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## Microwave promoted C-O coupling for synthesizing *O*-aryloxytriazole nucleoside analogues

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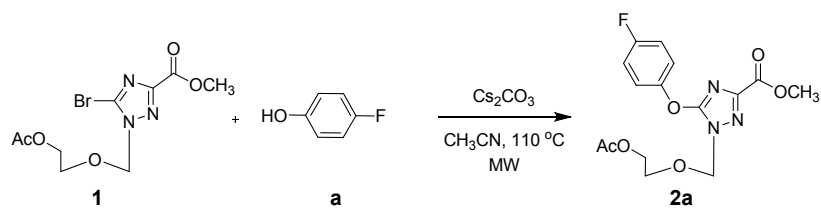
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## Table of Contents

Table S1 .....	S2
General.....	S3
Representative Procedure <b>A</b> for preparing <b>2a-2n</b> .....	S3
Representative Procedure <b>B</b> for preparing <b>4a-4n</b> .....	S3
<sup>1</sup> H NMR and <sup>13</sup> C NMR spectra. ....	S13

**Table S1.** Optimization of the reagent ratio.<sup>a</sup>



entry	phenol ( <b>a</b> )	$\text{Cs}_2\text{CO}_3$	yield %
1	1.0 eq	1.0 eq	58
2	2.0 eq	1.0 eq	72
3	3.0 eq	1.0 eq	78
4	3.0 eq	1.5 eq	3
5	3.0 eq	2.0 eq	4
6	3.0 eq	0.5 eq	58

<sup>a</sup> compound **1** (0.10 mmol), solvent (0.75 mL), MW,  $110\text{ }^\circ\text{C}$ , calculated yield with  $^1\text{H}$  NMR.

**General:** Chemicals were purchased from Sigma Aldrich or Alfa Aesar and were used directly without purification. The adducts were purified by flash chromatography on silica gel (Merck 200-300 mesh).  $^1\text{H}$  NMR spectra were recorded at 250 or 400 MHz and  $^{13}\text{C}$  NMR spectra recorded at 62.5 or 100 MHz, on Bruker Avance II 250, Bruker Avance III 400 spectrometers, JEOL 400 spectrometers, respectively. The chemical shifts ( $\delta$ ) are expressed in parts per million (ppm) with the residual peak of  $\text{CHCl}_3$  at 7.26 ppm. The high-resolution mass spectra (HRMS) were obtained with an MALDI/DHB or ESI-Positive mode on IonSpec 4.7 TESLA FTMS or Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS. Thin Layer Chromatography (TLC) was performed on TLC plates silica gel 60 F254, layer thickness 0.2 mm, Merck KGaA. The compound revelations were revealed by using UV light (254 nm).

**General procedure A for synthesizing 2a-2n.** Compound **1** (0.10 mmol),  $\text{Cs}_2\text{CO}_3$  (0.10 mmol) were mixed in  $\text{CH}_3\text{CN}$  (0.75 mL) in an oven-dried 10 mL MW tube with a stirring bar under 110 °C for 30 min. Reactions were monitored by TLC. The reaction mixture was concentrated under reduced pressure and the crude residue purified by flash chromatography on silica gel using the mixture dichloromethane and menthol as eluent. The purified material was dried in vacuum to afford the corresponding product **2a-2n**.

**General procedure B for synthesizing 4a-4n.** Compound **3** (0.10 mmol),  $\text{Cs}_2\text{CO}_3$  (0.10 mmol) were mixed in  $\text{CH}_3\text{CN}$  (0.75 mL) in an oven-dried 10 mL MW tube with a stirring bar under 110 °C for 30 min. Reactions were monitored by TLC. The reaction mixture was concentrated under reduced pressure and the crude residue purified by flash chromatography on silica gel using the mixture dichloromethane and menthol as eluent. The purified material was dried in vacuum to afford the corresponding product **4a-4n**.

**2a:** The desired product was obtained starting from compound **1** and 4-fluorophenol with a 78 % yield (27.6 mg) as white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.34-7.30 (m, 2H, phenyl-H), 7.09 (t, 2H, *J* = 8.6 Hz, phenyl-H), 5.57 (s, 2H, -OCH<sub>2</sub>N-), 4.21 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.94 (s, 3H, -C(O)OCH<sub>3</sub>), 3.89 (t, 2H, *J* = 4.4 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.03 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.6, 160.2 (*J*<sub>CF</sub> = 243.6 Hz), 159.7, 158.1, 150.8, 149.0 (*J*<sub>CF</sub> = 2.8 Hz), 121.0 (*J*<sub>CF</sub> = 8.5 Hz), 116.5 (*J*<sub>CF</sub> = 23.6 Hz), 76.2, 68.0, 62.8, 52.8, 20.7. R<sub>f</sub> = 0.34 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>15</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>6</sub><sup>+</sup>, 354.1096, found 354.1093.

**2b:** The desired product was obtained starting from compound **1** and 3-fluorophenol with a 74 % yield (26.1 mg) as c white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.41-7.32 (m, 1H, phenyl-H), 7.17-7.04 (m, 2H, phenyl-H), 7.00-6.93 (m, 1H, phenyl-H), 5.56 (s, 2H, -OCH<sub>2</sub>N-), 4.20 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.95 (s, 3H, -C(O)OCH<sub>3</sub>), 3.87 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.02 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.6, 163.0 (*J*<sub>CF</sub> = 247.1 Hz), 159.7, 157.4, 153.8 (*J*<sub>CF</sub> = 10.9 Hz), 150.9, 130.7 (*J*<sub>CF</sub> = 9.4 Hz), 115.0 (*J*<sub>CF</sub> = 3.4 Hz), 113.1 (*J*<sub>CF</sub> = 21.0 Hz), 107.5 (*J*<sub>CF</sub> = 25.5 Hz), 76.3, 68.1, 62.7, 52.8, 20.7. R<sub>f</sub> = 0.34 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>15</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>6</sub><sup>+</sup>, 354.1096, found 354.1100.

**2c:** The desired product was obtained starting from compound **1** and 2-fluorophenol with a 50 % yield (17.6 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.50-7.43 (m, 1H, phenyl-H), 7.28-7.15 (m, 3H, phenyl-H), 5.61 (s, 2H, -OCH<sub>2</sub>N-), 4.24 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.95 (s, 3H, -C(O)OCH<sub>3</sub>), 3.90 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.06 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 159.7, 158.0, 153.4 (*J*<sub>CF</sub> = 248.6 Hz), 150.9, 140.5 (*J*<sub>CF</sub> = 12.0 Hz), 127.6 (*J*<sub>CF</sub> = 7.1 Hz), 124.9 (*J*<sub>CF</sub> = 3.9 Hz), 122.4, 117.3 (*J*<sub>CF</sub> = 17.8 Hz), 76.3, 68.0, 62.8, 52.8, 20.7. R<sub>f</sub> = 0.31 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>15</sub>H<sub>17</sub>FN<sub>3</sub>O<sub>6</sub><sup>+</sup>, 354.1096, found 354.1096.

**2d:** The desired product was obtained starting from compound **1** and 4-(trifluoromethyl)phenol with a 62 % yield (24.9 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.69 (d, 2H, *J* = 9.0 Hz, phenyl-H), 7.51 (d, 2H, *J* = 9.0 Hz, phenyl-H), 5.59 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.97 (s, 3H, -

C(O)OCH<sub>3</sub>), 3.90 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.03 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 159.7, 157.2, 155.4, 150.9, 128.4 (*J*<sub>CF</sub> = 32.8 Hz), 127.4 (*J*<sub>CF</sub> = 3.8 Hz), 123.6 (*J*<sub>CF</sub> = 270.1 Hz), 119.7, 76.4, 68.2, 62.7, 52.9, 20.7. R<sub>f</sub> = 0.35 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>16</sub>H<sub>17</sub>F<sub>3</sub>N<sub>3</sub>O<sub>6</sub><sup>+</sup>, 404.1064, found 404.1068.

**2e:** The desired product was obtained starting from compound **1** and 3-(trifluoromethyl)phenol with a 80 % yield (32.1 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.62-7.52 (m, 4H, phenyl-H), 5.57 (s, 2H, -OCH<sub>2</sub>N-), 4.20 (t, 2H, *J* = 4.5 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.94 (s, 3H, -C(O)OCH<sub>3</sub>), 3.88 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.01 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.6, 159.6, 157.4, 153.1, 150.8, 132.4 (*J*<sub>CF</sub> = 33.0 Hz), 130.6, 123.2 (*J*<sub>CF</sub> = 270.8 Hz), 122.9 (*J*<sub>CF</sub> = 3.9 Hz), 116.7 (*J*<sub>CF</sub> = 3.9 Hz), 76.3, 68.1, 62.7, 52.8, 20.6. R<sub>f</sub> = 0.38 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>16</sub>H<sub>17</sub>F<sub>3</sub>N<sub>3</sub>O<sub>6</sub><sup>+</sup>, 404.1064, found 404.1064.

**2f:** The desired product was obtained starting from compound **1** and 2-(trifluoromethyl)phenol with a 35 % yield (14.1 mg) as white solid. <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>): δ 7.73-7.64 (m, 3H, phenyl-H), 7.39 (t, 1H, *J* = 7.6 Hz, phenyl-H), 5.60 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.96 (s, 3H, -C(O)OCH<sub>3</sub>), 3.88 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 170.8, 159.7, 157.3, 150.8, 150.1, 133.9, 127.3 (*J*<sub>CF</sub> = 7.3 Hz), 126.2, 122.8 (*J*<sub>CF</sub> = 271.2 Hz), 121.7 (*J*<sub>CF</sub> = 31.8 Hz), 76.3, 68.0, 62.8, 52.9, 20.7. R<sub>f</sub> = 0.34 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>16</sub>H<sub>17</sub>F<sub>3</sub>N<sub>3</sub>O<sub>6</sub><sup>+</sup>, 404.1064, found 404.1068.

**2g:** The desired product was obtained starting from compound **1** and 4-chlorophenol with a 61 % yield (22.5 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.40-7.29 (m, 4H, phenyl-H), 5.57 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.96 (s, 3H, -C(O)OCH<sub>3</sub>), 3.89 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.03 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 159.7, 157.7, 151.6, 150.9, 131.5, 130.0, 120.8, 76.3, 68.1, 62.8, 52.9, 20.8. R<sub>f</sub> = 0.33 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>15</sub>H<sub>16</sub>ClN<sub>3</sub>NaO<sub>6</sub><sup>+</sup>, 392.0620, found 392.0620.

**2h:** The desired product was obtained starting from compound **1** and phenol with a 44 % yield (14.7 mg) as a white solid.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.43-7.20 (m, 5H, -phenyl-H), 5.56 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.20 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.93 (s, 3H,  $-\text{C}(\text{O})\text{OCH}_3$ ), 3.87 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.02 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (62.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.8, 159.9, 158.1, 153.3, 150.9, 130.0, 126.1, 119.3, 76.2, 68.0, 62.8, 52.8, 20.8.  $R_f = 0.33$  (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for  $\text{C}_{15}\text{H}_{18}\text{N}_3\text{O}_6^+$ , 336.1190, found 336.1196.

**2i:** The desired product was obtained starting from compound **1** and 4-methylphenol with a 34 % yield (11.9 mg) as white solid.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.20 (s, 4H, phenyl-H), 5.56 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.22 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.94 (s, 3H,  $-\text{C}(\text{O})\text{OCH}_3$ ), 3.89 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.35 (s, 3H,  $-\text{PhCH}_3$ ), 2.04 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (62.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.7, 159.9, 158.4, 151.2, 135.8, 130.3, 119.2, 76.2, 68.0, 62.8, 52.8, 20.8.  $R_f = 0.38$  (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for  $\text{C}_{16}\text{H}_{20}\text{N}_3\text{O}_6^+$ , 350.1347, found 350.1348.

**2j:** The desired product was obtained starting from compound **1** and 3-methylphenol with a 37 % yield (12.9 mg) as white solid.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.31-7.24 (m, 1H, phenyl-H), 7.13-7.04 (m, 3H, phenyl-H), 5.56 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.22 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.95 (s, 3H,  $-\text{C}(\text{O})\text{OCH}_3$ ), 3.88 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.37 (s, 3H,  $-\text{PhCH}_3$ ), 2.04 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (62.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.7, 159.9, 158.2, 153.3, 150.9, 140.3, 129.6, 126.9, 119.8, 116.3, 76.2, 68.0, 62.8, 52.8, 21.3, 20.8.  $R_f = 0.38$  (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for  $\text{C}_{16}\text{H}_{20}\text{N}_3\text{O}_6^+$ , 350.1347, found 350.1349.

**2k:** The desired product was obtained starting from compound **1** and 2-methylphenol with a 32 % yield (11.2 mg) as white solid.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.30-7.13 (m, 4H, phenyl-H), 5.59 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.23 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.94 (s, 3H,  $-\text{C}(\text{O})\text{OCH}_3$ ), 3.90 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.26 (s, 3H,  $-\text{PhCH}_3$ ), 2.04 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (62.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.7, 159.9, 158.3, 151.7, 151.0, 131.7, 129.0, 127.5, 126.4, 119.9, 76.2, 67.9, 62.9, 52.8, 20.8, 16.0.  $R_f = 0.35$  (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for  $\text{C}_{16}\text{H}_{20}\text{N}_3\text{O}_6^+$ , 350.1347, found 350.1346.

**2l:** The desired product was obtained starting from compound **1** and 4-*n*-pentylphenol with a 44 % yield (17.8 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.25-7.17 (m, 4H, phenyl-H), 5.56 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.5 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.95 (s, 3H, -C(O)OCH<sub>3</sub>), 3.89 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.60 (t, 2H, *J* = 7.6 Hz, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>), 2.04 (s, 3H, -C(O)CH<sub>3</sub>), 1.66-1.57 (m, 2H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 1.34-1.30 (m, 4H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 0.92-0.87 (m, 3H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 159.9, 158.3, 151.3, 150.9, 140.9, 129.7, 119.1, 76.2, 68.0, 62.8, 52.8, 35.2, 31.2, 31.1, 26.9, 22.5, 20.8, 14.0. R<sub>f</sub> = 0.44 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>20</sub>H<sub>28</sub>N<sub>3</sub>O<sub>6</sub><sup>+</sup>, 406.1973, found 406.1975.

**2m:** The desired product was obtained starting from compound **1** and 4-*n*-heptylphenol with a 47 % yield (20.3 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.25-7.17 (m, 4H, phenyl-H), 5.56 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.95 (s, 3H, -C(O)OCH<sub>3</sub>), 3.89 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.59 (t, 2H, *J* = 7.6 Hz, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>), 2.04 (s, 3H, -C(O)CH<sub>3</sub>), 1.31-1.25 (m, 10H, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>), 0.91-0.85 (m, 3H, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.8, 159.9, 158.3, 151.3, 150.9, 140.9, 129.8, 129.7, 119.1, 76.2, 68.0, 62.9, 52.8, 35.3, 31.8, 31.4, 29.2, 29.1, 22.6, 20.8, 14.1. R<sub>f</sub> = 0.50 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>22</sub>H<sub>32</sub>N<sub>3</sub>O<sub>6</sub><sup>+</sup>, 434.2286, found 434.2291.

**2n:** The desired product was obtained starting from compound **1** and 4-methoxyphenol with a 40 % yield (14.6 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.27-7.22 (m, 2H, phenyl-H), 6.92-6.89 (m, 2H, phenyl-H), 5.56 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.94 (s, 3H, -C(O)OCH<sub>3</sub>), 3.89 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.81 (s, 3H, -OCH<sub>3</sub>), 2.04 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.8, 159.9, 158.7, 157.5, 150.9, 146.9, 120.6, 114.9, 76.2, 68.0, 62.9, 55.7, 52.8, 20.8. R<sub>f</sub> = 0.26 (cyclohexane/ethyl acetate = 1:1). HRMS: calcd. for C<sub>16</sub>H<sub>20</sub>FN<sub>3</sub>O<sub>7</sub><sup>+</sup>, 366.1296, found 366.1298.

**4a:** The desired product was obtained starting from compound **3** and 4-fluorophenol with a 86 % yield (29.0 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.35-7.29 (m, 2H, phenyl-H), 7.14-7.07 (m, 2H, phenyl-H), 6.78 (s, 1H, -C(O)NH<sub>2</sub>), 5.86 (s, 1H,

-C(O)NH<sub>2</sub>), 5.56 (s, 2H, -OCH<sub>2</sub>N-), 4.23 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.91 (t, 2H, *J* = 4.8 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 170.8, 160.5, 160.2 (*J*<sub>CF</sub> = 244.3 Hz), 157.8, 152.4, 149.0, 121.2 (*J*<sub>CF</sub> = 8.5 Hz), 116.5 (*J*<sub>CF</sub> = 23.6 Hz), 76.1, 68.1, 62.8, 20.8. *R*<sub>f</sub> = 0.49 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>14</sub>H<sub>15</sub>FN<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 361.0919, found 361.0909.

**4b:** The desired product was obtained starting from compound **3** and 3-fluorophenol with a 88 % yield (29.7 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.44-7.35 (m, 1H, phenyl-H), 7.17-7.11 (m, 2H, phenyl-H), 7.04-6.96 (m, 1H, phenyl-H), 6.81 (s, 1H, -C(O)NH<sub>2</sub>), 6.07 (s, 1H, -C(O)NH<sub>2</sub>), 5.56 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.91 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.04 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.8, 163.0 (*J*<sub>CF</sub> = 247.1 Hz), 160.4, 157.2, 153.8 (*J*<sub>CF</sub> = 10.8 Hz), 152.5, 130.8 (*J*<sub>CF</sub> = 9.4 Hz), 115.1 (*J*<sub>CF</sub> = 3.4 Hz), 113.2 (*J*<sub>CF</sub> = 20.9 Hz), 107.7 (*J*<sub>CF</sub> = 25.4 Hz), 76.2, 68.1, 62.8, 20.8. *R*<sub>f</sub> = 0.51 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>14</sub>H<sub>15</sub>FN<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 361.0919, found 361.0904.

**4c:** The desired product was obtained starting from compound **3** and 2-fluorophenol with a 84 % yield (28.4 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.46-7.42 (m, 1H, *J* = 7.8 Hz, phenyl-H), 7.31-7.19 (m, 3H, phenyl-H), 6.75 (s, 1H, -C(O)NH<sub>2</sub>), 5.69 (s, 1H, -C(O)NH<sub>2</sub>), 5.59 (s, 2H, -OCH<sub>2</sub>N-), 4.24 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.92 (t, 2H, *J* = 4.8 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, *d*<sub>6</sub>-DMSO and CDCl<sub>3</sub>): δ 171.1, 160.8, 157.5, 153.2 (*J*<sub>CF</sub> = 248.6 Hz), 152.2, 140.2 (*J*<sub>CF</sub> = 12.1 Hz), 127.5 (*J*<sub>CF</sub> = 7.1 Hz), 124.6 (*J*<sub>CF</sub> = 4.0 Hz), 122.3, 117.0 (*J*<sub>CF</sub> = 17.8 Hz), 76.0, 67.6, 62.8, 20.3. *R*<sub>f</sub> = 0.53 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>14</sub>H<sub>15</sub>FN<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 361.0919, found 361.0915.

**4d:** The desired product was obtained starting from compound **3** and 4-(trifluoromethyl)phenol with a 55 % yield (21.4 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.70 (d, 2H, *J* = 8.5 Hz, phenyl-H), 7.50 (d, 2H, *J* = 8.5 Hz, phenyl-H), 6.80 (s, 1H, -C(O)NH<sub>2</sub>), 6.12 (s, 1H, -C(O)NH<sub>2</sub>), 5.57 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t,



2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.91 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.04 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.8, 160.4, 157.0, 155.3, 152.5, 128.4 ( $J_{\text{CF}} = 32.8$  Hz), 127.3 ( $J_{\text{CF}} = 3.6$  Hz), 123.6 ( $J_{\text{CF}} = 270.4$  Hz), 119.8, 76.2, 68.2, 62.8, 20.8.  $R_f = 0.53$  (dichloromethane/methanol = 10:1). HRMS: calcd. for  $\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_4\text{NaO}_5^+$ , 411.0887, found 411.0879.

**4e:** The desired product was obtained starting from compound **3** and 3-(trifluoromethyl)phenol with a 81 % yield (31.4 mg) as white solid.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.61-7.54 (m, 4H, phenyl-H), 6.79 (s, 1H,  $-\text{C}(\text{O})\text{NH}_2$ ), 6.20 (s, 1H,  $-\text{C}(\text{O})\text{NH}_2$ ), 5.57 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.22 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.91 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.03 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (62.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.7, 160.4, 157.2, 153.1, 152.5, 132.5 ( $J_{\text{CF}} = 33.1$  Hz), 130.6, 123.3 ( $J_{\text{CF}} = 270.8$  Hz), 123.0 ( $J_{\text{CF}} = 10.2$  Hz), 121.1, 116.9 ( $J_{\text{CF}} = 3.8$  Hz), 76.2, 68.2, 62.8, 20.7.  $R_f = 0.53$  (dichloromethane/methanol = 10:1). HRMS: calcd. for  $\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_4\text{NaO}_5^+$ , 411.0887, found 411.0877.

**4f:** The desired product was obtained starting from compound **3** and 2-(trifluoromethyl)phenol with a 48 % yield (18.6 mg) as colorless oil.  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ):  $\delta$  7.73-7.65 (m, 3H, phenyl-H), 7.40 (t, 2H,  $J = 7.2$  Hz, phenyl-H), 6.79 (s, 1H,  $-\text{C}(\text{O})\text{NH}_2$ ), 6.10 (s, 1H,  $-\text{C}(\text{O})\text{NH}_2$ ), 5.57 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.22 (t, 2H,  $J = 4.6$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.89 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.05 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.8, 160.5, 157.2, 152.5, 150.1, 133.7, 127.2 ( $J_{\text{CF}} = 4.7$  Hz), 126.2, 122.7 ( $J_{\text{CF}} = 271.4$  Hz), 121.8 ( $J_{\text{CF}} = 31.8$  Hz), 76.2, 68.0, 62.8, 20.8.  $R_f = 0.58$  (dichloromethane/methanol = 10:1). HRMS: calcd. for  $\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_4\text{NaO}_5^+$ , 411.0887, found 411.0884.

**4g:** The desired product was obtained starting from compound **3** and 4-chlorophenol with a 84 % yield (29.7 mg) as white solid.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.41-7.28 (m, 4H, phenyl-H), 6.79 (s, 1H,  $-\text{C}(\text{O})\text{NH}_2$ ), 6.10 (s, 1H,  $-\text{C}(\text{O})\text{NH}_2$ ), 5.55 (s, 2H,  $-\text{OCH}_2\text{N}-$ ), 4.21 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 3.90 (t, 2H,  $J = 4.8$  Hz,  $-\text{OCH}_2\text{CH}_2\text{OAc}$ ), 2.04 (s, 3H,  $-\text{C}(\text{O})\text{CH}_3$ );  $^{13}\text{C}$  NMR (62.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.7, 160.4, 157.5, 152.5, 151.6, 131.5, 129.9, 120.9, 76.2, 68.1, 62.8, 20.8.  $R_f = 0.56$  (dichloromethane/methanol = 10:1). HRMS: calcd. for  $\text{C}_{14}\text{H}_{15}\text{ClN}_4\text{NaO}_5^+$ , 377.0623,

found 377.0621.

**4h:** The desired product was obtained starting from compound **3** and phenol with a 85 % yield (27.2 mg) as a white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.47-7.28 (m, 5H, -phenyl-H), 6.80 (s, 1H, -C(O)NH<sub>2</sub>), 5.64 (s, 1H, -C(O)NH<sub>2</sub>), 5.57 (s, 2H, -OCH<sub>2</sub>N-), 4.23 (t, 2H, *J* = 4.8 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.92 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 160.7, 157.7, 153.3, 152.5, 129.8, 126.1, 119.5, 76.1, 68.0, 62.8, 20.7. *R*<sub>f</sub> = 0.50 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>14</sub>H<sub>16</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 343.1013, found 343.1008.

**4i:** The desired product was obtained starting from compound **3** and 4-methylphenol with a 88 % yield (29.4 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.18 (s, 4H, phenyl-H), 6.83 (s, 1H, -C(O)NH<sub>2</sub>), 6.41 (s, 1H, -C(O)NH<sub>2</sub>), 5.53 (s, 2H, -OCH<sub>2</sub>N-), 4.20 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.89 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.34 (s, 3H, -PhCH<sub>3</sub>), 2.02 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 160.8, 158.0, 152.5, 151.1, 135.9, 130.2, 119.3, 76.0, 68.0, 62.8, 20.8. *R*<sub>f</sub> = 0.56 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>15</sub>H<sub>18</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 357.1169, found 357.1176.

**4j:** The desired product was obtained starting from compound **3** and 3-methylphenol with a 80 % yield (26.7 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.33-7.27 (m, 1H, phenyl-H), 7.10 (t, 3H, *J* = 7.3 Hz, phenyl-H), 6.81 (s, 1H, -C(O)NH<sub>2</sub>), 5.87 (s, 1H, -C(O)NH<sub>2</sub>), 5.55 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.91 (t, 2H, *J* = 4.8 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.39 (s, 3H, -PhCH<sub>3</sub>), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.8, 160.6, 157.9, 153.3, 152.6, 151.2, 140.3, 129.6, 126.9, 120.0, 116.4, 76.1, 68.0, 62.9, 21.3, 20.8. *R*<sub>f</sub> = 0.47 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>15</sub>H<sub>18</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 357.1169, found 357.1175.

**4k:** The desired product was obtained starting from compound **3** and 2-methylphenol with a 74 % yield (24.7 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.29-7.16 (m, 4H, phenyl-H), 6.77 (s, 1H, -C(O)NH<sub>2</sub>), 5.74 (s, 1H, -C(O)NH<sub>2</sub>), 5.58 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 5.0 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.92 (t, 2H, *J* = 4.6 Hz, -

OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.26 (s, 3H, -PhCH<sub>3</sub>), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 160.6, 157.9, 152.5, 151.7, 131.7, 129.3, 127.3, 126.4, 120.1, 76.1, 68.0, 62.9, 20.8, 16.0. R<sub>f</sub> = 0.51 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>15</sub>H<sub>18</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 357.1169, found 357.1183.

**4l:** The desired product was obtained starting from compound **3** and 4-*n*-pentylphenol with a 81 % yield (31.6 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.20 (s, 4H, phenyl-H), 6.83 (s, 1H, -C(O)NH<sub>2</sub>), 6.24 (s, 1H, -C(O)NH<sub>2</sub>), 5.54 (s, 2H, -OCH<sub>2</sub>N-), 4.21 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.90 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.60 (t, 2H, *J* = 7.8 Hz, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>), 2.03 (s, 3H, -C(O)CH<sub>3</sub>), 1.64-1.55 (m, 2H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 1.34-1.25 (m, 4H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 0.91-0.86 (m, 3H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 160.7, 158.0, 152.5, 151.3, 140.9, 129.6, 119.2, 76.0, 68.0, 62.8, 35.2, 31.4, 31.1, 22.4, 20.7, 13.9. R<sub>f</sub> = 0.53 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>19</sub>H<sub>26</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 413.1795, found 413.1779.

**4m:** The desired product was obtained starting from compound **3** and 4-*n*-heptylphenol with a 84 % yield (35.1 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.21 (s, 4H, phenyl-H), 6.81 (s, 1H, -C(O)NH<sub>2</sub>), 5.84 (s, 1H, -C(O)NH<sub>2</sub>), 5.55 (s, 2H, -OCH<sub>2</sub>N-), 4.22 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.91 (t, 2H, *J* = 4.8 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 2.61 (t, 2H, *J* = 7.6 Hz, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>), 2.05 (s, 3H, -C(O)CH<sub>3</sub>), 1.63-1.58 (m, 2H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>), 1.32-1.28 (m, 8H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>), 0.91-0.86 (m, 3H, -CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.7, 160.7, 158.0, 152.5, 151.3, 140.9, 129.6, 119.2, 76.0, 68.0, 62.9, 35.2, 31.7, 31.4, 29.2, 29.1, 22.6, 20.8, 14.0. R<sub>f</sub> = 0.49 (dichloromethane/methanol = 10:1). HRMS: calcd. for C<sub>21</sub>H<sub>30</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>, 441.2108, found 441.2114.

**4n:** The desired product was obtained starting from compound **3** and 4-methoxyphenol with a 80 % yield (28.0 mg) as white solid. <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 7.24-7.21 (m, 2H, phenyl-H), 6.94-6.91 (m, 2H, phenyl-H), 6.79 (s, 1H, -C(O)NH<sub>2</sub>), 5.63 (s, 1H, -C(O)NH<sub>2</sub>), 5.55 (s, 2H, -OCH<sub>2</sub>N-), 4.23 (t, 2H, *J* = 4.8 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.92 (t, 2H, *J* = 4.6 Hz, -OCH<sub>2</sub>CH<sub>2</sub>OAc), 3.82 (s, 3H, -OCH<sub>3</sub>), 2.05 (s, 3H, -C(O)CH<sub>3</sub>); <sup>13</sup>C NMR (62.5 MHz, CDCl<sub>3</sub>): δ 170.8, 160.7, 158.3, 157.5, 152.5,

146.9, 120.7, 114.7, 76.0, 68.0, 62.9, 55.6, 20.8.  $R_f = 0.50$  (dichloromethane/methanol = 10:1). HRMS: calcd. for  $C_{15}H_{18}N_4NaO_6^+$ , 373.1119, found 373.1119.

