Supporting Information
for DOI: 10.1055/s-0031-1290073
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Supporting Information

One-pot Synthesis of Fused Pyridazino[4,5-b][1,4]oxazepine-diones via Smiles Rearrangement

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Experimental Section

General

General Experimental Procedure for the Synthesis of (3a-l), (5a-f).

\textsuperscript{1}H NMR and \textsuperscript{13}C NMR Spectra of Compound (3a-l), (5a-f).

\textsuperscript{1}H NMR Spectra of Compound 13.

General

\textsuperscript{1}H NMR spectra were recorded on a Bruker Avance 400 (400 MHz) or 300 (300 MHz) spectrometer, using CDCl\textsubscript{3} as solvent and tetramethylsilane (TMS) as internal standard. \textsuperscript{13}C NMR spectra were recorded on a Bruker Avance 100 (100 MHz) or 75 (75 MHz) spectrometer, using CDCl\textsubscript{3} as solvent and tetramethylsilane (TMS) as internal standard. Melting points were determined on an XD-4 digital micro melting point apparatus. HRMS spectra were determined on a Q-TOF6510 spectrograph (Agilent).


To a solution of N-propyl salicylamide (150 mg, 0.9 mmol) in dry dimethylformamide (DMF, 10 mL) were added 4,5-dichloro-2-(tetrahydro-2H-pyran-2-yl)pyridazin-3(2H)-one (170 mg, 0.7 mmol) and K\textsubscript{2}CO\textsubscript{3} (290 mg, 2.1 mmol), then the mixture was stirred for 3 h at 80 °C (oil bath), and then H\textsubscript{2}O (30 mL) was added and the mixture was extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with sat. brine (2 × 20 mL), dried over MgSO\textsubscript{4}, filtered, and evaporated in vacuo. The crude product was purified by column chromatography on silica gel (PE/EtOAc = 3:1) to afford the desired product 3c as a white solid (214 mg, 89%).

11-Methyl-3-(tetrahydro-2H-pyran-2-yl)benzo[\textit{f}]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3a).

White crystal, m.p. 96.5-99.8 °C. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) 80.98 (dd, 1H, \textit{J} = 1.8, 7.8 Hz), 7.50-7.60 (m, 3H), 7.00-7.10 (m, 2H), 6.04 (dd, 1H, \textit{J} = 1.8, 7.8 Hz), 4.12-4.22 (m, 2H), 3.48-3.58 (m, 2H), 3.30-3.40 (m, 2H), 2.58-2.68 (m, 2H), 2.22-2.32 (m, 2H), 1.96-2.06 (m, 2H), 1.29-1.39 (m, 3H).
4.10-4.15 (m, 1H), 3.96-4.00 (q, 2H, J = 6.6 Hz), 7.24-7.30 (m, 1H), 6.03-6.07 (dd, 1H, J = 2.1, 10.8 Hz), 4.10-4.15 (m, 1H), 3.96-4.00 (q, 2H, J = 6.6 Hz), 2.03-2.20 (m, 2H), 1.56-1.83 (m, 6H), 0.96-1.00 (t, 3H, J = 7.2 Hz). 13C NMR (75 MHz, CDCl3) δ 166.08, 159.89, 156.77, 145.63, 134.28, 133.98, 132.55, 125.02, 125.73, 120.93, 83.19, 68.93, 48.68, 28.85, 24.86, 22.78, 21.65, 10.99. HRMS calcd for C21H21N3O4, 355.1532; found, 355.1626.

11-Isopropyl-3-(tetrahydro-2H-pyran-2-yl)benzo[fp]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3d). White crystal, m.p. 158.8-162.8 °C. 1H NMR (400 MHz, CDCl3) δ 7.82-7.87 (dd, 1H, J = 1.52, 7.8 Hz), 7.46-7.50 (m, 1H), 7.35-7.36 (dd, 1H, J = 0.9, 8.1 Hz), 7.24-7.28 (m, 1H), 6.03-6.06 (dd, 1H, J = 2.1, 10.8 Hz), 4.10-4.15 (m, 1H), 3.70-3.79 (m, 1H), 1.98-2.19 (m, 2H), 1.57-1.80 (m, 1H). 13C NMR (75 MHz, CDCl3) δ 165.87, 160.19, 156.90, 146.87, 134.21, 134.11, 133.33, 132.54, 126.03, 125.99, 128.81, 81.23, 68.95, 52.93, 28.92, 24.90, 22.81, 21.28, 21.23. HRMS calcd for C20H21N3O4, 355.1532; found, 355.1633.

11-Benzyl-3-(tetrahydro-2H-pyran-2-yl)benzo[fp]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3f). White crystal, m.p. 189.6-191.5 °C. 1H NMR (400 MHz, CDCl3) δ 7.80-7.85 (dd, 1H, J = 1.52, 7.8 Hz), 7.47-7.50 (m, 1H), 7.40-7.42 (t, 3H, J = 0.9 Hz), 7.26-7.33 (m, 6H), 5.98-6.02 (dd, 1H, J = 1.92, 10.76 Hz), 5.22-5.31 (q, 2H, J = 16.3 Hz), 4.05-4.14 (m, 1H), 3.67-3.73 (m, 1H), 1.97-2.07 (m, 2H), 1.51-1.65 (m, 4H). 13C NMR (75 MHz, CDCl3) δ 166.45, 159.87, 156.74, 145.10, 135.54, 134.64, 134.15, 132.60, 132.07, 129.14, 127.94, 126.55, 126.15, 125.36, 121.12, 83.21, 68.91, 50.65, 28.84, 24.84, 22.74. HRMS calcd for C25H25N3O4, 395.1845; found, 395.1913.

11-Phenyl-3-(tetrahydro-2H-pyran-2-yl)benzo[fp]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3g). White crystal, m.p. 193.5-196.7 °C. 1H NMR (400 MHz, CDCl3) δ 7.91-7.94 (dd, 1H, J = 1.8, 7.8 Hz), 7.50-7.60 (m, 3H), 7.44-7.49 (m, 2H), 7.29-7.40 (m, 4H), 6.02-6.06 (dd, 1H, J = 2.1, 10.8 Hz), 4.06-4.10 (m, 1H), 3.69-3.77 (m, 1H), 1.98-2.11 (m, 2H), 1.51-1.76 (m, 4H). 13C NMR (100 MHz, CDCl3) δ 166.03, 159.78, 156.83, 144.50, 143.58, 134.77, 133.71, 133.62, 132.13, 128.99, 129.11, 128.84, 126.17, 125.62, 121.27, 83.13, 68.89, 28.73, 24.85, 22.77. HRMS calcd for C19H17N3O4, 327.1219; found, 327.1295.
White crystal, m.p. 165.3-169.9 °C. 1H NMR (400 MHz, CDCl₃) δ 7.91-7.93 (dd, 1H, J = 1.64, 7.76 Hz), 7.54-7.58 (m, 1H), 7.43-7.45 (m, 1H), 7.26-7.33 (m, 5H), 7.24-7.26 (s, 1H), 6.02-6.05 (dd, 1H, J = 2.04, 10.6 Hz), 4.07-4.10 (m, 1H), 3.70-3.76 (m, 1H), 2.42 (s, 3H), 1.98-2.08 (m, 2H), 1.53-1.71 (m, 4H). 13C NMR (100 MHz, CDCl₃) δ 166.17, 159.80, 156.87, 144.33, 139.30, 135.84, 134.68, 134.04, 133.69, 132.68, 130.60, 128.53, 126.12, 125.71, 121.24, 83.13, 68.85, 28.70, 24.87, 22.78, 21.23. HRMS caleld for C₂₃H₁₈N₃O₅ 419.1481; found, 419.1569.

11-(4-fluorophenyl)-3-(tetrahydro-2H-pyran-2-yl)benzo[f]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3i). White crystal, m.p. 174.2-179.1 °C. 1H NMR (300 MHz, CDCl₃) δ 7.90-7.93 (dd, 1H, J = 1.8, 9.9 Hz), 7.53-7.59 (m, 1H), 7.42-7.46 (m, 1H), 7.27-7.34 (m, 4H), 6.99-7.05 (m, 2H), 6.01-6.05 (dd, 1H, J = 2.1, 10.8 Hz), 4.06-4.11 (dd, 1H, J = 2.1, 12 Hz), 3.86 (s, 3H), 3.69-3.77 (m, 1H), 1.98-2.13 (m, 2H), 1.52-1.76 (m, 4H). 13C NMR (75 MHz, CDCl₃) δ 166.33, 159.83, 159.80, 156.85, 144.21, 134.91, 134.14, 136.12, 133.67, 132.70, 131.02, 129.90, 126.11, 125.65, 121.23, 115.15, 83.13, 68.85, 55.60, 28.70, 24.86, 22.77. HRMS caleld for C₂₃H₁₈FN₃O₅ 407.1281; found, 407.1350.

11-(4-chlorophenyl)-3-(tetrahydro-2H-pyran-2-yl)benzo[f]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3k). White crystal, m.p. 199.5-206.8 °C. 1H NMR (300 MHz, CDCl₃) δ 7.90-7.93 (dd, 1H, J = 1.5, 7.8 Hz), 7.55-7.60 (m, 1H), 7.48-7.53 (m, 2H), 7.43-7.47 (m, 1H), 7.30-7.40 (m, 3H), 7.19-7.26 (m, 3H), 6.01-6.05 (dd, 1H, J = 2.1, 10.5 Hz), 4.06-4.11 (q, 1H, J = 9.9, 11.4 Hz), 3.69-3.77 (m, 1H), 1.99-2.13 (m, 2H), 1.53-1.78 (m, 4H). 13C NMR (75 MHz, CDCl₃) δ 166.06, 159.80, 156.76, 144.62, 134.91, 134.28, 133.77, 133.30, 132.73, 130.77, 130.66, 126.22, 125.34, 121.31, 117.43, 117.15, 116.84. HRMS caleld for C₂₃H₁₈ClN₃O₅ 423.0986; found, 423.1074.

11-(4-bromophenyl)-3-(tetrahydro-2H-pyran-2-yl)benzo[f]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (3l). White crystal, m.p. 216.2-221.5 °C. 1H NMR (300 MHz, CDCl₃) δ 7.90-7.93 (dd, 1H, J = 1.5, 7.8 Hz), 7.55-7.60 (m, 1H), 7.48-7.53 (m, 2H), 7.43-7.47 (m, 1H), 7.30-7.40 (m, 3H), 7.19-7.26 (m, 3H), 6.01-6.05 (dd, 1H, J = 2.1, 10.5 Hz), 4.06-4.11 (q, 1H, J = 9.9, 11.4 Hz), 3.69-3.77 (m, 1H), 1.99-2.13 (m, 2H), 1.53-1.78 (m, 4H). 13C NMR (75 MHz, CDCl₃) δ 166.06, 159.80, 156.76, 144.62, 134.91, 134.28, 133.77, 133.30, 132.73, 130.77, 130.66, 126.22, 125.34, 121.31, 117.43, 117.15, 116.84. HRMS caleld for C₂₃H₁₈BrN₃O₅ 437.1321; found, 437.1408.
135.61, 134.49, 132.05, 130.99, 129.13, 127.91, 126.59, 125.60, 125.41, 83.30, 68.92, 50.64, 28.89, 24.87, 22.80, 15.86. HRMS calcd for C_{24}H_{23}N_{3}O_{4}, 417.1689; found, 417.1772.

6-Methyl-11-phenyl-3-(tetrahydro-2H-pyran-2-yl)benzo[f]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (5b). White crystal, m.p. 211.2-214.8 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.71-7.74 (dd, 1H, J = 1.2, 7.8 Hz), 7.50-7.55 (m, 2H), 7.36-7.38 (m, 2H), 7.26 (d, 1H), 7.16-7.21 (t, 1H, J = 7.5 Hz), 6.01-6.05 (dd, 1H, J = 2.1, 10.5 Hz), 4.08-4.11 (m, 1H), 3.69-3.77 (m, 1H), 2.69 (s, 3H), 1.98-2.11 (m, 2H), 1.43-1.77 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 166.43, 158.67, 156.99, 145.08, 138.63, 136.19, 134.33, 133.59, 131.12, 130.27, 129.97, 129.08, 128.86, 125.68, 125.63, 83.25, 68.91, 28.75, 24.89, 22.83, 15.93. HRMS calcd for C_{23}H_{21}N_{3}O_{4}, 403.1532; found, 403.1605.

6-Methyl-11-phenyl-3-(tetrahydro-2H-pyran-2-yl)benzo[f]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (5b). White crystal, m.p. 211.2-214.8 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.71-7.74 (dd, 1H, J = 1.2, 7.8 Hz), 7.50-7.55 (m, 2H), 7.36-7.38 (m, 2H), 7.26 (d, 1H), 7.16-7.21 (t, 1H, J = 7.5 Hz), 6.01-6.05 (dd, 1H, J = 2.1, 10.5 Hz), 4.08-4.11 (m, 1H), 3.69-3.77 (m, 1H), 2.69 (s, 3H), 1.98-2.11 (m, 2H), 1.43-1.77 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 166.43, 158.67, 156.99, 145.08, 138.63, 136.19, 134.33, 133.59, 131.12, 130.27, 129.97, 129.08, 128.86, 125.68, 125.63, 83.25, 68.91, 28.75, 24.89, 22.83, 15.93. HRMS calcd for C_{23}H_{21}N_{3}O_{4}, 403.1532; found, 403.1605.

8-Chloro-11-phenyl-3-(tetrahydro-2H-pyran-2-yl)benzo[f]pyridazino[4,5-b][1,4]oxazepine-4,10(3H,11H)-dione (5d). White crystal, m.p. 202.4-206.5 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.89-7.90 (d, 1H, J = 2.4 Hz), 7.44-7.57 (m, 4H), 7.34-7.41 (m, 3H), 7.25 (d, 1H, J = 1.8 Hz), 6.00-6.04 (dd, 1H, J = 2.1, 10.5 Hz), 4.06-4.13 (m, 1H), 3.70-3.76 (m, 1H), 1.98-2.10 (m, 2H), 1.55-1.71 (m, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 164.78, 158.22, 156.63, 144.38, 138.21, 134.53, 133.78, 133.40, 132.27, 131.77, 130.07, 129.32, 128.73, 126.92, 122.75, 83.24, 68.88, 28.70, 24.85, 22.75. HRMS calcd for C_{27}H_{23}N_{3}O_{4}, 453.1689; found, 453.1785.

13-Benzyl-3-(tetrahydro-2H-pyran-2-yl)naphtho[2,3-f]pyridazino[4,5-b][1,4]oxazepine-4,12(3H,13H)-dione (5e). White crystal, m.p. 208.0-212.3 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.52 (s, 1H), 7.92-7.94 (d, 1H, J = 6.4 Hz), 7.89 (s, 1H), 7.83-7.85 (m, 2H), 7.28 (s, 1H), 6.03-6.06 (dd, 1H, J = 1.8, 10.6 Hz), 4.06-4.13 (m, 1H), 3.67-3.76 (m, 1H), 1.97-2.06 (m, 2H), 1.50-1.71 (m, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 166.15, 155.72, 144.21, 138.68, 136.85, 136.31, 134.31, 132.12, 130.80, 129.17, 129.10, 127.94, 127.43, 126.56, 124.74, 117.86, 83.25, 68.90, 50.86, 28.83, 24.84, 22.74. HRMS calcd for C_{26}H_{21}N_{3}O_{4}, 439.1532; found, 439.1617.

Appendix. NMR spectra of Titled compounds
\[ \text{\textsuperscript{1}H NMR Spectrum (400 MHz, CDCl}_3\text{) of Compound 3a} \]

\[ \text{\textsuperscript{13}C NMR Spectrum (100 MHz, CDCl}_3\text{) of Compound 3a} \]
$^1$H NMR Spectrum (400 MHz, CDCl$_3$) of Compound 3b

$^{13}$C NMR Spectrum (100 MHz, CDCl$_3$) of Compound 3b
\( ^1\)H NMR Spectrum (300 MHz, CDCl\(_3\)) of Compound 3c

\( ^{13}\)C NMR Spectrum (75 MHz, CDCl\(_3\)) of Compound 3c
$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 3d

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 3d
$^1$H NMR Spectrum (400 MHz, CDCl$_3$) of Compound 3e
$^{13}$C NMR Spectrum (100 MHz, CDCl$_3$) of Compound 3e

$^1$H NMR Spectrum (400 MHz, CDCl$_3$) of Compound 3f

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 3f
'H NMR Spectrum (300 MHz, CDCl₃) of Compound 3g

'C NMR Spectrum (100 MHz, CDCl₃) of Compound 3g
$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 3i

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 3i
$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 3j

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 3j
1H NMR Spectrum (300 MHz, CDCl₃) of Compound 3k

13C NMR Spectrum (75 MHz, CDCl₃) of Compound 3k
$^1$H NMR Spectrum (400 MHz, CDCl$_3$) of Compound 3l

$^{13}$C NMR Spectrum (100 MHz, CDCl$_3$) of Compound 3l
1H NMR Spectrum (400 MHz, CDCl₃) of Compound 5a

13C NMR Spectrum (100 MHz, CDCl₃) of Compound 5a
$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 5b

$^{13}$C NMR Spectrum (100 MHz, CDCl$_3$) of Compound 5b
$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 5c

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 5c
$^1$H NMR Spectrum (300 MHz, CDCl₃) of Compound 5d

$^{13}$C NMR Spectrum (100 MHz, CDCl₃) of Compound 5d
$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 5e

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 5e

$^1$H NMR Spectrum (300 MHz, CDCl$_3$) of Compound 5e

$^{13}$C NMR Spectrum (75 MHz, CDCl$_3$) of Compound 5e
H-H NOESY of product 3b
$^1$H NMR Spectrum (400 MHz, CDCl$_3$) of Compound 13