Gram-scale, Cheap, and Eco-friendly Iron-catalyzed Cross-Coupling between Alkyl Grignard reagents and Alkenyl or Aryl halides.

Supporting Information

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Instrumentation and Chemicals

Analyses
Gas chromatography analyses (GC) were performed on two different chromatographs. The first one was a Shimadzu Chromatograph 2010 Plus apparatus (GC2010) equipped with a flame ionization detector. The capillary column was a Zebron ZB-5MS (length: 10 m, I.D.: 0.10 mm, film thickness: 0.10 µm. 5% polysilslylene / 95% polydimethylsiloxane). The second one was a Shimadzu Chromatograph 2014 Plus apparatus (GC2014) equipped with a flame ionization detector. The capillary column was a Zebron ZB-35 (length: 10 m, I.D.: 0.10 mm, film thickness: 0.10 µm. 35% phenyl / 65% polydimethylsiloxane). Hydrogen was used as a carrier gas (1.14 mL/min, ratio split: 80). Three standard analysis conditions: 40 °C (hold 1 min) to 200 °C (hold 3.5 min), heating rate: 30 °C/min (Method 1); 80 °C (hold 0 min) to 200 °C (hold 4 min), heating rate: 20 °C/min (Method 2); 80 °C (hold 0 min) to 250 °C (hold 10 min), heating rate: 20 °C/min (Method 3).

Mass spectra were recorded on a Hewlett-Packard HP 5973 mass spectrometer via a GC/MS coupling with a Hewlett-Packard HP 6890 chromatograph equipped with a capillary column HP-5MS (50 m x 0.25 mm x 0.25 µm). Ionisation was performed by electronic impact (EI, 70 eV). Mass spectra are reported as m/z (molecular ion peak, % of relative intensity).

Thin layer chromatography (TLC) was carried out on silica gel plates (Carlo Erba 60 F254). Spots were detected with UV light.

Flash chromatography was performed on silica gel columns (Carlo Erba, spherical, neutral, 40-60 µm). 1H NMR (300 MHz, CDCl3), 13C NMR (75 MHz, CDCl3) and 19F NMR (282 MHz, CDCl3) were recorded on a Bruker Avance III HD 400 instrument. Chemical shifts (δ) are given in ppm from TMS (1H, 13C) and Trichlorofluoromethane (19F). Coupling constants (J) are given in Hz. The following abbreviations are used: s, singlet, d, doublet, t, triplet, q, quartet, m, multiplet, dm, multiplet of doublet.

Mass spectra were recorded on a Hewlett-Packard HP 5973 mass spectrometer via a GC/MS coupling with a Hewlett-Packard HP 6890 chromatograph equipped with a capillary column HP-5MS (50 m x 0.25 mm x 0.25 µm). Ionisation was performed by electronic impact (EI, 70 eV). Mass spectra are reported as m/z (% of relative intensity).

ESI-MS experiments were carried out using a LTQ-Orbitrap XL from Thermo Scientific (Thermo Fisher Scientific, Courtaboeuf, France) and operated in positive ionization mode, with a spray voltage at 3.6 kV. Sheath and auxiliary gas were set at a flow rate of 45 and 15 arbitrary units (a.u.), respectively. Applied voltages were 20 and 70 V for the ion transfer capillary and the tube lens, respectively. The ion transfer capillary was held at 275 °C. Detection was achieved in the Orbitrap with a resolution set to 60,000 (at m/z 400) and a m/z range between 110-1200 in profile mode. Spectrum was analyzed using the acquisition software XCalibur 2.1 (Thermo Fisher Scientific, Courtaboeuf, France). The automatic gain control (AGC) allowed accumulation of up to 2.105 ions for FTMS scans, Maximum injection time was set to 300 ms and 1 μscan was acquired. 5 μL was injected using a Thermo Finnigan Surveyor HPLC system (Thermo Fisher Scientific, Courtaboeuf, France) with a continuous infusion of methanol at 100 µL/min.

Purification of solvents and reagents
All reagents and solvents were obtained from either Sigma-Aldrich, Acros, Alfa, VWR, or TCI and were used as received unless otherwise stated. Dry solvents were obtained from commercial sources. Grignard reagents were titrated before use according to a modified version of the Watson protocol.1 All reactions were conducted in dry flasks under argon atmosphere. Room temperature is ca. 22 °C.
Synthesis of starting materials

(1, Z)-bromohexene (1a) was prepared according to the previously reported literature procedures. NMR spectra were in agreement with reported data. \(^2\)

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 6.16 – 6.07 (m, 2H), 2.24 – 2.18 (m, 2H), 1.46 – 1.31 (m, 4H), 0.93 (t, \(J = 7.2\) Hz, 3H).

\(^{13}\)C-NMR (CDCl\(_3\), 75 MHz): 135.2, 107.7, 30.4, 29.6, 22.4, 14.0.

2-butyl-1-bromohex-1-ene (1d) was prepared according to the previously reported literature procedures. NMR spectra were in agreement with reported data. \(^4\)

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 5.87 (s, 1H), 2.23 – 2.19 (m, 2H), 2.12 – 2.08 (m, 2H), 1.46 – 1.26 (m, 8H), 0.92 (dt, \(J = 10.8, 7.1\) Hz, 6H).

\(^{13}\)C-NMR (CDCl\(_3\), 75 MHz): 146.1, 100.9, 35.8, 32.5, 30.0, 29.4, 22.8, 22.5, 14.1, 14.0.

2-butyl-1-chlorohex-1-ene (1e) was prepared according to the previously reported literature procedures. NMR spectra were in agreement with reported data. \(^4\)

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 5.77 (s, 1H), 2.19 (t, \(J = 8.0\) Hz, 2H), 2.04 (t, \(J = 8.0\) Hz, 2H), 1.44 – 1.24 (m, 8H), 0.91 (dt, \(J = 9.0, 7.1\) Hz, 6H).

\(^{13}\)C-NMR (CDCl\(_3\), 75 MHz): 143.2, 111.8, 34.7, 30.0, 29.4, 22.8, 22.5, 14.1, 14.0.

Ethyl 4-(trifluoromethylsulfonate)-benzoate (3aa) was prepared according to the previously reported literature procedures. NMR spectra were in agreement with reported data. \(^6\)

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 8.18 – 8.14 (m, 2H), 7.38 – 7.34 (m, 2H), 4.41 (q, \(J = 7.1\) Hz, 2H), 1.41 (t, \(J = 7.1\) Hz, 3H).

\(^{13}\)C-NMR (CDCl\(_3\), 75 MHz): 165.1, 152.6, 132.0, 130.9, 121.5, 118.8 (q, \(J = 320.6\) Hz), 61.7, 14.4.

\(^{19}\)F-NMR (CDCl\(_3\), 282 MHz): -72.73 (s, 3F).

Ethyl 4-(phenylsulfonate)-benzoate (3ab) was prepared according to the previously reported literature procedures. NMR spectra were in agreement with reported data. \(^8\)

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 8.01 – 7.97 (m, 2H), 7.85 – 7.83 (m, 2H), 4.36 (q, \(J = 7.1\) Hz, 2H), 1.38 (t, \(J = 7.1\) Hz, 3H).

\(^{13}\)C-NMR (CDCl\(_3\), 75 MHz): 165.6, 152.9, 135.2, 134.6, 131.4, 129.5, 129.4, 128.6, 122.4, 61.4, 14.4.

Menthyl 4-chlorobenzoate (3c) was prepared according to the previously reported literature procedures. NMR spectra were in agreement with reported data. \(^9\)

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 8.00 – 7.97 (m, 2H), 7.43 – 7.40 (m, 2H), 4.93 (td, \(J = 10.9, 4.4\) Hz, 1H), 2.15 – 2.09 (m, 1H), 1.93 (m, 1H), 1.77 – 1.71 (m, 2H), 1.61 – 1.51 (m, 2H), 1.19 – 1.06 (m, 2H), 0.99 – 0.88 (m, 7H), 0.80 (d, \(J = 7.0\) Hz, 3H).

\(^{13}\)C-NMR (CDCl\(_3\), 75 MHz): 165.4, 139.3, 131.1, 129.4, 128.8, 75.3, 47.4, 41.1, 34.4, 31.6, 26.7, 23.8, 22.2, 20.9, 16.7.
**Table S1: Optimization of the substrate concentration for alkyl-vinyl cross-coupling reaction**

\[
\text{Br}_2 + n\text{BuMgCl} \quad 2.5 \text{ mol}\% \text{ FeCl}_3 \\
\quad 100 \text{ mol}\% \text{ EtOMgCl} \quad \text{THF, C, 0 °C, 5 min} \\
\Rightarrow \quad \text{Z > 99%} \\
\text{1a} \quad 1.2 \text{ equiv.} \\
\text{Z > 99%} \\
\text{2a}
\]

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**Table S2: Optimization of the temperature for alkyl-vinyl cross-coupling reaction**

\[
\text{Br}_2 + n\text{BuMgCl} \quad 2.5 \text{ mol}\% \text{ FeCl}_3 \\
\quad 100 \text{ mol}\% \text{ EtOMgCl} \quad \text{THF, 0,5 M, T, 5 min} \\
\Rightarrow \quad \text{Z > 99%} \\
\text{1a} \quad 1.2 \text{ equiv.} \\
\text{Z > 99%} \\
\text{2a}
\]

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**Table S3: Optimization of the nature of the RO[M] additive for alkyl-aryl cross-coupling reaction**

\[
\text{3a} \quad 1.2 \text{ equiv.} \\
\Rightarrow \quad \text{Z > 99%} \\
\text{4a}
\]

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Table S4: Optimization of the quantity of FeCl$_3$ for alkyl-aryl cross-coupling reaction

\[
\begin{array}{ccc}
\text{Entry} & \text{Quantity of FeCl}_3 (x \text{ mol%}) & \text{GC Yield (\%)} \\
1 & 5 & 96 \\
2 & 2.5 & 94 \\
3 & 1 & 100 \\
4 & 0.5 & 87 \\
5 & 0.1 & 15 \\
\end{array}
\]

Table S5: Optimization of the quantity of EtOMgCl for alkyl-aryl cross-coupling reaction

\[
\begin{array}{ccc}
\text{Entry} & \text{Quantity of EtOMgCl (y \text{ mol%})} & \text{GC Yield (\%)} \\
1 & 100 & 100 \\
2 & 150 & 100 \\
3 & 75 & 97 \\
4 & 50 & 99 \\
5 & 22 & 100 \\
6 & 15 & 100 \\
7 & 10 & 70 \\
\end{array}
\]
Table S6: Optimization of the temperature for alkyl-aryl cross-coupling reaction

\[
\text{3a} + n\text{BuMgCl} \quad \xrightarrow{1 \text{ mol}\% \text{ FeCl}_3 \quad 15 \text{ mol}\% \text{ EtOMgCl}} \quad \text{4a}
\]

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Table S7: Optimization of the substrate concentration for alkyl-aryl cross-coupling reaction

\[
\text{3a} + n\text{BuMgCl} \quad \xrightarrow{1 \text{ mol}\% \text{ FeCl}_3 \quad 15 \text{ mol}\% \text{ EtOMgCl}} \quad \text{4a}
\]

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<th>Entry</th>
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<td>1.92</td>
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General procedures for cross-coupling reactions

General procedure for alkyl-vinyl cross-coupling reaction: In a dry 250 mL four-necked round bottom flask under argon with mechanical stirring were added EtOH (50 mmol, 1.00 equiv.) and THF (22.5 mL). The solution was cooled to 0 °C and isopropylmagnesium chloride (45.5 mmol, 0.95 equiv.) was added dropwise in 30 min with a syringe pump. The reaction mixture was stirred for 30 min at room temperature. A solution of FeCl₃ in THF at 0.1 mol/L (1.25 mmol, 0.025 equiv.) and the vinyl halide (50 mmol, 1.00 equiv.) were added. The solution was cooled to 0 °C and Grignard reagent (65 mmol, 1.30 equiv.) was added dropwise in 30 min with a syringe pump. The reaction mixture was stirred for another 5 min, quenched with an aqueous solution of HCl 1 mol/L (130 mL), extracted with diethyl ether (3 × 100 mL) and the combined organic phase was carefully evaporated. The crude product was purified by distillation to obtain the product.

General procedure for alkyl-aryl cross-coupling reaction: In a dry 100 mL four-necked round bottom flask under argon with mechanical stirring were added EtOH (1.5 mmol, 1.00 equiv.) and THF (2 mL). The solution was cooled to 0 °C and butylmagnesium chloride (1.65 mmol, 0.165 equiv.) was added dropwise in 1 min with a syringe pump. The reaction mixture was stirred for 30 min at room temperature. A solution of FeCl₃ in THF at 0.1 mol/L (0.1 mmol, 0.01 equiv.) and the aryl halide (10 mmol, 1.00 equiv.) were added. The solution was cooled to 0 °C and butylmagnesium chloride (12 mmol, 1.20 equiv.) was added dropwise in 5 min with a syringe pump. The reaction mixture was stirred for another 60 min, quenched with an aqueous solution of HCl 1 mol/L (15 mL), extracted with diethyl ether (3 × 20 mL) and the combined organic phase was carefully evaporated. The crude product was purified by column chromatography to obtain the product.

General procedure for alkyl-heteroaryl cross-coupling reaction: In a dry 100 mL four-necked round bottom flask under argon with mechanical stirring were added EtOH (1.5 mmol, 1.00 equiv.) and THF (2 mL). The solution was cooled to 0 °C and butylmagnesium chloride (1.65 mmol, 0.165 equiv.) was added dropwise in 1 min with a syringe pump. The reaction mixture was stirred for 30 min at room temperature. A solution of FeCl₃ in THF at 0.1 mol/L (0.1 mmol, 0.01 equiv.) and the heteroaryl halide (10 mmol, 1.00 equiv.) were added. The solution was cooled to 0 °C and butylmagnesium chloride (12 mmol, 1.20 equiv.) was added dropwise in 5 min with a syringe pump. The reaction mixture was stirred for another 60 min, quenched with water (15 mL), extracted with diethyl ether (3 × 20 mL) and the combined organic phase was carefully evaporated. The crude product was purified by column chromatography to obtain the product.

General procedure for the one-pot amidification and alkyl-aryl cross-coupling reaction: In a dry 100 mL four-necked round bottom flask under argon with mechanical stirring were added secondary amine (11 mmol, 1.10 equiv.) and THF (20 mL). The solution was cooled to 0 °C and butylmagnesium chloride (12 mmol, 1.20 equiv.) was added dropwise in 5 min with a syringe pump. The reaction mixture was stirred for 30 min at room temperature followed by the addition of ethyl chlorobenzoate (10 mmol, 1.00 equiv.). The reaction mixture was stirred for another 30 min and a solution of FeCl₃ in THF at 0.1 mol/L (0.1 mmol, 0.01 equiv.) was added. The solution was cooled to 0 °C and butylmagnesium chloride (12 mmol, 1.20 equiv.) was added dropwise in 5 min with a syringe pump. The reaction mixture was stirred for another 60 min, quenched with an aqueous solution of HCl 1 mol/L (25 mL), extracted with diethyl ether (3 × 20 mL) and the combined organic phase was carefully evaporated. The crude product was purified by column chromatography to obtain the product.
Characterization Data

All $^1$H and $^{13}$C NMR spectra of already reported compounds were in agreement with literature. The corresponding references are cited thereafter.

(Z)-Dec-5-ene (2a).\(^{10}\)

GC2010, Method 1: $t_R = 1.984$ min.
$T_{eb} = 64 ^\circ C/20$ Torr.
**Purification**: Distillation under reduced pressure.
**Yield** = 82\% (5.75 g, colorless liquid).
$^1$H-NMR (CDCl$_3$, 400 MHz): 5.40 – 5.32 (m, 2H), 2.06 – 2.01 (m, 4H), 1.38 – 1.27 (m, 8H), 0.93 – 0.89 (m, 6H).
$^{13}$C-NMR (CDCl$_3$, 75 MHz): 130.0, 32.1, 27.1, 22.5, 14.1.

(Z)-Hexadec-5-ene (2b).\(^{11}\)

GC2010, Method 1: $t_R = 4.816$ min.
$T_{eb} = 105 ^\circ C/2$ Torr.
**Purification**: Distillation under reduced pressure.
**Yield** = 68\% (7.61 g, colorless liquid).
$^1$H-NMR (CDCl$_3$, 400 MHz): 5.40 – 5.32 (m, 2H), 2.06 – 2.00 (m, 4H), 1.35 – 1.24 (m, 20H), 0.90 – (m, 6H).
$^{13}$C-NMR (CDCl$_3$, 75 MHz): 130.1, 130.0, 32.1, 32.1, 29.9, 29.8, 29.7, 29.5, 29.5, 27.4, 27.1, 22.8, 22.5, 14.3, 14.2.

(Z)-2-Methyl-oct-3-ene (2c).\(^{12}\)

GC2010, Method 1: $t_R = 0.959$ min.
$T_{eb} = 115 ^\circ C$.
**Purification**: Distillation under atmospheric pressure.
**Yield** = 65\% (7.55 g, colorless liquid).
$^1$H-NMR (CDCl$_3$, 400 MHz): 5.28 – 5.16 (m, 2H), 2.60 (qd, $J = 13.4$, 6.7 Hz, 1H), 2.04 (q, $J = 6.7$ Hz, 2H), 1.35 – 1.28 (m, 4H), 0.96 (s, 3H), 0.94 (s, 3H), 0.92 – 0.89 (m, 3H).
$^{13}$C-NMR (CDCl$_3$, 75 MHz): 137.6, 127.6, 32.3, 27.2, 26.6, 23.4, 22.5, 14.1.

(Z)-1-Cyclohexanyl-hex-1-ene (2d).\(^{13}\)

GC2010, Method 1: $t_R = 3.172$ min.
**Tridec-2-ene (2e).**

\[
\begin{align*}
&\text{GC2010, Method 1: } t_R = 3.613 \text{ min.} \\
&T_{eb} = 113.7 \degree C/15.1 \text{ Torr.} \\
&\textbf{Purification: } \text{Distillation under reduced pressure.} \\
&\textbf{Yield} = 74\% (6.76 \text{ g, colorless liquid).} \\
&\text{\textsuperscript{1}H-NMR (CDCl}_3, 400 \text{ MHz}): 5.49 – 5.35 (m, 2H), 2.07 – 1.94 (m, 2H), 1.66 – 1.64 (m, 1.7H), 1.62 – 1.60 (m, 1.3H), 1.35 – 1.27 (m, 16H), 0.89 (t, J = 6.8 Hz, 3H). \\
&\text{\textsuperscript{13}C-NMR (CDCl}_3, 75 \text{ MHz)}: 131.8, 131.1, 124.7, 123.7, 32.8, 32.1, 29.8, 29.7, 29.5, 29.4, 27.0, 22.9, 18.1, 14.3.
\end{align*}
\]

**1-Phenyl-hex-(1, E)-ene (2f).**

This synthesis has been carried out on 10 mmol of starting material (1c).

\[
\begin{align*}
&\text{GC2010, Method 1: } t_R = 3.774 \text{ min.} \\
&T_{eb} = 99.5 \degree C/8.3 \text{ Torr.} \\
&\textbf{Purification: } \text{Chromatography, Eluent: Petroleum spirit.} \\
&\textbf{Yield} = 94\% (1.50 \text{ g, colorless liquid).} \\
&\text{\textsuperscript{1}H-NMR (CDCl}_3, 400 \text{ MHz}): 7.27 – 7.10 (m, 5H), 6.38 (m, 1H), 6.15 (dt, J = 15.8, 6.8 Hz, 1H), 2.32 – 2.08 (m, 2H), 1.41 – 1.25 (m, 4H), 0.83 (t, J = 7.2 Hz, 3H). \\
&\text{\textsuperscript{13}C-NMR (CDCl}_3, 75 \text{ MHz)}: 138.1, 131.4, 129.8, 128.6, 126.9, 126.0, 32.9, 31.7, 22.4, 14.1.
\end{align*}
\]

**5-Butyl-dec-5-ene (2g).**

\[
\begin{align*}
&\text{GC2010, Method 1: } t_R = 3.652 \text{ min.} \\
&T_{eb} = 99.5 \degree C/8.3 \text{ Torr.} \\
&\textbf{Purification: } \text{Distillation under reduced pressure.} \\
&\textbf{Yield}_{\text{chloride}} = 20\% (1.99 \text{ g, colorless liquid), } \textbf{Yield}_{\text{bromide}} = 37\% (3.64 \text{ g, colorless liquid).} \\
&\text{\textsuperscript{1}H-NMR (CDCl}_3, 400 \text{ MHz}): 5.10 (t, J = 7.0 Hz, 1H), 2.02 – 1.95 (m, 6H), 1.41 – 1.24 (m, 12H), 0.91 (m, 9H). \\
&\text{\textsuperscript{13}C-NMR (CDCl}_3, 75 \text{ MHz)}: 139.7, 124.8, 36.8, 32.6, 30.9, 30.7, 29.9, 27.6, 23.0, 22.7, 22.6, 14.2.
\end{align*}
\]
2-Methyl-tridec-2-ene (2h).\textsuperscript{16}

\[ \text{GC2010, Method 1: } t_R = 3.701 \text{ min.} \]
\[ T_{eb} = 99.6 \, ^\circ \text{C}/4.5 \text{ Torr.} \]

\textbf{Purification:} Distillation under reduced pressure.

\textit{Yield}\textsubscript{chloride} = 31\% (3.00 g, colorless liquid), \textit{Yield}\textsubscript{bromide} = 66\% (6.43 g, colorless liquid).

\textsuperscript{1}H-NMR (CDCl\textsubscript{3}, 400 MHz): 5.14 (t, J = 7.8 Hz, 1H), 1.98 (m, 2H), 1.71 (s, 3H), 1.62 (s, 3H), 1.29 (m, 16H), 0.90 (t, J = 6.8 Hz, 3H).

\textsuperscript{13}C-NMR (CDCl\textsubscript{3}, 75 MHz): 131.2, 125.2, 32.1, 30.1, 29.9, 29.8, 29.8, 29.5, 25.9, 22.9, 17.8, 14.3.

2-Methyl-dodec-1-ene (2i).\textsuperscript{17}

\[ \text{GC2010, Method 1: } t_R = 3.525 \text{ min.} \]
\[ T_{eb} = 85.7 \, ^\circ \text{C}/5.3 \text{ Torr.} \]

\textbf{Purification:} Distillation under reduced pressure.

\textit{Yield} = 81\% (7.38 g, colorless liquid).

\textsuperscript{1}H-NMR (CDCl\textsubscript{3}, 400 MHz): 4.68 (d, J = 8.8 Hz, 2H), 2.16 – 1.90 (t, J = 2.0 Hz, 2H), 1.72 (s, 3H), 1.47 – 1.37 (m, 2H), 1.28 (m, 16H), 0.89 (t, J = 6.8 Hz, 3H).

\textsuperscript{13}C-NMR (CDCl\textsubscript{3}, 75 MHz): 146.3, 109.4, 37.8, 31.8, 29.5, 29.4, 29.2, 27.5, 22.6, 22.3, 14.0.

3-Methyl-tridec-2-ene (2j).\textsuperscript{14}

\[ \text{GC2010, Method 1: } t_R = 4.024 \text{ min.} \]
\[ T_{eb} = 112 \, ^\circ \text{C}/8 \text{ Torr.} \]

\textbf{Purification:} Distillation under reduced pressure.

\textit{Yield} = 63\% (6.21 g, colorless liquid).

\textsuperscript{1}H-NMR (CDCl\textsubscript{3}, 400 MHz): 5.24 – 5.18 (m, 1H), 2.00 (dt, J = 21.8, 7.5 Hz, 2H), 1.70 – 1.57 (m, 6H), 1.43 – 1.28 (m, 16H), 0.91 (t, J = 6.8 Hz, 3H).

\textsuperscript{13}C-NMR (CDCl\textsubscript{3}, 75 MHz): 136.6, 136.4, 118.8, 118.1, 39.9, 32.1, 31.5, 29.8, 29.8, 29.5, 28.2, 28.0, 23.6, 22.9, 15.7, 14.3, 13.5, 13.4.

\textbf{Cl} (Z)-1-chlorododec-1-ene (2k).

\[ \text{GC2010, Method 1: } t_R = 4.155 \text{ min.} \]
\[ T_{eb} = 117.0 \, ^\circ \text{C}/9.8 \text{ Torr.} \]

\textbf{Purification:} Distillation under reduced pressure.

\textit{Yield} = 31\% (3.14 g, colorless liquid).

\textsuperscript{1}H-NMR (CDCl\textsubscript{3}, 400 MHz): 6.01 (dt, J = 7.0, 1.5 Hz, 1H), 5.76 (q, J = 7.1 Hz, 1H), 2.23 (qd, J = 7.3, 1.5 Hz, 2H), 1.31 – 1.27 (m, 16H), 0.89 (t, J = 6.8 Hz, 3H).

\textsuperscript{13}C-NMR (CDCl\textsubscript{3}, 75 MHz): 132.1, 117.9, 32.1, 29.7, 29.6, 29.5, 29.3, 28.5, 27.2, 22.8, 14.3.

\textbf{MS (EI, 70 eV) m/z :} 204 (M\textsuperscript{+}, 33), 202 (M\textsuperscript{+}, 100).
This synthesis has been carried out on 10 mmol of starting material (1k).

TLC: \( R_f = 0.79 \), Eluent: Petroleum spirit/Ethyl acetate 80:20.


**Yield** = 87% (1.56 g, colorless liquid).

\[^1\text{H-NMR (CDCl}_3, 400 \text{ MHz)}\]: 5.85 (s, 1H), 2.17 (d, \( J = 14.5 \text{ Hz} \), 6H), 1.50 – 1.42 (m, 2H), 1.37 – 1.27 (m, 2H), 1.01 (s, 6H), 0.90 (t, \( J = 7.3 \text{ Hz} \), 3H).

\[^{13}\text{C-NMR (CDCl}_3, 75 \text{ MHz)}\]: 200.2, 164.4, 124.7, 51.2, 44.0, 37.8, 33.7, 29.0, 28.4, 22.4, 13.9.

**Ethyl \( p \)-butylbenzoate (4a).**

GC2014, Method 2: \( t_R = 3.822 \text{ min} \).

**Yield** = 99% (2.06 g, yellow oil).

\[^1\text{H-NMR (CDCl}_3, 400 \text{ MHz)}\]: 7.96 (d, \( J = 8.2 \text{ Hz} \), 2H), 7.25 (d, \( J = 8.1 \text{ Hz} \), 2H), 4.37 (q, \( J = 7.1 \text{ Hz} \), 2H), 2.69 – 2.64 (m, 2H), 1.67 – 1.58 (m, 2H), 1.37 (dt, \( J = 15.1, 7.2 \text{ Hz} \), 5H), 0.94 (t, \( J = 7.3 \text{ Hz} \), 3H).

\[^{13}\text{C-NMR (CDCl}_3, 75 \text{ MHz)}\]: 166.9, 148.5, 129.7, 128.5, 128.1, 60.9, 35.8, 33.4, 22.4, 14.5, 14.0.

**Methyl \( p \)-hexylbenzoate (4b).**

GC2014, Method 2: \( t_R = 4.526 \text{ min} \).

**Yield** = 99% (2.22 g, yellow oil).

**Purification**: No further purification was required.

\[^1\text{H-NMR (CDCl}_3, 400 \text{ MHz)}\]: 6.97 – 7.94 (m, 2H), 7.25 (d, \( J = 8.3 \text{ Hz} \), 2H), 3.91 (s, 3H), 2.68 – 2.64 (m, 2H), 1.67 – 1.61 (m, 2H), 1.36 – 1.28 (m, 6H), 0.90 – 0.87 (m, 3H).

\[^{13}\text{C-NMR (CDCl}_3, 75 \text{ MHz)}\]: 167.4, 148.7, 129.8, 128.6, 127.5, 52.1, 36.2, 31.8, 31.2, 29.1, 22.7, 14.2.

**Menthyl \( p \)-butylbenzoate (4c).**

GC2014, Method 2: \( t_R = 8.019 \text{ min} \).

**Yield** = 99% (3.30 g, orange oil).

**Purification**: No further purification was required.

\[^1\text{H-NMR (CDCl}_3, 400 \text{ MHz)}\]: 6.97 – 7.95 (m, 2H), 7.25 (d, \( J = 8.3 \text{ Hz} \), 2H), 4.93 (td, \( J = 10.9, 4.4 \text{ Hz} \), 1H), 2.69 – 2.65 (m, 2H), 2.15 – 2.10 (m, 1H), 1.97 (ddt, \( J = 13.9, 7.0, 2.7 \text{ Hz} \), 1H), 1.76 – 1.71
(m, 2H), 1.66 – 1.51 (m, 4H), 1.36 (dq, $J = 14.6, 7.3$ Hz, 2H), 1.19 – 1.05 (m, 2H), 0.98 – 0.89 (m, 10H), 0.80 (d, $J = 7.0$ Hz, 3H).

$^{13}$C-NMR (CDCl$_3$, 75 MHz): 166.3, 148.4, 129.8, 128.5, 128.5, 74.7, 47.4, 41.2, 35.8, 34.5, 33.5, 31.6, 26.6, 23.8, 22.5, 22.2, 20.9, 16.7, 14.1.


85:15

1-butynaphthalene/2-butynaphthalene 85:15 (4d).$^{19}$

GC2014, Method 2: $t_R = 3.950$ min.

TLC: $R_f = 0.54$, Eluent: Petroleum spirit.


Yield = 85% (1.57 g, colorless liquid).

$^1$H-NMR (CDCl$_3$, 400 MHz): 8.07 (d, $J = 8.1$ Hz, 0.85H), 7.87 (d, $J = 7.7$ Hz, 0.85H), 7.83 – 7.77 (m, 0.45H), 7.72 (d, $J = 8.1$ Hz, 0.85H), 7.63 (s, 0.15H), 7.55 – 7.46 (m, 1.70H), 7.45 – 7.39 (m, 1H), 7.36 – 7.33 (m, 1H), 7.27 (d, $J = 2.1$ Hz, 0.15H), 3.09 (t, $J = 8.0$ Hz, 1.70H), 2.80 (t, $J = 7.7$ Hz, 0.30H), 1.80 – 1.69 (m, 2H), 1.53 – 1.39 (m, 2H), 0.99 (t, $J = 7.4$ Hz, 3H).

$^{13}$C-NMR (CDCl$_3$, 75 MHz): 140.6, 139.1, 134.0, 133.8, 132.1, 128.9, 127.9, 127.7, 127.6, 127.5, 126.5, 126.4, 126.0, 125.7, 125.7, 125.5, 125.1, 124.1, 36.0, 33.7, 33.2, 33.0, 23.0, 22.5, 14.2.

$^{14}$p-butylnaphthalene (4i).$^{15}$

GC2014, Method 2: $t_R = 2.897$ min.

TLC: $R_f = 0.21$, Eluent: Petroleum spirit/Ethyl acetate 95:5.


Yield = 80% (1.27 g, colorless liquid).

$^1$H-NMR (CDCl$_3$, 400 MHz): 7.58 (d, $J = 8.2$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 2.72 – 2.66 (m, 2H), 1.66 – 1.58 (m, 2H), 1.42 – 1.33 (dq, $J = 14.6$, 7.3 Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H).

$^{13}$C-NMR (CDCl$_3$, 75 MHz): 148.7, 132.2, 129.3, 119.4, 109.6, 36.0, 33.2, 22.4, 14.0.

$^{15}$2-butylquinoline (4k).$^{20}$

GC2014, Method 2: $t_R = 4.054$ min.

Yield = 97% (1.79 g, yellow oil).

Purification: No further purification was required.

$^1$H-NMR (CDCl$_3$, 400 MHz): 8.09 (d, $J = 8.2$ Hz, 2H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.50 (t, $J = 7.5$ Hz, 1H), 7.32 (d, $J = 8.4$ Hz, 1H), 3.00 (t, $J = 8.0$ Hz, 2H), 1.85 – 1.77 (m, 2H), 1.51 – 1.41 (sex, $J = 8.0$ Hz, 2H), 0.97 (t, $J = 7.4$ Hz, 3H).
13C-NMR (CDCl3, 75 MHz): 163.2, 147.9, 136.4, 129.5, 128.8, 127.6, 126.8, 125.8, 121.5, 39.2, 32.3, 22.8, 14.1.

This synthesis has been carried out on 50 mmol of starting material (3m).

GC2014, Method 2: \( t_R = 1.221 \) min.

Yield = 86% (5.82 g, colorless liquid).

Purification: No further purification was required.

1H-NMR (CDCl3, 400 MHz): 8.68 (d, \( J = 4.9 \) Hz, 2H), 7.13 (t, \( J = 4.9 \) Hz, 1H), 2.98 (t, \( J = 8.0 \) Hz, 2H), 1.86 – 1.78 (m, 2H), 1.42 (sex, \( J = 7.2 \) Hz, 2H), 0.96 (t, \( J = 7.4 \) Hz, 3H).

13C-NMR (CDCl3, 75 MHz): 171.8, 157.1, 118.5, 39.4, 31.0, 22.7, 14.1.

OCN

N

2-butylpyrimidine (4l).

GC2014, Method 2: \( t_R = 5.665 \) min.

TLC: \( R_f = 0.13 \), Eluent: Petroleum spirit/Ethyl acetate 90:10.


Yield = 96% (2.23 g, yellow oil).

1H-NMR (CDCl3, 400 MHz): 7.29 – 7.27 (m, 2H), 7.18 (d, \( J = 8.1 \) Hz, 2H), 3.40 (d, \( J = 76.3 \) Hz, 4H), 2.62 (t, \( J = 6.0 \) Hz, 2H), 1.63 – 1.56 (m, 2H), 1.35 (sex, \( J = 7.2 \) Hz, 2H), 1.17 (s, 6H), 0.92 (t, \( J = 7.3 \) Hz, 3H).

13C-NMR (CDCl3, 75 MHz): 171.6, 144.1, 134.6, 128.4, 126.4, 43.4, 39.3, 35.5, 33.5, 22.3, 14.3, 14.0, 13.0.


O

N, N-diethyl p-butyLBenzamide (5a).

GC2014, Method 3: \( t_R = 16.595 \) min.

TLC: \( R_f = 0.10 \), Eluent: Petroleum spirit/Diethyl ether 50:50.


Yield = 90% (3.17 g, white solid).

1H-NMR (CDCl3, 400 MHz): 7.28 (d, \( J = 8.0 \) Hz, 2H), 7.14 (d, \( J = 8.0 \) Hz, 2H), 6.99 – 6.95 (m, 1H), 6.86 – 6.80 (m, 3H), 3.80 (s, 3H), 3.73 (d, \( J = 127.8 \) Hz, 4H), 3.00 (d, \( J = 41.9 \) Hz, 4H), 2.56 (t, \( J = 8.0 \) Hz, 2H), 1.57 – 1.49 (m, 2H), 1.28 (sex, \( J = 7.2 \) Hz, 2H), 0.85 (t, \( J = 7.3 \) Hz, 3H).

13C-NMR (CDCl3, 75 MHz): 170.7, 152.4, 145.0, 140.8, 133.1, 128.6, 127.3, 123.7, 121.2, 118.6, 111.4, 55.5, 51.3, 50.9, 48.2, 42.5, 35.6, 33.6, 22.4, 14.0.


(4-butyLphenyl)-(o-anisylpiperazinyl)methanone (5b).
(4-butylphenyl)-4-morpholinylmethanone (5c).\textsuperscript{22}

**GC2014, Method 2:** \( t_R = 7.607 \) min.

**Yield** = 99\% (2.48 g, orange oil).

**Purification:** No further purification was required.

\[ ^1H-NMR \text{ (CDCl}_3\text{, 400 MHz)}: 7.41 – 7.21 \text{ (m, 4H), 3.97 – 3.33 \text{ (m, 8H), 2.63 \text{ (t, } J = 8.0 \text{ Hz 2H), 1.59} \text{ (quint, } J = 7.0 \text{ Hz, 2H), 1.35 \text{ (sex, } J = 7.2 \text{ Hz, 2H), 0.92 \text{ (t, } J = 7.3 \text{ Hz, 3H).}} \]

\[ ^13C-NMR \text{ (CDCl}_3\text{, 75 MHz)}: 170.7, 145.1, 132.6, 128.6, 127.3, 126.0, 48.4, 42.9, 35.6, 33.5, 22.3, 14.0. \]

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N-methyl-N-phenyl \( p \)-butyl-benzamide (5d).

**GC2014, Method 2:** \( t_R = 8.155 \) min.

**TLC:** \( R_f = 0.60 \), Eluent: Petroleum spirit/Diethyl ether 50:50.

**Purification:** Chromatography, Eluent: Petroleum spirit/Diethyl ether 50:50.

**Yield** = 99\% (2.64 g, orange oil).

\[ ^1H-NMR \text{ (CDCl}_3\text{, 400 MHz)}: 7.25 – 7.20 \text{ (m, 4H), 7.16 – 7.12 \text{ (m, 1H), 7.05 – 7.03 \text{ (m, 2H), 6.97 \text{ (d, } J = 8.1 \text{ Hz, 2H), 3.50 \text{ (s, 3H), 2.53 – 2.49 \text{ (m, 2H), 1.55 – 1.47 \text{ (m, 2H), 1.33 – 1.22 \text{ (m, 2H), 0.88 \text{ (t, } J = 7.3 \text{ Hz, 3H).}} \]

\[ ^13C-NMR \text{ (CDCl}_3\text{, 75 MHz)}: 170.9, 145.3, 144.8, 133.2, 129.2, 129.0, 127.8, 127.0, 126.4, 38.6, 35.5, 33.3, 22.3, 14.0. \]

**HRMS (ESI):** \([M + Na]^+\) Calculated for C\textsubscript{18}H\textsubscript{21}NONa: 290.1515; Found: 290.1511.
Bibliography

$^1$H and $^{13}$C NMR spectra of synthesized compounds

2a