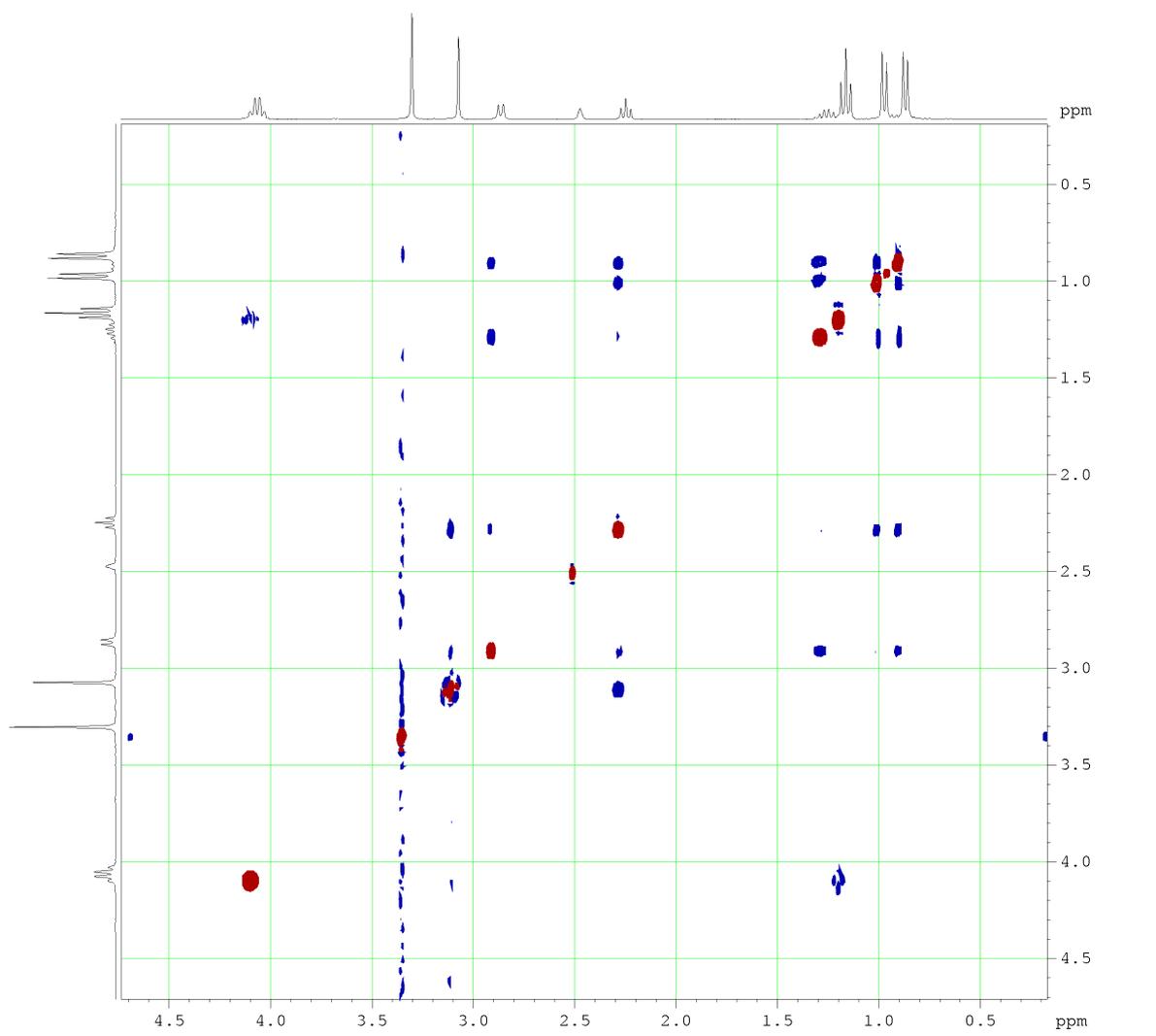


Diastereoselective synthesis of 1,3-di- and 1,3,3-trisubstituted diaziridines coupled with neurotransmitter amino acids

Vladimir V. Kuznetsov, Alexander V. Shevtsov, Mikhail I. Pleshchev, Yurii A. Strelenko and Nina N. Makhova

Experimental

Elemental analysis was performed by the CHN Analyzer Perkin–Elmer 2400. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 (300.13 and 75.47 MHz, respectively) spectrometer. The chemical shifts of the signals of CDCl_3 residual proton (δ 7.27 ppm) and carbon (δ 77.0 ppm) were used as the internal standard. The spectra were measured at 30 °C. 2D-spectra were recorded on a Bruker AV-600 (600 and 150 MHz for ^1H and ^{13}C , respectively) spectrometer and standard Bruker methods with Z-gradient. Mass spectra were measured using a Finnigan MAT INCOS-50 instrument. High resolution mass spectra were recorded on a Bruker microTOF spectrometer with electrospray ionization (ESI). All measurements were performed in a positive (+MS) ion mode (interface capillary voltage: 4500 V) with scan range m/z : 50-3000 The IR spectra were recorded on a Bruker “Alpha” spectrometer in the range 400-4000 cm^{-1} (resolution 2 cm^{-1}) as a thin layer. Analytical thin-layer chromatography (TLC) was carried out on Merck 25 TLC silica gel 60 F₂₅₄ aluminum sheets. The visualization of the TLC plates was accomplished in I_2 vapors. Value of pH was measured with handy waterproof Pen-type pH Meter PH-033. All reagents and solvents were purchased (Sigma Aldrich, Merck) and used without further purification.



{¹H-¹H}gNOESY spectrum of compound **8a** (DMSO-*d*₆)

Ethyl (1S,2S*,3S*)-2-(3-isopropyl diaziridin-1-yl)acetate* **8a**. ¹H NMR (300 MHz, CDCl₃) δ: 0.95, 1.10 (both d, 6H, 2 Me, *J* 6.0 Hz), 1.20 (t, 3H, Me in Et, *J* 6.2 Hz), 1.43 (m, 1H, CH), 1.80 (d, 1H, NH, *J* 6.5 Hz), 2.18 (t, 1H, CH_{ring}, *J* 6.5 Hz), 3.47 (d, 1H, N-CH_A, ²*J* 15.3 Hz), 3.57 (d, 1H, N-CH_B, ²*J* 15.3 Hz), 4.35 (q, 2H, OCH₂, *J* 6.2 Hz).

Ethyl (1R,2R*,3S*)-2-(3-isopropyl-2-(phenylcarbamoyl)diaziridin-1-yl)acetate* **8a'**. To a stirred solution of diastereomer (*1R*,2R*,3S**)-**8a** (1.72 g, 10 mmol) in 50 ml of dry Et₂O phenyl isocyanate (1.20 g, 10 mmol) dissolved in 50 ml of dry Et₂O was added dropwise. The resulting mixture was refluxed for 5 h, the solvent was then removed on a rotatory evaporator, and the solid residue was suspended in 30 ml of hexane. The precipitate was filtered, washed with 15 ml of hexane and dried on air. White solid, yield 88%, mp 65.0 °C. ¹H NMR (300 MHz, CDCl₃) δ: 1.08 (d, 3H, Me, *J* 6.5 Hz), 1.22 (d, 3H, Me, *J* 6.5 Hz), 1.30 (t, 3H, MeCH₂O, *J* 5.0 Hz), 1.53 (m, 1H, CH), 2.87 (d, 1H, CH_{ring}, *J* 8.2 Hz), 2.89 (d, 1H, NCH_A, ²*J* 17.4 Hz), 3.89 (d, 1H, NCH_B, ²*J* 17.4 Hz), 4.28 (q, 2H, OCH₂, *J* 5.0 Hz), 7.05 (t, 1H, CH_{Ph}, *J* 10.0 Hz), 7.31 (t, 2H, CH_{Ph}, *J* 10.0

Hz), 7.64 (d, 2H, CH_{Ph}, *J* 10.0 Hz), 9.57 (s, 1H, NH). ¹³C NMR (75 MHz, CDCl₃) δ: 14.21 (OCH₂Me), 18.47, 19.53 (both d, 6H, CHMe), 30.20 (CH(Me)₂), 60.37 (NCH₂), 61.74 (OCH₂), 70.82 (C_{ring}), 119.07, 123.67, 128.99, 138.21, 159.75 (Ph), 159.80, 171.31 (CO). IR (KBr, v/cm⁻¹): 3434, 3391, 3309, 2983, 1726, 1703, 1615, 1601, 1551, 1446, 1317, 1246, 1221, 1199, 756, 697, 637. MS (EI, 70 eV), *m/z*: 291 [M]⁺, 248 [M - Pr]⁺, 199 [M - NHC₆H₅]⁺, 172 [M -]⁺, 119 [CONHC₆H₅]⁺, 99 [M - CONHC₆H₅ - C(O)OC₂H₅ + H]. Found (%): C, 61.80; H, 7.31; N, 14.50. Calc. for C₁₅H₂₁N₃O₃ (%): C, 61.84; H, 7.27; N, 14.42.

Ethyl (1R,2R*,3S*)-3-(3-isopropylidiaziridin-1-yl)propanoate 8b*. Colorless liquid, yield 57%, bp 90–92 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.02 (d, 3H, Me-CH, *J* 10.0 Hz), 1.12 (d, 3H, Me-CH, *J* 10.0 Hz), 1.31 (t, 3H, Me-CH₂O, *J* 12.0 Hz), 1.44 (m, 1H, HC(Me)₂), 1.76 (d, 1H, NH, *J* 8.0 Hz), 2.39 (m, 1H, HC_{ring}), 2.45–2.65 (m, 4H, N-CH₂CH₂), 4.15 (q, 2H, OCH₂, *J* 12.0 Hz). ¹³C NMR (75 MHz, CDCl₃) δ: 14.2 (MeCH), 18.2 (MeCH), 18.8 (CH(Me)₂), 33.1 (MeCH₂O), 33.8 (CH₂CH₂C(O)), 56.4 (CH₂N), 60.5 (CH₂O), 66.4 (C_{ring}), 172.1 (C(O)). IR (v/cm⁻¹): 3254, 3210, 2962, 2875, 1737, 1674, 1469, 1448, 1374, 1305, 1257, 1176, 1096, 1063, 1029. HRMS (ESI), *m/z*: 187.1446 [M+H]⁺ (calc. for C₉H₁₈N₂O₂, *m/z*: 187.1442). Found (%): C, 57.97; H, 9.76; N, 15.09. Calc. for C₉H₁₈N₂O₂ (%): C, 58.04; H, 9.74; N, 15.04.

Ethyl (1R,2R*,3S*)-4-(3-isopropylidiaziridin-1-yl)butanoate 8c*. Colorless liquid, yield 58%, bp 107–109 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.03 (d, 3H, Me-CH, *J* 11.0 Hz), 1.15 (d, 3H, Me-CH, *J* 12.0 Hz), 1.31 (t, 3H, Me-CH₂O, *J* 7.3 Hz), 1.40 (dq, 1H, HC(Me)₂, *J* 11.0 Hz, 12 Hz), 1.69 (d, 1H, NH, *J* 8.0 Hz), 1.85 (m, 2H, CH₂-CH₂-CH₂), 2.19 (d, 1H, HC_{ring}, *J* 8.0 Hz), 2.35 (m, 4H, CH₂N, CH₂C(O)), 4.05 (q, 2H, OCH₂, *J* 7.3 Hz). ¹³C NMR (75 MHz, CDCl₃) δ: 14.3 (MeCH), 18.2 (MeCH), 18.8 (CHMe₂), 24.0 (CH₂-CH₂-CH₂), 31.9 (MeCH₂O), 32.1 (CH₂CH₂C(O)), 33.1 (CH₂N), 60.3 (CH₂O), 65.9 (C_{ring}), 173.4 (C(O)). IR (v/cm⁻¹): 3251, 3213, 2960, 2876, 1734, 1697, 1469, 1449, 1420, 1369, 1349, 1314, 1302, 1255, 1166, 1097, 1077, 1031, 916, 879, 837. HRMS (ESI), *m/z*: 201.1601 [M+H]⁺ (calc. for C₁₀H₂₀N₂O₂, *m/z*: 201.1598). Found (%): C, 60.02; H, 10.03; N, 13.90. Calc. for C₁₀H₂₀N₂O₂ (%): C, 59.97; H, 10.07; N, 13.99.

Ethyl (1R,2R*,3S*)-2-(3-methyldiaziridin-1-yl)acetate 8d*. Colorless liquid, yield 32%, bp 59–61 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.25 (t, 3H, MeCH₂O, *J* 7.1 Hz), 1.41 (d, 3H, MeC_{ring}, *J* 4.8 Hz), 1.79 (m, 1H, NH), 2.63 (m, 1H, CH_{ring}), 3.12 (d, 1H, N-CH_A, ²*J* 16.6.0 Hz), 3.22 (d, 1H, N-CH_B, ²*J* 16.6 Hz), 4.18 (q, 2H, CH₂O, *J* 7.1 Hz). ¹³C NMR (75 MHz, CDCl₃) δ: 14.09 (Me), 19.70 (Me), 55.90 (C_{ring}), 60.77 (CH₂N), 61.50 (CH₂O), 169.60 (C=O). IR (v/cm⁻¹): 3387, 3260, 2984, 2934, 2909, 1741, 1613, 1447, 1418, 1374, 1348, 1200, 1097, 1026, 937, 861.

HRMS (ESI), m/z : 145.0973 $[M+H]^+$ (calc. for $C_6H_{12}N_2O_2$, m/z : 145.0972). Found (%): C, 50.03; H, 8.31; N, 19.45. Calc. for $C_6H_{12}N_2O_2$ (%): C, 49.98; H, 8.39; N, 19.43.

Ethyl (1R,2R*,3S*)-3-(3-methyldiaziridin-1-yl)propanoate 8e*. Colorless liquid, yield 28%, bp 65–66 °C (1 Torr). 1H NMR (300 MHz, $CDCl_3$) δ : 1.22 (t, 3H, $\underline{Me}CH_2O$, J 7.3 Hz), 1.34 (d, 3H, $\underline{Me}C_{ring}$, J 4.4 Hz), 1.51 (m, 1H, NH), 2.42 (m, 1H, CH_{ring}), 2.56 (m, 3H, $NCHCH_2$), 2.86 (m, 1H, NCH), 4.10 (q, 2H, CH_2O , J 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 14.19 (Me), 20.02 (Me), 33.78 ($\underline{CH_2}(CO)$), 56.07 (NCH₂), 56.42 (C_{ring}), 60.43 (CH_2O), 172.10 (C=O). IR (ν/cm^{-1}): 3258, 3213, 2983, 2932, 2873, 1735, 1448, 1414, 1374, 1313, 1258, 1224, 1177, 1096, 1058, 1046, 1027, 995. HRMS (ESI), m/z : 159.1135 $[M+H]^+$ (calc. for $C_7H_{14}N_2O_2$, m/z : 159.1128). Found (%): C, 53.09; H, 8.98; N, 17.66. Calc. for $C_7H_{14}N_2O_2$ (%): C, 53.15; H, 8.92; N, 17.71.

Ethyl (1R,2R*,3S*)-2-(3-ethyldiaziridin-1-yl)acetate 8f*. Colorless liquid, yield 25%, bp 65–66 °C (1 Torr). 1H NMR (300 MHz, $CDCl_3$) δ : 1.03 (t, 3H, $\underline{Me}-CH_2-HC_{ring}$, J 7.5 Hz), 1.23 (t, 3H, $\underline{Me}-CH_2O$, J 7.1 Hz), 1.58 (m, 2H, $Me-CH_2-C_{ring}$), 1.85 (m, 1H, NH), 2.51 (t, 1H, HC_{ring} , J 4.6 Hz), 3.19 (m, 2H, NCH₂), 4.17 (q, 2H, OCH_2 , J 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 9.60 (Me), 14.21 (Me), 27.45 (CH_2), 60.86 (C_{ring}), 61.41 (CH_2), 61.82 (CH_2), 169.68 (C=O). IR (film, ν/cm^{-1}): 3468, 3256, 2973, 2938, 2879, 2360, 2340, 1745, 1632, 1465, 1439, 1417, 1374, 1348, 1268, 1194, 1098, 1030, 998, 941, 877. HRMS (ESI), m/z : 159.1133 $[M+H]^+$ (calc. for $C_7H_{14}N_2O_2$, m/z : 159.1129). Found (%): C, 53.20; H, 8.88; N, 17.65. Calc. for $C_7H_{14}N_2O_2$ (%): C, 53.15; H, 8.92; N, 17.71.

Ethyl (1R,2R*,3S*)-3-(3-ethyldiaziridin-1-yl)propanoate 8g*. Colorless liquid, yield 32%, bp 72–73 °C (1 Torr). 1H NMR (300 MHz, $CDCl_3$) δ : 1.00 (t, 3H, $\underline{Me}-CH_2-C_{ring}$, J 7.5 Hz), 1.21 (t, 3H, $\underline{Me}-CH_2O$, J 7.1 Hz), 1.60 (m, 3H, $Me-CH_2-C_{ring}$, NH), 2.52 (m, 4H, HC_{ring} , NCH_A , $CH_2C(O)$), 2.80 (m, 1H, NCH_B), 4.15 (q, 2H, CH_2O , J 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 9.68 (Me), 14.23 (Me), 27.59 ($\underline{CH_2}C_{ring}$), 33.76 ($\underline{CH_2}CO$), 56.28 (C_{ring}), 60.49 (CH_2), 61.86 (CH_2), 172.10 (C=O). IR (ν/cm^{-1}): 3254, 3212, 2972, 2938, 2878, 2361, 2341, 1734, 1667, 1612, 1465, 1375, 1314, 1256, 1177, 1097, 1030, 991, 931, 880, 857. MS (EI, 70 eV), m/z : 173 $[M+H]^+$, 172 $[M]^+$, 157, 156, 127, 116, 99, 85, 70, 56. HRMS (ESI), m/z : 173.1287 $[M+H]^+$ (calc. for $C_8H_{16}N_2O_2$, m/z : 173.1285). Found (%): C, 55.73; H, 9.31; N, 16.32. Calc. for $C_8H_{16}N_2O_2$ (%): C, 55.79; H, 9.36; N, 16.27.

Ethyl (1R,2R*,3S*)-3-(3-isobutyldiaziridin-1-yl)propanoate 8i*. Colorless liquid, yield 46%, bp 101–102 °C (1 Torr). 1H NMR (300 MHz, $CDCl_3$) δ : 0.95 (d, 6H, $(\underline{Me})_2-CH$, J 7.1 Hz), 1.25 (t, 3H, $\underline{Me}-CH_2$, J 7.5 Hz), 1.41 (m, 2H, CH_2C_{ring}), 1.68 (m, 1H, NH), 1.80 (m, 1H, $\underline{HC}(\underline{Me}_2)$), 2.41 (m, 1H, HC_{ring}), 2.57 (m, 3H, $CH_2C(O)$, NCH_A), 2.92 (m, 1H, NCH_B), 4.13 (q, 2H, OCH_2 , J 7.5

Hz). ^{13}C NMR (75 MHz, CDCl_3) δ : 14.25 ($\underline{\text{Me}}\text{CH}_2\text{O}$), 22.76 ($\underline{\text{Me}}\text{CH}$), 22.79 ($\underline{\text{Me}}\text{CH}$), 26.38 ($\underline{\text{C}}\text{H}(\text{Me})_2$), 33.83 ($\underline{\text{C}}\text{H}_2\text{C}_{\text{ring}}$), 43.70 ($\underline{\text{C}}\text{H}_2\text{C}=\text{O}$), 56.22 ($\underline{\text{C}}\text{H}_2\text{O}$), 59.58 (C_{ring}), 60.52 ($\text{N}\underline{\text{C}}\text{H}_2$), 172.14 ($\text{C}=\text{O}$). IR (v/cm^{-1}): 3475, 3371, 3254, 3217, 2959, 2935, 2907, 2873, 1736, 1667, 1549, 1467, 1448, 1373, 1344, 1316, 1253, 1177, 1114, 1097, 1051, 1028, 924, 899, 857. HRMS (ESI), m/z : 201.1601 $[\text{M}+\text{H}]^+$ (calc. for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2$, m/z : 201.1598). Found (%): C, 60.03; H, 10.01; N, 13.94. Calc. for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2$ (%): C, 59.97; H, 10.07; N, 13.99.

Ethyl (1R,2R*,3S*)-4-(3-isobutyldiaziridin-1-yl)butanoate 8j*. Colorless liquid, yield 52%, bp 104–105 °C (1 Torr). ^1H NMR (300 MHz, CDCl_3) δ : 0.90 (d, 6H, ($\underline{\text{Me}}\text{CH}_2$)-CH, J 6.7 Hz), 1.25 (t, 3H, $\underline{\text{Me}}\text{-CH}_2\text{O}$, J 6.9 Hz), 1.41 (m, 2H, $\text{CH}_2\text{C}_{\text{ring}}$), 1.60 (m, 1H, NH), 1.88 (m, 3H, $\underline{\text{H}}\text{C}(\text{Me}_2)$, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.20 (m, 1H, HC_{ring}), 2.42 (m, 3H, $\text{CH}_2\text{C}(\text{O})$, NCH_A), 2.60 (m, 1H, NCH_B), 4.13 (q, 2H OCH_2 , J 6.9 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ : 14.27 ($\underline{\text{Me}}\text{CH}_2$), 22.75 ($\underline{\text{Me}}\text{CH}$), 22.80 ($\underline{\text{Me}}\text{CH}$), 24.13 ($\text{CH}_2\text{CH}_2\text{CH}_2$), 26.41 ($\underline{\text{C}}\text{H}(\text{Me})_2$), 32.11 ($\underline{\text{C}}\text{H}_2\text{C}_{\text{ring}}$), 43.79 ($\underline{\text{C}}\text{H}_2\text{C}=\text{O}$), 58.99 (C_{ring}), 60.01 ($\underline{\text{C}}\text{H}_2\text{O}$), 60.32 ($\text{N}\underline{\text{C}}\text{H}_2$), 173.60 ($\text{C}=\text{O}$). IR (v/cm^{-1}): 3221, 3106, 2958, 2936, 2907, 2872, 1735, 1696, 1466, 1447, 1438, 1422, 1370, 1347, 1285, 1260, 1172, 1112, 1097, 1081, 1069, 1030, 996, 923, 900. HRMS (ESI), m/z : 215.1761 $[\text{M}+\text{H}]^+$ (calc. for $\text{C}_{11}\text{H}_{22}\text{N}_2\text{O}_2$, m/z : 215.1755). Found (%): C, 60.03; H, 10.01; N, 13.94. Calc. for $\text{C}_{11}\text{H}_{22}\text{N}_2\text{O}_2$ (%): C, 59.97; H, 10.07; N, 13.99.

Ethyl (1R,2R*,3S*)-2-[3-(pentan-3-yl)diaziridin-1-yl]acetate 8k*. Colorless liquid, yield 32%, bp 85–87 °C (1 Torr). ^1H NMR (300 MHz, CDCl_3) δ : 0.90 (m, 7H, ($\underline{\text{Me}}\text{-CH}_2\text{-CH}$) $_2$, $\underline{\text{H}}\text{C}(\text{Et})_2$), 1.23 (t, 3H, $\underline{\text{Me}}\text{-CH}_2\text{O}$, J 7.0 Hz), 1.45 (m, 4H ($\text{Me-CH}_2\text{-CH}$) $_2$), 2.05 (m, 1H, NH), 2.35 (d, 1H, HC_{ring} , J 8.0 Hz), 3.07, 3.28 (both d, 2H, NCH_2 , 2J 16.1 Hz), 4.17 (q, 2H, OCH_2 , J 7.0 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ : 11.19 (Me), 11.40 (Me), 14.07 (Me), 23.42 (CH_2), 24.24 (CH_2), 46.24 (CH), 60.70 (CH_2N), 61.69 (OCH_2), 63.99 (C_{ring}), 169.5 ($\text{C}=\text{O}$). IR (v/cm^{-1}): 3244, 3090, 3965, 2935, 2878, 1747, 1532, 1462, 1378, 1348, 1269, 1197, 1097, 1033, 946, 895, 854, 784, 758. Found (%): C, 59.92; H, 9.95; N, 14.10. HRMS (ESI), m/z : 201.1596 $[\text{M}+\text{H}]^+$ (calc. for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2$, m/z : 201.1598). Calc. for $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2$ (%): C, 59.97; H, 10.07; N, 13.99.

Ethyl (1R,2R*,3S*)-3-[3-(pentan-3-yl)diaziridin-1-yl]propanoate 8l*. Colorless liquid, yield 41%, bp 95–97 °C (1 Torr). ^1H NMR (300 MHz, CDCl_3) δ : 0.92 (m, 7H, ($\underline{\text{Me}}\text{CH}_2\text{CH}$) $_2$, $\underline{\text{H}}\text{C}(\text{Et})_2$), 1.23 (t, 3H, $\underline{\text{Me}}\text{CH}_2\text{O}$, J 7.1 Hz), 1.45 (m, 4H, (MeCH_2CH) $_2$), 1.70 (m, 1H, NH), 2.30 (d, 1H, HC_{ring} , J 7.9 Hz), 2.40 (m, 1H, NCH_A), 2.55 (m, 2H, $\text{CH}_2\text{C}=\text{O}$), 2.92 (m, 1H, NCH_B), 4.12 (q, 2H, OCH_2 , J 7.1 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ : 11.23 (Me), 11.26 (Me), 14.11 (Me), 23.65 (CH_2), 24.51 (CH_2), 33.71 ($\underline{\text{C}}\text{H}_2\text{C}=\text{O}$), 46.48 (CH), 56.19 (NCH_2), 60.34 (OCH_2), 64.43 (C_{ring}), 171.94 ($\text{C}=\text{O}$). IR (v/cm^{-1}): 3447, 3254, 3210, 2965, 2939, 2878, 1737, 1619, 1462, 1378, 1313, 1254, 1175, 1096, 1028, 957, 936, 878, 858, 831, 779. MS (EI, 70 eV), m/z : 200 $[\text{M}$

– CH₃ + H]⁺, 199 [M – CH₃]⁺, 185 [M – C₂H₅]⁺, 170 [M – Me, C₂H₅]⁺, 169 [M – OC₂H₅]⁺, [M – (C₂H₅, CH₃, H)]⁺, [M – (CH₃, CH₃, CH₃)]⁺, 141 [M – C(O)OC₂H₅]⁺, 127 [M – (Et₂CH-CH, CH₃, H)]⁺, 70 [Et₂CH-C]. HRMS (ESI), *m/z*: 215.1753 [M+H]⁺ (calc. for C₁₁H₂₂N₂O₂, *m/z*: 215.1755). Found (%): C, 61.63; H, 10.42; N, 13.00. Calc. for C₁₁H₂₂N₂O₂ (%): C, 61.65; H, 10.35; N, 13.07.

Ethyl (1R,2R*)-2-(3,3-dimethyldiaziridin-1-yl)acetate 9a*. Colorless liquid, yield 25%, bp 66–68 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.25 (t, 3H, MeCH₂O, *J* 7.1 Hz), 1.32, 1.42 (both s, 6H, 2Me), 2.04 (br.s, 1H, NH), 3.31 (br.s, 2H, NCH₂), 4.21 (q, 2H, OCH₂, *J* 7.1 Hz). ¹³C NMR (75 MHz, CDCl₃) δ: 14.06 (Me), 17.30 (Me)₂, 27.60 (CH₂O), 55.26 (NCH₂), 60.69 (HC_{ring}), 170.18 (C=O).

Ethyl (1R,2R*)-2-(1,2-diazaspiro[2.5]octan-1-yl)acetate 9b*. Colorless liquid, yield 15%, bp 115–120 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.23 (t, 3H, MeCH₂, *J* 7.5 Hz), 1.65 (m, 10H, (CH₂)₅), 2.15 (s, 1H, NH), 3.32 (d, 1H, N-CH_A, ²*J* 15.3 Hz), 3.38 (d, 1H, N-CH_B, ²*J* 15.3 Hz), 4.45 (q, 2H, OCH₂, *J* 7.5 Hz).

Ethyl (1R,2R*)-3-(3,3-dimethyldiaziridin-1-yl)propanoate 9c*. Colorless liquid, yield 24%, bp 72–73 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.25 (t, 3H, *J* 8.1 Hz, MeCH₂), 1.35 (s, 3H, MeC_{ring}), 1.40 (s, 3H, MeC_{ring}), 1.95 (br s, 1H, NH), 2.60 (m, 3H, CH₂C(O), CH_aN), 2.95 (m, 1H, CH_bN), 4.15 (q, 2H, OCH₂, *J* 8.1 Hz). ¹³C NMR (75 MHz, CDCl₃) δ: 14.22 (MeCH₂), 17.28 (MeC_{ring}), 28.10 (MeC_{ring}), 34.48 (CH₂CH₂C(O)), 49.24 (CH₂N), 57.52 (C_{ring}), 60.39 (CH₂O), 172.30 (C=O). IR (ν/cm⁻¹): 3368, 3259, 3209, 2981, 2933, 2360, 2341, 1735, 1447, 1378, 1309, 1257, 1176, 1131, 1061, 1029, 821, 759, 668, 510. MS (EI, 70 eV), *m/z*: 172 [M]⁺, 156 [M – O]⁺, 143 [M – C₂H₅]⁺, 127 [M – OC₂H₅]⁺, 116 [NCH₂CH₂C(O)OC₂H₅]⁺, 99 [M – C(O)OC₂H₅]⁺, 85 [M – CH₂C(O)OC₂H₅]⁺, 72 [(CH₃)₂CN₂]⁺, 56 [(CH₃)₂CN]⁺, 42 [(CH₃)₂C]⁺. HRMS (ESI), *m/z*: 173.1284 [M+H]⁺ (calc. for C₈H₁₆N₂O₂, *m/z*: 173.1285). Found (%): C, 55.82; H, 9.39; N, 16.21. Calc. for C₈H₁₆N₂O₂ (%): C, 55.79; H, 9.36; N, 16.27.

Ethyl (1R,2R*)-3-(1,2-diazaspiro[2.5]octan-1-yl)propanoate 9d*. Colorless liquid, yield 25%, bp 132–134 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.23 (t, 3H, MeCH₂, *J* 8.2 Hz), 1.65 (m, 10H, (CH₂)₅), 2.26 (br s, 1H, NH), 2.60 (m, 3H, CH₂C(O), NCH_a), 3.10 (m, 1H, NCH_b), 4.15 (q, 2H, OCH₂, *J* 8.2 Hz). ¹³C NMR (75 MHz, CDCl₃) δ: 14.26 Me, 25.50, 25.93, 28.09, 32.27, 38.87 ((CH₂)₅), 48.40 (CH₂C=O), 49.21 (CH₂N), 60.41 (OCH₂), 62.06 (CH_{ring}), 172.37 (C=O). IR (ν/cm⁻¹): 3245, 2980, 2927, 2853, 1748, 1449, 1416, 1373, 1348, 1270, 1245, 1193, 1130, 1100, 1035, 949, 924, 835. HRMS (ESI), *m/z*: 213.1602 [M+H]⁺ (calc. for C₁₁H₂₀N₂O₂, *m/z*:

213.1598). Found (%): C, 62.18; H, 9.45; N, 13.28. Calc. for C₁₁H₂₀N₂O₂ (%): C, 62.23; H, 9.50; N, 13.20.

Ethyl (1R,2R*)-4-(3,3-dimethyldiaziridin-1-yl)butanoate 9e*. Colorless liquid, yield 22%, bp 69.5 °C (1 Torr). ¹H NMR (300 MHz, CDCl₃) δ: 1.21 (t, 3H, MeCH₂, *J* 7.1 Hz), 1.30 (s, 3H, Me), 1.34 (s, 3H, Me), 1.78 (s, 1H, NH), 1.87 (m, 2H, NCH₂CH₂, *J* 7.3 Hz), 2.37 (m, 3H, CH₂C=O, NCH_b), 2.61 (dt, 2H, NCH₂, ²*J* 12.4, ³*J* 7.3 Hz), 4.09 (q, 2H, OCH₂, *J* 7.1 Hz). HRMS (ESI), *m/z*: 187.1447 [M+H]⁺ (calc. for C₉H₁₈N₂O₂, *m/z*: 187.1442). Found (%): C, 57.98; H, 9.77; N, 15.02. Calc. for C₉H₁₈N₂O₂ (%): C, 58.04; H, 9.74; N, 15.04.