Supporting Information

LiCl-Promoted Amination of β-Methoxy amides (γ-Lactones)
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Supporting Information

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1. General remarks
Unless otherwise noted, all reagents and solvents were purchased from Innochem Co., Ltd. and Aldrich Inc. Flash column chromatography was performed with silica gel (200-300 mesh, 300-400 mesh, Qingdao Haiyang Chemical Co., Ltd.). Melting points (not corrected) were measured with RY-2. Optical rotations were measured with a Perkin-Elmer 240. NMR spectra were taken on MERCURY-400M or BRUKER-500M spectrometer. HRMS (ESI) experiments were carried out on a LC-ESI-JMS T100CS.
2. Synthesis

3-Methoxy-N-phenylpropanamide (1a). To a suspension of aniline (1.02 g, 1.0 eq) in dichloromethane (DMF, 15 mL) was added 3-methoxypropanoic acid (1.25 g, 1.1 eq), N1-((Ethylimino)methylene)-N3,N3-dimethylpropane-1,3-diamine hydrochloride (EDCI, 2.3 g, 1.1 eq), and triethylamine (4.5 mL, 3.0 eq), subsequently. After stirring at room temperature for 12 hours, the reaction mixture was added diluted with EA and washed with 5% HCl aqueous solution, water and brine, dried over MgSO$_4$ and concentrated under reduce pressure. The residue was purified by column chromatography on silica gel to afford 1a (1.50 g, 69%) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.32 (s, 1H), 7.51 (d, $J= 8.0$ Hz, 2H), 7.37 – 7.22 (m, 2H), 7.09 (d, $J= 7.4$ Hz, 1H), 3.73 (m, 2H), 3.54 – 3.36 (s, 3H), 2.71 – 2.52 (m, 2H).

3-Methoxy-N-(4-methoxyphenyl) propenamide (1b). According to the general procedure analogous to that described for 1a, 1b (1.59 g, 76%) was obtained from $p$-Anisidin (1.23 g, 10 mmol) as a gray solid. Mp: 56-58 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.16 (s, 1H), 7.49 – 7.35 (m, 2H), 6.95 – 6.72 (m, 2H), 3.78 (s, 3H), 3.72 (t, $J= 5.7$ Hz, 2H), 3.43 (s, 3H), 2.61 (t, $J= 5.7$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.6, 156.3, 131.2, 121.7, 114.1, 114.1, 68.7, 58.9, 55.5, 37.8; HRMS (ESI) m/z calcd. for C$_{11}$H$_{16}$O$_3$N [M+H]$^+$ 210.10519, found 210.11269.
**N-(4-Chlorophenyl)-3-methoxypropanamide (1c).** According to the general procedure analogous to that described for 1a, 1c (1.50 g, 70%) was obtained from 4-chloroaniline (1.28 g, 10 mmol) as a white solid. Mp: 60-62 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.27 (s, 1H), 7.54 – 7.38 (m, 2H), 7.30 – 7.23 (m, 2H), 3.72 (t, J=5.6Hz, 2H), 3.45 (s, 3H), 2.63 (t, J=5.6Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 136.6, 129.0, 128.9, 121.1, 68.5, 59.0, 37.9; HRMS (ESI) m/z calcd. for C₁₀H₁₃O₂NCl [M+H]⁺ 214.05566, found 214.06340.

**N-(4-Bromophenyl)-3-methoxypropanamide (1d).** According to the general procedure analogous to that described for 1a, 1d (1.89 g, 73%) was obtained from 4-chloroaniline (1.72 g, 10 mmol) as a white solid. Mp: 58-60 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.31 (s, 1H), 7.41 (s, 4H), 3.72 (t, J=5.6 Hz, 2H), 3.45 (s, 3H), 2.62 (t, J = 5.6 Hz, 2H).

**N-Benzyl-3-methoxypropanamide (1e).** To a suspension of benzylamine (547 µL, 5 mmol) in DMF (8 mL) was added 3-methoxypropanoic acid (500 mg, 5 mmol), EDCI (1.5 g, 7.5 mmol), 1-Hydroxybenzotriazole (675 mg, 5 mmol) and triethylamine (1.4 mL, 10 mmol), subsequently. After stirring at room temperature for 12 hours, the reaction mixture was diluted with EA (30 mL) and washed with saturated NaHCO₃ aqueous solution (30 mL), NH₄Cl aqueous solution (30 mL), water (30 mL) and brine (30 mL), dried over MgSO₄ and concentrated under reduce pressure. The residue
was purified by column chromatography on silica gel to afford 1e (314 mg, 33%) as a yellow solid. Mp: 48-50 °C; 1H NMR (400 MHz, CDCl₃) δ 7.34 – 7.22 (m, 5H), 4.44 (d, J = 5.7 Hz, 2H), 3.71 – 3.55 (m, 2H), 3.38 – 3.24 (s, 3H), 2.49 (t, J = 5.7 Hz, 2H).

**tert-Butyl 4-(3-methoxypropanoyl) piperazine-1-carboxylate (1f).** To a suspension of 1-boc-piperazine (745 mg, 4 mmol) in DMF (8 mL) was added 3-methoxypropanoic acid (500 mg, 5 mmol), EDCI (1.5 g, 7.5 mmol), and 1-Hydroxybenzotriazole (675 mg, 5 mmol). After stirring at room temperature for 12 hours, the reaction mixture was added EA (30 mL) and was washed with NaHCO₃ aqueous solution (30 mL), NH₄Cl aqueous solution (30 mL), H₂O (30 mL) and NaCl aqueous solution (30 mL), dried over MgSO₄ and concentrated. The residue was purified by column chromatography on silica gel to afford 1f (676mg, 62%) as a white solid. Mp: 68-70 °C; 1H NMR (500 MHz, CDCl₃) δ 3.75 (t, J = 6.1 Hz, 2H), 3.65 (s, 2H), 3.48 (d, J = 14.0 Hz, 6H), 3.40 (s, 3H), 2.66 (t, J = 6.1 Hz, 2H), 1.52 (s, 9H).

**General procedure for the amination of carbonyl β-methoxy group in the presence of LiCl.**

\[ \text{Ph} \text{N} \text{O} \text{O} \text{H} + \text{LiCl (2.0 equiv)} \xrightarrow{\text{iPrOH (0.15 M), 12 h}} \text{Ph} \text{N} \text{N} \text{O} \text{H} \text{N} \text{H} \text{iPrOH} \]

(2.0 equiv)

\(120 \text{ °C, sealed tube}\)

**N-Phenyl-3-(piperidin-1-yl) propenamide (3aa).** To a mixture of 1a (150 mg, 0.8 mmol) and 2a (136 mg, 1.6 mmol) in i-PrOH (5.3 mL) was added LiCl (67mg, 1.6 mmol). The mixture was stirred at 120 °C for 12 hours in a sealed tube. After cooling down to room temperature, the reaction mixture was added diluted with DCM (10 mL) was washed with saturated NaHCO₃ aqueous solution (10 mL), water (10 mL) and brine (10 mL),
dried over MgSO₄ and concentrated under reduce pressure. The residue was purified by column chromatography on silica gel to afford **3aa** (130 mg, 70%) as a yellow oil. $^1$H NMR (400 MHz, CDCl₃) $\delta$ 11.21 (s, 1H), 7.59 – 7.50 (m, 2H), 7.35 – 7.28 (m, 2H), 7.11 – 7.02 (m, 1H), 2.76 – 2.68 (m, 2H), 2.65 – 2.50 (m, 6H), 1.77 – 1.67 (m, 4H), 1.56 (s, 2H); $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 170.7, 138.9, 129.0, 123.6, 119.5, 54.4, 53.7, 32.6, 26.1, 24.1; HRMS (ESI) m/z calcd. for C$_{14}$H$_{21}$ON$_2$ [M+H]$^+$ 233.15756, found 233.16441.

![N-(4-Methoxyphenyl)-3-(piperidin-1-yl) propenamide](image)

**N-(4-Methoxyphenyl)-3-(piperidin-1-yl) propenamide (3ba).** According to the general procedure analogous to that described for **3aa**, **3ba** (132 mg, 72%) was obtained from **1b** (150 mg, 0.7 mmol) as a white solid. Mp: 104-106 °C; $^1$H NMR (400 MHz, CDCl₃) $\delta$ 11.14 (s, 1H), 7.54 – 7.38 (m, 2H), 7.00 – 6.74 (m, 2H), 3.78 (s, 3H), 2.70 – 2.63 (m, 2H), 2.51 (m, 6H), 1.74 – 1.63 (m, 4H), 1.54 (s, 2H); $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 170.5, 155.8, 132.3, 120.9, 114.2, 55.5, 54.4, 53.7, 32.44, 26.2, 24.2; HRMS (ESI) m/z calcd. for C$_{15}$H$_{23}$O$_2$N$_2$ [M+H]$^+$ 263.16813, found 263.17493.

![Cl](image)

**N-(4-Chlorophenyl)-3-(piperidin-1-yl) propenamide (3ca).** According to the general procedure analogous to that described for **3aa, 3ca** (134 mg, 72%) was obtained from **1c** (150 mg, 0.7 mmol) as a yellow solid. Mp: 70-72 °C; $^1$H NMR (400 MHz, CDCl₃) $\delta$ 11.44 (s, 1H), 7.53 – 7.46 (m, 2H), 7.27 – 7.23 (m, 2H), 2.71 – 2.64 (m, 2H), 2.52 (m, 6H), 1.75 – 1.62 (m, 4H), 1.56 (m, 2H); $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 170.8, 137.6, 129.0, 128.3, 120.6, 54.3, 53.6, 32.5, 26.2, 24.2; HRMS (ESI) m/z calcd. for C$_{14}$H$_{20}$ON$_2$Cl [M+H]$^+$ 267.11859, found 267.12555.
**N-(4-Bromophenyl)-3-(piperidin-1-yl) propenamide** (3da). According to the general procedure analogous to that described for 3aa, 3da (143 mg, 77%) was obtained from 1d (150 mg, 0.6 mmol) as a yellow solid. Mp: 74-76 °C; 1H NMR (400 MHz, CDCl₃) δ 11.44 (s, 1H), 7.47 – 7.42 (m, 2H), 7.42 – 7.37 (m, 2H), 2.67 (m, 2H), 2.63 – 2.47 (m, 6H), 1.74 – 1.64 (m, 4H), 1.56 (m, 2H); 13C NMR (100 MHz, CDCl₃) δ 170.9, 138.1, 131.9, 121.0, 115.9, 54.2, 53.6, 32.5, 26.2, 24.1; HRMS (ESI) m/z calcd. for C₁₄H₂₀ON₂Br [M+H]⁺ 311.06808, found 311.07364.

**N-Phenyl-3-(pyrrolidin-1-yl) propenamide** (3ab). According to the general procedure analogous to that described for 3aa, 3ab (127 mg, 73%) was obtained from 1a (150 mg, 0.8 mmol) as a yellow oil. 1H NMR (400 MHz, CDCl₃) δ 11.13 (s, 1H), 7.49 (m, 2H), 7.28 (m, 2H), 7.04 (t, 𝑗 = 7.4 Hz, 1H), 2.83 (t, 𝑗 = 6.0 Hz, 2H), 2.65 (s, 4H), 2.56 – 2.47 (m, 2H), 1.88 (s, 4H); 13C NMR (100 MHz, CDCl₃) δ 170.9, 138.9, 123.6, 119.7, 53.2, 51.4, 34.7, 23.7; HRMS (ESI) m/z calcd. for C₁₃H₁₉ON₂ [M+H]⁺ 219.14191, found 219.14943.

**N-(4-Methoxyphenyl)-3-(pyrrolidin-1-yl) propenamide** (3bb). According to the general procedure analogous to that described for 3aa, 3bb (120 mg, 69%) was obtained from 1b (150 mg, 0.7 mmol) as a white
solid. Mp: 76-80 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.19 – 10.73 (m, 1H), 7.40 (dd, J = 9.0 Hz, 2H), 6.84 (d, J = 9.0 Hz, 2H), 3.78 (s, 3H), 2.88 – 2.80 (m, 2H), 2.67 (t, J = 8.6, 3.5 Hz, 4H), 2.56 – 2.48 (m, 2H), 1.88 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 155.8, 132.2, 121.2, 114.1, 55.5, 53.2, 51.5, 34.6, 23.7; HRMS (ESI) m/z calcd. for C₁₄H₂₀N₂O₂ [M+H]^+ 249.15248, found 249.16005.

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\text{N-(4-Chlorophenyl)-3-(pyrrolidin-1-yl) propenamide (3cb).} According to the general procedure analogous to that described for 3aa, 3cb (118 mg, 67%) was obtained from 1c (150 mg, 0.7 mmol) as a yellow solid. Mp: 88-90 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.67 (s, 1H), 7.57 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.8 Hz, 2H), 3.24 (t, J = 6.0 Hz, 2H), 3.06 (s, 4H), 2.91 (t, J = 6.0 Hz, 2H), 2.00 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 169.1, 137.2, 128.9, 128.7, 121.0, 53.8, 51.3, 33.8, 23.5; HRMS (ESI) m/z calcd. for C₁₃H₁₈ON₂Cl [M+H]^+ 253.10294, found 253.11082.

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\text{N-(4-Bromophenyl)-3-(pyrrolidin-1-yl) propenamide (3db).} According to the general procedure analogous to that described for 3aa, 3db (130 mg, 73%) was obtained from 1d (150 mg, 0.6 mmol) as a white solid. Mp: 140-142 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.85 (s, 1H), 7.61 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.8 Hz, 2H), 3.51 (t, J = 6.6 Hz, 2H), 3.16 (t, J = 6.6 Hz, 2H), 2.12 (s, 4H), 1.74 (s, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 167.6, 137.3, 131.8, 121.5, 116.9, 54.4, 51.6, 33.5, 23.4; HRMS (ESI) m/z calcd. for C₁₃H₁₈ON₂Br [M+H]^+ 297.05243, found 297.06082.
3-(Diethylamino)-N-phenylpropanamide (3ac). According to the general procedure analogous to that described for 3aa, 3ac (110 mg, 63%) was obtained from 1a (150 mg, 0.8 mmol) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.93 (s, 1H), 7.62 – 7.53 (m, 2H), 7.33 – 7.24 (m, 2H), 7.06 (t, $J$ = 7.4 Hz, 1H), 2.95 (t, $J$ = 6.2 Hz, 2H), 2.80 (q, $J$ = 7.2 Hz, 4H), 2.69 (t, $J$ = 6.2 Hz, 2H), 1.19 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.1, 138.7, 128.9, 123.7, 119.7, 48.9, 46.3, 32.8, 10.7; HRMS (ESI) m/z calcd. for C$_{13}$H$_{21}$ON$_2$ [M+H]$^+$ 221.15756, found 221.16490.

3-(Diethylamino)-N-(4-methoxyphenyl) propenamide (3bc). According to the general procedure analogous to that described for 3aa, 3bc (137 mg, 78%) was obtained from 1b (150 mg, 0.7 mmol) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.45 (s, 1H), 7.52 (d, $J$ = 8.8 Hz, 2H), 6.78 (d, $J$ = 8.8 Hz, 2H), 3.73 (d, $J$ = 1.0 Hz, 3H), 3.17 (t, $J$ = 6.3 Hz, 2H), 2.98 – 2.86 (m, 6H), 1.25 (t, $J$ = 7.3 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.8, 156.2, 131.6, 121.6, 114.0, 55.5, 48.7, 47.0, 31.9, 8.8; HRMS (ESI) m/z calcd. for C$_{14}$H$_{23}$O$_2$N$_2$ [M+H]$^+$ 251.16813, found 251.17552.

$N$-(4-Chlorophenyl)-3-(diethylamino) propenamide (3cc). According to the general procedure analogous to that described for 3aa, 3cc (124 mg, 70%) was obtained from 1c (150 mg, 0.7 mmol) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 11.36 (s, 1H), 7.52 – 7.47 (m, 2H), 7.28 – 7.22 (m,
2H), 2.83 – 2.76 (m, 2H), 2.69 (q, \( J = 7.2 \) Hz, 4H), 2.56 – 2.48 (m, 2H), 1.13 (dd, \( J = 7.7, 6.7 \) Hz, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 170.6, 137.4, 128.9, 128.4, 120.7, 48.9, 46.1, 32.9, 11.2; HRMS (ESI) m/z calcd. for C\(_{13}\)H\(_{20}\)ON\(_2\)Cl [M+H]\(^+\) 255.11859, found 255.12634.

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  \draw[thick,->] (0,0) -- (0.5,0);
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  \node at (-0.5,0) {Br};
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\textit{N-(4-Bromophenyl)-3-(diethylamino) propenamide (3dc).} According to the general procedure analogous to that described for 3aa, 3dc (138 mg, 77%) was obtained from 1d (150 mg, 0.6 mmol) as a yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 10.24 (s, 1H), 7.50 – 7.43 (m, 2H), 7.41 – 7.34 (m, 2H), 3.15 (t, \( J = 6.4 \) Hz, 2H), 2.97 (q, \( J = 7.2 \) Hz, 4H), 2.81 (t, \( J = 6.4 \) Hz, 2H), 1.25 (t, \( J = 7.2 \) Hz, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 169.8, 137.2, 131.9, 121.6, 116.8, 48.9, 46.8, 31.4, 9.9; HRMS (ESI) m/z calcd. for C\(_{13}\)H\(_{20}\)ON\(_2\)Br [M+H]\(^+\) 299.06808, found 299.07632.

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  \draw[thick,->] (0,0) -- (-0.5,0);
  \draw[thick,->] (0,0) -- (-0.5,-0.5);
  \node at (-0.5,0) {Br};
\end{tikzpicture}} \]

\textit{3-(Dimethylamino)-N-phenylpropanamide (3ad).} According to the general procedure analogous to that described for 3aa, 3ad (98 mg, 64%) was obtained from 1a (150 mg, 0.8 mmol) as a yellow solid. Mp: 52-54 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 10.78 (s, 1H), 7.56 (dd, \( J = 8.5, 0.9 \) Hz, 2H), 7.33 (t, \( J = 7.9 \) Hz, 2H), 7.10 (t, \( J = 7.4 \) Hz, 1H), 2.78 – 2.71 (m, 2H), 2.62 – 2.54 (m, 2H), 2.43 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 170.5, 138.7, 128.9, 123.7, 119.9, 55.0, 44.3, 33.5; HRMS (ESI) m/z calcd. for C\(_{11}\)H\(_{17}\)ON\(_2\) [M+H]\(^+\) 193.12626, found 193.13383.
3-(Dimethylamino)-N-(4-methoxyphenyl) propenamide (3bd).
According to the general procedure analogous to that described for 3aa, 3bd (113 mg, 73%) was obtained from 1b (150 mg, 0.7 mmol) as a yellow solid. Mp: 50-52 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.70 (s, 1H), 7.54 – 7.36 (m, 2H), 6.93 – 6.78 (m, 2H), 3.80 (d, \(J = 1.2\) Hz, 3H), 2.72 – 2.63 (m, 2H), 2.51 (m, 2H), 2.38 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.5, 155.9, 132.0, 121.5, 114.1, 55.5, 55.2, 44.5, 33.4; HRMS (ESI) m/z calcd. for \(\text{C}_{12}\text{H}_{19}\text{O}_2\text{N}_2\) [M+H]\(^+\) 223.13683, found 223.14442.

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N-(4-Chlorophenyl)-3-(dimethylamino) propenamide (3cd). According to the general procedure analogous to that described for 3aa, 3cd (106 mg, 67%) was obtained from 1c (150 mg, 0.7 mmol) as a white solid. Mp: 56-62 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.05 (s, 1H), 7.53 – 7.45 (m, 2H), 7.33 – 7.23 (m, 2H), 2.72 – 2.64 (m, 2H), 2.56 – 2.49 (m, 2H), 2.40 (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.8, 137.3, 128.9, 128.4, 121.1, 55.0, 44.4, 33.3; HRMS (ESI) m/z calcd. for \(\text{C}_{11}\text{H}_{16}\text{ON}_{2}\text{Cl}\) [M+H]\(^+\) 227.08729, found 227.09523.

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N-(4-Bromophenyl)-3-(dimethylamino) propenamide (3dd). According to the general procedure analogous to that described for 3aa, 3dd (104 mg, 64%) was obtained from 1d (150 mg, 0.6 mmol) as a yellow solid. Mp: 52-56 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 11.23 – 10.77 (m, 1H), 7.45 – 7.33
(m, 4H), 2.63 (t, J = 6.6, 5.0 Hz, 2H), 2.47 (t, J = 6.6, 4.9 Hz, 2H), 2.35 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.8, 137.9, 131.8, 121.4, 116.0, 55.1, 44.5, 33.4; HRMS (ESI) m/z calcd. for C$_{11}$H$_{16}$ON$_2$Br [M+H]$^+$ 271.03678, found 271.04501.

3-Morpholino-N-phenylpropanamide (3ae). According to the general procedure analogous to that described for 3aa, 3ae (120 mg, 64%) was obtained from 1a (150 mg, 0.8 mmol) as a white solid. Mp: 62-64 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.71 (s, 1H), 7.53 (dd, J = 8.5, 1.0 Hz, 2H), 7.37 – 7.28 (m, 2H), 7.13 – 7.04 (m, 1H), 3.82 (t, J = 4.6 Hz, 4H), 2.79 – 2.70 (m, 2H), 2.62 (s, 4H), 2.57 – 2.50 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.3, 138.6, 129.1, 123.8, 119.5, 67.1, 54.2, 52.9, 32.3; HRMS (ESI) m/z calcd. for C$_{13}$H$_{19}$O$_2$N$_2$ [M+H]$^+$ 235.13683, found 235.14270.

$\text{HN}$
\begin{center}
\includegraphics[width=1cm]{benzene.png}
\end{center}

$\text{O}$

$\text{O}$

N-(4-Methoxyphenyl)-3-morpholinopropanamide (3be). According to the general procedure analogous to that described for 3aa, 3be (122 mg, 66%) was obtained from 1b (150 mg, 0.7 mmol) as a yellow solid. Mp: 110-112 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.48 (s, 1H), 7.41 (d, J = 8.9 Hz, 2H), 6.92 – 6.73 (m, 2H), 3.90 – 3.66 (m, 7H), 2.69 (t, J = 5.9 Hz, 2H), 2.56 (s, 4H), 2.49 (t, J = 5.9 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.1, 156.0, 131.9, 121.1, 114.2, 67.1, 55.5, 54.3, 52.9, 32.3; HRMS (ESI) m/z calcd. for C$_{14}$H$_{21}$O$_3$N$_2$ [M+H]$^+$ 265.14739, found 265.15491.
**N-(4-Chlorophenyl)-3-morpholinopropanamide (3ce).** According to the general procedure analogous to that described for 3aa, 3ce (120 mg, 64%) was obtained from 1c (150 mg, 0.7 mmol) as a white solid. Mp: 94-96 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.84 (s, 1H), 7.53 – 7.45 (m, 2H), 7.28 (dd, $J = 7.4$, 4.0 Hz, 2H), 3.82 (t, $J = 4.5$ Hz, 4H), 2.79 – 2.70 (m, 2H), 2.62 (s, 4H), 2.57 – 2.50 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.3, 137.2, 129.0, 128.6, 120.7, 67.1, 54.1, 52.8, 32.2; HRMS (ESI) m/z calcd. for C$_{13}$H$_{18}$O$_2$N$_2$Cl [M+H]$^+$ 269.09786, found 269.10410.

**N-(4-Bromophenyl)-3-morpholinopropanamide (3de).** According to the general procedure analogous to that described for 3aa, 3de (140 mg, 75%) was obtained from 1d (150 mg, 0.6 mmol) as a white solid. Mp: 82-84 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.82 (s, 1H), 7.50 – 7.34 (m, 4H), 3.83 – 3.76 (m, 4H), 2.76 – 2.68 (m, 2H), 2.60 (s, 4H), 2.55 – 2.48 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.4, 137.7, 132.0, 121.1, 116.2, 67.1, 54.1, 52.8, 32.2; HRMS (ESI) m/z calcd. for C$_{13}$H$_{18}$O$_2$N$_2$Br [M+H]$^+$ 313.04734, found 313.05566.

**3-(methylamino)-N-phenylpropanamide (3af).** According to the general procedure analogous to that described for 3aa, 3af (22 mg, 15%) was obtained from 1d (150 mg, 0.8 mmol) as a colorless oil. $^1$H NMR (400 MHz, CD$_3$OD) $\delta$ 7.55 (d, $J = 7.7$ Hz, 2H), 7.29 (t, $J = 7.9$ Hz, 2H), 7.07 (t, $J = 7.4$ Hz, 1H), 2.88 (t, $J = 6.7$ Hz, 2H), 2.57 (t, $J = 6.8$ Hz, 2H), 2.40 (s,
3H); $^{13}$C NMR (100 MHz, CD$_3$OD) $\delta$ 172.6, 139.8, 129.8, 125.1, 121.2, 48.2, 36.8, 35.8. HRMS (ESI) m/z calcd. for C$_{10}$H$_{15}$N$_2$O [M+H]$^+$ 179.11789, found 179.11823.

N-Benzyl-3-(dimethylamino) propenamide (3ed). According to the general procedure analogous to that described for 3aa, 3ed (170 mg, 83%) was obtained from 1e (200 mg, 1 mmol) as a colorless oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.67 (s, 1H), 7.31 (m, 2H), 7.28 – 7.21 (m, 3H), 4.45 (d, $J$ = 5.4 Hz, 2H), 2.55 (t, $J$ = 5.8 Hz, 2H), 2.41 (t, $J$ = 5.8 Hz, 2H), 2.22 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.6, 139.0, 128.6, 127.3, 127.1, 55.3, 44.6, 43.0, 33.0; HRMS (ESI) m/z calcd. for C$_{12}$H$_{19}$O$_2$N [M+H]$^+$ 207.14923.

**tert-Butyl 4-(3-(piperidin-1-yl) propanoyl) piperazine-1-carboxylate (3fa).** According to the general procedure analogous to that described for 3aa, 3fa (93 mg, 52%) was obtained from 1f (150 mg, 0.55 mmol) as a white solid. Mp: 96-98 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.64 – 3.52 (m, 2H), 3.50 – 3.30 (m, 6H), 2.76 – 2.65 (m, 2H), 2.58 (m, 2H), 2.45 (s, 4H), 1.69 – 1.54 (m, 4H), 1.45 (m, 11H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.5, 154.6, 80.3, 54.8, 54.7, 45.4, 41.4, 31.1, 28.4, 25.8, 24.2; HRMS (ESI) m/z calcd. for C$_{17}$H$_{32}$O$_3$N$_3$ [M+H]$^+$ 326.23654, found 326.24277.
According to the general procedure analogous to that described for 3aa, 3fe (140 mg, 78%) was obtained from 1f (150 mg, 0.55 mmol) as a white solid. Mp: 80-82 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.65 (Brs, 4H), 3.54 (s, 2H), 3.38 (d, $J = 17.9$ Hz, 6H), 2.75 – 2.61 (m, 2H), 2.57 – 2.36 (m, 6H), 1.48 – 1.34 (m, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.2, 154.5, 80.4, 66.9, 54.4, 53.7, 45.4, 41.4, 30.8, 28.4; HRMS (ESI) m/z calcd. for C$_{16}$H$_{30}$O$_4$N$_3$ [M+H]$^+$ 328.21581, found 328.22339.

tert-Butyl 4-(3-(pyrrolidin-1-yl) propanoyl) piperazine-1-carboxylate (3fb). According to the general procedure analogous to that described for 3aa, 3fb (121 mg, 71%) was obtained from 1f (150 mg, 0.55 mmol) as a yellow solid. Mp: 88-90 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.51 (Brs, 2H), 3.48 – 3.32 (m, 8H), 3.25 (s, 4H), 2.99 (t, $J = 7.0$ Hz, 2H), 2.06 (s, 4H), 1.41 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.7, 154.4, 80.4, 54.0, 51.0, 45.2, 41.6, 29.6, 28.3, 23.2; HRMS (ESI) m/z calcd. for C$_{16}$H$_{30}$O$_3$N$_3$ [M+H]$^+$ 312.22089, found 312.22852.

tert-Butyl 4-(3-(diethylamino) propanoyl) piperazine-1-carboxylate (3fc). According to the general procedure analogous to that described for 3aa, 3fc (124 mg, 72%) was obtained from 1f (150 mg, 0.55 mmol) as a yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.60 – 3.53 (m, 2H), 3.43 (s, 4H), 3.41 – 3.35 (m, 2H), 2.93 – 2.78 (m, 2H), 2.57 (m, 6H), 1.45 (s, 9H), 1.06 (t, $J = 7.2$ Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.5, 154.6, 80.3, 48.8, 47.0, 45.4, 41.4, 31.2, 28.4, 11.4; HRMS (ESI) m/z calcd. for C$_{16}$H$_{32}$O$_3$N$_3$ [M+H]$^+$ 314.23654, found 314.24405.
**tert-Butyl 4-(3-(dimethylamino) propanoyl) piperazine-1-carboxylate (3fd).** According to the general procedure analogous to that described for 3aa, 3fd (110 mg, 70%) was obtained from 1f (150 mg, 0.55 mmol) as a yellow solid. Mp: 78-80 °C; ¹H NMR (500 MHz, CDCl₃) δ 3.59 (Brs, 2H), 3.42 (m, 6H), 2.64 (t, J = 7.3 Hz, 2H), 2.51 (t, J = 7.4 Hz, 2H), 2.26 (s, 6H), 1.47 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 154.6, 80.3, 55.2, 45.6, 45.4, 41.4, 31.8, 28.4; HRMS (ESI) m/z calcd. for C₁₄H₂₈O₃N₃ [M+H]⁺ 286.20524, found 286.21231.

**3-((Dimethylamino)methyl) dihydrofuran-2(3H)-one (5ad).** According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 5 hours. 5ad (133 mg, 85%) was obtained from 4a (142 mg, 1 mmol) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 4.32 (m, 1H), 4.16 (m, 1H), 2.74 – 2.61 (m, 2H), 2.49 – 2.34 (m, 2H), 2.22 (s, 6H), 2.12 – 2.02 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 177.4, 65.8, 58.8, 44.5, 37.4, 27.0; HRMS (ESI) m/z calcd. for C₇H₁₄O₂N [M+H]⁺ 144.09463, found 144.10182.

**(3R,3aS,9R,9bS)-9-Hydroxy-6,9-dimethyl-3-(piperidin-1-ylmethyl)-3a,4,5,7,8,9,9a,9b-octahydroazuleno[4,5-b] furan-2(3H)-one (5ba).** According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 10 hours. 5ba (111 mg, 93%) was obtained from 4b (100 mg, 0.3 mmol) as a yellow oil. [α]₂₀°D = +16.2 (c 0.47, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 3.82 (s, 1H), 2.77 (s, 1H),
2.63 (d, \(J = 15.3\) Hz, 3H), 2.52 – 2.31 (m, 5H), 2.17 (s, 3H), 2.02 (d, \(J = 16.5\) Hz, 1H), 1.78 (dd, \(J = 19.1, 8.5\) Hz, 2H), 1.67 (s, 3H), 1.56 (s, 4H), 1.42 (s, 2H), 1.27 (d, \(J = 17.4\) Hz, 5H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 176.4, 130.8, 130.4, 83.1, 79.3, 57.4, 56.7, 54.0, 50.1, 43.2, 37.4, 34.4, 29.0, 26.4, 24.9, 23.2, 22.8, 21.8; HRMS (ESI) m/z calcd. for C\(_{20}\)H\(_{32}\)O\(_3\)N [M+H]\(^+\) 334.23039, found 334.23825.

\((3R,3aS,9R,9bS)-9\text{-Hydroxy-6,9-dimethyl-3-(pyrrolidin-1-ylmethyl)-3a,4,5,7,8,9,9a,9b-octahydroazuleno[4,5-b]furan-2(3H)-one}\ (5bb).\)

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 5 hours. 5bb (78 mg, 63%) was obtained from 4b (100 mg, 0.3 mmol) as a yellow solid. Mp: 142-144 °C; \([\alpha]_{D}^{20} = +20.2\) (c 0.50, CHCl\(_3\)); \(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 3.80 (t, \(J = 10.3\) Hz, 1H), 2.91 – 2.78 (m, 2H), 2.69 – 2.58 (m, 2H), 2.51 (d, \(J = 13.2\) Hz, 4H), 2.38 (m, 2H), 2.26 – 2.02 (m, 4H), 1.84 – 1.70 (m, 6H), 1.67 (s, 3H), 1.28 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.2, 131.8, 131.4, 84.2, 80.4, 58.4, 54.7, 54.3, 50.7, 45.7, 38.4, 35.5, 30.0, 27.4, 23.8, 23.7, 22.9; HRMS (ESI) m/z calcd. for C\(_{19}\)H\(_{30}\)O\(_3\)N [M+H]\(^+\) 320.21474, found 320.22211.

\((3R,3aS,9R,9bS)-3-((\text{Dimethylamino})methyl)-9\text{-hydroxy-6,9-dimethyl-3a,4,5,7,8,9,9a,9b-octahydroazuleno[4,5-b]furan-2(3H)-one}\ (5bd).\)

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 5 hours. 5bd (107 mg, 92%) was obtained from 4b (120 mg, 0.4 mmol) as a yellow solid. Mp: 118-120 °C; \([\alpha]_{D}^{20} = +15.6\) (c 0.49, CHCl\(_3\)); \(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 3.82 (t, \(J = 10.2\) Hz, 1H), 2.72 (dd, \(J = 12.7, 4.1\) Hz, 1H), 2.68 – 2.54 (m, 3H), 2.38
(m, 2H), 2.26 (s, 6H), 2.16 (m, 4H), 2.08 – 1.98 (m, 1H), 1.77 (m, 2H),
1.69 (s, 3H), 1.30 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 177.1, 131.8,
131.4, 84.1, 80.3, 58.3, 58.2, 50.9, 46.0, 44.6, 38.3, 35.3, 30.0, 27.3, 23.8,
22.8; HRMS (ESI) m/z calcd. for C\(_{17}\)H\(_{28}\)O\(_3\)N [M+H]\(^+\) 294.19909, found
294.20700.

(3R,3aS,9R,9bS)-9-Hydroxy-6,9-dimethyl-3-(morpholinomethyl)3a,4,5,7,8,9,9a,9b-octahydroazuleno[4,5-b]furan-2(3H)-one (5be).
According to the general procedure analogous to that described for 3aa,
except that the reaction was allowed for 5 hours. 5be (91 mg, 91%) was
obtained from 4b (100 mg, 0.3 mmol) as a yellow solid. Mp: 115-117 °C;
\([\alpha]\)^{20}_D\(=\) +20.6 (c 0.50, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.82 (t, \(J\) =
10.2 Hz, 1H), 3.67 (s, 4H), 2.79 (d, \(J\) = 11.3 Hz, 1H), 2.71 – 2.56 (m, 3H),
2.54 – 2.31 (m, 6H), 2.16 (t, \(J\) = 12.8 Hz, 4H), 2.05 (d, \(J\) = 11.2 Hz, 1H),
1.78 (dd, \(J\) = 18.9, 8.3 Hz, 2H), 1.67 (s, 3H), 1.29 (s, 3H); \(^{13}\)C NMR (100
MHz, CDCl\(_3\)) \(\delta\) 176.7, 131.9, 131.4, 84.2, 80.4, 66.9, 58.4, 57.1, 54.2, 50.9,
44.2, 38.4, 35.4, 30.0, 27.4, 23.8, 22.9; HRMS (ESI) m/z calcd. for C\(_{19}\)H\(_{30}\)O\(_4\)N [M+H]\(^+\) 336.20966, found 336.21619.

(3R,3aS,9R,9bS)-9-Hydroxy-6,9-dimethyl-3-(thiomorpholinomethyl)-
3a,4,5,7,8,9,9a,9b-octahydroazuleno[4,5-b]furan-2(3H)-one (5bh).
According to the general procedure analogous to that described for 3aa,
except that the reaction took 5 hours. 5bh (86 mg, 82%) was obtained from
4b (100 mg, 0.3 mmol) as a yellow solid. Mp: 96-100 °C; \([\alpha]\)^{20}_D\(=\) +20.7 (c
0.52, CHCl\(_3\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 3.81 (t, \(J\) = 10.5 Hz, 1H), 2.83
(m, 1H), 2.75 (s, 4H), 2.64 (s, 5H), 2.59 (s, 1H), 2.38 (s, 2H), 2.17 (s, 3H),
2.10 (d, \(J\) = 14.0 Hz, 1H), 2.02 (d, \(J\) = 11.5 Hz, 1H), 1.84 – 1.73 (m, 2H),

1.68 (s, 3H), 1.29 (s, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 177.5, 132.3, 131.8, 84.6, 80.8, 58.9, 57.7, 56.1, 51.2, 45.1, 38.9, 35.9, 30.5, 28.3, 27.8, 24.3, 23.3; HRMS (ESI) m/z calcd. for C$_{19}$H$_{30}$O$_3$NS [M+H]$^+$ 352.18681, found 352.19336.

(3R,3aS,9R,9bS)-3-((Benzylamino)methyl)-9-hydroxy-6,9-dimethyl-$\beta$-octahydroazuleno[4,5-b] furan-2(3H)-one (5bi).

According to the general procedure analogous to that described for 3aa, except that the reaction took 20h. 5bi (26 mg, 36%) was obtained from 4b (58 mg, 0.2 mmol) as a yellow oil. $[\alpha]^{20}_D = -16.5$ (c 0.22, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.33 (m, 5H), 3.83 (m, 3H), 2.96 (dd, $J = 12.2$, 3.8 Hz, 1H), 2.77 (dd, $J = 12.2$, 6.7 Hz, 1H), 2.65 (d, $J = 10.0$ Hz, 1H), 2.49 – 2.33 (m, 3H), 2.25 – 2.06 (m, 3H), 1.77 (m, 3H), 1.67 (s, 3H), 1.28 (d, $J = 10.0$ Hz, 5H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 177.5, 139.7, 131.9, 131.3, 128.5, 128.1, 127.1, 84.5, 80.3, 58.2, 53.9, 48.8, 46.6, 46.0, 38.4, 35.2, 30.0, 27.0, 23.8, 22.8; HRMS (ESI) m/z calcd. for C$_{22}$H$_{30}$O$_3$N [M+H]$^+$ 356.21474, found 356.22107.

(3R,3aS,9R,9bS)-9-Hydroxy-6,9-dimethyl-3-((methylamino)methyl)-$\beta$-octahydroazuleno[4,5-b] furan-2(3H)-one (5bf).

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 15 hours. 5bf (27 mg, 49%) was obtained from 4b (60 mg, 0.2 mmol) as a white solid. Mp: 110-112 °C; $[\alpha]^{20}_D = -13.8$ (c 0.23, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.86 (t, $J = 10.3$ Hz, 1H), 2.91 (dd, $J = 12.0$, 4.0 Hz, 1H), 2.80 (dd, $J = 12.1$, 7.2 Hz, 1H), 2.66 (d, $J = 10.4$ Hz, 1H), 2.53 – 2.45 (m, 4H), 2.37 (d, $J = 8.9$ Hz, 1H), 2.24 – 2.11 (m, 4H), 2.12 – 1.99 (m, 2H), 1.92 (dd, $J = 13.8$, 2.2 Hz,
1H), 1.79 (dd, J = 18.4, 7.7 Hz, 2H), 1.68 (s, 3H), 1.35 – 1.26 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 177.7, 132.1, 131.5, 84.7, 80.5, 58.4, 49.5, 49.3, 46.6, 38.6, 37.0, 35.4, 30.2, 27.3, 24.0, 23.0; HRMS (ESI) m/z calcd. for C$_{16}$H$_{26}$O$_3$N [M+H]$^+$ 280.18344, found 280.19034.

**tert-Butyl (2-(((3R,3aS,9R,9bS)-9-Hydroxy-6,9-dimethyl-2-oxo-2,3,3a,4,5,7,8,9,9a,9b-decahydroazuleno[4,5-b]furan-3-yl)methyl)amino)ethyl)(methyl)carbamate (5bj).** According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 15 hours. 5bj (88 mg, 70%) was obtained from 4b (100 mg, 0.3 mmol) as a white solid. Mp: 120-122 ºC; [α]$^{20}_D$ = –10.0 (c 0.48, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 3.98 – 3.78 (m, 1H), 3.37 (s, 2H), 3.09 – 2.97 (m, 1H), 2.92 (s, 3H), 2.82 (s, 2H), 2.69 (d, J = 9.7 Hz, 1H), 2.50 – 2.38 (m, 2H), 2.22 (s, 3H), 2.15 – 2.05 (m, 2H), 1.96 (d, J = 12.8 Hz, 1H), 1.81 (tt, J = 22.7, 11.3 Hz, 3H), 1.72 (s, 3H), 1.50 (s, 9H), 1.41 – 1.26 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.3, 155.9, 132.0, 131.2, 84.5, 80.3, 79.5, 60.4, 58.3, 48.9, 46.8, 38.4, 35.3, 30.1, 28.5, 27.2, 23.8, 22.9, 21.1, 14.2; HRMS (ESI) m/z calcd. for C$_{23}$H$_{39}$O$_5$N$_2$ [M+H]$^+$ 423.27807, found 423.28516.

**((3aR,4aS,6aS,7R,9aS)-7-((Dimethylamino)methyl)-1,4a-dimethyl-5,6,6a,7,9a,9b-hexahydro-3H-oxireno[2',3':8,8a] azuleno[4,5-b]furan-8(4aH)-one (5cd).** According to the general procedure analogous to that described for 3aa, except that the reaction took 5h. 5cd (58 mg, 99%) was obtained from 4c (60 mg, 0.2 mmol) as a white solid. Mp: 84-86 ºC; [α]$^{20}_D$ = +72.5 (c 0.49, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 5.55 (s, 1H), 4.02 (d, J = 9.5 Hz, 1H), 2.84 (d, J = 9.4 Hz, 1H), 2.73 (m, 2H), 2.58 (s, 1H), 2.31
(s, 1H), 2.24 (s, 5H), 2.17 – 2.04 (m, 2H), 2.02 – 1.83 (m, 6H), 1.63 (d, J = 10.6 Hz, 1H), 1.53 – 1.40 (m, 1H), 1.29 (d, J = 37.0 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.8, 140.7, 124.8, 82.6, 72.5, 62.7, 58.0, 52.4, 51.9, 46.1, 44.6, 39.6, 33.7, 22.9, 22.8, 18.3; HRMS (ESI) m/z calcd. for C\(_{17}\)H\(_{26}\)O\(_3\)N [M+H]\(^+\) 292.18344, found 292.19095.

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 5 hours. 5dd (40 mg, 70%) was obtained from 4d (60 mg, 0.2 mmol) as a brown oil. \([\alpha]^{20}_D\) = +40.9 (c 0.18, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.40 (s, 1H), 5.12 (s, 1H), 4.00 (t, J = 10.1 Hz, 1H), 2.85 (d, J = 9.8 Hz, 1H), 2.72 (s, 1H), 2.67 – 2.53 (m, 2H), 2.51 – 2.40 (m, 1H), 2.28 (s, 6H), 2.13 (m, 2H), 2.06 – 1.98 (m, 1H), 1.93 (m, 1H), 1.78 – 1.61 (m, 3H), 1.54 – 1.40 (m, 1H), 1.40 – 1.31 (m, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.5, 148.3, 110.8, 82.1, 73.2, 63.3, 57.9, 50.6, 49.2, 46.1, 44.7, 34.3, 32.5, 31.2, 23.0, 23.0; HRMS (ESI) m/z calcd. for C\(_{17}\)H\(_{26}\)O\(_3\)N [M+H]\(^+\) 292.18344, found 292.19116.

(3aR,4aS,6aS,7R,9aS)-7-((Dimethylamino)methyl)-4a-methyl-1-methylenoctahydo-1H-oxireno[2',3':8,8a]azuleno[4,5-b]furan-8(4aH)-one (5dd). According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 18 hours. 5ed (46 mg, 61%) was obtained from 4e (75 mg, 0.25 mmol) as a white solid. Mp: 162-164 °C; \([\alpha]^{20}_D\) = +55.5 (c 0.48, CHCl\(_3\)); \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) \(\delta\) 3.95 (t, J = 10.3 Hz, 1H), 3.32 (s, 1H), 3.29 (s, 3H), 2.60 –
2.53 (m, 2H), 2.34 (d, J = 15.3 Hz, 1H), 2.13 (d, J = 13.5 Hz, 6H), 1.93 (m, 1H), 1.83 (dd, J = 24.5, 11.7 Hz, 2H), 1.67 (m, 2H), 1.49 (s, 3H), 1.20 (s, 3H); \(^{13}\)C NMR (126 MHz, DMSO-\(d_6\)) \(\delta\) 177.9, 80.5, 69.7, 65.5, 62.3, 59.5, 58.7, 51.4, 49.2, 46.4, 44.0, 36.5, 33.2, 23.2, 22.8, 19.2; HRMS (ESI) m/z calcd. for C\(_{17}\)H\(_{26}\)O\(_4\)N [M+H]\(^+\) 308.17836, found 308.18463.

(3\(aS\),6\(Z\),10\(Z\),11\(aS\))-3-((Dimethylamino)methyl)-6,10-dimethyl-3\(a\),4,5,8,9,11\(a\)-hexahydrocycloeca[b]furan-2(3\(H\))-one (5fd).

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 5 hours. 5fd (33 mg, 60%) was obtained from 4f (60 mg, 0.2 mmol) as a yellow solid. Mp: 101-103 °C; \([\alpha]\)\(^{20}\)D = +0.84 (c 0.47, CHCl\(_3\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 4.83 (d, J = 9.9 Hz, 1H), 4.67 (d, J = 9.7 Hz, 1H), 4.56 (d, J = 9.5 Hz, 1H), 2.73 (d, J = 4.7 Hz, 1H), 2.61 (d, J = 4.5 Hz, 1H), 2.35 (d, J = 6.4 Hz, 2H), 2.26 (d, J = 13.4 Hz, 8H), 2.18 (s, 1H), 2.12 – 2.06 (m, 2H), 2.01 (m, 2H), 1.69 (s, 3H), 1.62 (d, J = 11.5 Hz, 1H), 1.41 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.6, 140.5, 137.1, 127.4, 127.0, 81.4, 58.1, 51.2, 46.2, 46.1, 41.1, 39.6, 28.4, 26.2, 17.3, 16.2; HRMS (ESI) m/z calcd. for C\(_{17}\)H\(_{28}\)O\(_2\)N [M+H]\(^+\) 278.20418, found 278.21207.

(3\(R\),3\(aS\),9\(aR\),10\(aS\),10\(bS\),E)-3-((Dimethylamino)methyl)-6,9a-dimethyl-3\(a\),4,5,8,9,9a,10a,10b-octahydrooxireno[2',3':9,10]cycloeca[1,2-b]furan-2(3\(H\))-one (5gd).

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 5 hours. 5fd (30 mg, 48%) was obtained from 4g (60 mg, 0.2 mmol) as a yellow solid. Mp: 128-130 °C; \([\alpha]\)\(^{20}\)D = -21.2 (c 0.53, CHCl\(_3\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 5.17 (d, J = 11.5 Hz, 1H), 3.80 (t, J = 8.9 Hz, 1H), 2.76 – 2.67 (m, 2H), 2.60 (dd, J =
13.1, 4.2 Hz, 1H), 2.37 (dq, $J = 10.2, 5.2$ Hz, 2H), 2.21 (d, $J = 19.6$ Hz, 8H), 2.18 – 1.99 (m, 4H), 1.67 (s, 3H), 1.64 – 1.57 (m, 1H), 1.27 (s, 3H), 1.19 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 176.5, 134.7, 125.0, 82.1, 66.5, 61.5, 57.7, 47.9, 46.5, 46.2, 41.1, 36.7, 29.9, 24.1, 17.2, 17.0; HRMS (ESI) m/z calcd. for C$_{17}$H$_{28}$O$_3$N [M+H]$^+$ 294.19909, found 294.20697.

$\textit{N}$-(3-Methoxypropyl) aniline (6a). $[^1]$ 6a was prepared according to the literature procedures as a yellow oil. $^1$H NMR (400 MHz, Acetone-$d_6$) $\delta$ 7.13 – 6.98 (m, 2H), 6.68 – 6.49 (m, 3H), 3.46 (t, $J = 6.1$ Hz, 2H), 3.28 (s, 3H), 3.16 (t, $J = 6.2$ Hz, 2H), 1.84 (m, 2H).

2-Methoxy-$\textit{N}$-phenylacetamide (7a). yellow oil. According to the general procedure analogous to that described for 1a. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.26 (s, 1H), 7.57 (m, 2H), 7.33 (m, 2H), 7.12 (t, $J = 7.4$ Hz, 1H), 4.00 (s, 2H), 3.49 (s, 3H).

3-(Benzyloxy)-$\textit{N}$-phenylpropanamide (8a). colorless oil. According to the general procedure analogous to that described for 1a. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31 (s, 1H), 7.44 (d, $J = 7.8$ Hz, 2H), 7.38 – 7.26 (m, 7H), 7.08 (t, $J = 7.4$ Hz, 1H), 4.60 (s, 2H), 3.84 (t, $J = 5.6$ Hz, 2H), 2.66 (t, $J = 5.6$ Hz, 2H).
3-Phenoxy-N-phenylpropanamide (8b). A yellow oil. According to the general procedure analogous to that described for 1a. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 10.07 (s, 1H), 7.62 (d, $J = 8.4$ Hz, 2H), 7.39 – 7.22 (m, 4H), 7.06 (d, $J = 7.4$ Hz, 1H), 6.94 (t, $J = 8.1$ Hz, 3H), 4.27 (t, $J = 6.0$ Hz, 2H), 2.80 (t, $J = 6.0$ Hz, 2H).

According to the general procedure analogous to that described for 3aa, except that the reaction was allowed for 12 hours. 9a (32 mg, 27%) and 10a (35 mg, 21%) and raw material 1a (39 mg, 26%) was obtained from 1a (150 mg, 0.8 mmol).

N-phenylacrylamide (9a). White solid. Mp: 104-106 °C; $^1$H NMR (400 MHz, ) $\delta$ 7.58 (d, $J = 7.5$ Hz, 2H), 7.33 (t, $J = 7.9$ Hz, 2H), 7.13 (t, $J = 7.3$ Hz, 1H), 6.44 (d, $J = 16.5$ Hz, 1H), 6.26 (m, 1H), 5.77 (m, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 163.5, 137.7, 131.2, 129.1, 127.86, 124.6, 120.0; HRMS (ESI) m/z calcd. for C$_9$H$_{10}$ON [M+H]$^+$ 148.06841, found 148.07492.
3-Isopropoxy-N-phenylpropanamide (10a). colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.67 (s, 1H), 7.51 (dd, $J$ = 8.5, 0.9 Hz, 2H), 7.35 – 7.27 (m, 2H), 7.15 – 7.01 (m, 1H), 3.78 – 3.64 (m, 3H), 2.74 – 2.50 (m, 2H), 1.24 (d, $J$ = 6.1 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.2, 138.3, 129.0, 124.0, 119.6, 72.4, 64.1, 38.2, 22.1; HRMS (ESI) m/z calcd. for C$_{12}$H$_{18}$O$_2$N [M+H]$^+$ 208.12593, found 208.13239.
References

3. NMR spectra

$^1$H NMR spectra of 1a

$^1$H NMR spectra of 1b
$\text{C NMR spectra of 1b}$

$\text{H NMR spectra of 1c}$
$^{13}$C NMR spectra of 1c

$^1$H NMR spectra of 1d
$^1$H NMR spectra of 1e

$^1$H NMR spectra of 1f
$^1$H NMR spectra of 3aa

$^{13}$C NMR spectra of 3aa
$^1$H NMR spectra of 3ba

$^{13}$C NMR spectra of 3ba
$^1$H NMR spectra of 3ca

$^{13}$C NMR spectra of 3ca
$^1$H NMR spectra of 3da

$^{13}$C NMR spectra of 3da
$^1$H NMR spectra of 3ab

$^{13}$C NMR spectra of 3ab
$^1$H NMR spectra of 3bb

$^{13}$C NMR spectra of 3bb
$^1$H NMR spectra of 3cb

$^{13}$C NMR spectra of 3cb
$^1$H NMR spectra of 3db

$^{13}$C NMR spectra of 3db
$^1$H NMR spectra of 3ac

$^{13}$C NMR spectra of 3ac
$^1$H NMR spectra of 3bc

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\text{NMR spectra}
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$^{13}$C NMR spectra of 3bc

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\text{NMR spectra}
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$^1$H NMR spectra of 3cc

$^{13}$C NMR spectra of 3cc
$^1$H NMR spectra of 3dc

$^{13}$C NMR spectra of 3dc
$^1$H NMR spectra of 3ad

$^{13}$C NMR spectra of 3ad
$^1$H NMR spectra of $3bd$

$^{13}$C NMR spectra of $3bd$
$^1$H NMR spectra of 3cd

$^{13}$C NMR spectra of 3cd
$^1$H NMR spectra of 3dd

$^{13}$C NMR spectra of 3dd
$^1$H NMR spectra of 3ae

$^{13}$C NMR spectra of 3ae
$^1$H NMR spectra of 3be

$^{13}$C NMR spectra of 3be
$^1$H NMR spectra of 3ce

$^{13}$C NMR spectra of 3ce
$^1$H NMR spectra of 3de

$^{13}$C NMR spectra of 3de
\( ^1H \) NMR spectra of 3af

\[ \text{Diagram of } ^1H \text{ NMR spectra} \]

\( ^{13}C \) NMR spectra of 3af

\[ \text{Diagram of } ^{13}C \text{ NMR spectra} \]
$^1$H NMR spectra of 3ed

13C NMR spectra of 3ed
$^1$H NMR spectra of 3fa

$^{13}$C NMR spectra of 3fa
$^1$H NMR spectra of 3fe

$^{13}$C NMR spectra of 3fe
$^1$H NMR spectra of 3fb
$^{13}$C NMR spectra of $3fb$

$^1$H NMR spectra of $3fc$
$^{13}$C NMR spectra of $3\text{fe}$

$^1$H NMR spectra of $3\text{fd}$

$^{13}$C NMR spectra of $3\text{fd}$
$^1$H NMR spectra of 5ad

$^{13}$C NMR spectra of 5ad
$^{1}H$ NMR spectra of 5ba

$^{13}C$ NMR spectra of 5ba
$^1$H NMR spectra of 5bb

$^{13}$C NMR spectra of 5bb
$^1$H NMR spectra of 5bd

$^{13}$C NMR spectra of 5bd
$^1$H NMR spectra of 5be

$^{13}$C NMR spectra of 5be
\(^1\)H NMR spectra of 5bh

\(^{13}\)C NMR spectra of 5bh
$^1$H NMR spectra of 5bi

$^{13}$C NMR spectra of 5bi
$^1$H NMR spectra of 5bf

$^{13}$C NMR spectra of 5bf
$^{1}$H NMR spectra of 5bj

$^{13}$C NMR spectra of 5bj
$^{1}$H NMR spectra of 5cd

$^{13}$C NMR spectra of 5cd
$^1$H NMR spectra of 5dd

$^{13}$C NMR spectra of 5dd
$^1$H NMR spectra of 5ed

$^{13}$C NMR spectra of 5ed
$^1$H NMR spectra of 5fd

$^{13}$C NMR spectra of 5fd
\(^1\)H NMR spectra of 5gd

\(^{13}\)C NMR spectra of 5gd
$^1$H NMR spectra of 6a

$^1$H NMR spectra of 7a
$^1$H NMR spectra of 8a

$^1$H NMR spectra of 8b
$^1$H NMR spectra of 9a

$^{13}$C NMR spectra of 9a
$\text{H NMR spectra of 10a}$

$\text{C NMR spectra of 10a}$