Supporting Information

Iron-Catalyzed C–H/N–H Activation by Triazole Guidance: Versatile Alkyne Annulation

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General Remarks

All reactions were carried out in Schlenk tubes under a N\textsubscript{2} atmosphere using pre-dried glassware. THF was dried using a solvent purification system (SPS) from MBRAUN. All starting materials were synthesized according to previously described methods.\textsuperscript{[1-2]} Alkynes 4 were synthesized according to known procedures.\textsuperscript{[3]} \(i\text{PrMgBr} (3.0\ \text{M in 2Me-THF})\) was purchased from Sigma-Aldrich. Other chemicals were obtained from commercial sources and were used without further purification. Yields refer to isolated compounds, estimated to be > 95% pure as determined by \(^1\text{H}-\text{NMR}\) and GC analysis. Chromatography: Merck silica gel 60 (40-63 \(\mu\text{m}\)). NMR: Spectra were recorded on Varian Unity 300, Mercury 300 or Inova 500 in the solvent indicated; chemical shifts (\(\delta\)) are given in ppm. All IR spectra were recorded on a Bruker FT-IR Alpha device. MS: EI-MS-spectra were recorded with Finnigan MAT 95, 70 eV; High resolution mass spectrometry (HRMS) with APEX IV 7T FTICR, Bruker Daltonic. Preparative HPLC was performed on a system from JAI (LC-92XX II Series, Injection- and Control-Valve, UV and RI Detector) connected to JAIGEL HH series columns. CHCl\textsubscript{3} of HPLC-grade was employed. M. p.: Stuart melting point apparatus SMP3, Barlworld Scientific, values are uncorrected.
Representative procedure for the synthesis of amides 1

Oxalyl chloride (1.1 equiv) was added dropwise to a mixture of carboxylic acid (1.0 equiv), DMF (20 µl) in CH₂Cl₂ (10 ml) under N₂ atmosphere at 0 °C. The mixture was stirred at the same temperature for 5 h upon which it was allowed to warm up to ambient temperature. The crude acid chloride was cooled to 0 °C and it was added dropwise to a solution of propargylamine (1.5 equiv), NEt₃ (3.0 equiv) in dry CH₂Cl₂ (10 ml) at 0 °C. The mixture was initially stirred at the same temperature and then at ambient temperature for 12 h. To the reaction was added sat. aqueous NaHCO₃ (20 ml). The aqueous layers were extracted with CH₂Cl₂ (3x20 ml). The combined organic extracts were washed with HCl (1 M, 20 ml), brine and dried over Na₂SO₄ and the filtrate was concentrated under reduced pressure. The crude product was further submitted to the corresponding alkylazide (1.5 equiv), CuSO₄·5H₂O (10 mol %), sodium ascorbate (20 mol %) in a mixture of tBuOH/H₂O (2:1, 40:20 ml). After 3 h, to the reaction was added with sat. aqueous NH₄Cl (40 ml). The aqueous layers were extracted with EtOAc (3x40 ml). The combined organic extracts were dried over Na₂SO₄ and the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel.
**N-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (1b)**

![Chemical Structure of 1b](attachment:structure1b.png)

The representative procedure was followed using benzoic acid (366 mg, 3.00 mmol) and 1-azido-n-hexane (571 mg, 4.50 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1b (705 mg, 82%) as a white solid. M. p. = 92-94 °C.

$^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ = 7.85-7.77 (m, 2H), 7.64-7.60 (s, 1H), 7.48-7.43 (m, 2H), 7.41-7.35 (m, 2H), 4.66 (d, $J$ = 5.3 Hz, 2H), 4.33-4.25 (m, 2H), 1.89-1.82 (m, 2H), 1.33-1.24 (m, 6H), 0.88-0.81 (m, 3H).

$^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta$ = 167.4 (C$q$), 134.0 (C$q$), 131.5 (C$q$), 128.4 (CH), 127.3 (CH), 127.0 (CH), 122.4 (CH), 50.4 (CH$_2$), 35.3 (CH$_2$), 31.1 (CH$_2$), 30.1 (CH$_2$), 26.1 (CH$_2$), 22.3 (CH$_2$), 13.9 (CH$_3$). IR (ATR): 2954, 1638, 1486, 1373, 1059, 748, 589 cm$^{-1}$. MS (ESI) $m/z$ (relative intensity): 595 (21) [2M+Na]$^+$, 309 (100) [M+Na]$^+$, 287 (43) [M+H]$^+$. HR-MS (ESI) $m/z$ calcd for C$_{16}$H$_{23}$N$_4$O [M+H]$^+$ 287.1872 found 287.1870.

**N-[(1-n-Octyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (1c)**

![Chemical Structure of 1c](attachment:structure1c.png)

The representative procedure was followed using benzoic acid (366 mg, 3.00 mmol) and 1-azido-n-octane (698 mg, 4.50 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1c (791 mg, 84%) as a white solid. M. p. = 105-107 °C.

$^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ = 7.80 (d, $J$ = 7.6 Hz, 2H), 7.62 (s, 1H), 7.49-7.41 (m, 1H), 7.38-7.34 (m, 2H), 7.32 (s, 1H), 4.66 (d, $J$ = 5.3 Hz, 2H), 4.28 (t, $J$ = 7.2 Hz, 2H), 1.89-1.81 (m, 2H), 1.30-1.19 (m, 10H), 0.85-0.80 (m, 3H). $^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta$ = 167.4 (C$q$), 134.0 (C$q$), 131.5 (C$q$), 128.4 (CH), 128.4 (CH), 127.0 (CH), 122.3 (CH), 50.4 (CH$_2$), 35.3 (CH$_2$), 31.6 (CH$_2$), 30.2 (CH$_2$), 29.0 (CH$_2$), 28.9 (CH$_2$), 26.4 (CH$_2$), 22.5 (CH$_2$), 14.0 (CH$_3$). IR (ATR): 2955, 1637, 1523, 1290, 1059, 785, 692, cm$^{-1}$. MS (ESI) $m/z$ (relative
intensity): 651 (5) [2M+Na]^+, 337 (18) [M+Na]^+, 315 (100) [M+H]^+. HR-MS (ESI) m/z calcd for C_{18}H_{27}N_{4}O [M+H]^+ 315.2185 found 315.2181.

\[ \text{N-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methylbenzamide (1f)} \]

The representative procedure was followed using 4-methylbenzoic acid (409 mg, 3.00 mmol) and 1-azido-n-hexane (571 mg, 4.50 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1f (721 mg, 80%) as a white solid. M. p. = 126-128 °C.

\[ \text{^1H-NMR (300 MHz, CDCl}_3\text{): } \delta = 7.68 (d, J = 8.3 Hz, 2H), 7.60 (s, 1H), 7.29-7.23 (m, 1H), 7.17 (d, J = 8.3 Hz, 2H), 4.65 (d, J = 5.6 Hz, 2H), 4.28 (t, J = 7.2 Hz, 2H), 2.34 (s, 3H), 1.89-1.81 (m, 2H), 1.30-1.24 (m, 6H), 0.86-0.82 (m, 3H). \]

\[ \text{\textsuperscript{13}C-NMR (125 MHz, CDCl}_3\text{): } \delta = 167.4 (C\textsubscript{q}), 144.7 (C\textsubscript{q}), 142.0 (C\textsubscript{q}), 131.1 (CH), 129.1 (CH), 127.0 (CH), 122.3 (C\textsubscript{q}), 50.4 (CH\textsubscript{2}), 35.3 (CH\textsubscript{2}), 31.1 (CH\textsubscript{2}), 30.2 (CH\textsubscript{2}), 26.1 (CH\textsubscript{2}), 22.4 (CH\textsubscript{2}), 21.4 (CH\textsubscript{3}), 13.9 (CH\textsubscript{3}). \]

\[ \text{IR (ATR): 2857, 1636, 1547, 1261, 1052, 798, 752, cm}^{-1}. \]

\[ \text{MS (ESI) m/z (relative intensity): 623 (5) [2M+Na]^+, 323 (22) [M+Na]^+, 301 (100) [M+H]^+. HR-MS (ESI) m/z calcd for C_{17}H_{25}N_{4}O [M+H]^+ 301.2028 found 301.2027.} \]

\[ \text{N-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-[1,1'-biphenyl]-4-carboxamide (1g)} \]

The representative procedure was followed using 4-phenylbenzoic acid (597 mg, 3.00 mmol) and 1-azido-n-hexane (571 mg, 4.50 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1g (946 mg, 87%) as a white solid. M. p. = 178-180 °C.

\[ \text{\textsuperscript{1H-NMR (300 MHz, CDCl}_3\text{): } \delta = 7.89-7.86 (m, 2H), 7.63-7.61 (m, 2H), 7.62-7.60 (m, 2H), 7.58-7.56 (m, 3H), 7.38-7.32 (m, 2H), 4.70 (d, J = 5.7 Hz, 2H), 4.32-4.28 (m, 2H), 1.92-1.84 (m, 2H), 1.32-1.24 (m, 6H), 0.87-0.82 (m, 3H). \]

\[ \text{\textsuperscript{13}C-NMR (125 MHz, CDCl}_3\text{): } \delta = 167.1 (C\textsubscript{q}), \]
144.3 (C<sub>q</sub>), 139.9 (C<sub>q</sub>), 132.6 (CH), 128.9 (CH), 127.9 (C<sub>q</sub>), 127.9 (CH), 127.6 (CH), 127.2 (CH), 127.2 (CH), 122.4 (C<sub>q</sub>), 50.4 (CH<sub>2</sub>), 35.4 (CH<sub>2</sub>), 31.1 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 26.1 (CH<sub>2</sub>), 22.4 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>), IR (ATR): 2953, 1636, 1532, 1058, 851, 741, 685 cm<sup>-1</sup>. MS (ESI) m/z (relative intensity): 747 (39) [2M+Na]<sup>+</sup>, 385 (47) [M+Na]<sup>+</sup>, 363 (100) [M+H]<sup>+</sup>. HR-MS (ESI) m/z calcd for C<sub>22</sub>H<sub>27</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 363.2185 found 363.2181.

4-(tert-Butyl)-N-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (1h)

The representative procedure was followed using 4-(tert-butyl)benzoic acid (356 mg, 2.00 mmol) and 1-azido-n-hexane (381 mg, 3.00 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3 → 1:1) yielded 1h (581 mg, 85%) as a white solid. M. p. = 126-129 °C. 1H-NMR (300 MHz, CDCl<sub>3</sub>): δ = 7.73-7.69 (m, 2H), 7.59 (s, 1H), 7.42-7.39 (m, 2H), 6.96 (bs, 1H), 4.68 (d, J = 5.7 Hz, 2H), 4.29 (t, J = 7.3 Hz, 2H), 1.89-1.81 (m, 2H), 1.30 (s, 9H), 1.30-1.23 (m, 6H), 0.88-0.83 (m, 3H). 13C-NMR (125 MHz, CDCl<sub>3</sub>): δ = 167.3 (C<sub>q</sub>), 155.1 (C<sub>q</sub>), 131.1 (C<sub>q</sub>), 126.9 (CH), 125.5 (CH), 125.2 (C<sub>q</sub>), 122.3 (CH), 50.4 (CH<sub>2</sub>), 35.3 (CH<sub>2</sub>), 34.9 (C<sub>q</sub>), 31.2 (CH<sub>3</sub>), 31.1 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 26.1 (CH<sub>2</sub>), 22.4 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>). IR (ATR): 2951, 1638, 1549, 1313, 854, 667 cm<sup>-1</sup>. MS (ESI) m/z (relative intensity): 707 (37) [2M+Na]<sup>+</sup>, 365 (59) [M+Na]<sup>+</sup>, 343 (100) [M+H]<sup>+</sup>. HR-MS (ESI) m/z calcd for C<sub>20</sub>H<sub>31</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 343.2498 found 343.2492.
N-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methoxybenzamide (1i)

\[
\begin{align*}
\text{MeO} & \quad \text{H} & \quad \text{N} & \quad \text{N} \rightarrow \text{n-Hex} \\
\end{align*}
\]

The representative procedure was followed using 4-methoxybenzoic acid (457 mg, 3.00 mmol) and 1-azido-n-hexane (571 mg, 4.50 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1i (703 mg, 74%) as a white solid. M. p. = 109-110 °C. \( ^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta = 7.76 \) (d, \( J = 8.5 \) Hz, 2H), 7.60 (s, 1H), 7.40-7.35 (m, 1H), 6.84 (d, \( J = 8.5 \) Hz, 2H), 4.63 (d, \( J = 5.7 \) Hz, 2H), 4.28 (t, \( J = 7.2 \) Hz, 2H), 3.78 (s, 3H), 1.88-1.81 (m, 2H), 1.31-1.23 (m, 6H), 0.86-0.81 (m, 3H). \( ^{13}\)C-NMR (125 MHz, CDCl\(_3\)): \( \delta = 166.9 \) (C\( _q \)), 162.2 (C\( _q \)), 128.8 (C\( _q \)), 126.3 (CH), 122.3 (C\( _q \)), 113.7 (CH), 113.5 (CH), 55.3 (CH\( _2 \)), 50.4 (CH\( _3 \)), 35.3 (CH\( _2 \)), 31.1 (CH\( _2 \)), 30.2 (CH\(_2\)), 26.1 (CH\(_2\)), 22.2 (CH\(_2\)), 13.8 (CH\(_3\)). IR (ATR): 2954, 1634, 1503, 1175, 1059, 839, 611 cm\(^{-1}\). MS (ESI) \( m/z \) (relative intensity): 339 (21) [M+Na]\(^+\), 317 (100) [M+H]\(^+\). HR-MS (ESI) \( m/z \) calcd for C\(_{17}\)H\(_{25}\)N\(_4\)O [M+H]\(^+\) 317.1978 found 317.1980.

4-Ethoxy-N-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (1j)

\[
\begin{align*}
\text{EtO} & \quad \text{H} & \quad \text{N} & \quad \text{N} \rightarrow \text{n-Hex} \\
\end{align*}
\]

The representative procedure was followed using 4-ethoxybenzoic acid (500 mg, 3.00 mmol) and 1-azido-n-hexane (571 mg, 4.50 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1j (635 mg, 64%) as a white solid. M. p. = 134-136 °C. \( ^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta = 7.73 \) (d, \( J = 8.8 \) Hz, 2H), 7.60 (s, 1H), 6.93 (bs, 1H), 6.86 (d, \( J = 8.8 \) Hz, 2H), 4.66 (d, \( J = 5.0 \) Hz, 2H), 4.29 (t, \( J = 7.3 \) Hz, 2H), 4.04 (q, \( J = 7.0 \) Hz, 2H), 1.91-1.82 (m, 2H), 1.40 (t, \( J = 7.0 \) Hz, 3H), 1.33-1.23 (m, 6H), 0.87-0.82 (m, 3H). \( ^{13}\)C-NMR (125 MHz, CDCl\(_3\)): \( \delta = 167.1 \) (C\( _q \)), 161.7 (C\( _q \)), 128.8 (CH), 125.7 (C\( _q \)), 122.3 (C\( _q \)), 116.2 (CH), 114.1 (CH), 63.6 (CH\(_2\)), 50.4 (CH\(_2\)), 35.3 (CH\(_2\)), 31.1 (CH\(_2\)), 30.2 (CH\(_2\)), 26.1 (CH\(_2\)), 22.4 (CH\(_2\)), 14.7 (CH\(_3\)), 13.9 (CH\(_3\)). IR (ATR): 2932, 1634, 1551, 1251, 1050, 651 cm\(^{-1}\). MS
(ESI) m/z (relative intensity): 683 (18) [2M+Na]+, 353 (100) [M+Na]+, 331 (47) [M+H]+. HR-MS (ESI) m/z calcd for C_{18}H_{27}N_{4}O_{2} [M+H]+ 331.2134 found 331.2129.

N-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-(methylthio)benzamide (1k)

![Structure](image)

The representative procedure was followed using 4-(methylthio)benzoic acid (336 mg, 2.00 mmol) and 1-azido-n-hexane (381 mg, 3.00 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1k (439 mg, 66%) as a white solid. M. p. = 137-139 °C. ¹H-NMR (300 MHz, CDCl₃): δ = 7.73-7.68 (m, 2H), 7.60 (s, 1H), 7.24 (s, 1H), 7.23-7.18 (m, 2H), 4.66 (d, J = 5.7 Hz, 2H), 4.29 (t, J = 7.6 Hz, 2H), 2.46 (s, 3H), 1.92-1.79 (m, 2H), 1.32-1.21 (m, 6H), 0.87-0.81 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 166.9 (C_q), 144.7 (C_q), 143.5 (C_q), 130.1 (C_q), 127.4 (CH), 125.3 (CH), 122.5 (CH), 50.4 (CH₂), 36.3 (CH₂), 31.1 (CH₂), 30.1 (CH₂), 26.1 (CH₂), 22.3 (CH₂), 15.0 (CH₃), 13.9 (CH₃). IR (ATR): 2954, 1634, 1523, 1059, 837, 789 cm⁻¹. MS (ESI) m/z (relative intensity): 687 (44) [2M+Na]+, 355 (92) [M+Na]+, 333 (100) [M+H]+. HR-MS (ESI) m/z calcd for C_{17}H_{23}N_{4}O_{2}S [M+H]+ 333.1749 found 333.1744.

4-(Dimethylamino)-N-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (II)

![Structure](image)

The representative procedure was followed using 4-(dimethylamino)benzoic acid (330 mg, 2.00 mmol) and 1-azido-n-hexane (381 mg, 3.00 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded II (363 mg, 55%) as a white solid. M. p. = 176-178 °C. ¹H-NMR (300 MHz, CDCl₃): δ = 7.69-7.66 (m, 2H), 7.57 (s, 1H), 6.82 (s, 1H), 6.63-6.60 (m, 2H), 4.66 (d, J = 5.7 Hz, 2H), 4.27 (t, J = 7.3 Hz, 2H), 2.97 (s, 6H), 1.88-1.76 (m, 2H), 1.33-1.19 (m, 6H), 0.86-0.82 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 167.3 (C_q), 152.5 (C_q),
145.2 (C<sub>q</sub>), 128.5 (CH), 122.3 (CH), 120.7 (C<sub>q</sub>), 111.0 (CH), 50.4 (CH<sub>2</sub>), 40.1 (CH<sub>3</sub>), 35.2 (CH<sub>2</sub>), 31.1 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 26.1 (CH<sub>2</sub>), 22.4 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>). IR (ATR): 2922, 1624, 1606, 1517, 1310, 1213, 631 cm<sup>-1</sup>. MS (ESI) m/z (relative intensity): 681 (28) [2M+Na]<sup>+</sup>, 352 (76) [M+Na]<sup>+</sup>, 330 (100) [M+H]<sup>+</sup>. HR-MS (ESI) m/z calcd for C<sub>18</sub>H<sub>28</sub>N<sub>5</sub>O [M+H]<sup>+</sup> 330.2294 found 330.2299.

4-Fluoro-N-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (1m)

The representative procedure was followed using 4-fluorobenzoic acid (280 mg, 2.00 mmol) and 1-azido-n-hexane (381 mg, 3.00 mmol). Purification by column chromatography (n-hexane/EtOAc 7:3→ 1:1) yielded 1m (413 mg, 68%) as a white solid. M. p. = 108-110 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): δ = 7.98-7.78 (m, 2H), 7.71-7.59 (m, 1H), 7.11-6.96 (m, 1H), 4.69-4.57 (m, 2H), 4.38-4.23 (m, 2H), 1.92-1.79 (m, 2H), 1.37-1.18 (m, 6H), 0.90-0.77 (m, 3H). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>): δ = 166.4 (C<sub>q</sub>), 165.9 (d, <sup>1</sup>J<sub>C-F</sub> = 251 Hz, C<sub>q</sub>), 144.7 (C<sub>q</sub>), 130.1 (d, <sup>4</sup>J<sub>C-F</sub> = 3 Hz, C<sub>q</sub>), 129.5 (d, <sup>3</sup>J<sub>C-F</sub> = 9 Hz, CH), 122.6 (CH), 115.5 (d, <sup>2</sup>J<sub>C-F</sub> = 22 Hz, CH), 50.4 (CH<sub>2</sub>), 35.2 (CH<sub>2</sub>), 31.0 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 26.1 (CH<sub>2</sub>), 22.3 (CH<sub>2</sub>), 13.8 (CH<sub>3</sub>). <sup>19</sup>F-NMR (283 MHz, CDCl<sub>3</sub>): δ = -108.1 (m). IR (ATR): 2956, 2856, 1637, 1604, 1461, 1286, 1239, 1059, 849 cm<sup>-1</sup>. MS (ESI) m/z (relative intensity): 327 (17) [M+Na]<sup>+</sup>, 305 (100) [M+H]<sup>+</sup>. HR-MS (ESI) m/z calcd for C<sub>16</sub>H<sub>22</sub>F<sub>4</sub>N<sub>5</sub>O [M+H]<sup>+</sup> 305.1778 found 305.1774.
Variation of key parameters for iron-catalyzed C–H/N–H alkyne annulation

To a stirred solution of 1b (85.8 mg, 0.30 mmol), ZnBr₂•TMEDA (204.6 mg, 0.60 mmol), dppe (17.9 mg, 0.045 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol) in THF (0.50 ml), iPrMgBr (3.0 M in 2-MeTHF) (500 µl, 1.5 mmol) was added dropwise and the reaction mixture was stirred for 5 min at ambient temperature. Then, Fe(acac)₃ (10.6 mg, 0.03 mmol) was added in a single portion. After stirring the solution for additional 5 min, an oxidant (0.60 mmol, 2.0 equiv) was added. Then, the mixture was placed in a pre-heated oil bath at 60 °C. After stirring for 16 h, sat. aqueous NH₄Cl (15 ml) was added to the reaction mixture, which was then extracted with CH₂Cl₂ (3 x15 ml). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated. The crude product was purified by column chromatography (n-hexane/EtOAc 9:1→ 3:1).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidant</th>
<th>Yield (%)[a]</th>
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<tbody>
<tr>
<td>1</td>
<td>DCIB[b]</td>
<td>81</td>
</tr>
<tr>
<td>2</td>
<td>DCP[c]</td>
<td>--</td>
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<tr>
<td>3</td>
<td>2,3-DCB[d]</td>
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<tr>
<td>4</td>
<td>1,2-trans-dichloro-cyclohexane</td>
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</tr>
<tr>
<td>5</td>
<td>DCE[e]</td>
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</table>

[a] Reaction conditions: 1b (0.30 mmol), 2a (0.60 mmol), Fe(acac)₃ (0.03 mmol), dppe (0.045 mmol), ZnBr₂•TMEDA (0.60 mmol, 2.0 equiv), iPrMgBr (1.50 mmol, 5.0 equiv), oxidant (0.60 mmol), THF (0.50 ml), 60 °C, 16 h, isolated yields; [b] 1,2-dichloro-isobutane; [c] 1,2-dichloropropane; [d] 2,3-trans-dichlorobutane; [e] dichloroethane.
Representative procedure for the iron-catalyzed C–H/N–H alkyne annulation

To a stirred solution of 1 (0.30 mmol), ZnBr₂·TMEDA (204.6 mg, 0.60 mmol), dppe (17.9 mg, 0.045 mmol) and the corresponding alkyne (0.60 mmol) in THF (0.50 ml), iPrMgBr (3.0 M in 2-MeTHF, 500 µl, 1.5 mmol) was added dropwise and the reaction mixture was stirred for 5 min at ambient temperature. Then, Fe(acac)₃ (10.6 mg, 0.03 mmol) was added in a single portion. After stirring the solution for additional 5 min, DCIB (70 µl, 0.60 mmol) was added. Then, the mixture was placed in a pre-heated oil bath at 60 °C. After stirring for 16 h, sat. aqueous NH₄Cl (15 ml) was added to the reaction mixture, which was extracted with CH₂Cl₂ (3 x15 ml). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated. The crude product was purified by column chromatography (n-hexane/EtOAc).
2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propylisoquinolin-1(2H)-one (3ba)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3ba (95.6 mg, 81%) as a yellowish oil. Rf (n-hexane/EtOAc 1:1) = 0.57. 1H-NMR (300 MHz, CDCl3): δ = 7.76 (d, J = 8.7 Hz, 1H), 7.69 (s, 1H), 7.63-7.59 (m, 2H), 7.43-7.37 (m, 1H), 5.38 (s, 2H), 4.23 (t, J = 7.3 Hz, 2H), 3.04-2.95 (m, 2H), 2.71-2.63 (m, 2H), 1.89-1.78 (m, 2H), 1.72-1.63 (m, 2H), 1.60-1.49 (m, 2H), 1.28 (t, J = 7.4 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H), 0.85-0.80 (m, 3H). 13C-NMR (125 MHz, CDCl3): δ = 162.7 (Cq), 144.4 (Cq), 140.0 (Cq), 136.8 (Cq), 132.2 (CH), 128.1 (CH), 125.6 (CH), 124.8 (Cq), 123.8 (CH), 122.8 (CH), 114.4 (Cq), 50.3 (CH2), 39.9 (CH2), 31.4 (CH2), 31.1 (CH2), 30.1 (CH2), 29.8 (CH2), 26.1 (CH2), 23.5 (CH2), 23.3 (CH2), 22.3 (CH2), 14.5 (CH3), 14.3 (CH3), 13.9 (CH3). IR (ATR): 2957, 1643, 1591, 1341, 1049, 910, 771 cm⁻¹. MS (ESI) m/z (relative intensity): 811 (26) [2M+Na]+, 417 (34) [M+Na]+, 395 (100) [M+H]+. HR-MS (ESI) m/z calcd for C24H35N4O [M+H]+ 395.2811 found 395.2806.

2-[(1-n-Octyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propylisoquinolin-1(2H)-one (3ca)

The representative procedure was followed using 1c (94.2 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3ca (78.4 mg, 62%) as a yellowish oil. Rf (n-hexane/EtOAc 2:1) = 0.54. 1H-NMR (300 MHz, CDCl3): δ = 8.42 (d, J = 8.4 Hz, 1H), 7.69 (s, 1H), 7.64-7.59 (m, 2H), 7.45-7.36 (m, 1H), 5.38 (s, 2H), 4.23 (t, J = 7.4 Hz, 2H), 3.05-2.96 (m, 2H), 2.70-2.6 (m, 2H), 1.87-1.78 (m, 2H), 1.70-1.49 (m, 6H), 1.32-1.19 (m, 8H), 1.13 (t, J = 7.4 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H), 0.87-0.78 (m, 3H). 13C-NMR (125 MHz, CDCl3): δ =162.6 (Cq), 144.3 (Cq), 140.0 (Cq), 14.5 (CH3), 14.3 (CH3), 13.9 (CH3).
136.8 (Cq), 132.2 (Cq), 128.1 (CH), 125.6 (CH), 124.8 (CH), 123.8 (CH), 122.8 (CH), 114.4 (Cq), 50.3 (CH2), 39.9 (CH2), 31.4 (CH2), 31.1 (CH2), 31.0 (CH2), 30.1 (CH2), 29.8 (CH2), 26.1 (CH2), 23.5 (CH2), 23.3 (CH2), 22.4 (CH2), 22.3 (CH2), 14.5 (CH3), 14.3 (CH3), 13.9 (CH3). IR (ATR): 2957, 2870, 1646, 1590, 1465, 1378, 1047 cm⁻¹. MS (ESI) m/z (relative intensity): 867 (35) [2M+Na]⁺, 445 (100) [M+Na]⁺, 423 (76) [M+H]⁺. HR-MS (ESI) m/z calcd for C₂₆H₃₉N₄O [M+H]⁺ 423.3124 found 423.3118.

2-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propyloquinolin-1(2H)-one (3da)

The representative procedure was followed using 1d (87.6 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1 → 3:1) yielded 3da (85.2 mg, 71%) as a white solid. M. p. = 101-103 °C. Rₜ (n-hexane/EtOAc 1:1) = 0.38. ¹H-NMR (300 MHz, CDCl₃): δ = 8.38 (ddd, J = 8.2, 1.3, 0.7 Hz, 1H), 7.66 (s, 1H), 7.62-7.59 (m, 2H), 7.38 (ddd, J = 8.2, 5.4, 2.7 Hz, 1H), 7.33-7.27 (m, 3H), 7.22-7.19 (m, 2H), 5.41 (s, 2H), 5.37 (s, 2H), 3.02-2.98 (m, 2H), 2.68-2.64 (m, 2H), 1.70-1.61 (m, 2H), 1.58-1.49 (m, 2H), 1.13 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 162.6 (Cq), 144.8 (Cq), 140.0 (Cq), 136.8 (Cq), 134.5 (Cq), 132.2 (CH), 129.0 (CH), 128.6 (CH), 128.1 (CH), 128.0 (CH), 125.6 (CH), 124.7 (Cq), 123.9 (CH), 122.8 (CH), 114.4 (Cq), 54.1 (CH₂), 39.8 (CH₂), 31.4 (CH₂), 29.8 (CH₂), 23.5 (CH₂), 23.2 (CH₂), 14.4 (CH₃), 14.2 (CH₃). IR (ATR): 1629, 1581, 1053, 778, 725, 690, 661 cm⁻¹. MS (ESI) m/z (relative intensity): 823 (54) [2M+Na]⁺, 423 (29) [M+Na]⁺, 401 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C₂₅H₂₉N₄O [M+H]⁺ 401.2341 found 401.2336.
2-[[1-(4-Methoxyphenyl)-1H-1,2,3-triazol-4-yl]methyl]-3,4-di-n-propylisoquinolin-1(2H)-one (3ea)

![Chemical Structure](image)

The representative procedure was followed using 1e (92.4 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3ea (74.3 mg, 60%) as a viscous yellowish oil. Rf (n-hexane/EtOAc 1:1) = 0.53. **1H-NMR** (300 MHz, CDCl₃): δ = 8.43 (dd, J = 8.0, 1.0 Hz, 1H), 8.09 (s, 1H), 7.64-7.61 (m, 2H), 7.47-7.54 (m, 2H), 7.41 (ddd, J = 8.0, 4.9, 3.2 Hz, 1H), 6.97-6.91 (m, 2H), 5.46 (s, 2H), 3.81 (s, 3H), 3.09-3.00 (m, 2H), 2.72-2.64 (m, 2H), 1.83-1.66 (m, 2H), 1.65-1.48 (m, 2H), 1.16 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H). **13C-NMR** (125 MHz, CDCl₃): δ = 162.6 (C_q), 159.6 (C_q), 144.8 (C_q), 139.8 (C_q), 136.8 (C_q), 132.1 (CH), 130.4 (C_q), 128.1 (CH), 125.6 (CH), 124.7 (C_q), 122.8 (CH), 122.3 (CH), 122.0 (CH), 114.6 (CH), 114.5 (C_q), 55.6 (CH₃), 39.9 (CH₂), 31.5 (CH₂), 30.0 (CH₂), 23.6 (CH₂), 23.4 (CH₂), 23.4 (CH₂), 14.6 (CH₃), 14.4 (CH₃). **IR (ATR):** 1636, 1516, 1255, 1029, 825, 761 cm⁻¹. **MS (ESI) m/z** (relative intensity): 855 (31) [2M+Na]^+, 439 (38) [M+Na]^+, 417 (100) [M+H]^+. **HR-MS (ESI) m/z** calcd for C_{25}H_{29}N_{4}O_{2} [M+H]^+ 417.2291 found 417.2289.

2-[[1-n-Hexyl-1H-1,2,3-triazol-4-yl]methyl]-6-methyl-3,4-di-n-propylisoquinolin-1(2H)-one (3fa)

![Chemical Structure](image)

The representative procedure was followed using 1f (98.4 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3fa (103.7 mg, 82%) as a colorless oil. Rf (n-hexane/EtOAc 2:1) = 0.43. **1H-NMR** (300 MHz, CDCl₃): δ = 8.31 (d, J = 8.6 Hz, 1H), 7.67 (s, 1H), 7.37 (s, 1H), 7.25-7.21 (d, J = 8.6 Hz, 1H), 5.37 (s, 2H), 4.22 (t, J = 7.4 Hz, 2H), 3.01-2.93 (m, 2H), 2.68-2.61 (m, 2H), 2.47

S-13
(s, 3H), 1.86-1.77 (m, 2H), 1.70-1.60 (m, 2H), 1.60-1.48 (m, 2H), 1.27-1.20 (m, 6H), 1.12 (t, \(J = 7.3\) Hz, 3H), 1.03 (t, \(J = 7.4\) Hz, 3H), 0.84-0.79 (m, 3H). \(^1^3\)C-NMR (125 MHz, CDCl\(_3\)): \(\delta = 162.6\) (C\(_q\)), 144.5 (C\(_q\)), 142.6 (C\(_q\)), 140.1 (C\(_q\)), 137.0 (C\(_q\)), 128.1 (C\(_q\)), 127.3 (CH), 123.8 (CH), 122.6 (CH), 122.6 (CH), 114.2 (C\(_q\)), 50.3 (CH\(_2\)), 39.8 (CH\(_2\)), 31.4 (CH\(_2\)), 31.1 (CH\(_2\)), 30.1 (CH\(_2\)), 29.8 (CH\(_2\)), 26.1 (CH\(_2\)), 23.5 (CH\(_2\)), 23.2 (CH\(_2\)), 22.4 (CH\(_2\)), 22.3 (CH\(_2\)), 14.5 (CH\(_2\)), 14.2 (CH\(_3\)), 13.9 (CH\(_3\)). IR (ATR): 2957, 2870, 1643, 1618, 1490, 1458, 1047, 793 cm\(^{-1}\). MS (ESI) \(m/z\) (relative intensity): 839 (26) [2M+Na\(^+\)], 431 (45) [M+Na\(^+\)], 409 (100) [M+H\(^+\)]. HR-MS (ESI) \(m/z\) calcd for C\(_{25}\)H\(_{37}\)N\(_4\)O [M+H\(^+\)] 409.2967 found 409.2962.

2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-6-phenyl-3,4-di-n-propylisoquinolin-1(2H)-one (3ga)

![Structure of 3ga](image)

The representative procedure was followed using 1g (117.0 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→3:1) yielded 3ga (72.9 mg, 54%) as a white solid. M. p. = 114-116 °C. R\(_f\) (n-hexane/EtOAc 1:1) = 0.52. \(^1^H\)-NMR (300 MHz, CDCl\(_3\)): \(\delta = 8.48\) (dd, \(J = 8.2\), 0.7 Hz, 1H), 7.77 (dd, \(J = 1.4\), 0.7 Hz, 1H), 7.70 (s, 1H), 7.66-7.61 (m, 3H), 7.51-7.44 (m, 2H), 7.43-7.37 (m, 1H), 5.34 (s, 2H), 4.24 (t, \(J = 7.2\) Hz, 2H), 3.05-2.99 (m, 2H), 2.77-2.70 (m, 2H), 1.89-1.78 (m, 2H), 1.74-1.54 (m, 4H), 1.32-1.21 (m, 6H), 1.15 (t, \(J = 7.5\) Hz, 3H), 1.05 (t, \(J = 7.5\) Hz, 3H), 0.86-0.80 (m, 3H). \(^1^3\)C-NMR (125 MHz, CDCl\(_3\)): \(\delta = 162.4\) (C\(_q\)), 145.0 (C\(_q\)), 144.3 (C\(_q\)), 140.8 (C\(_q\)), 140.5 (C\(_q\)), 137.1 (C\(_q\)), 128.9 (CH), 128.7 (CH), 127.9 (CH), 127.5 (CH), 125.0 (CH), 123.7 (CH), 123.6 (C\(_q\)), 121.2 (CH), 114.4 (C\(_q\)), 50.4 (CH\(_2\)), 40.0 (CH\(_2\)), 31.5 (CH\(_2\)), 31.1 (CH\(_2\)), 30.2 (CH\(_2\)), 29.9 (CH\(_2\)), 26.2 (CH\(_2\)), 23.7 (CH\(_2\)), 23.4 (CH\(_2\)), 22.4 (CH\(_2\)), 14.6 (CH\(_3\)), 14.4 (CH\(_3\)), 14.0 (CH\(_3\)). IR (ATR): 1638, 1616, 1588, 1045, 796, 699 cm\(^{-1}\). MS (ESI) \(m/z\) (relative intensity): 963 (41) [2M+Na\(^+\)], 493 (21) [M+Na\(^+\)], 471 (100) [M+H\(^+\)]. HR-MS (ESI) \(m/z\) calcd for C\(_{30}\)H\(_{39}\)N\(_4\)O [M+H\(^+\)] 471.3124 found 471.3118.
6-(tert-Butyl)-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propylosoquinolin-1(2H)-one (3ha)

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{N} & \quad \text{N}
\end{align*}
\]

The representative procedure was followed using \textbf{1h} (102.6 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (\textit{n}-hexane/EtOAc 9:1 → 3:1) yielded 3ha (67.9 mg, 50%) as a viscous colourless oil. Rf \textit{n}-hexane/EtOAc 1:1 = 0.56. \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 8.36 \ (d, J = 7.8 \ Hz, 1\ H), 7.68 \ (s, 1\ H), 7.60 \ (d, J = 1.7 \ Hz, 1\ H), 7.49 \ (dd, J = 7.8, 1.7 \ Hz, 1\ H), 5.41 \ (s, 2\ H), 4.23 \ (t, J = 7.3 \ Hz, 2\ H), 3.04-2.96 \ (m, 2\ H), 2.70 \ (dd, J = 10.5, 5.5 \ Hz, 2\ H), 1.93-1.76 \ (m, 2\ H), 1.73-1.50 \ (m, 4\ H), 1.38 \ (s, 9\ H), 1.31-1.20 \ (m, 6\ H), 1.14 \ (t, J = 7.3 \ Hz, 3\ H), 1.05 \ (t, J = 7.3 \ Hz, 3\ H), 0.86-0.80 \ (m, 3\ H).

\textsuperscript{13}C-NMR (125 MHz, CDCl\textsubscript{3}): \(\delta = 162.5 \ (C_q), 155.4 \ (C_q), 144.5 \ (C_q), 139.9 \ (C_q), 136.6 \ (C_q), 127.9 \ (CH), 123.8 \ (CH), 123.7 \ (CH), 122.5 \ (C_q), 118.7 \ (CH), 114.5 \ (C_q), 50.3 \ (CH2), 39.7 \ (CH2), 35.3 \ (C_q), 31.4 \ (CH2), 31.2 \ (CH2), 31.0 \ (CH2), 30.0 \ (CH2), 29.8 \ (CH2), 26.1 \ (CH2), 23.5 \ (CH2), 23.3 \ (CH2), 22.3 \ (CH2), 14.4 \ (CH3), 14.2 \ (CH3), 13.9 \ (CH3). \text{IR (ATR): } 1641, 1614, 1587, 1463, 795, 730 \ \text{cm}^{-1}. \text{MS (ESI) } m/z \ \text{(relative intensity): } 923 \ (44 \ [2M+Na]^+), 451 \ (100 \ [M+H]^+). \text{HR-MS (ESI) } m/z \ \text{calcd for } C_{28}H_{43}N_{4}O \ [M+H]^+ \ 451.3437 \ \text{found 451.3431.}

2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-6-methoxy-3,4-di-n-propylosoquinolin-1(2H)-one (3ia)

\[
\begin{align*}
\text{MeO} & \quad \text{n-Pr} \\
\text{N} & \quad \text{N}
\end{align*}
\]

The representative procedure was followed using \textbf{1i} (103.2 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (\textit{n}-hexane/EtOAc 9:1 → 3:1) yielded 3ia (73.7 mg, 58%) as viscous colourless oil. Rf \textit{n}-hexane/EtOAc 2:1 = 0.30. \textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 8.35 \ (d, J = 8.7 \ Hz, 1\ H), 7.68 \ (s, 1\ H), 7.02-6.95 \ (m, 1\ H), 7.43-7.37 \ (m, 1\ H), 5.36 \ (s, 2\ H), 4.23 \ (t, J = 7.2 \ Hz, 2\ H), 3.89 \ (s, 3\ H), 3.01-2.93 \ (m, 2\ H), 2.66-2.60
(m, 2H), 1.86-1.77 (m, 2H), 1.71-1.52 (m, 4H), 1.27-1.20 (m, 6H), 1.13 (t, J = 7.4 Hz, 3H), 1.03 (t, J = 7.5 Hz, 3H), 0.85-0.79 (m, 3H). \[^{13}\text{C}-\text{NMR (125 MHz, CDCl}_3\text{): } \delta = 162.8 \text{ (C} \text{q}), 162.3 \text{ (C} \text{q}), 144.5 \text{ (C} \text{q}), 140.7 \text{ (C} \text{q}), 138.8 \text{ (C} \text{q}), 130.3 \text{ (C} \text{q}), 123.8 \text{ (CH)}, 118.8 \text{ (CH)}, 114.2 \text{ (CH)}, 113.9 \text{ (C} \text{q}), 104.9 \text{ (CH)}, 55.3 \text{ (CH} \text{)}, 50.3 \text{ (CH} \text{)}, 39.7 \text{ (CH} \text{)}, 31.5 \text{ (CH} \text{)}, 31.1 \text{ (CH} \text{)}, 30.1 \text{ (CH} \text{)}, 30.0 \text{ (CH} \text{)}, 26.1 \text{ (CH} \text{)}, 23.3 \text{ (CH} \text{)}, 23.3 \text{ (CH} \text{)}, 22.4 \text{ (CH} \text{)}, 14.5 \text{ (CH} \text{)}, 14.3 \text{ (CH} \text{)}, 13.9 \text{ (CH} \text{)}. \text{IR (ATR): 2957, 2929, 1639, 1611, 1491, 1238, 1213, 1035, 789, 729 cm}^{-1}. \text{MS (ESI) } m/z \text{ (relative intensity): 871 (20) [2M+Na}^+\text{], 447 (28) [M+Na}^+\text{], 425 (100) [M+H}^+\text{]. HR-MS (ESI) } m/z \text{ calcd for C}_{25}\text{H}_{37}\text{N}_4\text{O} [\text{M+H}^+] 425.2917 \text{ found 425.2912.}\)

**6-Ethoxy-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propyloisoquinolin-1(2H)-one (3ja)**

![Chemical structure](image)

The representative procedure was followed using 1j (99.2 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3ja (97.0 mg, 74%) as a white solid. M. p. = 134-136 °C. Rf (n-hexane/EtOAc 1:1) = 0.39. \[^{1}\text{H-NMR (300 MHz, CDCl}_3\text{): } \delta = 8.33 \text{ (d, } J = 8.7 \text{ Hz, 1H}), 7.65 \text{ (s, 1H)}, 6.99 \text{ (d, } J = 2.1 \text{ Hz, 1H}), 6.96-6.93 \text{ (m, 1H)}, 5.37 \text{ (s, 2H)}, 4.22 \text{ (t, } J = 7.2 \text{ Hz, 2H}), 4.11 \text{ (q, } J = 6.8 \text{ Hz, 2H)}, 3.00-2.91 \text{ (m, 2H)}, 2.64-2.57 \text{ (m, 2H)}, 1.87-1.76 \text{ (m, 2H)}, 1.71-1.60 \text{ (m, 2H)}, 1.59-1.48 \text{ (m, 2H)}, 1.44 \text{ (t, } J = 6.8 \text{ Hz, 3H)}, 1.29-1.19 \text{ (m, 6H)}, 1.11 \text{ (t, } J = 7.5 \text{ Hz, 3H)}, 1.02 \text{ (t, } J = 7.5 \text{ Hz, 3H)}, 0.81-0.77 \text{ (m, 3H).} \[^{13}\text{C}-\text{NMR (125 MHz, CDCl}_3\text{): } \delta = 162.3 \text{ (C} \text{q}), 162.1 \text{ (C} \text{q}), 144.5 \text{ (C} \text{q}), 140.6 \text{ (C} \text{q}), 138.8 \text{ (C} \text{q}), 130.2 \text{ (CH)}, 123.7 \text{ (CH)}, 118.6 \text{ (C} \text{q}), 114.5 \text{ (CH)}, 113.9 \text{ (C} \text{q}), 105.5 \text{ (CH)}, 63.6 \text{ (CH} \text{)}, 50.3 \text{ (CH} \text{)}, 39.6 \text{ (CH} \text{)}, 31.4 \text{ (CH} \text{)}, 31.0 \text{ (CH} \text{)}, 30.0 \text{ (CH} \text{)}, 29.9 \text{ (CH} \text{)}, 26.1 \text{ (CH} \text{)}, 23.3 \text{ (CH} \text{)}, 23.2 \text{ (CH} \text{)}, 22.3 \text{ (CH} \text{)}, 14.7 \text{ (CH} \text{)}, 14.5 \text{ (CH} \text{)}, 14.2 \text{ (CH} \text{)}, 13.8 \text{ (CH} \text{)}. \text{IR (ATR): 1639, 1610, 1239, 1216, 1187, 1045 cm}^{-1}. \text{MS (ESI) } m/z \text{ (relative intensity): 899 (23) [2M+Na}^+\text{], 461 (22) [M+Na}^+\text{], 439 (100) [M+H}^+\text{]. HR-MS (ESI) } m/z \text{ calced for C}_{26}\text{H}_{39}\text{N}_4\text{O}_2 [\text{M+H}^+] 439.3073 \text{ found 439.3068.}\)
2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-6-(methylthio)-3,4-di-n-propylisoquinolin-1(2H)-one (3ka)

The representative procedure was followed using [Fe(acac)]$_3$ (21.1 mg, 0.06 mmol), dppe (29.9 mg, 0.075 mmol), 1k (99.6 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1→1:1) yielded 3ka (69.7 mg, 53 %) as a yellowish solid. M. p. = 143-145 °C. R$_f$ (n-hexane/EtOAc 1:1) = 0.38. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta$ = 8.29 (d, $J$ = 8.6 Hz, 1H), 7.67 (s, 1H), 7.34 (d, $J$ = 1.7 Hz, 1H), 7.25 (dd, $J$ = 8.6, 1.7 Hz, 1H), 5.36 (s, 2H), 4.22 (t, $J$ = 7.3 Hz, 2H), 3.01-2.94 (m, 2H), 2.65-2.60 (m, 2H), 2.53 (s, 3H), 1.86-1.78 (m, 2H), 1.70-1.61 (m, 2H), 1.57-1.49 (m, 2H), 1.28-1.20 (m, 6H), 1.12 (m, 3H), 1.02 (m, 3H), 0.84-0.79 (m, 3H). $^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta$ = 162.4 (C$_q$), 144.3 (C$_q$), 141.0 (C$_q$), 137.1 (C$_q$), 129.6 (C$_q$), 128.5 (CH), 123.8 (CH), 123.4 (CH), 121.8 (C$_q$), 118.4 (CH), 113.7 (C$_q$), 50.3 (CH$_2$), 39.8 (CH$_2$), 31.4 (CH$_2$), 31.0 (CH$_2$), 30.0 (CH$_2$), 29.8 (CH$_2$), 26.1 (CH$_2$), 23.4 (CH$_2$), 23.2 (CH$_2$), 22.3 (CH$_2$), 15.1 (CH$_3$), 14.5 (CH$_3$), 14.2 (CH$_3$), 13.8 (CH$_3$). IR (ATR): 1638, 1601, 1581, 1425, 789, 729 cm$^{-1}$. MS (ESI) m/z (relative intensity): 903 (66) [2M+Na]$^+$, 463 (68) [M+Na]$^+$, 441 (100) [M+H]$^+$. HR-MS (ESI) m/z calcd for C$_{25}$H$_{37}$N$_4$O$_2$ [M+H]$^+$ 441.2688 found 441.2686.

6-(Dimethylamino)-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propylisoquinolin-1(2H)-one (3la)

The representative procedure was followed using [Fe(acac)]$_3$ (21.1 mg, 0.06 mmol), dppe (29.9 mg, 0.075 mmol), 1l (98.7 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1→1:1) yielded 3la (84.7 mg, 65 %) as a yellowish solid. M. p. = 143-145 °C. R$_f$ (n-hexane/EtOAc 1:1) = 0.22. $^1$H-
NMR (300 MHz, CDCl₃): δ = 8.26 (d, J = 9.1 Hz, 1H), 7.65 (s, 1H), 6.86 (dd, J = 9.1, 2.5 Hz, 1H), 6.61 (d, J = 2.5 Hz, 1H), 5.35 (s, 2H), 4.21 (t, J = 7.2 Hz, 2H), 3.06 (s, 6H), 2.97-2.88 (m, 2H), 2.64-2.60 (m, 2H), 1.87-1.78 (m, 2H), 1.68-1.52 (m, 4H), 1.30-1.20 (m, 6H), 1.11 (t, J = 7.2 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H), 0.85-0.80 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 162.5 (C₉), 152.9 (C₉), 145.0 (C₉), 140.1 (C₉), 138.3 (C₉), 129.5 (CH), 123.7 (CH), 114.8 (C₉), 113.8 (C₉), 112.1 (CH), 102.1 (CH), 50.3 (CH₃), 40.2 (CH₃), 39.5 (CH₂), 31.5 (CH₂), 31.1 (CH₂), 30.1 (CH₂), 30.0 (CH₂), 26.1 (CH₂), 23.3 (CH₂), 23.1 (CH₂), 22.3 (CH₂), 14.6 (CH₃), 14.3 (CH₃), 13.9 (CH₃). IR (ATR): 1629, 1606, 1574, 1507, 1047, 788 cm⁻¹. MS (ESI) m/z (relative intensity): 897 (13) [2M+Na]+, 460 (28) [M+Na]+, 438 (100) [M+H]+. HR-MS (ESI) m/z calcd for C₂₆H₄₀N₅O [M+H]+ 438.3233 found 438.3228.

6-Fluoro-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]-3,4-di-n-propylisoquinolin-1(2H)-one (3ma)

The representative procedure was followed using [Fe(acac)₃] (21.1 mg, 0.06 mmol), dppe (29.9 mg, 0.075 mmol), 1m (91.2 mg, 0.30 mmol) and 4-octyne (2a) (66.0 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3ma (49.3 mg, 40%) as a viscous yellow oil. Rₜ (n-hexane/EtOAc 1:1) = 0.55. ¹H-NMR (300 MHz, CDCl₃): δ = 8.41 (dd, J = 10.6, 6.1 Hz, 1H), 7.68 (s, 1H), 7.20 (dd, J = 10.6, 2.4 Hz, 1H), 7.09 (dd, J = 6.1, 2.4, 1H), 5.35 (s, 2H), 4.23 (t, J = 7.3 Hz, 2H), 3.03-2.97 (m, 2H), 2.62-2.57 (m, 2H), 1.90-1.77 (m, 2H), 1.71-1.63 (m, 2H), 1.57-1.47 (m, 2H), 1.31-1.19 (m, 6H), 1.13 (t, J = 7.3 Hz, 3H), 1.03 (t, J = 7.3 Hz, 3H), 0.87-0.79 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 165.4 (d, JₐC-F = 249 Hz, C₉), 161.9 (C₉), 144.0 (C₉), 141.5 (C₉), 139.2 (d, JₐC-F = 10 Hz, C₉), 131.2 (d, JₐC-F = 10 Hz, CH), 123.7 (CH), 121.3 (C₉), 114.2 (d, JₐC-F = 24 Hz, CH), 113.8 (d, JₐC-F = 4 Hz, C₉), 107.9 (d, JₐC-F = 22 Hz, CH), 50.4 (CH₂), 39.9 (CH₂), 31.6 (CH₂), 31.1 (CH₂), 30.1 (CH₂), 30.0 (CH₂), 26.2 (CH₂), 23.4 (CH₂), 23.3 (CH₂), 22.4 (CH₂), 14.5 (CH₃), 14.4 (CH₃), 13.9 (CH₃). ¹⁹F-NMR (285 MHz, CDCl₃): δ = -106.4 (ddd, J = 11, 9, 8 Hz). IR (ATR): 1646, 1615, 1597, 1487, 1170, 788 cm⁻¹. MS (ESI) m/z (relative intensity): 847 (42) [2M+Na]+, 431
(100) [M+Na]⁺, 413 (63) [M+H]⁺. HR-MS (ESI) m/z calcd for C₁₄H₂₄FN₄O [M+H]⁺ 413.2717 found 413.2711.

3,4-Di-n-butyl-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]isoquinolin-1(2H)-one (3bb)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 5-decyne (2b) (82.8 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→3:1) yielded 3bb (106.3 mg, 84%) as a yellow oil. Rᵋ (n-hexane/EtOAc 1:1) = 0.55. ¹H-NMR (300 MHz, CDCl₃): δ = 8.42 (d, J = 8.5 Hz, 1H), 7.69 (s, 1H), 7.65-7.60 (m, 2H), 7.42-7.36 (m, 1H), 5.39 (s, 2H), 4.23 (t, J = 7.3 Hz, 2H), 3.08-2.97 (m, 2H), 2.73-2.64 (m, 2H), 1.89-1.76 (m, 2H), 1.68-1.41 (m, 8H), 1.35-1.18 (m, 6H), 1.07-0.98 (m, 3H), 0.96-0.92 (m, 3H), 0.85-0.79 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 162.7 (C₉), 144.4 (C₉), 140.1 (C₉), 136.9 (C₉), 132.2 (CH), 128.1 (CH), 125.6 (CH), 124.8 (C₉), 123.8 (CH), 122.7 (CH), 114.4 (C₉), 50.3 (CH₂), 39.8 (CH₂), 32.4 (CH₂), 32.0 (CH₂), 31.1 (CH₂), 30.1 (CH₂), 29.1 (CH₂), 27.4 (CH₂), 26.1 (CH₂), 23.1 (CH₂), 22.9 (CH₂), 22.3 (CH₂), 13.9 (CH₂), 13.9 (CH₂), 13.9 (CH₃). IR (ATR): 2957, 2859, 1642, 1590, 1260, 1087, 1020, 800, 734, 703 cm⁻¹. MS (ESI) m/z (relative intensity): 867 (24) [2M+Na]⁺, 445 (26) [M+Na]⁺, 423 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C₂₆H₃₉N₄O [M+H]⁺ 423.3124 found 423.3118.
3,4-Diethyl-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]isoquinolin-1(2H)-one (3bc)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 3-hexyne (2c) (51.6 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1 → 3:1) yielded 3bc (82.9 mg, 76%) as a viscous orange oil. R_f (n-hexane/EtOAc 2:1) = 0.41. ¹H-NMR (300 MHz, CDCl₃): δ = 8.43 (dd, J = 8.0, 1.1 Hz, 1H), 7.71 (s, 1H), 7.67–7.59 (m, 2H), 7.40 (ddd, J = 8.0, 5.4, 2.8 Hz, 1H), 4.23 (t, J = 7.4 Hz, 2H), 3.09 (q, J = 7.2 Hz, 2H), 2.75 (q, J = 7.2 Hz, 2H), 1.89–1.75 (m, 2H), 1.31 (t, J = 7.2 Hz, 3H), 1.27–1.21 (m, 8H), 1.17 (t, J = 7.2 Hz, 3H), 0.83–0.79 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 162.6 (C_q), 144.3 (C_q), 140.8 (C_q), 136.7 (C_q), 132.2 (CH), 128.1 (CH), 125.6 (CH), 124.8 (C_q), 123.9 (CH), 122.6 (CH), 115.3 (C_q), 50.3 (CH₂), 39.6 (CH₂), 31.0 (CH₂), 30.0 (CH₂), 26.1 (CH₂), 22.4 (CH₂), 22.3 (CH₂), 20.5 (CH₂), 14.7 (CH₃), 14.1 (CH₃), 13.8 (CH₃). IR (ATR): 1640, 1588, 1463, 1049, 771, 702 cm⁻¹. MS (ESI) m/z (relative intensity): 755 (23) [2M+Na]⁺, 389 (31) [M+Na]⁺, 367 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C₂₂H₃₁N₄O [M+H]⁺ 367.2498 found 367.2493.

2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methyl-3-phenylisoquinolin-1(2H)-one (5ba)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and prop-1-yn-1-ylbenzene (4a) (69.6 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1 → 3:1) yielded 5ba (88.4 mg, 74%) as a yellowish solid. M. p. = 88–91 °C. R_f (n-hexane/EtOAc 1:1) = 0.33. ¹H-NMR (300 MHz, CDCl₃): δ = 8.49 (d,
\[ J = 8.0 \text{ Hz}, 1H \], 7.72-7.66 (m, 2H), 7.55 (s, 1H), 7.53-7.49 (m, 1H), 7.48-7.43 (m, 3H), 7.27-7.22 (m, 2H), 5.02 (s, 2H), 4.20 (t, \( J = 7.2 \text{ Hz}, 2H \)), 1.97 (s, 3H), 1.86-1.75 (m, 2H), 1.30-1.19 (m, 6H), 0.86-0.79 (m, 3H). \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)): \( \delta = 162.1 (C_q), 143.9 (C_q), 140.1 (C_q), 137.2 (C_q), 134.7 (C_q), 132.3 (CH), 130.0 (CH), 128.9 (CH), 128.6 (CH), 128.6 (CH), 128.0 (CH), 126.4 (CH), 125.2 (C_q), 123.2 (CH), 110.9 (C_q), 50.2 (CH\(_2\)), 42.1 (CH\(_2\)), 31.1 (CH\(_2\)), 30.1 (CH\(_2\)), 26.1 (CH\(_2\)), 22.4 (CH\(_2\)), 15.0 (CH\(_3\)), 13.9 (CH\(_2\)). \] IR (ATR): 1651, 1613, 1321, 762, 726, 696 cm\(^{-1}\). MS (ESI) m/z (relative intensity): 823 (61) [2M+Na]\(^+\), 423 (33) [M+Na]\(^+\), 401 (100) [M+H]\(^+\). HR-MS (ESI) m/z calcd for C\(_{25}\)H\(_{29}\)N\(_4\)O \([M+H]\)^{+} 401.2341 found 401.2340.

\[ n-\text{Hexyl-1H-1,2,3-triazol-4-yl)methyl]-3-(3-methoxyphenyl)-4-methylisoquinolino}
\[ n-\text{1(2H)-one (5bb) } \]

The representative procedure was followed using \( 1b \) (85.8 mg, 0.30 mmol) and 1-methoxy-3-(prop-1-yn-1-yl)benzene (4b) (87.6 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 5bb (52.7 mg, 41%) as a viscous yellow oil. R\(_f\) (n-hexane/EtOAc 1:1) = 0.37. \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta = 8.51 (dd, J = 8.2, 2.6 \text{ Hz}, 1H), 7.73-7.69 (m, 2H), 7.60 (s, 1H), 7.52 (ddd, \( J = 8.2, 5.2, 2.6 \text{ Hz}, 1H), 7.41-7.35 (m, 1H), 7.01 (ddd, \( J = 8.2, 2.6, 1.1 \text{ Hz}, 1H), 6.87-6.81 (m, 2H), 5.15-4.96 (m, 2H), 4.23 (t, \( J = 7.2 \text{ Hz}, 2H), 3.82 (s, 3H), 2.03 (s, 3H), 1.88-1.73 (m, 2H), 1.31-1.19 (m, 6H), 0.84 (t, \( J = 7.2 \text{ Hz}, 3H). \] \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)): \( \delta = 162.1 (C_q), 159.6 (C_q), 144.0 (C_q), 140.0 (C_q), 137.2 (C_q), 135.9 (C_q), 132.3 (CH), 129.7 (CH), 128.0 (CH), 126.4 (CH), 125.2 (C_q), 123.2 (CH), 122.2 (CH), 115.4 (CH), 115.1 (CH), 110.8 (C_q), 55.4 (CH\(_3\)), 50.2 (CH\(_2\)), 42.1 (CH\(_2\)), 31.1 (CH\(_2\)), 30.2 (CH\(_2\)), 26.2 (CH\(_2\)), 22.4 (CH\(_2\)), 15.0 (CH\(_3\)), 13.9 (CH\(_3\)). \] IR (ATR): 1645, 1589, 1045, 766, 708, 697 cm\(^{-1}\). MS (ESI) m/z (relative intensity): 883 (44) [2M+Na]\(^+\), 453 (35) [M+Na]\(^+\), 431 (100) [M+H]\(^+\). HR-MS (ESI) m/z calcd for C\(_{26}\)H\(_{31}\)N\(_4\)O \([M+H]\)^{+} 431.2447 found 431.2442.
3-(4-Fluorophenyl)-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methylisoquinolin-1(2H)-one (5bc)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 1-fluoro-3-(prop-1-yn-1-yl)benzene (4c) (80.4 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→3:1) yielded 5bc (63.8 mg, 51%) as viscous yellow oil. Rf (n-hexane/EtOAc 1:1) = 0.41. 1H-NMR (300 MHz, CDCl3): δ = 8.50-8.48 (m, 1H), 7.72-7.66 (m, 2H), 7.61 (s, 1H), 7.53-7.49 (m, 1H), 7.29-7.26 (m, 2H), 7.20-7.14 (m, 2H), 5.03 (s, 2H), 4.23 (t, J = 7.2 Hz, 2H), 1.97 (s, 3H), 1.85-1.78 (m, 2H), 1.28-1.22 (m, 6H), 0.85-0.80 (m, 3H). 13C-NMR (125 MHz, CDCl3): δ = 163.9 (d, 1J_{C,F} = 249 Hz, C_q), 161.6 (C_q), 139.1 (C_q), 137.2 (C_q), 132.5 (CH), 132.1 (d, 3J_{C,F} = 8 Hz, CH), 130.8, (d, 4J_{C,F} = 4 Hz, C_q), 128.1 (CH), 126.7 (CH), 125.9 (C_q), 125.5 (C_q) 123.6 (CH), 123.4 (CH), 115.9 (d, 2J_{C,F} = 22 Hz, CH), 111.5 (C_q), 50.2 (CH2), 41.9 (CH2), 31.1 (CH2), 30.1 (CH2), 26.1 (CH2), 22.4 (CH2), 14.9 (CH3), 13.9 (CH3). 19F-NMR (285 MHz, CDCl3): δ = -111.6 (tt, J = 9, 6 Hz). IR (ATR): 1645, 1509, 1220, 849, 766, 729 cm⁻¹. MS (ESI) m/z (relative intensity): 859 (58) [2M+Na]+, 441 (33) [M+Na]+, 419 (100) [M+H]+. HR-MS (ESI) m/z calcd for C_{25}H_{28}FN_{4}O [M+H]^+ 419.2247 found 419.2242.
2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methyl-3-phenylisoquinolin-1(2H)-one (5bd)

![Chemical Structure](image)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 1-methyl-4-(prop-1-yn-1-yl)benzene (4d) (78.2 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 5bd (87.7 mg, 71%) as viscous yellow oil. Rf (n-hexane/EtOAc 1:1) = 0.39. 1H-NMR (300 MHz, CDCl3): δ = 8.51 (d, J = 8.1 Hz, 1H), 7.74-7.66 (m, 2H), 7.57 (s, 1H), 7.51 (ddd, J = 8.1, 5.6, 2.1 Hz, 1H), 7.28 (d, J = 7.8 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 5.07 (s, 2H), 4.22 (t, J = 7.2 Hz, 2H), 2.43 (s, 3H), 1.99 (s, 3H), 1.89-1.76 (m, 2H), 1.32-1.20 (m, 6H), 0.88-0.81 (m, 3H). 13C-NMR (125 MHz, CDCl3): δ = 162.3 (Cq), 144.1 (Cq), 140.3 (Cq), 138.8 (Cq), 137.3 (Cq), 132.4 (CH), 131.8 (Cq), 129.9 (CH), 129.4 (CH), 128.0 (CH), 126.4 (CH), 125.2 (Cq), 123.4 (CH), 123.3 (CH), 111.1 (Cq), 50.1 (CH2), 42.0 (CH2), 31.0 (CH2), 30.0 (CH2), 26.0 (CH2), 22.3 (CH2), 21.4 (CH3), 14.9 (CH3) 13.9 (CH3). IR (ATR): 1645, 1613, 1592, 1322, 804, 765, 696 cm⁻¹. MS (ESI) m/z (relative intensity): 851 (40) [2M+Na]⁺, 437 (45) [M+Na]⁺, 415 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C26H31N4O [M+H]⁺ 415.2498 found 415.2492.

2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methyl-3-(4-n-propylphenyl)isoquinolin-1(2H)-one (5be)

![Chemical Structure](image)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 1-(prop-1-yn-1-yl)-4-propylbenzene (4e) (194.8 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 5be (87.3 mg, 66%) as a viscous yellow oil. Rf (n-
hexane/EtOAc 1:1) = 0.47. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 8.51$-$8.48$ (m, 1H), 7.69-$7.66$ (m, 2H), 7.55 (s, 1H), 7.51-$7.48$ (m, 1H), 7.25 (d, $J = 7.8$ Hz, 2H), 7.14 (d, $J = 7.8$ Hz, 2H), 5.05 (s, 2H), 4.21 (t, $J = 7.2$ Hz, 2H), 2.64 (t, $J = 7.8$ Hz, 2H), 1.98 (s, 3H), 1.85-$1.76$ (m, 2H), 1.73-$1.63$ (m, 2H), 1.27-$1.21$ (m, 6H), 0.97 (t, $J = 6.8$ Hz, 3H). $^1^3$C-NMR (125 MHz, CDCl$_3$): $\delta = 162.2$ (C$_{q}$), 144.3 (C$_{q}$), 143.5 (C$_{q}$), 140.4 (C$_{q}$), 137.4 (C$_{q}$), 132.4 (CH), 132.1 (CH), 129.9 (CH), 128.8 (CH), 128.7 (C$_{q}$), 128.0 (CH), 126.4 (CH), 125.1 (C$_{q}$), 123.3 (CH), 111.1 (C$_{q}$), 50.2 (CH$_2$), 42.0 (CH$_2$), 37.9 (CH$_2$), 31.1 (CH$_2$), 30.1 (CH$_2$), 26.0 (CH$_2$), 24.2 (CH$_2$), 22.4 (CH$_2$), 15.0 (CH$_3$), 13.9 (CH$_3$), 13.9 (CH$_3$). IR (ATR): 1646, 1613, 1592, 1322, 1047, 765, 697 cm$^{-1}$. MS (ESI) $m/z$ (relative intensity): 907 (35) [2M+Na]$^+$, 443 (100) [M+H]$^+$.

HR-MS (ESI) $m/z$ calcd for C$_{28}$H$_{35}$N$_4$O [M+H]$^+$ 443.2811 found 443.2805.

2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-3-(4-methoxyphenyl)-4-methylisoquinolin-1(2H)-one (5bf)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 1-methoxy-4-(prop-1-yn-1-yl)benzene (4f) (87.6 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→3:1) yielded 5bf (99.0 mg, 77%) as a yellowish solid. M. p. = 101-$103$ °C. R$_f$ (n-hexane/EtOAc 1:1) = 0.25. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 8.48$ (d, $J = 8.0$ Hz, 1H), 7.70-$7.65$ (m, 2H), 7.57 (s, 1H), 7.49 (ddd, $J = 8.0$, 5.9, 2.0 Hz, 1H), 7.16 (d, $J = 7.6$ Hz, 2H), 6.97 (d, $J = 7.6$ Hz, 2H), 5.06 (s, 2H), 4.21 (t, $J = 7.2$ Hz, 2H), 3.85 (s, 3H), 1.98 (s, 3H), 1.85-$1.77$ (m, 2H), 1.29-$1.20$ (m, 6H), 0.83-$0.80$ (m, 3H). $^1^3$C-NMR (125 MHz, CDCl$_3$): $\delta = 159.8$ (C$_{q}$), 140.0 (C$_{q}$), 137.3 (C$_{q}$), 133.3 (CH), 131.3 (CH), 130.4 (C$_{q}$), 128.0 (CH), 127.0 (C$_{q}$), 126.4 (CH), 125.2 (C$_{q}$), 123.4 (C$_{q}$), 123.3 (CH), 114.0 (CH), 113.3 (CH), 111.5 (C$_{q}$), 55.2 (CH$_3$), 50.1 (CH$_2$), 42.0 (CH$_2$), 31.0 (CH$_2$), 30.0 (CH$_2$), 26.1 (CH$_2$), 22.3 (CH$_2$), 15.0 (CH$_3$), 13.9 (CH$_3$). IR (ATR): 1644, 1508, 1245, 843, 766, 694 cm$^{-1}$. MS (ESI) $m/z$ (relative

3-[(1,1'-Biphenyl]-4-yl)-2-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methylisoquinolin-1(2H)-one (5bg)

![Chemical Structure](image)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 4-(prop-1-yn-1-yl)-1,1'-biphenyl (4g) (115.2 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 5bg (76.7 mg, 54%) as a yellowish solid. M. p. = 125-128 °C. Rf (n-hexane/EtOAc 1:1) = 0.38. ¹H-NMR (300 MHz, CDCl₃): δ = 8.53 (d, J = 8.0 Hz, 1H), 7.76-7.65 (m, 6H), 7.60 (s, 1H), 7.57-7.51 (m, 1H), 7.50-7.44 (m, 2H), 7.41-7.37 (m, 3H), 5.12 (s, 2H), 4.24 (t, J = 7.2 Hz, 2H), 2.05 (s, 3H), 1.89-1.79 (m, 2H), 1.30-1.23 (m, 6H), 0.87-0.82 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 162.1 (C₉), 143.9 (C₆), 141.6 (C₇), 140.1 (C₈), 139.9 (C₉), 137.2 (C₁₀), 133.7 (C₁₁), 132.3 (CH), 130.5 (CH), 128.7 (CH), 128.0 (CH), 127.6 (CH), 127.2 (CH), 127.0 (CH), 126.4 (CH), 125.3 (C₉), 123.3 (CH), 123.2 (CH), 111.1 (C₇), 50.2 (CH₂), 42.1 (CH₂), 31.1 (CH₂), 30.2 (CH₂), 26.2 (CH₂), 22.4 (CH₃), 15.1 (CH₃), 13.9 (CH₃). IR (ATR): 1644, 1591, 1484, 764, 728, 696 cm⁻¹. MS (ESI) m/z (relative intensity): 975 (71) [2M+Na]⁺, 499 (41) [M+Na]⁺, 477 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C₃₁H₃₃N₄O [M+H]⁺ 477.2654 found 477.2649.
2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methyl-3-(naphthalen-1-yl)isoquinolin-1(2H)-one (5bh)

The representative procedure was followed using [Fe(acac)₃] (21.1 mg, 0.06 mmol), dppe (29.9 mg, 0.075 mmol), 1b (85.8 mg, 0.30 mmol) and 1-(prop-1-yn-1-yl)naphthalene (4h) (99.6 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 5bh (75.1 mg, 56%) as a viscous brownish oil. Rf (n-hexane/EtOAc 1:1) = 0.35. ¹H-NMR (300 MHz, CDCl₃): δ = 8.59 (d, J = 8.1 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.78-7.72 (m, 2H), 7.62-7.54 (m, 2H), 7.53-7.45 (m, 2H), 7.45-7.32 (m, 3H), 5.27 (d, J = 14.5 Hz, 1H), 4.57 (d, J = 14.5 Hz, 1H), 4.22-4.11 (m, 2H), 1.92 (s, 3H), 1.83-1.72 (m, 2H), 1.34-1.16 (m, 6H), 0.90-0.78 (m, 3H). ¹³C-NMR (125 MHz, CDCl₃): δ = 162.5 (C₉), 144.0 (C₉), 138.0 (C₉), 137.3 (C₉), 133.5 (C₉), 132.5 (CH), 131.8 (C₉), 131.7 (C₉), 129.7 (CH), 129.1 (CH), 128.7 (CH), 128.2 (CH), 127.0 (CH), 126.7 (CH), 126.3 (CH), 125.6 (C₉), 125.5 (CH), 124.6 (CH), 123.4 (CH), 123.1 (CH), 112.2 (C₉), 50.1 (CH₂), 41.9 (CH₂), 31.0 (CH₂), 30.1 (CH₂), 26.1 (CH₂), 22.4 (CH₂), 14.6 (CH₃), 13.9 (CH₃). IR (ATR): 1645, 1592, 799, 775, 727, 696 cm⁻¹. MS (ESI) m/z (relative intensity): 923 (76) [2M+Na]⁺, 473 (18) [M+Na]⁺, 451 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C₂₉H₃₁N₄O [M+H]⁺ 451.2498 found 451.2492.
2-[(1-n-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-4-methyl-3-(2-methylthiophen-3-yl)isoquinolin-1(2H)-one (5bi)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 2-methyl-3-(prop-1-yn-1-yl)thiophene (4i) (81.6 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 5bi (85.4 mg, 68%) as a yellowish oil. Rf (n-hexane/EtOAc 1:1) = 0.39. 1H-NMR (300 MHz, CDCl3): δ = 8.50 (ddd, J = 8.1, 1.4, 0.6 Hz, 1H), 7.72-7.67 (m, 2H), 7.56 (s, 1H), 7.51 (ddd, J = 8.1, 6.4, 2.0 Hz, 1H), 7.22 (d, J = 5.1 Hz, 1H), 6.85 (dd, J = 5.1, 0.6 Hz, 1H), 5.13-5.02 (m, 2H), 4.20 (t, J = 7.2 Hz, 2H), 2.07 (s, 2H), 2.00 (s, 2H), 1.84-1.77 (m, 2H), 1.28-1.19 (m, 6H), 0.85-0.79 (m, 3H). 13C-NMR (125 MHz, CDCl3): δ = 162.5 (Cq), 143.9 (Cq), 139.1 (Cq), 137.1 (Cq), 134.7 (Cq), 132.4 (CH), 131.6 (Cq), 128.6 (CH), 128.0 (CH), 126.6 (CH), 125.4 (Cq), 123.4 (CH), 123.3 (CH), 123.2 (CH), 112.5 (Cq), 50.1 (CH2), 41.6 (CH2), 31.0 (CH2), 30.1 (CH2), 26.0 (CH2), 22.3 (CH2), 14.2 (CH3), 13.9 (CH3), 13.4 (CH3). IR (ATR): 1644, 1612, 1593, 1046, 766, 679 cm⁻¹. MS (ESI) m/z (relative intensity): 863 (28) [2M+Na]⁺, 443 (38) [M+Na]⁺, 421 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C24H29N4O5S [M+H]⁺ 421.2062 found 421.2057.
Reaction on one gram-scale

To a stirred solution of 1 (1.00 g, 3.5 mmol), ZnBr₂·TMEDA (2.40 g, 7.0 mmol), dppe (209 mg, 0.52 mmol) and the 4-octyne (1.1 ml, 7.0 mmol) in THF (4.0 ml), iPrMgBr (3.0 M in 2-MeTHF, 5.9 ml, 17.5 mmol) was added dropwise and the reaction mixture was stirred for 5 min at ambient temperature. Then, Fe(acac)₃ (124 mg, 0.35 mmol) was added in a single portion. After stirring the solution for additional 5 min, DCIB (0.8 ml, 7.0 mmol) was added. Then, the mixture was placed in a pre-heated oil bath at 60 °C. After stirring for 16 h, sat. aqueous NH₄Cl (15 ml) was added to the reaction mixture, which was extracted with CH₂Cl₂ (3 x15 ml). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated. Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3ba (952 mg, 69%) as a yellowish oil. Rₜ (n-hexane/EtOAc 1:1) = 0.57.
Probing SET-type mechanism

To a stirred solution of 1b (0.30 mmol), ZnBr$_2$·TMEDA (204.6 mg, 0.60 mmol), dppe (17.9 mg, 0.045 mmol) and the alkyne 2b (0.60 mmol) in THF (0.50 ml), iPrMgBr (3.0 M in 2-MeTHF, 500 µl, 1.5 mmol) was added dropwise and the reaction mixture was stirred for 5 min at ambient temperature. Then, Fe(acac)$_3$ (10.6 mg, 0.03 mmol) was added in a single portion. After stirring the solution for additional 5 min, an additive (0.30 mmol, 1.0 equiv) and DCIB (70 µl, 0.60 mmol) were added. Then, the mixture was placed in a pre-heated oil bath at 60 °C. After stirring for 16 h, sat. aqueous NH$_4$Cl (15 ml) was added to the reaction mixture, which was extracted with CH$_2$Cl$_2$ (3 x15 ml). The combined organic extracts were dried over Na$_2$SO$_4$, filtered and concentrated. The crude product was purified by column chromatography (n-hexane/EtOAc 9:1→ 3:1→1:1).

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<tr>
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</table>

[a] Reaction conditions: 1b (0.30 mmol), 2b (0.60 mmol), Fe(acac)$_3$ (0.03 mmol), dppe (0.045 mmol), additive (0.30 mmol), ZnBr$_2$·TMEDA (0.60 mmol, 2.0 equiv), iPrMgBr (1.50 mmol, 5.0 equiv), DCIB (0.60 mmol), THF (0.50 ml), 60 °C, 16 h, isolated yields; [b] TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl; [c] BHT = 2,6-bis(1,1-dimethylethyl)-4-methylphenol; [d] Galvinoxyl = 2,6-di-tert-butyl-α-(3,5-di-tert-butyl-4-oxo-2,5-cyclohexadien-1-ylidene)-p-tolyloxy.
(E)-2-(Dec-5-en-5-yl)-N-[(1-n-hexyl-1H-1,2,3-triazol-4-yl)methyl]benzamide (3bb´)

The representative procedure was followed using 1b (85.8 mg, 0.30 mmol) and 5-decyne (2b) (82.8 mg, 0.60 mmol). Purification by column chromatography (n-hexane/EtOAc 9:1→ 3:1) yielded 3bb´ (68.6 mg, 54%) as a white solid. M. p. = 76-79 °C. Rf (n-hexane/EtOAc 1:1) = 0.35. 1H-NMR (300 MHz, CDCl3): δ = 7.71 (dd, J = 7.4, 1.8 Hz, 1H), 7.58 (s, 1H), 7.39-7.24 (m, 2H), 7.09 (dd, J = 7.4, 1.8 Hz, 1H), 6.90 (t, J = 5.8 Hz, 1H), 5.46 (t, J = 7.0 Hz, 1H), 4.62 (t, J = 5.8 Hz, 2H), 4.31 (t, J = 7.0 Hz, 2H), 2.15-2.08 (m, 4H), 1.93-1.82 (m, 2H), 1.41-1.24 (m, 10H), 1.18-1.06 (m, 4H), 0.96-0.83 (m, 6H), 0.77 (t, J = 6.8 Hz, 3H). 13C-NMR (125 MHz, CDCl3): δ = 169.0 (Cq), 144.2 (Cq), 142.6 (Cq), 141.5 (Cq), 133.2 (Cq), 131.8 (CH), 131.6 (CH), 130.3 (CH), 128.9 (CH), 127.0 (CH), 122.1 (CH), 50.3 (CH₂), 35.4 (CH₂), 31.9 (CH₂), 31.7 (CH₂), 31.1 (CH₂), 30.4 (CH₂), 30.2 (CH₂), 27.9 (CH₂), 26.2 (CH₂), 22.6 (CH₂), 22.5 (CH₂), 22.3 (CH₂), 14.0 (CH₃), 13.9 (CH₃), 13.8 (CH₃). IR (ATR): 2925, 1653, 1260, 1060, 1021, 797 cm⁻¹. MS (ESI) m/z (relative intensity): 871 (26) [2M+Na]⁺, 447 (92) [M+Na]⁺, 425 (100) [M+H]⁺. HR-MS (ESI) m/z calcd for C₂₆H₄₁N₄O [M+H]⁺ 425.3280 found 425.3275.
Intermolecular KIE

To a stirred solution of 1b (0.15 mmol), [D]$_5$-1b (0.15 mmol), ZnBr$_2$•TMEDA (204.6 mg, 0.60 mmol), dppe (17.9 mg, 0.045 mmol) and 4-octyne (2a) (0.60 mmol) in THF (0.50 ml), iPrMgBr (3.0 M in 2-MeTHF, 500 µl, 1.5 mmol) was added dropwise and the reaction mixture was stirred for 5 min at ambient temperature. Then, Fe(acac)$_3$ (10.6 mg, 0.03 mmol) was added in a single portion. After stirring the solution for additional 5 min, DCIB (70 µl, 0.60 mmol) was added. Then, the mixture was placed in a pre-heated oil bath at 60 °C. After stirring for 3 h, sat. aqueous NH$_4$Cl (15 ml) was added to the reaction mixture, which was extracted with CH$_2$Cl$_2$ (3 x 15 ml). The combined organic extracts were dried over Na$_2$SO$_4$, filtered and concentrated. The crude product was purified by column chromatography (n-hexane/EtOAc 9:1→ 1:1). The mixture was analyzed by 600 MHz $^1$H-NMR spectroscopy to determine the ratio of 3ba'$/[D]_4$-3ba'$. 
\[ 3ba' / [D]_\text{aq}-3ba' = (0.55/0.45) = 1.2 \]
Intramolecular KIE

To a stirred solution of [D]-1b (0.30 mmol), ZnBr$_2$•TMEDA (204.6 mg, 0.60 mmol), dppe (17.9 mg, 0.045 mmol) and 4-octyne (2a) (0.60 mmol) in THF (0.50 ml), $i$PrMgBr (3.0 M in 2-MeTHF) (500 µl, 1.5 mmol) was added dropwise and the reaction mixture was stirred for 5 min at ambient temperature. Then, Fe(acac)$_3$ (10.6 mg, 0.03 mmol) was added in a single portion. After stirring the solution for additional 5 min, DCIB (70 µl, 0.60 mmol) was added. Then, the mixture was placed in a pre-heated oil bath at 60 °C. After stirring for 3 h, sat. aqueous NH$_4$Cl (15 ml) was added to the reaction mixture, which was extracted with CH$_2$Cl$_2$ (3 x15 ml). The combined organic extracts were dried over Na$_2$SO$_4$, filtered and concentrated. The crude product was purified by column chromatography (n-hexane/EtOAc 9:1→ 1:1). The mixture was analyzed by $^1$H-NMR spectroscopy to determine the ratio of [D]-3ba'/3ba'.

$k_4/k_0 = 1.1$
\[ \text{[D]-3ba}^-/3\text{ba}^- (1-0.48)/0.48 = 1.1 \]
References


$^1$H-, $^{13}$C-, $^{19}$F-NMR Spectra

$1b$ (300 MHz, CDCl$_3$)

$1b$ (125 MHz, CDCl$_3$)
1c (300 MHz, CDCl$_3$)

1c 125 MHz, CDCl$_3$)
$1f$ (300 MHz, CDCl$_3$)

$1f$ (125 MHz, CDCl$_3$)
$1g$ (300 MHz, CDCl$_3$)

$1g$ (125 MHz, CDCl$_3$)
1i (300 MHz, CDCl₃)

1i (125 MHz, CDCl₃)
$\text{Me}_2\text{N}$

$\text{H}$

$\text{N} \equiv \text{n-Hex}$

$\text{1I (300 MHz, CDCl}_3\text{)}$

\[\begin{array}{c}
\text{Me}_2\text{N} \\
\text{H} \\
\text{N} \equiv \text{n-Hex}
\end{array}\]

$\text{1I (125 MHz, CDCl}_3\text{)}$

\[\begin{array}{c}
\text{Me}_2\text{N} \\
\text{H} \\
\text{N} \equiv \text{n-Hex}
\end{array}\]
$1m$ (300 MHz, CDCl$_3$)

$1m$ (125 MHz, CDCl$_3$)
$1m$ (275 MHz, CDCl$_3$)
3ba (300 MHz, CDCl₃)

3ba (125 MHz, CDCl₃)
3ca (300 MHz, CDCl₃)

3ca (125 MHz, CDCl₃)
3ea (300 MHz, CDCl₃)

3ea (125 MHz, CDCl₃)
3fa (300 MHz, CDCl₃)

3fa (125 MHz, CDCl₃)
3ma (275 MHz, CDCl$_3$)
3bb (300 MHz, CDCl₃)

3bb (125 MHz, CDCl₃)
3bc (300 MHz, CDCl$_3$)

3bc (125 MHz, CDCl$_3$)
$5ba$ (300 MHz, CDCl$_3$)

$5ba$ (125 MHz, CDCl$_3$)
$5bc$ (300 MHz, CDCl$_3$)

$5bc$ (125 MHz, CDCl$_3$)
$5bc$ (275 MHz, CDCl$_3$)
$5\text{be (300 MHz, CDCl}_3)$

$5\text{be (125 MHz, CDCl}_3)$
5bf (300 MHz, CDCl₃)

5bf (125 MHz, CDCl₃)