</th>
<th>(R^1)</th>
<th>Product</th>
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<tbody>
<tr>
<td>1</td>
<td>3-Br</td>
<td>0</td>
<td>Me</td>
<td>A 90%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B 10%</td>
</tr>
<tr>
<td>2</td>
<td>4-Br</td>
<td>0</td>
<td>OMe</td>
<td>A 99%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B -</td>
</tr>
<tr>
<td>3</td>
<td>3-Br</td>
<td>0</td>
<td>OMe</td>
<td>A 99%</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>B -</td>
</tr>
<tr>
<td>4</td>
<td>4-Br</td>
<td>1</td>
<td>OMe</td>
<td>A 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B -</td>
</tr>
<tr>
<td>5</td>
<td>4-Br</td>
<td>2</td>
<td>OMe</td>
<td>A 99%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B -</td>
</tr>
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\(^a\)BuLi (1 equiv. over 1 h.) added to a solution of 0.3 mmol of substrate in toluene at room temperature.
Experimental details and spectral data of compounds

1-(1,1'-biphenyl-4-yl)pentan-1-one (3a): Reaction temperature: 40 °C. White solid (m.p. 78-79 °C) obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [81% yield]. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 7.9 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 3.00 (t, J = 7.4 Hz, 2H), 1.84 – 1.69 (m, 2H), 1.51 – 1.36 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 200.2, 145.5, 139.9, 135.8, 128.9, 128.6, 128.1, 127.2, 127.2, 38.4, 24.4, 31.7. HRMS (APCI+, m/z): calculated for C₁₇H₁₉O [M+H⁺]: 239.1430; found: 239.1431.

1-(1,1'-biphenyl-4-yl)heptan-1-one (3b): Reaction temperature: 40 °C. White solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [76% yield]. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 2.99 (t, J = 7.4 Hz, 2H), 1.83 – 1.70 (m, 2H), 1.48 – 1.28 (m, 6H), 0.90 (t, J = 6.7 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 200.2, 145.5, 139.9, 135.8, 128.9, 128.6, 128.1, 127.24, 127.18, 38.7, 31.7, 29.1, 24.4, 22.5, 14.0. HRMS (APCI+, m/z): calculated for C₁₉H₂₃O [M+H⁺]: 267.1743; found: 267.1742. The physical data were identical in all respects to those previously reported.⁴

1-(4-(furan-2-yl)phenyl)pentan-1-one (3c): Reaction temperature: 40 °C. White solid (m.p. 71-72 °C) obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [84% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 8.3 Hz, 2H), 7.51 (s, 1H), 6.78 (d, J = 3.3 Hz, 1H), 6.56 – 6.41 (m, 1H), 2.95 (t, J = 7.4 Hz, 2H), 1.84 – 1.61 (m, 2H), 1.56 – 1.33 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H). ¹³C NMR

(100 MHz, CDCl$_3$) $\delta$ 199.7, 152.9, 143.2, 135.5, 134.6, 128.7, 123.5, 112.0, 107.3, 38.2, 26.5, 22.5, 13.9. HRMS (APCI+, m/z): calculated for C$_{17}$H$_{19}$O [M+H$^+$]: 239.1430; found: 239.1431.

4-Phenylbenzophenone (3d): Reaction temperature: 40 °C. White solid obtained after column chromatography (SiO$_2$, n-pentane/EtOAc 100:3), [85% yield]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.90 (dd, $J$ = 7.9, 1.7 Hz, 2H), 7.84 (dd, $J$ = 8.4, 1.4 Hz, 2H), 7.71 (dd, $J$ = 8.3, 1.7 Hz, 2H), 7.66 (dd, $J$ = 8.4, 1.4 Hz, 2H), 7.63 – 7.58 (m, 1H), 7.52 (d, $J$ = 7.8 Hz, 2H), 7.48 (dd, $J$ = 7.7, 1.3 Hz, 2H), 7.41 (dt, $J$ = 7.3, 1.3 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.3, 145.2, 140.0, 137.8, 136.2, 132.4, 130.7, 130.0, 129.0, 128.3, 128.2, 127.3, 127.0. The physical data were identical in all respects to those previously reported.$^5$

phenyl(3'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methanone (3e): Reaction temperature: 40 °C. Yellow solid (m.p. 74-76 °C) obtained after column chromatography (SiO$_2$, n-pentane/EtOAc 100:3), [84% yield]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 (d, $J$ = 8.0 Hz, 2H), 7.89 (s, 1H), 7.83 (t, $J$ = 6.6 Hz, 3H), 7.72 (d, $J$ = 8.0 Hz, 2H), 7.67 (d, $J$ = 7.6 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.51 (t, $J$ = 7.6 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.1, 143.5, 140.8, 137.5, 137.0, 132.5, 131.6, 131.2, 130.8, 130.0, 129.5, 128.3, 127.1, 124.79 (q, $J$ = 3.8 Hz, 1H), 124.06 (q, $J$ = 3.8 Hz, 1H). HRMS (APCI+, m/z): calculated for C$_{20}$H$_{14}$F$_3$O [M+H$^+$]: 327.0991; found: 327.0994.

4'-Methylvalerophenone (3f): Reaction temperature: 40 °C. Yellowish oil obtained after column chromatography (SiO$_2$, n-pentane/EtOAc 100:2), [87% yield]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.85 (d, $J$ = 8.0 Hz, 2H), 7.24 (d, $J$ = 7.9 Hz, 2H), 2.93 (t, $J$ = 7.4 Hz, 2H), 2.40 (s, 3H), 1.76 – 1.64 (m, 2H), 1.47 – 1.32 (m, 2H), 0.94 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 200.2, 143.5, 134.6, 129.1, 128.2, 38.2, 26.6, 22.5, 21.6, 13.9. The physical data were identical in all respects to those previously reported.$^6$

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1-(4-cyclopropylphenyl)pentan-1-one (3g): Reaction temperature: 40 °C. Yellow oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [80% yield]. \( ^1H \) NMR (400 MHz, CDCl₃) \( \delta \) 7.85 (d, \( J = 8.0 \) Hz, 2H), 7.10 (d, \( J = 8.0 \) Hz, 2H), 2.91 (t, \( J = 7.1 \) Hz, 2H), 2.01 – 1.86 (m, 1H), 1.82 – 1.61 (m, 2H), 1.49 – 1.33 (m, 2H), 1.09–1.00 (m, 2H), 0.94 (t, \( J = 7.2 \) Hz, 3H), 0.81 – 0.70 (m, 2H). \(^{13}C\) NMR (100 MHz, CDCl₃) \( \delta \) 200.0, 150.0, 134.5, 128.2, 125.4, 38.2, 26.6, 22.5, 15.7, 13.9, 10.3. HRMS (APCI+, \( m/z \)): calculated for C₁₇H₁₉O [M+H⁺]: 239.1430; found: 239.1431.

(4-cyclopropylphenyl)(phenyl)methanone (3h): Reaction temperature: 40 °C. Off white solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:2), [80% yield]. \(^1H\) NMR (400 MHz, CDCl₃) \( \delta \) 7.77 (d, \( J = 8.2 \) Hz, 2H), 7.72 (d, \( J = 8.2 \) Hz, 2H), 7.56 (t, \( J = 7.5 \) Hz, 1H), 7.47 (t, \( J = 7.6 \) Hz, 2H), 7.14 (d, \( J = 8.1 \) Hz, 2H), 2.02 – 1.92 (m, 1H), 1.11 – 1.04 (m, 2H), 0.83 – 0.77 (m, 2H). \(^{13}C\) NMR (100 MHz, CDCl₃) \( \delta \) 196.3, 149.7, 138.0, 134.7, 132.1, 130.4, 129.9, 128.2, 125.2, 15.7, 10.3. The physical data were identical in all respects to those previously reported.⁷

Thiophen-2-yl(4-(thiophen-2-yl)phenyl)methanone (3i): Reaction temperature: 40 °C. Yellow solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [86% yield]. \(^1H\) NMR (400 MHz, CDCl₃) \( \delta \) 7.91 (d, \( J = 8.3 \) Hz, 2H), 7.78 – 7.71 (m, 3H), 7.68 (d, \( J = 3.3 \) Hz, 1H), 7.44 (d, \( J = 3.1 \) Hz, 1H), 7.37 (d, \( J = 4.7 \) Hz, 1H), 7.18 (t, \( J = 4.3 \) Hz, 1H), 7.13 (t, \( J = 4.3 \), 1H). \(^{13}C\) NMR (100 MHz, CDCl₃) \( \delta \) 187.3, 143.6, 143.0, 138.2, 136.7, 134.5, 134.1, 130.1, 128.4, 127.9, 126.3, 125.6, 124.5. HRMS (APCI+, \( m/z \)): calculated for C₁₅H₁₁OS₂ [M+H⁺]: 271.0246; found: 271.0248.

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1-(4-(furan-2-yl)phenyl)heptan-3-one (3j): Reaction temperature: 40 °C. Off white solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [81% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, J = 8.1 Hz, 2H), 7.44 (s, 1H), 7.19 (d, J = 8.0 Hz, 2H), 6.60 (d, J = 3.3 Hz, 1H), 6.50 – 6.41 (m, 1H), 2.90 (t, J = 7.6 Hz, 2H), 2.73 (t, J = 7.6 Hz, 2H), 2.38 (t, J = 7.4 Hz, 2H), 1.65 – 1.46 (m, 2H), 1.38 – 1.18 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 210.2, 154.0, 141.8, 140.4, 128.9, 128.6, 123.9, 111.5, 104.5, 44.1, 42.8, 29.5, 25.9, 22.3, 13.8. HRMS (APCI+, m/z): calculated for C₁₇H₂₁O₂ [M+H⁺]: 257.1536; found: 257.1536.

1-([1,1'-biphenyl]-4-yl)heptan-3-one (3k): Reaction temperature: r.t. White solid (m.p. 54-55 °C) obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [77% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, J = 7.9, 1.4 Hz, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 2.95 (t, J = 7.6 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.41 (t, J = 7.4 Hz, 2H), 1.64 – 1.50 (m, 2H), 1.38 – 1.23 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 210.3, 140.9, 140.3, 139.0, 128.7, 128.7, 127.2, 127.1, 127.0, 44.2, 42.8, 29.4, 25.9, 22.3, 13.8. HRMS (APCI+, m/z): calculated for C₁₉H₂₃O [M+H⁺]: 267.1743; found: 267.1741.

1-([1,1'-biphenyl]-4-yl)nonan-3-one (3l): Reaction temperature: 40 °C. White solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [74% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, J = 7.2 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.27 (d, J = 7.4 Hz, 2H), 2.95 (t, J = 7.6 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.41 (t, J = 7.4 Hz, 2H), 1.63 – 1.52 (m, 2H), 1.36 – 1.20 (m, 6H), 0.88 (t, J = 6.6 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 210.3, 140.9, 140.3, 139.0, 128.74, 128.71, 127.2, 127.1, 127.0, 44.2, 43.1, 31.6, 29.4, 28.9, 23.8, 22.5, 14.0. HRMS (APCI+, m/z): calculated for C₂₁H₂₇O [M+H⁺]: 295.2056; found: 295.2056.
1-(4'-methyl-[1,1'-biphenyl]-4-yl)heptan-3-one (3m): Reaction temperature: 40 °C. White solid (m.p. 57-59 °C) obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [83% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.50 (t, J = 8.7 Hz, 4H), 7.26 (d, J = 7.8 Hz, 4H), 2.95 (t, J = 7.6 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.46 – 2.37 (m, 5H), 1.65 – 1.52 (m, 2H), 1.40 – 1.23 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H). HRMS (APCI+, m/z): calculated for C₂₀H₂₅O [M+H⁺]: 281.1900; found: 281.1901.

1-(2',6'-dimethoxy-[1,1'-biphenyl]-4-yl)heptan-3-one (3n): Reaction temperature: 40 °C. White solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:7.5), [71% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, J = 7.8 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 8.4 Hz, 2H), 3.74 (s, 6H), 3.03 – 2.87 (m, 2H), 2.86 – 2.71 (m, 2H), 2.43 (t, J = 7.4 Hz, 2H), 1.58 (m, 2H), 1.33 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H). HRMS (APCI+, m/z): calculated for C₂₁H₂₆O₃Na [M+Na⁺]: 349.1774; found: 349.1800.

1-(4-((trimethylsilyl)methyl)phenyl)heptan-3-one (3o): Reaction temperature: 40 °C. Transparent oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:7.5), [78% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.02 (d, J = 7.8 Hz, 2H), 6.91 (d, J = 7.8 Hz, 2H), 2.84 (t, J = 7.6 Hz, 2H), 2.70 (t, J = 7.5 Hz, 2H), 2.37 (t, J = 7.4 Hz, 2H), 2.04 (s, 2H), 1.62 – 1.46 (m, 2H), 1.35 – 1.22 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H), -0.02 (s, 9H). HRMS (APCI+, m/z): calculated for C₁₇H₂₉OSi [M+H⁺]: 277.1982; found: 277.1984.
3-(4-(furan-2-yl)phenyl)-1-phenylpropan-1-one (3p): Reaction temperature: 40 °C. yellowish oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [80% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 8.1 Hz, 2H), 7.56 (m, 1H), 7.46 (t, J = 7.6 Hz, 3H), 7.28 (d, J = 8.1 Hz, 2H), 6.61 (d, J = 3.2 Hz, 1H), 6.46 (dd, J = 3.1, 1.5 Hz, 1H), 3.31 (t, J = 7.6 Hz, 2H), 3.09 (t, J = 7.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 199.1, 154.0, 141.8, 140.5, 136.8, 133.1, 129.0, 128.7, 128.6, 128.0, 124.0, 111.6, 104.5, 40.2, 29.9. HRMS (APCI+, m/z): calculated for C₁₉H₁₇O₂ [M+H⁺]: 277.1223; found: 277.1222.

3-[(1,1'-biphenyl)-4-yl]-1-(thiophen-2-yl)propan-1-one (3q): Reaction temperature: 40 °C. yellowish oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [71% yield]. ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 3.6 Hz, 1H), 7.63 (d, J = 4.9 Hz, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 7.9 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.39 – 7.31 (m, 3H), 7.12 (t, J = 4.3 Hz, 1H), 3.29 (t, J = 7.7 Hz, 2H), 3.13 (t, J = 7.6 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 192.1, 144.2, 140.9, 140.1, 139.2, 133.6, 131.8, 128.9, 128.7, 128.1, 127.3, 127.1, 127.0, 41.1, 30.0. HRMS (APCI+, m/z): calculated for C₁₉H₁₇OS [M+H⁺]: 293.0995; found: 293.0996.

3-(4'-methyl-[1,1'-biphenyl]-4-yl)-1-phenylpropan-1-one (3r): Reaction temperature: 40 °C. yellow solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [89% yield]. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (dd, J = 7.7, 1.3 Hz, 2H), 7.62 – 7.41 (m, 7H), 7.34 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 3.36 (t, J = 7.5 Hz, 2H), 3.13 (t, J = 7.6 Hz, 2H), 2.41 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 199.2, 140.1, 139.1, 138.1, 136.9, 136.8, 133.1, 129.5, 128.8, 128.1, 127.1, 126.8, 40.4, 29.7, 21.1. The physical data were identical in all respects to those previously reported.⁸

3-(2',6'-dimethoxy-[1,1'-biphenyl]-4-yl)-1-phenylpropan-1-one (3s): Reaction temperature: 40 °C. Off white solid obtained after column chromatography (SiO₂, n-pentane/EtOAc 10:1), [84% yield]. \(^{1}\)H NMR (400 MHz, CDCl₃) δ 8.01 (d, \(J = 7.4\) Hz, 1H), 7.57 (t, \(J = 7.3\) Hz, 1H), 7.48 (t, \(J = 7.5\) Hz, 2H), 7.32 (s, 4H), 7.28 (d, \(J = 8.3\) Hz, 1H), 6.68 (d, \(J = 8.4\) Hz, 2H), 3.75 (s, 6H), 3.39 (t, \(J = 7.5\) Hz, 2H), 3.13 (t, \(J = 7.3\) Hz, 2H). \(^{13}\)C NMR (100 MHz, CDCl₃) δ 199.4, 157.7, 139.5, 136.9, 133.0, 131.8, 128.6, 128.5, 128.1, 127.8, 119.3, 104.2, 55.9, 40.4, 30.0. HRMS (APCI+, \(m/z\)) calculated for C₂₃H₂₂O₃Na [M+Na⁺]: 369.1461; found: 369.1490.

1-([1,1'-biphenyl]-2-yl)nonan-3-one (3t): Reaction temperature: 40 °C. Transparent oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 10:1), [84% yield]. \(^{1}\)H NMR (400 MHz, CDCl₃) δ 7.42 (t, \(J = 7.3\) Hz, 2H), 7.39 – 7.20 (m, 7H), 2.90 (t, \(J = 7.6\) Hz, 2H), 2.49 (t, \(J = 8.0\) Hz, 2H), 2.22 (t, \(J = 7.4\) Hz, 2H), 1.53 – 1.40 (m, 2H), 1.37 – 1.12 (m, 6H) 0.89 (t, \(J = 6.9\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl₃) δ 210.3, 141.9, 141.6, 138.5, 130.2, 129.2, 129.1, 128.2, 127.0, 126.1, 43.7, 42.7, 31.5, 28.8, 27.4, 23.8, 22.5, 14.0. HRMS (APCI+, \(m/z\)) calculated for C₂₁H₂₇O [M+H⁺]: 295.2057; found: 295.2058.

1-([1,1'-biphenyl]-3-yl)ethanone (3u): Reaction temperature: 40 °C. Yellow oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:4), [72% yield]. \(^{1}\)H NMR (400 MHz, CDCl₃) δ 8.19 (s, 1H), 7.94 (d, \(J = 7.7\) Hz, 1H), 7.80 (d, \(J = 7.7\) Hz, 1H), 7.62 (d, \(J = 7.6\) Hz, 2H), 7.54 (t, \(J = 7.7\) Hz, 1H), 7.47 (t, \(J = 7.5\) Hz, 2H), 7.39 (t, \(J = 7.3\) Hz, 1H), 2.66 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl₃) δ 198.0, 141.7, 140.2, 137.6, 131.7, 129.0, 128.9, 127.8, 127.2, 127.1 126.9, 26.7. The physical data were identical in all respects to those previously reported.\(^9\)

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**1-((1,1'-biphenyl)-3-yl)pentan-1-one (3v):** Reaction temperature: r.t. Transparent oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [71% yield].

¹H NMR (400 MHz, CDCl₃) δ 8.18 (s, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.7 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 3.02 (t, J = 7.4 Hz, 2H), 1.84 – 1.69 (m, 2H), 1.53 – 1.36 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 200.5, 141.7, 140.3, 137.6, 131.5, 129.0, 128.9, 127.7, 127.2, 126.9, 126.7, 38.5, 26.5, 22.5, 13.9. HRMS (APCI+, m/z): calculated for C₁₇H₁₉O [M+H⁺]: 239.1430; found: 239.1431.

**2'-methoxy-[(1,1'-biphenyl)-3-yl](phenyl)methanone (3w):** Reaction temperature: r.t. Transparent oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [72% yield].

¹H NMR (400 MHz, CDCl₃) δ 8.02 (s, 1H), 7.96 – 7.74 (m, 4H), 7.67 – 7.45 (m, 4H), 7.38 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 7.8 Hz, 1H), 6.93 (dd, J = 8.3, 2.3 Hz, 1H), 3.87 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 196.6, 160.0, 141.6, 141.3, 138.2, 137.5, 132.5, 131.1, 130.1, 129.9, 129.0, 128.7, 128.6, 128.3, 119.7, 113.1, 113.0, 55.34. MS (ESI): m/z 288.

**[1,1'-biphenyl]-3-yl(cyclopropyl)methanone (3x):** Reaction temperature: 40 °C. Transparent oil obtained after column chromatography (SiO₂, n-pentane/EtOAc 100:3), [85% yield].

¹H NMR (400 MHz, CDCl₃) δ 8.19 (s, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 7.9 Hz, 2H), 7.51 (t, J = 7.7 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.3 Hz, 1H), 2.77 – 2.57 (m, 1H), 1.27 – 1.21 (m, 2H), 1.08 – 0.98 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 200.6, 141.6, 140.3, 138.5, 131.3, 129.0, 128.9, 127.7, 127.2, 126.9, 126.7, 17.3, 11.8. HRMS (APCI+, m/z): calculated for C₁₆H₁₅O [M+H⁺]: 223.1117; found: 223.1116.
$^1$H and $^{13}$C NMR of isolated compounds