Palladium-catalyzed selective synthesis of 3,4-dihydroquinazolines from electron-rich aryamines, electron-poor arylamines and glyoxalates

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1. General information

Unless otherwise specified, all reagents and solvents were obtained from commercial suppliers and used without further purification. All reagents were weighed and handled in air at room temperature. Chromatographic purifications were carried out on a Biotage Isolera Four instrument. $^1$H NMR and $^{13}$C NMR spectra were obtained in CDCl$_3$ with TMS as internal standard (600 MHz $^1$H and 150 MHz $^{13}$C) at room temperature, the chemical shifts ($\delta$) were expressed in ppm and $J$ values were given in Hz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), doublet of quartets (dq) and multiplet (m). All first order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). In a few cases the number of signals in the $^{13}$C NMR spectrum is than due, which may be caused by the superimposition of signals. HRMS data were obtained by ESI on a TOF mass analyzer.
3. Screening of reaction conditions

Table S1

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<sup>a</sup> Reaction conditions: 1<sub>a</sub> (0.6 mmol), 2<sub>a</sub> (0.5 mmol), 3<sub>a</sub> (1.2 mmol), 5 mol% catalyst, MeCN (2 mL), 60°C, 24h; <sup>b</sup>isolated yields.

Table S2

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<td>16&lt;sup&gt;f&lt;/sup&gt;</td>
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4. General procedure

3.1 Palladium-catalyzed synthesis of 3,4-dihydroquinazolines from electron-rich arylamines, electron-poor arylamines and glyoxalates

To a mixture of electron-rich arylamine 1 (0.6 mmol), electron-poor arylamine 2 (0.5 mmol), glyoxalate 3 (1.2 mmol), PdCl₂ (5 mol%), and 4-nitrothiophenol (10 mol %) in a 25 mL round-bottomed flack at room temperature, was added CH₃CN (2 ml). The reaction vessel was allowed to stir at 60°C for 24-36h. After the reaction, the solvent was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product 4.

3.2 Palladium-catalyzed synthesis of 3,4-dihydroquinazolines from arylamines and glyoxalates
To a mixture of arylamine 1 (0.5 mmol), glyoxalate 3 (1.2 mmol), PdCl$_2$ (5 mol%), and 4-nitrothiophenol (10 mol %) in a 25 mL round-bottomed flack at room temperature, was added CH$_3$CN (2 ml). The reaction vessel was allowed to stir at 60°C for 24-36h. After the reaction, the solvent was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product 5.

4. Characterization data of products (4a-5i, 7b)

4a, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta = 1.15$ (t, $J = 7.1$ Hz, 3H), 1.24 (t, $J = 7.1$ Hz, 3H), 3.81 (s, 3H), 4.17-4.30 (m, 4H), 5.28 (s, 1H), 6.76 (d, $J = 2.7$ Hz, 1H), 6.91 (dd, $J = 2.8, 8.7$ Hz, 1H), 6.97-6.99 (m, 1H), 7.12 (t, $J = 8.6$ Hz, 1H), 7.19 (dd, $J = 2.8, 6.2$ Hz, 1H), 7.40 (d, $J = 8.7$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta =$ 13.8, 14.0, 55.6, 62.30, 62.33, 63.5, 111.7, 115.1, 117.0 (d, $J_{C-F} = 22.3$ Hz), 121.6, 121.8 (d, $J_{C-F} = 18.7$ Hz), 122.9 (d, $J_{C-F} = 7.1$ Hz), 125.4, 127.6, 133.2, 140.6, 144.3, 156.2 (d, $J_{C-F} = 247.8$ Hz), 159.3, 161.9, 169.3; HRMS calculated for C$_{21}$H$_{20}$ClFN$_2$NaO$_5$(ESI), 457.0942; found, 457.0937.

4b, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta = 1.06$ (t, $J = 7.1$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H), 3.80 (s, 3H), 4.11-4.26 (m, 4H), 5.29 (s, 1H), 6.74 (d, $J = 2.5$ Hz, 1H), 6.88 (dd, $J = 2.6, 8.7$ Hz, 1H), 7.03 (t, $J = 8.5$ Hz, 2H), 7.09 (dd, $J = 4.6, 8.8$ Hz, 2H), 7.37 (d, $J = 8.8$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta =$ 13.7, 14.1, 55.6, 62.2,
63.6, 111.6, 115.1, 116.3 (d, $J_{CF} = 22.6$ Hz), 121.4, 124.9 (d, $J_{CF} = 8.2$ Hz), 127.5, 133.3, 140.0, 145.0, 159.0, 160.8 (d, $J_{CF} = 239.1$ Hz), 162.2, 169.7; HRMS calculated for C$_{21}$H$_{22}$FN$_2$O$_5$ (ESI): 401.1519; found, 401.1507.

4c, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.10 (t, $J = 7.1$ Hz, 3H), 1.23 (t, $J = 7.1$ Hz, 3H), 3.81 (s, 3H), 4.14-4.26 (m, 4H), 5.29 (s, 1H), 6.76 (s, 1H), 6.90 (d, $J = 8.6$ Hz, 1H), 7.01 (d, $J = 8.4$ Hz, 2H), 7.31 (d, $J = 8.4$ Hz, 2H), 7.40 (d, $J = 8.7$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 55.6, 62.19, 62.23, 63.3, 111.7, 115.1, 121.7, 123.9, 127.6, 129.5, 131.6, 133.3, 142.5, 144.5, 159.2, 162.1, 169.5; HRMS calculated for C$_{21}$H$_{21}$ClN$_2$NaO$_5$ (ESI): 439.1037; found, 439.1031.

4d, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.10 (t, $J = 7.1$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H), 3.80 (s, 3H), 4.13-4.27 (m, 4H), 5.28 (s, 1H), 6.76 (d, $J = 2.6$ Hz, 1H), 6.90 (dd, $J = 2.6$, 8.8 Hz, 1H), 6.94 (d, $J = 8.4$ Hz, 2H), 7.40 (d, $J = 8.7$ Hz, 1H), 7.46 (d, $J = 8.5$ Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.1, 55.6, 62.28, 62.35, 63.1, 111.7, 115.1, 119.2, 121.8, 123.9, 127.6, 132.4, 133.2, 142.9, 144.4, 159.2, 162.1, 169.6; HRMS calculated for C$_{21}$H$_{21}$BrN$_2$NaO$_5$ (ESI): 483.0512; found, 483.0526.

4e, reaction time 36h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.12 (t, $J = 7.1$ Hz, 3H), 1.23 (t, $J = 7.1$ Hz, 3H), 2.57 (s, 3H), 3.81 (s, 3H), 4.11-4.29 (m, 4H), 5.34 (s, 1H), 6.79 (d, $J = 2.6$ Hz, 1H), 6.91 (dd, $J = 2.7$, 8.7 Hz, 1H), 7.07 (d, $J = 8.6$ Hz, 2H), 7.44
(d, J = 8.7 Hz, 1H), 7.95 (d, J = 8.6 Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 26.5, 55.6, 62.3, 62.4, 62.7, 111.9, 115.2, 120.9, 122.3, 127.8, 129.8, 133.1, 133.8, 143.9, 147.7, 159.5, 162.0, 169.3, 196.5; HRMS calculated for C$_{23}$H$_{24}$N$_2$NaO$_6$(ESI): 447.1505; found, 447.1527.

$^{4f}$, reaction time 36h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.09 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 3.82 (s, 3H), 3.91 (s, 3H), 4.13-4.28 (m, 4H), 5.34 (s, 1H), 6.79 (d, J = 2.6 Hz, 1H), 6.91 (dd, J = 2.8, 8.7 Hz, 1H), 7.05 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.8 Hz, 1H), 8.02 (d, J = 8.6 Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 52.2, 55.6, 62.28, 62.35, 62.7, 111.8, 115.2, 120.8, 122.3, 126.8, 127.8, 130.9, 133.2, 144.0, 147.7, 159.4, 162.1, 166.2, 169.4; HRMS calculated for C$_{23}$H$_{24}$N$_2$NaO$_7$(ESI): 463.1457; found, 463.1476.

$^{4g}$, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.14 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 4.16-4.27 (m, 4H), 5.26 (s, 1H), 6.70 (s, 1H), 6.98-7.00 (m, 1H), 7.01 (s, 1H), 7.12 (t, J = 8.6 Hz, 1H), 7.19 (dd, J = 2.7, 6.1 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.8, 14.1, 56.0, 56.2, 62.2, 62.4, 63.2, 108.8, 109.3, 111.9, 117.1 (d, $J_{CF} = 22.3$ Hz), 121.8 (d, $J_{CF} = 18.5$ Hz), 123.0 (d, $J_{CF} = 7.1$ Hz), 125.6, 133.3, 140.6, 144.8, 149.9, 156.3 (d, $J_{CF} = 248.2$ Hz), 161.8, 169.5; HRMS calculated for C$_{22}$H$_{23}$ClFN$_2$O$_6$ (ESI): 465.1219; found, 465.1223.

$^{4h}$, reaction time 24h, $^1$H NMR (600 MHz, (CD$_3$)$_2$CO): $\delta$ = 1.09 (t, J = 7.1
Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 4.09-4.20 (m, 4H), 5.59 (s, 1H), 6.80 (d, J = 2.6 Hz, 1H), 6.85 (dd, J = 2.7, 8.5 Hz, 1H), 7.14-7.18 (m, 2H), 7.33-7.36 (m, 2H), 8.70 (brs, 1H); $^{13}$C NMR (150 MHz, [D$_6$]-Acetone): $\delta$ = 13.1, 13.4, 61.4, 61.6, 62.6, 113.4, 116.3, 117.1 (d, $J_{CF}$ = 22.3 Hz), 120.6 (d, $J_{CF}$ = 18.7 Hz), 122.2, 124.0 (d, $J_{CF}$ = 7.3 Hz), 125.5, 126.9, 132.4, 140.9, 144.0, 155.9 (d, $J_{CF}$ = 244.9 Hz), 157.2, 161.8, 169.4; HRMS calculated for C$_{20}$H$_{18}$ClFN$_2$NaO$_5$ (ESI): 443.0776; found, 443.0780.

4i, reaction time 24h, $^1$H NMR (600 MHz, (CD$_3$)$_2$CO): $\delta$ = 1.13 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H), 4.13-4.23 (m, 4H), 5.71 (s, 1H), 6.87-6.90 (m, 2H), 7.24 (d, J = 8.5 Hz, 1H), 7.26 (d, J = 9.1 Hz, 2H), 8.27 (d, J = 9.1 Hz, 2H), 8.93 (brs, 1H); $^{13}$C NMR (150 MHz, [D$_6$]-Acetone): $\delta$ = 13.2, 13.4, 61.5, 61.7, 61.8, 113.7, 116.4, 121.0, 123.3, 124.8, 127.3, 132.3, 142.7, 144.0, 149.4, 157.7, 161.6, 169.0; HRMS calculated for C$_{20}$H$_{20}$N$_3$O$_7$ (ESI): 414.1294; found, 414.1296.

4j, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.14 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H), 2.61 (s, 1H), 4.17-4.22 (m, 4H), 5.27 (s, 1H), 6.76 (d, J = 2.5 Hz, 1H), 6.83 (dd, J = 2.6, 8.6 Hz, 1H), 7.26-7.30 (m, 2H), 7.35-7.37 (m, 1H), 7.79 (dd, J = 2.8, 6.0 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 62.7, 62.9, 63.2, 113.6, 117.2, 119.4 (d, $J_{CF}$ = 21.9 Hz), 120.2, 121.8, 127.4, 129.8 (d, $J_{CF}$ = 8.1 Hz), 131.8, 137.3 (d, $J_{CF}$ = 8.3 Hz), 140.3, 143.4, 153.2 (d, $J_{CF}$ = 264.4 Hz), 157.0, 161.3, 169.1; HRMS calculated for C$_{20}$H$_{19}$FNO$_4$ (ESI): 432.1201; found, 432.1202.
4k, reaction time 36h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.14 (t, $J$ = 7.1 Hz, 3H), 1.23 (t, $J$ = 7.1 Hz, 3H), 2.61 (s, 1H), 4.17-4.30 (m, 4H), 5.30 (s, 1H), 6.78 (d, $J$ = 2.5 Hz, 1H), 6.84 (dd, $J$ = 2.6, 8.5 Hz, 1H), 6.91 (s, 1H), 6.94 (dd, $J$ = 2.2, 8.8 Hz, 1H), 7.34 (d, $J$ = 8.6 Hz, 1H), 8.05 (d, $J$ = 8.8 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 21.2, 62.4, 62.6, 62.7, 113.5, 117.0, 119.0, 122.5, 124.5, 126.6, 127.7, 132.3, 136.1, 143.4, 145.4, 147.5, 156.7, 161.6, 169.1; HRMS calculated for C$_{21}$H$_{21}$ClFN$_3$NaO$_7$(ESI): 450.1268; found, 450.1272.

4l, reaction time 36h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.09 (t, $J$ = 7.1 Hz, 3H), 1.23 (t, $J$ = 7.1 Hz, 3H), 2.48 (s, 3H), 4.13-4.27 (m, 4H), 5.29 (s, 1H), 7.03 (d, $J$ = 8.6 Hz, 2H), 7.09 (s, 1H), 7.22 (d, $J$ = 8.3 Hz, 1H), 7.32 (d, $J$ = 8.6 Hz, 2H), 7.36 (d, $J$ = 8.3 Hz, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 16.0, 62.29, 62.33, 63.2, 121.1, 124.2, 124.3, 126.6, 127.6, 129.5, 132.0, 137.1, 138.2, 142.2, 145.8, 162.0, 169.3; HRMS calculated for C$_{21}$H$_{22}$ClN$_2$O$_4$S(ESI): 433.0991; found, 433.0983.

4m, reaction time 24h, $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 1.09 (t, $J$ = 7.1 Hz, 3H), 1.24 (t, $J$ = 7.1 Hz, 3H), 4.13-4.28 (m, 8H), 5.21 (s, 1H), 6.74 (s, 1H), 6.99-7.01 (m, 3H), 7.31 (dd, $J$ = 1.9, 6.8 Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 13.7, 14.0, 62.1, 62.2, 62.7, 64.3, 64.4, 113.9, 114.71, 114.73, 124.0, 129.5, 131.7, 133.9, 142.4, 143.3, 144.3, 145.2, 162.1, 169.7; HRMS calculated for C$_{22}$H$_{21}$ClN$_2$NaO$_6$(ESI): 467.0988; found, 467.0980.
4n, reaction time 36h, (isomers mixture); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 0.54\) (d, \(J = 6.9\) Hz, 6H), 0.59 (d, \(J = 6.9\) Hz, 3H), 0.70-0.74 (m, 10H), 0.77-0.79 (m, 5H), 0.83 (d, \(J = 6.6\) Hz, 6H), 0.85-0.89 (m, 17H), 0.91-1.06 (m, 10H), 1.24-1.28 (m, 3H), 1.30-1.37 (m, 4H), 1.40-1.45 (m, 5H), 1.56-1.59 (m, 2H), 1.62-1.67 (m, 9H), 1.72 (m, 3H), 1.80-1.85 (m, 1H), 1.89-1.91 (m, 2H), 2.01-2.03 (m, 2H), 3.788 (s, 3H), 3.79 (s, 3H), 4.62-4.74 (m, 4H), 5.22 (s, 1H), 5.25 (s, 1H), 6.70 (d, \(J = 2.6\) Hz, 1H), 6.74 (d, \(J = 2.6\) Hz, 1H), 6.86-6.89 (m, 2H), 6.99-7.00 (m, 2H), 7.08-7.12 (m, 2H), 7.18-7.20 (m, 2H), 7.34-7.40 (m, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta = 15.5, 15.7, 15.9, 16.0, 20.6, 20.8, 21.8, 21.9, 22.0, 22.77, 22.8, 23.1, 23.2, 25.3, 25.7, 25.91, 25.95, 31.2, 31.3, 31.4, 33.97, 34.0, 34.07, 34.1, 39.8, 40.2, 40.5, 40.6, 46.61, 46.64, 47.0, 47.1, 55.5, 55.6, 63.6, 64.0, 111.0, 111.6, 115.1, 115.2, 116.9 (d, \(J_{CF} = 22.3\) Hz), 117.2 (d, \(J_{CF} = 22.2\) Hz), 121.57, 121.6, 121.7 (d, \(J_{CF} = 18.8\) Hz), 122.1 (d, \(J_{CF} = 18.8\) Hz), 122.7 (d, \(J_{CF} = 6.7\) Hz), 123.3 (d, \(J_{CF} = 6.8\) Hz), 125.2, 125.9, 127.6, 127.9, 133.2, 133.4, 140.6, 140.8, 144.6, 144.7, 156.2 (d, \(J_{CF} = 237.7\) Hz), 156.4 (d, \(J_{CF} = 248.0\) Hz), 159.1, 161.7, 162.3, 169.0, 169.1; HRMS calcd for C\(_{37}\)H\(_{48}\)ClFN\(_2\)NaO\(_5\): 677.3139; found, 677.3128.

5a, reaction time 24h, \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 1.06\) (t, \(J = 7.1\) Hz, 3H), 1.23 (t, \(J = 7.1\) Hz, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 4.10-4.27 (m, 4H), 5.31 (s, 1H), 6.74 (d, \(J = 2.7\) Hz, 1H), 6.85-6.89 (m, 3H), 7.07 (d, \(J = 8.8\) Hz, 2H), 7.36 (d, \(J = 8.8\) Hz, 1H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta = 13.7, 14.0, 55.51, 55.56, 61.92, 61.98, 64.0, 111.5, 114.5, 115.0, 121.2, 125.3, 127.3, 133.6, 136.7, 145.8, 158.2, 158.7, 162.5, 169.8; HRMS calculated for C\(_{22}\)H\(_{25}\)N\(_2\)O\(_6\)(ESI): 413.1708; found, 413.1713.
5b, reaction time 24h, \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 1.06 (t, J = 7.1\) Hz, 3H), 1.22 (t, \(J = 7.1\) Hz, 3H), 2.33 (s, 3H), 2.34 (s, 3H), 4.10-4.27 (m, 4H), 5.31 (s, 1H), 6.99 (d, \(J = 8.2\) Hz, 2H), 7.02 (s, 1H), 7.14 (d, \(J = 8.1\) Hz, 3H), 7.32 (d, \(J = 8.0\) Hz, 1H); \(^1\)C NMR (150 MHz, CDCl\(_3\)): \(\delta = 13.6, 14.0, 20.9, 21.1, 61.9, 62.0, 63.5, 120.3, 123.0, 125.9, 126.8, 129.9, 130.3, 136.2, 137.2, 137.6, 141.2, 146.6, 162.5, 170.0\); HRMS calculated for C\(_{22}\)H\(_{25}\)N\(_2\)O\(_4\) (ESI): 381.1818; found, 381.1814.

5c, reaction time 24h, \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 1.08 (t, J = 7.1\) Hz, 3H), 1.23 (t, \(J = 7.1\) Hz, 3H), 2.47 (s, 3H), 2.48 (s, 3H), 4.11-4.28 (m, 4H), 5.30 (s, 1H), 7.03 (d, \(J = 8.6\) Hz, 2H ), 7.10 (d, \(J = 2.0\) Hz, 1H), 7.22 (d, \(J = 8.7\) Hz, 3H), 7.36 (d, \(J = 8.4\) Hz, 1H); \(^1\)C NMR (150 MHz, CDCl\(_3\)): \(\delta = 13.7, 14.0, 16.1, 62.2, 63.3, 121.0, 123.6, 124.3, 126.5, 127.6, 127.65, 137.0, 137.4, 137.8, 140.8, 146.3, 162.2, 169.5\); HRMS calculated for C\(_{22}\)H\(_{25}\)N\(_2\)O\(_4\)S\(_2\) (ESI): 445.1260; found, 445.1256.

5d, reaction time 24h, \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 1.07 (t, J = 7.1\) Hz, 3H), 1.23 (t, \(J = 7.1\) Hz, 3H), 2.22 (s, 3H), 2.23 (s, 3H), 2.24 (s, 3H), 2.25 (s, 3H), 4.11-4.26 (m, 4H), 5.30 (s, 1H), 6.82 (d, \(J = 8.0\) Hz, 1H), 6.86 (s, 1H), 6.96 (s, 1H), 7.07 (d, \(J = 8.0\) Hz, 1H), 7.21 (s, 1H); \(^1\)C NMR (150 MHz, CDCl\(_3\)): \(\delta = 13.7, 14.0, 19.2, 19.4, 19.6, 19.8, 61.8, 61.9, 63.2, 117.8, 120.4, 124.2, 126.9, 127.2, 130.4, 134.8, 135.9, 137.7, 137.8, 138.0, 141.5, 146.7, 162.6, 170.2\); HRMS calculated for C\(_{24}\)H\(_{29}\)N\(_2\)O\(_4\) (ESI): 409.2114; found, 409.2127.
5e, reaction time 36h, ¹H NMR (600 MHz, CDCl₃): δ = 0.96 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H), 4.07-4.15 (m, 4H), 5.23 (s, 1H), 6.94 (d, J = 8.7 Hz, 2H), 7.09 (d, J = 1.7 Hz, 1H), 7.16-7.25 (m, 33H), 7.31 (d, J = 8.4 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃): δ = 13.6, 14.0, 61.9, 62.1, 62.9, 64.6, 64.8, 119.4, 121.6, 124.9, 126.1, 127.4, 127.57, 127.6, 129.4, 130.9, 131.1, 132.0, 132.2, 137.8, 141.2, 145.0, 146.1, 146.4, 146.5, 147.0, 162.6, 169.6; HRMS calculated for C₅₈H₄₅N₂O₄(ESI): 837.3669; found, 837.3692.

5f, reaction time 36h, ¹H NMR (600 MHz, CDCl₃): δ = 0.95 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.25-1.28 (m, 2H), 1.34-1.42 (m, 8H), 1.74 (d, J = 12.7 Hz, 2H), 1.83-1.86 (m, 8H), 2.48 (d, J = 7.7 Hz, 2H), 4.06-4.18 (m, 3H), 4.23-4.29 (m, 1H), 5.35 (s, 1H), 7.01 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 1.6 Hz, 1H), 7.16-7.18 (m, 3H), 7.34 (d, J = 8.1 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃): δ = 13.5, 14.0, 26.0, 26.1, 26.8, 34.3, 34.4, 34.5, 44.0, 44.2, 61.9, 63.5, 120.3, 122.9, 124.7, 125.8, 127.7, 128.0, 137.9, 141.4, 146.4, 146.6, 147.4, 162.6, 170.0; HRMS calculated for C₃₂H₄₁N₂O₄(ESI): 517.3072; found, 517.3066.

5g, reaction time 36h, ¹H NMR (600 MHz, CDCl₃): δ = 1.08 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 1.75-1.77 (m, 8H), 2.70-2.76 (m, 8H), 4.11-4.27 (m, 4H), 5.28 (s, 1H), 6.76 (s, 1H), 6.80 (dd, J = 2.3, 8.1 Hz, 1H), 6.90 (s, 1H), 7.00 (d, J = 8.0 Hz, 1H), 7.13 (s, 1H); ¹³C NMR (150 MHz, CDCl₃): δ = 13.7, 14.0, 22.9, 22.96, 23.0,
23.1, 28.9, 29.19, 29.22, 29.4, 61.86, 61.9, 63.2, 118.0, 120.2, 123.3, 126.1, 126.7, 129.9, 135.4, 136.6, 137.4, 138.3, 138.5, 141.1, 146.6, 162.6, 170.3; HRMS calculated for \( \text{C}_{28}\text{H}_{32}\text{N}_{2}\text{NaO}_{4} \) (ESI): 483.2266; found, 483.2254.

5h, reaction time 24h, \(^1\)H NMR (600 MHz, CDCl$_3$): \( \delta = 1.04 \) (t, \( J = 7.1 \) Hz, 3H), 1.25 (t, \( J = 7.1 \) Hz, 3H), 3.90 (d, \( J = 3.7 \) Hz, 1H), 3.93 (s, 2H), 4.13-4.31 (m, 4H), 5.57 (s, 1H), 7.16 (dd, \( J = 2.0, 8.1 \) Hz, 1H), 7.29-7.40 (m, 5H), 7.54 (t, \( J = 6.4 \) Hz, 2H), 7.62 (s, 1H), 7.64 (s, 1H), 7.74-7.77 (m, 3H); \(^{13}\)C NMR (150 MHz, CDCl$_3$): \( \delta = 13.7, 14.1, 36.9, 37.0, 62.12, 62.14, 64.1, 117.7, 119.6, 119.8, 119.9, 120.0, 120.4, 122.0, 122.7, 125.09, 125.11, 126.9, 127.0, 139.0, 140.1, 140.7, 140.9, 141.1, 142.4, 143.3, 143.6, 144.6, 144.7, 146.6, 162.6, 170.1 \); HRMS calculated for \( \text{C}_{34}\text{H}_{29}\text{N}_{2}\text{O}_{4} \) (ESI): 529.2128; found, 529.2127.

5i, reaction time 36h, (isomers mixture); \(^1\)H NMR (600 MHz, CDCl$_3$): \( \delta = 0.48 \) (d, \( J = 7.0 \) Hz, 3H), 0.50 (d, \( J = 6.8 \) Hz, 3H), 0.59 (d, \( J = 6.9 \) Hz, 3H), 0.67-0.71 (m, 9H), 0.78-0.79 (m, 9H), 0.82-0.89 (18H), 0.92-1.05 (m, 8H), 1.30-1.38 (m, 6H), 1.40-1.46 (m, 3H), 1.51-1.64 (m, 6H), 1.76-1.81 (m, 1H), 1.86-1.97 (m, 3H), 3.78-3.79 (m, 12H), 4.57-4.72 (m, 4H), 5.25 (s, 1H), 5.30 (s, 1H), 6.68 (d, \( J = 2.7 \) Hz, 1H), 6.72 (d, \( J = 2.7 \) Hz, 1H), 6.83-6.87 (m, 6H), 7.06-7.09 (m, 4H), 7.34-7.37 (m, 2H); \(^{13}\)C NMR (150 MHz, CDCl$_3$): \( \delta = 15.5, 15.7, 15.9, 16.1, 20.6, 20.91, 20.92, 21.0, 21.91, 21.93, 22.0, 22.8, 23.0, 23.2, 24.9, 25.6, 25.7, 25.8, 31.2, 31.3, 31.4, 34.00, 34.07, 34.1, 34.2, 39.6, 40.2, 40.5, 40.6, 46.5, 46.6, 47.0, 47.1, 55.4, 55.5, 55.6, 64.1, 64.5, 110.7, 111.4, 114.5, 114.6, 115.0, 115.1, 121.3, 121.4, 124.9, 125.5, 127.2, 127.5,
133.7, 133.9, 136.7, 137.1, 146.1, 158.1, 158.3, 158.5, 162.4, 162.9, 169.5, 169.6; HRMS calculated for $\text{C}_{38}\text{H}_{53}\text{N}_{2}\text{O}_{6}$ (ESI): 633.3909; found, 633.3904.

$\textbf{7b}$, $^1\text{H}$ NMR (600 MHz, CDCl$_3$): $\delta = 1.09$ (t, $J = 7.1$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H), 2.25 (s, 6H), 4.06-4.15 (m, 2H), 4.18-4.22 (m, 2H), 4.70 (brs, 1H), 5.15 (s, 1H), 5.63 (s, 1H), 6.66 (d, $J = 8.0$ Hz, 1H), 6.88 (d, $J = 8.3$ Hz, 2H), 6.94 (d, $J = 7.9$ Hz, 1H), 7.03 (d, $J = 8.2$ Hz, 2H), 7.11 (s, 1H); $^{13}\text{C}$ NMR (150 MHz, CDCl$_3$): $\delta = 14.0$, 14.1, 20.5, 20.7, 61.4, 61.5, 62.9, 67.7, 116.6, 118.6, 118.9, 127.9, 129.1, 129.3, 129.7, 131.4, 139.0, 144.8, 170.2, 172.1; HRMS calculated for $\text{C}_{22}\text{H}_{26}\text{N}_{2}\text{NaO}_{4}$ (ESI): 405.1791; found, 405.1785.
5. Copies of NMR spectra for 4a–5i, 7b
4C

4C