Supporting Information

Construction of Highly Functional α-Amino Nitriles via a Novel Multicomponent Tandem Organocatalytic Reaction: a Facile Access to α-Methylene γ-Lactams

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I. General Information

Flasks and reaction tubes were sealed with rubber plugs. Reactions were monitored by thin-layer chromatography (TLC) visualizing with ultraviolet light (UV), KMnO₄, iodine, p-anisaldehyde stain, and phosphomolybdic acid (PMA) stain. Organic solutions were concentrated under reduced pressure using a rotary evaporator with an ice-water bath. Column chromatography was performed using silica gel (200-300) mesh.

II. Preparation of Substrates

III. General Procedure for Screening Reaction

IV. General Procedure for Tandem Organocatalytic Strecker-Allylic-Alkylation Reaction

V. General Procedure for the Synthesis of α-Methylene-γ-Butyrolactones

VI. Procedure for Chemical Transformations

VII. NMR Spectra

VIII. References

Materials. All reagents were obtained commercially and used without further purification with the following exceptions. Dichloromethane (DCM), toluene, acetonitrile (CH₃CN), and tert-butyl alcohol (t-BuOH) were dried by distillation from CaH₂; tetrahydrofuran (THF) and 1,4-Dioxane were dried by distillation from Na; benzaldehyde and furaldehyde were purified by distillation at reduced pressure; 1,4-diazabicyclo[2.2.2]octane (DABCO) was purified by recrystallization; triethylamine (TEA) was purified by distillation from CaH₂.

Instrumentation. Proton nuclear magnetic resonance (¹H NMR) spectra and carbon nuclear magnetic resonance (¹³C NMR) spectra were recorded on a Varian Mercury (300 or 400 and 75 or 100 MHz, respectively). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane (TMS) and are referenced to residual protium in the NMR solvent (CHCl₃ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane (TMS) and are referenced to the carbon resonances of the solvent residual peak (CDCl₃ = δ 77.16 ppm). NMR data are presented as follows: chemical shift (δ ppm), multiplicity.
(s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hertz (Hz), integration.

Mass spectra were in general recorded on the Bruker MicrOTOF Q II.

II. Preparation of Substrates

\[
\text{HN}^\text{Ph} \quad \text{PhCN} \\
\text{1a}
\]

\(\text{α-Aminonitriles (1a) was prepared according to a published procedure}^1; \text{ the spectral data were in agreement with literature values.}\)

\[
\text{OR}^4 \quad \text{CO}_2\text{R}^3 \\
\text{2}
\]

\(\text{MBH carbonates 2 were prepared according to a published procedure}^2,^3,^4; \text{ spectral data were in agreement with literature values.}\)

III. General Procedure for Screening Reaction

To a dried reaction tube were added \(1a\) (0.3 mmol), DABCO (20%), CH\(_3\)CN (3 ml) and \(2\) (0.45 mmol). The mixture was stirred at \(30 \, ^\circ\text{C}\) and the reaction was monitored by TLC. Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide following compounds.

Table 1 Optimization of Lewis base-Catalyzed Direct Allylic Alkylation of α-Amino Nitrile \(1a\) with MBH Carbonate \(2^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>solvent</th>
<th>(t) (h)</th>
<th>yield (%) (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DABCO</td>
<td>PhCH(_3)</td>
<td>4</td>
<td>52(3a); 14(13)</td>
</tr>
<tr>
<td>2</td>
<td>DABCO</td>
<td>DCM</td>
<td>9</td>
<td>50(3a); 18(13)</td>
</tr>
<tr>
<td>3</td>
<td>DABCO</td>
<td>THF</td>
<td>4</td>
<td>36(3a); 33(13)</td>
</tr>
<tr>
<td>4</td>
<td>DABCO</td>
<td>CHCl(_3)</td>
<td>22</td>
<td>40(3a); 43(12)</td>
</tr>
<tr>
<td>5</td>
<td>DABCO</td>
<td>1,4-dioxane</td>
<td>15</td>
<td>62(3a)</td>
</tr>
<tr>
<td>6</td>
<td>DABCO</td>
<td>(t)-BuOH</td>
<td>9</td>
<td>56(3a)</td>
</tr>
<tr>
<td>7</td>
<td>DABCO</td>
<td>DMF</td>
<td>2</td>
<td>79(3a); 5(4a)</td>
</tr>
<tr>
<td>8</td>
<td>DABCO</td>
<td>CH(_3)CN</td>
<td>3.5</td>
<td>32(3a); 50(4a)</td>
</tr>
<tr>
<td>9(^c)</td>
<td>DABCO</td>
<td>CH(_3)CN</td>
<td>14</td>
<td>93(3a)</td>
</tr>
</tbody>
</table>
IV. General Procedure for Tandem Organocatalytic Strecker-Allylic-Alkylation Reaction

To a dried reaction tube were added aldehyde (0.3 mmol) and amine (0.315 mmol). After the mixture was stirred at rt for 10 min, TMSCN (0.33 mmol) was added, and the mixture was vigorously stirred. After 50 min, CH₃CN (3 ml), DABCO (20%) and compound 2 (0.45 mmol) were added. The reaction was monitored by TLC. Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide 3.

3aa: This compound was synthesized according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:2), which afforded 87 mg of a white solid (95%, yield). mp 118 -119 °C. ¹H NMR (300 MHz, CDCl₃) 7.61-7.58 (m, 2H), 7.42 - 7.34 (m, 3H), 7.11 - 7.06 (m, 2H), 6.76-6.71 (m, 1H), 6.52 – 6.47 (m, 2H), 6.46 - 6.44 (m, 1H), 5.86 (br,1H), 5.73 - 5.72 (m, 1H), 3.82 (s, 3H), 3.08 (d, J = 13.8 Hz, 1H), 3.01 (d, J = 13.8 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 168.60, 143.40, 138.07, 133.19, 132.82, 128.91, 125.66, 119.16, 119.04, 61.98, 52.56, 46.14. IR (KBr): 3371, 3065, 3028, 2925, 2869, 2245, 1726, 1632, 1527, 1499, 1321, 1203, 756, 732, 696 cm⁻¹. HRMS (ESI): calcd. for C₁₀H₁₆N₂O₂Na ([M+Na⁺]: 329.1260, found 329.1258.

Unless otherwise noted, reactions were performed with 0.3 mmol of 1a, 0.45 mmol of 2a, and 20 mol % of catalyst in 3.0 mL of solvent at 30 °C. Isolated yield. 4Å molecular sieve was added and the reaction was performed at 0 °C. MBH acetate 2e (0.45 mmol) was employed. Based on ¹H NMR of the mixture 1a and 12 which can’t be separated by column chromatography.
3ab: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 87 mg of a white amorphous solid (85%, yield). \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.57-7.54 (m, 2H), 7.43-7.35 (m, 3H), 7.03 (d, J = 8.7 Hz, 2H), 6.46 (s, 1H), 6.42 (d, J = 8.6 Hz, 2H), 6.07 (br, 1H), 5.74 (s, 1H), 3.83 (s, 3H), 3.06 (d, J = 13.9 Hz, 1H), 2.98 (d, J = 13.9 Hz, 1H). \(^1\)C NMR (75 MHz, CDCl\(_3\)) δ 168.79, 142.03, 137.61, 133.10, 133.00, 129.01, 128.79, 128.65, 125.55, 123.79, 118.88, 116.16, 62.05, 52.66, 46.10. IR (KBr): 3357, 3063, 2951, 2928, 2229, 1727, 1630, 1600, 1493, 1446, 1310, 1203, 818, 735, 698 cm\(^{-1}\). HRMS (ESI): calcd. for C\(_{19}\)H\(_{18}\)ClN\(_2\)O\(_2\) ([M+H]\(^+\)): 341.1051, found 341.1052.

3ac: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded an oil (inseparate mixture of 3ac (77%, yield) and ether 8 \(^8\) (3ac/8 = 7.2/1, based on \(^1\)H NMR).\(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.67 – 7.63 (m, 2H), 7.43 – 7.24 (m, 8H), 6.28 (s, 1H), 5.45 (s, 1H), 3.86 (d, J = 12.5 Hz, 1H), 3.67-2.52 (m, 1H), 3.62 (s, 3H), 3.14 (d, J = 13.5 Hz, 1H), 2.94 (d, J = 13.5 Hz, 1H), 2.16 (br, 1H). HRMS (ESI): calcd. for C\(_{20}\)H\(_{20}\)N\(_2\)O\(_2\)Na ([M+H]\(^+\)): 343.1417, found 343.1410.

3ad: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:13), which afforded 97 mg of a white solid (96%, yield). mp 105 -107 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.61-7.57 (m, 2H), 7.42-7.34(m, 3H), 6.68 – 6.65 (m, 2H), 6.47 – 6.44 (m, 2H), 6.43-6.41 (m, 1H), 5.67-5.66 (m, 1H), 5.42 (br, 1H), 3.80 (s, 3H), 3.68 (s, 3H), 3.04 (s, 2H). \(^1\)C NMR (75 MHz, CDCl\(_3\)) δ 163.25, 148.08, 133.11, 132.22, 128.24, 127.29, 123.76, 123.53, 120.77, 114.39, 111.70, 109.25, 57.69, 50.48, 47.56, 40.85. IR (KBr): 3378, 3034, 2929, 2854, 2227, 1724, 1629, 1521, 1464, 1461, 1246, 1170, 813, 746, 693 cm\(^{-1}\). HRMS (ESI): calcd. for C\(_{20}\)H\(_{21}\)N\(_2\)O\(_3\) ([M+H]\(^+\)): 337.1547, found 337.1541.

SI-4
This compound was prepared according to the general procedure, except that 2 (3.0 eq) was added before the excess of TMSCN was evaporated under reduced pressure when the first step was finished. The product was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 60 mg of a white solid (67%, yield). mp 56 – 59 °C. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.51 - 7.48 (m, 2H), 7.35 – 7.31 (m, 3H), 6.13 (s, 1H), 5.49 (s, 1H), 3.82 – 3.69 (m, 4H), 3.43 (s, 3H), 3.20 (d, $J = 12.9$ Hz, 1H), 2.97 (d, $J = 12.9$ Hz, 1H), 2.76-2.73 (m, 2H), 2.56-2.50 (m, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 161.40, 130.55, 129.05, 124.86, 123.60, 123.19, 122.47, 111.36, 66.13, 61.66, 46.58, 43.55, 34.60. IR (KBr): 3002, 2959, 2891, 2852, 2217, 1721, 1631, 1487, 1246, 1202, 724, 703 cm$^{-1}$. HRMS (ESI): calcd. for C$_{17}$H$_{21}$N$_2$O$_3$ ([M+H]$^+$): 301.1547, found 301.1544.

3b: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:13), which afforded 78 mg of a white solid (70%, yield). mp 90 -91 °C. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.53 (d, $J = 8.6$ Hz, 2H), 6.67 (d, $J = 8.9$ Hz, 2H), 6.45 – 6.43 (m, 3H), 5.67 (s, 1H), 5.44 (s, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.02 (s, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.27, 153.22, 136.89, 136.79, 134.48, 133.01, 132.70, 128.99, 127.34, 119.05, 116.74, 114.33, 62.11, 55.36, 52.52, 45.77. IR (KBr): 3336, 3045, 2938, 2838, 1724, 1512, 1487, 1314, 1248, 1199, 815, 772 cm$^{-1}$. HRMS (ESI): calcd. For C$_{20}$H$_{19}$ClN$_2$O$_3$Na ([M+Na]$^+$): 393.0976, found 393.0972.

3c: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 95 mg of a white solid (91%, yield). mp 70 - 72 °C. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.46 (d, $J = 8.2$ Hz, 2H), 6.68 – 6.64 (m, 2H), 6.49 – 6.44 (m, 2H), 6.42 (s, 1H), 5.67 (s, 1H), 5.38 (br, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.02 (s, 2H), 2.35 (s, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.41, 153.16, 138.49, 137.46, 135.29, 133.44, 132.41, 129.53, 125.79, 119.60, 116.82, 114.35, 62.47, 55.43, 52.48, 46.06, 20.99. IR (KBr): 3371, 3033, 2951, 2857, 1732, 1511, 1248, 1203, 814, 774 cm$^{-1}$. HRMS (ESI): calcd. for C$_{21}$H$_{22}$N$_2$O$_3$Na ([M+Na]$^+$): 373.1523, found 373.1521.
3d: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 87 mg of a colourless oil (79%, yield). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.30 (t, $J = 7.9$ Hz, 1H), 7.20-7.18 (m, 1H), 7.14–7.12 (m, 1H), 6.87 (dd, $J = 8.0$, 2.4 Hz, 1H), 6.69 – 6.66 (m, 2H), 6.49 – 6.46 (m, 2H), 6.44 (s, 1H), 5.71 (s, 1H), 5.43 (br, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.68 (s, 3H), 3.08 – 2.98 (m, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.50, 160.03, 153.25, 140.08, 137.36, 133.41, 132.50, 129.96, 119.38, 118.06, 116.75, 114.35, 114.02, 111.55, 62.69, 55.44, 55.27, 52.52, 45.97. IR (film): 3365, 3057, 2838, 2229, 1706, 1511, 1488, 1243, 1199, 825, 739 cm$^{-1}$. HRMS (ESI): calcd. for C$_{21}$H$_{22}$N$_2$O$_4$Na ($[M+Na]^+$): 389.1472, found 389.1475.

3f: This compound was prepared according to the general procedure except that the excess of TMSCN was evaporated under reduced pressure after the 1$^{st}$ step Strecker reaction was run for 4 h. The product was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded an inseparable mixture of 3f (78%, yield) and $\alpha$-amino nitrile 9 which was generated from 2-Bromobenzaldehyde, $p$-anisidine and TMSCN (3f/9 = 8.4/1, based on $^1$H NMR). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.73 – 7.63 (m, 2H), 7.34 – 7.28 (m, 1H), 7.24 – 7.18 (m, 1H), 6.72 – 6.66 (m, 2H), 6.51 – 6.46 (m, 3H), 5.89-5.87 (m, 2H), 3.84 (s, 3H), 3.69 (s, 3H), 3.40 (d, $J = 13.5$ Hz, 1H), 3.22 (d, $J = 13.9$ Hz, 1H). HRMS (ESI): calcd. for C$_{20}$H$_{20}$BrN$_2$O$_3$ ($[M+H]^+$): 415.0652, found 415.0647.

3g: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 96 mg of a white solid (83%, yield). mp 103-104 ºC. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.09 (s, 1H), 7.87-7.82 (m, 3H), 7.69-7.66 (m, 1H), 7.52-7.49 (m, 2H), 6.63 (d, $J = 8.9$ Hz, 2H), 6.50 (d, $J = 8.9$ Hz, 2H), 6.42 (s, 1H), 5.69 (s, 1H), 5.51 (s, 1H), 3.73 (s, 3H), 3.64 (s, 3H), 3.15 (d, $J = 13.8$ Hz, 1H), 3.09 (d, $J = 13.8$ Hz, 1H). $^{13}$C (75 MHz, CDCl$_3$) $\delta$ 168.39, 153.34, 137.45, 135.88, 133.50, 133.28, 133.05, 132.59, 129.03, 128.30, 127.65, 126.73, 126.64, 125.51, 123.09, 119.56, 117.03, 114.45, 63.02, 55.42, 52.49, 45.91. IR (KBr): 3402, 3062, 2955, 2852, 1657, 1513, 1305, 1253, 1244, 1174, 818 cm$^{-1}$. HRMS (ESI): calcd. for C$_{23}$H$_{22}$N$_2$O$_3$Na ($[M+Na]^+$): 409.1523, found 409.1519.
**3h**: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:13), which afforded 74 mg of a yellow oil (76%, yield). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.44 (dd, $J = 1.7$, 0.8 Hz, 1H), 6.74 – 6.70 (m, 2H), 6.66 – 6.63 (m, 2H), 6.45-6.43 (m, 1H), 6.39 (dd, $J = 3.3$, 0.8 Hz, 1H), 6.33 (dd, $J = 3.3$, 1.8 Hz, 1H), 5.73-5.71 (m, 1H), 4.90 (br, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.26 (d, $J = 13.8$ Hz, 2H), 3.15 (d, $J = 13.8$ Hz, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 167.86, 154.24, 149.21, 143.04, 136.94, 133.14, 131.93, 118.78, 117.77, 114.24, 110.54, 109.81, 58.76, 55.35, 52.44, 42.05. IR (film): 3062, 3035, 2954, 2192, 1718, 1650, 1509, 1150, 819 cm$^{-1}$. HRMS (ESI): calcd. for C$_{18}$H$_{19}$N$_2$O$_4$ ([M+H]$^+$): 327.1339, found 327.1338.

**3af**: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 100 mg of a white solid (95%, yield). mp 80 - 82 °C. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.61 – 7.58 (m, 2H), 7.42 – 7.33 (m, 3H), 6.68-6.64 (m, 2H), 6.47-6.43 (m, 3H), 5.66 (s, 1H), 5.50 (br, 1H), 4.25 (q, $J = 7.1$ Hz, 2H), 3.68 (s, 3H), 3.04 (s, 2H), 1.33 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.04, 153.15, 138.45, 137.37, 133.63, 132.24, 128.87, 128.60, 125.85, 119.48, 116.71, 114.38, 62.68, 61.68, 55.54, 46.00, 14.05. IR (KBr): 3376, 2997, 2832, 2231, 1718, 1627, 1518, 1240, 1161, 818, 754, 698 cm$^{-1}$. HRMS (ESI): calcd. for C$_{21}$H$_{22}$N$_2$O$_3$Na ([M+Na]$^+$): 373.1523, found 373.1521.

**3ag**: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 106 mg of a white solid (94%, yield). mp 93 - 95 °C. $^1$H NMR (300 MHz, CDCl$_3$) 7.61-7.58 (m, 2H), 7.42 – 7.33 (m, 3H), 6.68 – 6.65 (m, 2H), 6.45 – 6.42 (m, 2H), 6.34 (s, 1H), 5.64 (s, 1H), 5.58 (br, 1H), 3.67 (s, 3H), 3.02 (d, $J = 13.7$ Hz, 1H), 2.96 (d, $J = 13.8$ Hz, 1H), 1.53 (s, 9H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 167.46, 153.13, 138.70, 137.58, 135.01, 131.54, 128.95, 128.61, 125.85, 119.55, 116.58, 114.47, 82.17, 62.84, 55.52, 45.94, 27.99. IR (KBr): 3381, 3065, 3031, 2949, 2234, 1709, 1626, 1525, 1507, 1246, 1161, 818, 754, 692 cm$^{-1}$. HRMS (ESI): calcd. for C$_{23}$H$_{26}$N$_2$O$_3$Na ([M+Na]$^+$): 401.1836, found 401.1834.
**3ah**: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:10), which afforded a crude product which was recrystallized to provide a white solid (9%, yield). mp 167-168 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.63 – 7.62 (m, 4H), 7.45 – 7.34 (m, 6H), 7.03 (t, \(J = 7.8\) Hz, 2H), 6.75 (t, \(J = 7.3\) Hz, 1H), 6.55 (s, 1H), 6.36 (d, \(J = 8.0\) Hz, 2H), 6.33 (s, 1H), 4.76 (s, 1H), 4.48 (s, 1H), 3.42 (s, 3H). IR (KBr): 3373, 3113, 3060, 2872, 2241, 1726, 1631, 1602, 1500, 1450, 1248, 1146, 750, 698 cm\(^{-1}\). HRMS (ESI): calcd. for C\(_{25}\)H\(_{23}\)N\(_2\)O\(_2\) ([M+H]+): 383.1754, found 383.1747.

**13**: (see Table 1); mp 91-94 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.71 – 7.67 (m, 2H), 7.53 – 7.50 (m, 2H), 7.40 – 7.33 (m, 5H), 7.30-7.26 (m, 1H), 6.09 (s, 1H), 6.06 (t, \(J = 1.3\) Hz, 1H), 5.63-5.61 (m, 1H), 5.40-5.38 (m, 1H), 4.06 (d, \(J = 14.7\) Hz, 1H), 3.70 (dt, \(J = 15.0, 3.0\) Hz, 1H), 3.63 (s, 3H), 3.34 (s, 3H), 2.93 (d, \(J = 13.0\) Hz, 1H), 2.47 (d, \(J = 13.0\) Hz, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ 166.56, 166.50, 145.22, 136.64, 136.54, 134.17, 130.29, 129.18, 128.96, 128.49, 128.23, 127.69, 127.43, 118.73, 71.03, 52.63, 51.69, 42.74. IR (KBr): 3348, 3061, 2929, 2854, 2224, 1725, 1633, 1494, 1200, 1155, 729, 703 cm\(^{-1}\). HRMS (ESI): calcd. for C\(_{24}\)H\(_{25}\)N\(_2\)O\(_4\) ([M+H]+): 405.1809, found 405.1815.

**12**: Inseparate mixture of 12, 1a and ether 8 (See Table 1). \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 7.52 – 7.38 (m, 5H), 7.30 – 7.25 (m, 2H), 6.99 – 6.89 (m, 3H), 6.25 – 6.24 (m, 1H), 5.85 (s, 1H), 5.74 – 5.73 (m, 1H), 4.20 (d, \(J = 18.0\) Hz, 1H), 4.07 (d, \(J = 17.8\) Hz, 1H). HRMS (ESI): calcd. for C\(_{19}\)H\(_{19}\)N\(_2\)O\(_2\) ([M+H]+): 307.1441, found 307.1435.

**V. General Procedure for the Synthesis of α-Methylene-γ-Butyrolactones**

![V. General Procedure for the Synthesis of α-Methylene-γ-Butyrolactones](SI-8)
To a dried round-bottom flask were added 3 (0.25 mmol) and CH\textsubscript{3}CN (2.5 mL). To this solution was added DBU (20%) at 0 °C and the mixture was warmed to rt. The reaction was monitored by TLC. Upon completion, the reaction mixture was washed with brine. The mixture was extracted with ethyl acetate. The combined organic extract was dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated \textit{in vacuo}. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide 4.

4a: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 61 mg of a white solid (89%, yield). mp 80-82 °C. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.49 – 7.45 (m, 2H), 7.41 – 7.37 (m, 3H), 7.31 – 7.20 (m, 5H), 6.38 (t, J = 2.6 Hz, 1H), 5.66 (t, J = 2.3 Hz, 1H), 3.75 (dt, J = 17.0, 2.4 Hz, 1H), 3.32 (dt, J = 17.0, 2.7 Hz, 1H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 166.42, 136.76, 135.47, 134.78, 129.45, 129.22, 128.89, 127.45, 125.79, 125.35, 119.69, 118.81, 63.61, 43.16. IR (KBr): 3062, 3008, 2927, 2854, 1717, 1661, 1592, 1491, 1452, 1350, 759, 699 cm\textsuperscript{-1}. HRMS (ESI): calcd. for C\textsubscript{18}H\textsubscript{15}N\textsubscript{2}O ([M+H]+): 275.1179, found 275.1172.

4b: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 51 mg of a white solid (66%, yield). mp 75-77 °C. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.47 – 7.39 (m, 5H), 7.25 (d, J = 8.8 Hz, 2H), 7.16 (d, J = 8.8 Hz, 2H), 6.38 (t, J = 2.5 Hz, 1H), 5.67 (t, J = 2.1 Hz, 1H), 3.75 (dt, J = 17.0, 2.2 Hz, 1H), 3.30 (dt, J = 17.0, 2.4 Hz, 1H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 166.41, 136.51, 134.49, 134.07, 133.22, 129.71, 129.45, 129.19, 126.99, 125.34, 120.22, 118.68, 63.58, 43.17. IR (KBr): 3105, 3049, 2955, 2921, 1714, 1665, 1493, 1452, 1340, 828, 759, 696 cm\textsuperscript{-1}. HRMS (ESI): calcd. for C\textsubscript{18}H\textsubscript{14}ClN\textsubscript{2}O([M+H]+): 309.0789, found 309.0798.

4c: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 70 mg of a white solid (92%, yield). mp 100-102°C. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.48-7.44 (m, 2H), 7.40-7.37 (m, 3H), 7.05 (d, J = 9.0 Hz, 2H), 6.77 (d, J = 9.1 Hz, 2H), 6.34 (t, J = 2.7 Hz, 1H), 5.63 (t, J = 2.3 Hz, 1H),
3.76 – 3.69 (m, 1H), 3.71 (s, 3H), 3.33 (dt, $J = 17.2, 2.6$ Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 166.63, 158.77, 136.82, 134.80, 129.46, 129.15, 127.95, 127.87, 125.50, 119.38, 118.82, 114.24, 63.95, 55.14, 42.58. IR (KBr): 3106, 3063, 2959, 2937, 2909, 1716, 1670, 1511, 1451, 1356, 1255, 828, 751, 699 cm$^{-1}$. HRMS (ESI): calcd. for C$_{19}$H$_{17}$N$_2$O$_2$ ([M+H]$^+$): 305.1285, found 305.1281.

To a solution of 3ac (98 mg, 0.3 mmol) in toluene (3 ml) was added $p$-TsOH (10 mg, 0.06 mmol) and stirred at 80°C for 56 h. The mixture was filtrated through a pad of Celite and the precipitate washed with dichloromethane (3×10 ml). The organic phase was evaporated in vapor and the residue was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6) to give 4d (45 mg, 52%) as yellow oil.

4d: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.38 – 7.33 (m, 5H), 7.21 – 7.16 (m, 3H), 7.12 – 7.09 (m, 2H), 6.30 (t, $J = 2.7$ Hz, 1H), 5.56 (t, $J = 2.3$ Hz, 1H), 4.73 (d, $J = 14.9$ Hz, 1H), 4.18 (d, $J = 14.9$ Hz, 1H), 3.58 (dt, $J = 17.3, 2.4$ Hz, 1H), 3.14 (dt, $J = 17.3, 2.7$ Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 167.48, 136.02, 135.20, 134.60, 129.60, 129.25, 129.00, 128.28, 127.78, 125.62, 119.00, 118.15, 62.20, 45.67, 42.81. IR (KBr): 3065, 3040, 2972, 2841, 1714, 1663, 1513, 1356, 764, 701 cm$^{-1}$. HRMS (ESI): calcd. for C$_{19}$H$_{17}$N$_2$O ([M+H]$^+$): 289.1335, found 289.1338.

4e: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 69 mg of a white solid (82%, yield). mp 136-137°C. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42 – 7.35 (m, 4H), 7.05 (d, $J = 9.0$ Hz, 2H), 6.80 (d, $J = 9.0$ Hz, 2H), 6.37 (t, $J = 2.7$ Hz, 1H), 5.66 (t, $J = 2.3$ Hz, 1H), 3.78-3.71 (m, 1H), 3.75 (s, 3H), 3.28 (dt, $J = 17.1, 2.6$ Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 161.52, 153.90, 130.51, 130.31, 129.36, 124.33, 122.84, 122.63, 122.02, 114.76, 113.51, 109.34, 58.42, 50.15, 37.44. IR (KBr): 3057, 3040, 2972, 2841, 1714, 1663, 1513, 1356, 1250, 823 cm$^{-1}$. HRMS (ESI): calcd. for C$_{19}$H$_{16}$ClN$_2$O$_2$ ([M+H]$^+$): 339.0895, found 339.0903.

4f: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 50 mg of a white solid (55%, yield). mp 136-137°C. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42 – 7.35 (m, 4H), 7.05 (d, $J = 9.0$ Hz, 2H), 6.80 (d, $J = 9.0$ Hz, 2H), 6.37 (t, $J = 2.7$ Hz, 1H), 5.66 (t, $J = 2.3$ Hz, 1H), 3.78-3.71 (m, 1H), 3.75 (s, 3H), 3.28 (dt, $J = 17.1, 2.6$ Hz, 1H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 161.52, 153.90, 130.51, 130.31, 129.36, 124.33, 122.84, 122.63, 122.02, 114.76, 113.51, 109.34, 58.42, 50.15, 37.44. IR (KBr): 3057, 3040, 2972, 2841, 1714, 1663, 1513, 1356, 1250, 823 cm$^{-1}$. HRMS (ESI): calcd. for C$_{19}$H$_{16}$ClN$_2$O$_2$ ([M+H]$^+$): 339.0895, found 339.0903.
chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 64 mg of a white amorphous solid (81%, yield). ¹H NMR (300 MHz, CDCl₃) δ 7.34 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 9.0 Hz, 2H), 6.78 (d, J = 9.0 Hz, 2H), 6.34 (t, J = 2.7 Hz, 1H), 5.63 (t, J = 2.3 Hz, 1H), 3.76 – 3.68 (m, 1H), 3.74 (s, 3H), 3.31 (dt, J = 17.1, 2.6 Hz, 1H), 2.35 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 161.65, 153.75, 134.49, 129.89, 128.73, 124.74, 122.87, 120.40, 114.20, 113.93, 109.17, 58.78, 50.10, 37.61, 15.87. IR (KBr): 3031, 2957, 2933, 2839, 1713, 1663, 1513, 1358, 1249, 830, 815 cm⁻¹. HRMS (ESI): calcd. for C₂₀H₁₉N₂O₂ ([M+H]+): 319.1441, found 319.1446.

4g: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 58 mg of a white solid (70%, yield). mp 107-109°C. ¹H NMR (300 MHz, CDCl₃) δ 7.31 (t, J = 8.0 Hz, 1H), 7.12-7.08 (m, 2H), 7.06-7.03 (m, 1H), 6.98 – 6.96 (m, 1H), 6.91-6.88 (m, 1H), 6.82 – 6.79 (m, 2H), 6.35 (t, J = 2.7 Hz, 1H), 5.64 (t, J = 2.3 Hz, 1H), 3.78 (s, 3H), 3.76 – 3.68 (m, 1H), 3.75 (s, 3H), 3.31 (dt, J = 17.2, 2.6 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 166.72, 160.04, 158.81, 138.39, 134.76, 130.36, 127.99, 127.77, 119.49, 118.84, 117.58, 114.58, 111.52, 63.88, 55.26, 55.19, 42.63. IR (KBr): 3069, 2967, 2840, 2239, 1714, 1662, 1514, 1494, 1465, 1355, 1248, 812, 793, 704 cm⁻¹. HRMS (ESI): calcd. for C₂₀H₁₉N₂O₃ ([M+H]+): 335.1390, found 335.1394.

4h: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 55 mg of a colorless oil (58%, yield). ¹H NMR (300 MHz, CDCl₃) δ 7.77-7.74 (m, 1H), 7.67-7.64 (m, 1H), 7.35-7.30 (m, 1H), 7.28 – 7.21 (m, 3H), 6.82-6.77 (m, 2H), 6.37 (t, J = 2.6 Hz, 1H), 5.64 (t, J = 2.3 Hz, 1H), 3.79 (dt, J = 17.6, 2.7 Hz, 1H), 3.73 (s, 3H), 3.67 (dt, J = 17.6, 2.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 167.11, 158.75, 136.18, 135.14, 132.69, 131.19, 130.80, 127.98, 127.86, 127.21, 120.52, 119.46, 118.91, 114.22, 65.35, 55.18, 39.52. IR (film): 3059, 2961, 2840, 1714, 1663, 1514, 1362, 1264, 736, 702 cm⁻¹. HRMS (ESI): calcd. for C₁₉H₁₆BrN₂O₂ ([M+H]+): 383.0390, found 383.0393.

4i: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:12), which afforded 75 mg of a white solid (85%, yield). mp 135-136 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.00 – 7.99 (m, 1H), 7.90 (d, J = 8.7 Hz, 1H), 7.86 – 7.82 (m, 2H), 7.59 – 7.51 (m, 2H), 7.45 (dd, J = 8.8, 2.1 Hz, 1H), 7.08 (d, J = 9.1 Hz, 1H), 6.39 (s, 3H), 3.34 (dt, J = 17.6, 2.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 167.11, 158.75, 136.18, 135.14, 132.69, 131.19, 130.80, 127.98, 127.86, 127.21, 120.52, 119.46, 118.91, 114.22, 65.35, 55.18, 39.52. IR (film): 3059, 2961, 2840, 1714, 1663, 1514, 1362, 1264, 736, 702 cm⁻¹. HRMS (ESI): calcd. for C₁₉H₁₆BrN₂O₂ ([M+H]+): 383.0390, found 383.0393.
Hz, 2H), 6.74 (d, \( J = 9.1 \) Hz, 2H), 6.40 (t, \( J = 2.6 \) Hz, 1H), 5.67 (t, \( J = 2.2 \) Hz, 1H), 3.80 (dt, \( J = 17.3 \), 2.3 Hz, 1H), 3.70 (s, 3H), 3.42 (dt, \( J = 17.3 \), 2.6 Hz, 1H), 3.80 (dt, \( J = 17.3 \), 2.3 Hz, 1H), 3.70 (s, 3H), 3.42 (dt, \( J = 17.3 \), 2.6 Hz, 1H), 3.80 (dt, \( J = 17.3 \), 2.3 Hz, 1H), 3.70 (s, 3H), 3.42 (dt, \( J = 17.3 \), 2.6 Hz, 1H). 13C NMR (75 MHz, CDCl3) δ 161.83, 153.84, 129.80, 128.77, 128.14, 127.46, 124.71, 123.25, 122.96, 122.89, 122.55, 122.33, 122.10, 120.96, 116.54, 114.55, 113.90, 109.27, 59.22, 50.05, 37.33. IR (KBr): 3003, 2966, 2853, 1719, 1653, 1559, 1541, 1251, 828 cm-1. HRMS (ESI): calcd. For C23H19N2O2 ([M+H]+): 355.1441, found 355.1443.

4j: This compound was prepared according to the general procedure and was purified by flash chromatography (silica gel, EtOAc/Petroleum = 1:6), which afforded 40 mg of a yellow oil (55%, yield). 1H NMR (300 MHz, CDCl3) δ 7.47 (dd, \( J = 1.9 \), 0.9 Hz, 1H), 6.93-6.89 (m, 2H), 6.87-6.82 (m, 2H), 6.48 (dd, \( J = 3.4 \), 0.9 Hz, 1H), 6.34-6.32 (m, 2H), 5.66 (t, \( J = 2.3 \) Hz, 1H), 3.78 (s, 3H), 3.64 (dt, \( J = 17.1 \), 2.7 Hz, 1H), 3.56 (dt, \( J = 16.8 \), 2.1 Hz, 1H). 13C NMR (75 MHz, CDCl3) δ 166.50, 159.64, 146.79, 144.29, 134.36, 128.97, 127.17, 119.43, 117.64, 114.53, 112.04, 110.97, 59.07, 55.28, 37.68. IR (film): 3061, 2963, 2935, 2840, 1711, 1668, 1512, 1362, 1265, 829 cm-1. HRMS (ESI): calcd. for C17H15N2O3 ([M+H]+): 295.1077, found 295.1080.

Procedure for the One Pot Synthesis of α-Methylene-γ-Butyrolactam

\[ \text{R}^1\text{CHO} + \text{R}^2\text{NH}_2 + \text{TMS-CN} \rightarrow \text{DABCO(20%)} \rightarrow \text{DBU(60%) CH}_3\text{CN} \rightarrow \text{N}^\text{O} \rightarrow \text{4a, yield: 78%} \]

To a dried reaction tube were added aldehyde (0.3 mmol) and amine (0.315 mmol). After the mixture was stirred at rt for 10 min, TMS-CN (0.33 mmol) was added. After the mixture was vigorously stirred for 50 min, CH3CN (3 ml), DABCO (20%) and 2a (0.45 mmol) were added. The reaction was monitored by TLC. After 2.5 h, DBU (60%) was added to the above mixture. Upon completion, the stirring bar was removed and the mixture was evaporated under reduced pressure to give the crude products. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum) to provide 4a.

VI. Procedure for Chemical Transformations

\[ \text{MeO}_2\text{C} + \text{PMP} \rightarrow \text{AgNO}_3, \text{THF/H}_2\text{O, rt} \rightarrow \text{MeO}_2\text{C} \]

3a (33.6 mg, 0.1 mmol) was dissolved in THF (0.68 mL) and treated with an aqueous solution (0.1 mL) of AgNO3 (33.9 mg, 0.2 mmol). After stirring at room temperature for 18h, the solution was
filtrated through a pad of Celite and the precipitate washed with ether (2×5 mL) and water (5 mL). The aqueous phase was extracted with ether (3×5 mL), the combined organic phase washed with brine (2×5 mL) and water (5 mL), dried over anhydrous Na₂SO₄, filtered and the solvent removed in vacuo. Purification by flash chromatography (silica gel, EtOAc/Petroleum 1/10) afforded the (16 mg, 78%) as red brown oil.⁹

¹H NMR (300 MHz, CDCl₃) δ 8.09 – 7.90 (m, 2H), 7.66 – 7.31 (m, 3H), 6.51 – 6.30 (m, 1H), 5.79 – 5.60 (m, 1H), 4.10 – 3.95 (m, 2H), 3.74 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 196.84, 166.95, 136.59, 134.64, 133.33, 128.71, 128.66, 128.32, 52.15, 41.78.

⁹

To a solution of 4c (213 mg, 0.7 mmol) in CH₃CN (5.0 ml) was added aqueous cerium ammonium nitrate (1.9 g, 3.43 mmol) solution (5.0 ml) at 0 ˚C. ⁶ After being stirred at 0 ˚C for 4 h, the reaction mixture was quenched by addition of sat. NaHCO₃ (aq.) solution (15 ml). The aqueous layer was extracted with diethyl ether (10 ml) and the combined organic layers were successively washed with 5% Na₂SO₃ solution, sat. NaHCO₃ (aq.) solution and brine, and dried over anhydrous Na₂SO₄. The solvent was evaporated in vacuo to leave crude material, which was purified by column chromatography (silica gel, EtOAc/Petroleum = 1:5) to afford 58 mg of a white solid in 42% yield. mp 88-90 °C.

¹H NMR (300 MHz, CDCl₃) δ 7.56-7.42 (m, 5H), 6.20 (t, J = 2.7 Hz, 1H), 5.55 – 5.54 (m, 1H), 3.65 (dt, J = 17.1, 2.1 Hz, 1H), 3.10 (dt, J = 17.1, 2.7 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 169.87, 138.23, 135.11, 129.48, 129.43, 124.62, 119.98, 119.57, 57.20, 43.76. IR (KBr): 3438, 3011, 2927, 2856, 1680, 1632, 1527, 1346, 740 cm⁻¹. HRMS (ESI): calcd. for C₁₂H₁₁N₂O ([M+H]+): 199.0866, found 199.0868.

VII. NMR Spectra and HPLC Spectra

VIII. References