Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Chemical genetics approach to identify new small molecule modulators of cell growth by phenotypic screening of *Saccharomyces cerevisiae* strains with a library of morpholine-derived compounds

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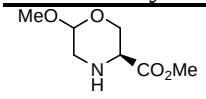
ELECTRONIC SUPPLEMENTARY INFORMATION

Table S1. Library members grouped by scaffold similarity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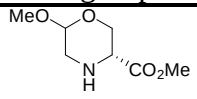
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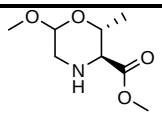
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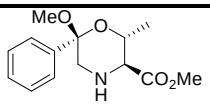
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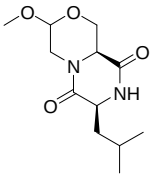
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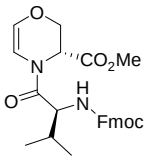
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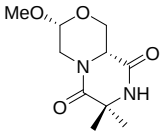
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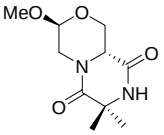
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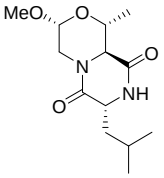
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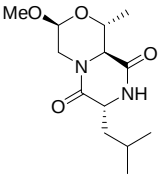
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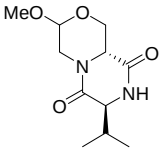
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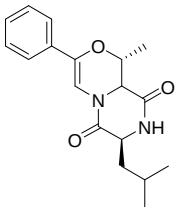
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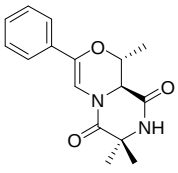
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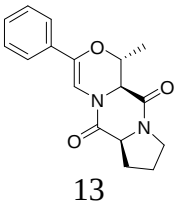
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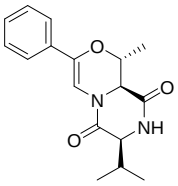
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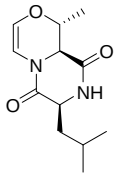
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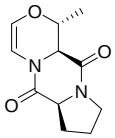
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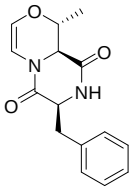
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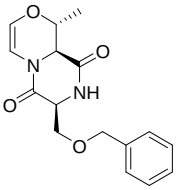
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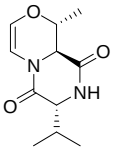
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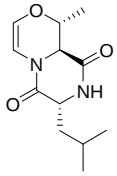
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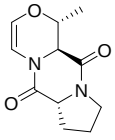
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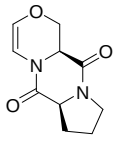
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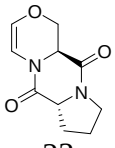
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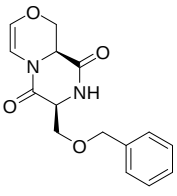
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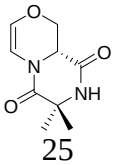
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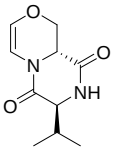
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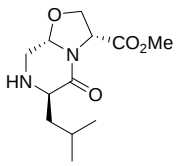
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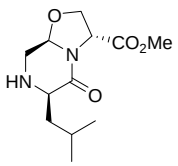
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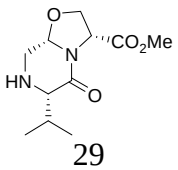
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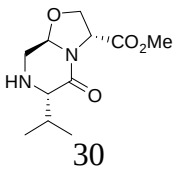
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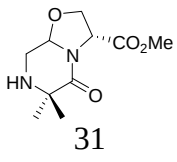
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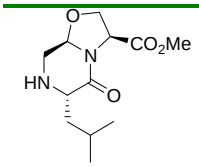

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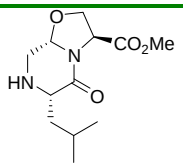

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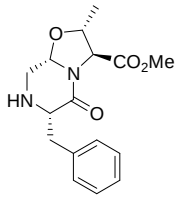

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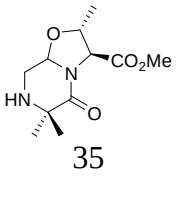

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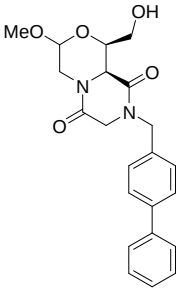

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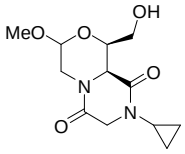

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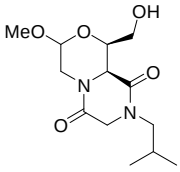

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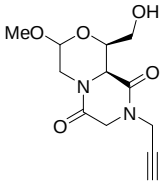

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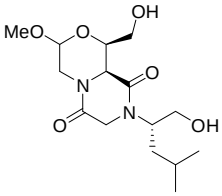

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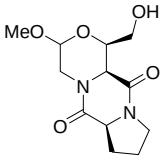

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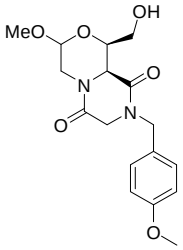

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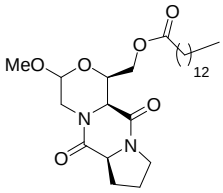

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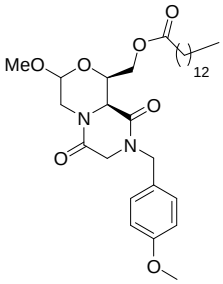

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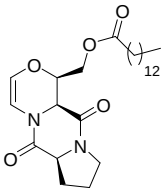

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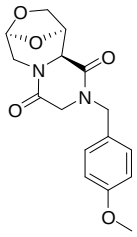

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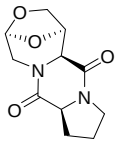

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Experimental Section

General

Chromatographic separations were performed on silica gel (Kieselgel 60, Merck) using flash-column techniques; R_f values refer to TLC carried out on 25-mm silica gel plates (Merck F_{254}) with the same eluant as indicated for column cromatography. ^1H and ^{13}C NMR spectra were recorded with Varian Gemini spectrometers operating at 200 MHz for ^1H and 50 MHz for ^{13}C, respectively. ESI mass spectra were carried out on a ion-trap double quadrupole mass spectrometer using electrospray (ES^+) ionization techniques. Purity grade of library members was assessed by HPLC with an analytical C-18 10 μm, 250 × 4.6 mm, reverse-phase column, and H_2O – CH_3CN eluant buffered with 0.1% TFA using the following gradient: 10% acetonitrile/5 min, then 10 – 25% acetonitrile/20 min, then 25 – 30% acetonitrile/5 min, then 30 – 90% acetonitrile/15 min. All the compounds showed a purity grade > 90%.

Compounds **1a**, **1b** and **2** were prepared following reported procedures (Sladojevich, F.; Trabocchi, A.; Guarna, A.; Convenient route to enantiopure Fmoc-protected morpholine-3-carboxylic acid, *J. Org. Chem.* **2007**, *72*, 4254; F. Sladojevich, A. Trabocchi, A. Guarna, *Org. Biomol. Chem.*, **2008**, *6*, 3328).

(2*R*,3*S*,6*S*)-6-Methoxy-2-methyl-6-phenyl-morpholine-3-carboxylic acid methyl ester (3). L-Threonine methyl ester hydrochloride (730 mg, 4.30 mmol) was dissolved in *N*-methylpyrrolidone (4 mL), then DIPEA (1.47 mL, 8.61 mmol) and phenacyl bromide (571 mg, 2.87 mmol) were successively added, and the resulting mixture was stirred at room temperature for 6 h. Subsequently, water (30 mL) was added, and the organic phase was extracted with EtOAc and washed with brine. Crude product was obtained after filtration over Celite and solvent evaporation. The resulting mixture was partitioned between water and Et_2O. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Then, the crude mixture was dissolved in MeOH (14 mL) and $SOCl_2$ (1.02 mL, 14 mmol) was added dropwise, at 0

°C. The resulting mixture was refluxed for 4.5 h, and then concentrated under reduced pressure. The crude material was dissolved again in MeOH, treated with Amberlist A-21, and the solvent was evaporated to dryness. Pure **3** (265 mg) was obtained in 50% yield after purification through flash column chromatography EtOAc - Petr. ether 1:1, Rf = 0.37). (Found: C, 63.52; H, 7.23; N, 5.12. $C_{14}H_{19}NO_4$ requires C, 63.38; H, 7.22; N, 5.28%). $[\alpha]^{25}_D$ +45.6 (*c* = 1.2, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.48-7.46 (m, 2H), 7.39-7.32 (m, 3H), 3.97-3.93 (m, 1H), 3.77 (s, 3H), 3.30 (d, *J* = 9.9 Hz, 1H), 3.09 (d, *J* = 13.9 Hz, 1H), 3.05 (s, 3H), 2.67 (d, *J* =13.9 Hz, 1H), 2.10 (br, 1H), 1.27 (d, *J* = 6.0 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 171.3 (s), 150.8 (s), 139.6 (d), 128.1 (d, 2C), 128.0 (d), 125.9 (d, 2C), 97.1 (s), 67.4 (d), 63.2 (d), 54.0 (t), 52. (q), 49.2 (q), 18.4 (q) ppm. ESI-MS *m*/*z* 266.25 (M^++1).

(3*R/S*,7*S*,9a*S*)-7-Isobutyl-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (4). Compound **4** was obtained from morpholine acetal **1a** (66 mg, 0.38 mmol) and Fmoc-(L)-Leu-Cl (130 mg, 0.38 mmol) following general procedure A. Pure **4** was obtained after flash chromatography purification (1:1 EtOAc/petr. ether, R_f = 0.2), in 84% yield. (Found: C, 56.51; H, 7.91; N, 10.68. $C_{12}H_{20}N_2O_4$ requires C, 56.23; H, 7.87; N, 10.93%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 6.20 (br, 1H), 4.56 (dd, *J* = 13.4, 2.9 Hz, 1H), 4.45-4.37 (m, 2H), 4.10 (m, 1H), 3.79 (m, 1H), 3.65 (dd, *J* = 11.7, 9.9 Hz, 1H), 3.53 (s, 3H), 2.65 (dd, *J* = 13.2, 8.7 Hz, 1H), 1.66 (m, 3H), 0.98 (dd, *J* = 6.7, 6.6 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 163.7 (s), 162.5 (s), 95.1 (d), 72.3 (d), 69.0 (d), 66.1 (t), 53.7 (q), 40.5 (t), 33.4 (t), 23.2 (d), 22.5 (q), 20.5 (q) ppm. ESI-MS *m*/*z* 257.3 (M^++1).

4-[2(*S*)-(9H-Fluoren-9-ylmethoxycarbonylamino)-3-methyl-butyryl]-3,4-dihydro-2H-[1,4]oxazine-3(*R*)-carboxylic acid methyl ester (5). Morpholine compound **1b** (100 mg, 0.57 mmol) was dissolved in anhydrous CH_2Cl_2 (2 mL), then 2,6-lutidine (133 µL, 1.14 mmol) and Fmoc-(L)-Val (245 mg, 0.69 mmol) were added. The reaction mixture was brought to 60 °C and stirred for 2 h under a nitrogen atmosphere. The reaction mixture was then diluted with CH_2Cl_2 and sequentially washed with 5% HCl, 5% $NaHCO_3$ and brine. The organic layers were dried over Na_2SO_4, filtered and evaporated to give a brownish foam. Then, toluene (10 mL) and pTsOH (180

mg, 0.91 mmol) were added, and the mixture was refluxed over molecular sieves for 2 h. Then, the mixture was diluted with EtOAc (20 mL) and sequentially washed with 5% HCl, 5% $NaHCO_3$ and brine. The organic layers were dried over Na_2SO_4, filtered and evaporated to give pure **5** after flash chromatography purification (1:3 EtOAc/petr. ether), in 54% yield. (Found: C, 67.61; H, 6.28; N, 5.74. $C_{26}H_{28}N_2O_6$ requires C, 67.23; H, 6.08; N, 6.03%). $[\alpha]^{25}_D$ +27.7 (*c* = 0.8, $CHCl_3$). 1:1 Mixture of rotamers δ_H (200 MHz, $CDCl_3$) 7.78 (d, *J* = 7.3 Hz, 2H), 7.59 (m, 2H), 7.37 (m, 4H), 6.40 (d, *J* = 5.1 Hz, 1H, rot. A), 6.18 (d, *J* = 4.2 Hz, 1H, 0.5 rot. A and 0.5 rot. B), 5.63 (m, 2H), 4.68-4.46 (m, 3H), 4.31-4.07 (m, 2H), 3.90-3.73 (m, 2H), 3.81 (s, 1.5H, rot. A), 3.79 (s, 1.5H, rot. B), 2.44-2.34 (m, 1H), 0.89 (m, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 162.5, 161.8, 143.3, 141.3, 127.8, 127.5, 127.1, 125.0, 124.9, 124.8, 124.5, 124.3, 124.1, 120.0, 114.3, 113.9, 109.7, 108.8, 68.0, 67.8, 67.7, 67.6, 52.6, 47.2, 31.9, 30.0, 22.7, 19.1 ppm. ESI-MS *m*/*z* 465.3 (M^++1).

(3*R*,9a*R*)-3-Methoxy-7,7-dimethyl-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (6) and (3*S*,9a*R*)-3-methoxy-7,7-dimethyl-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (7). Compounds **6** and **7** were obtained from compound **1a** (100 mg, 0.57 mmol) and Fmoc-α-Me-Ala-Cl (217 mg, 0.63 mmol) following the general procedure A in 41% and 35% yields, respectively, after flash chromatography purification (1:1 EtOAc/petr. ether, 6: R_f = 0.11, 7: R_f = 0.09). **6**: (Found: C, 52.88; H, 7.12; N, 12.01. $C_{10}H_{16}N_2O_4$ requires C, 52.62; H, 7.07; N, 12.27%). $[\alpha]^{24}_D$ +100.7 (*c* = 1.3, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.41 (br, 1H), 4.54, (dd, *J* = 13.2, 2.9 Hz, 1H), 4.38 (m, 2H), 4.09 (m, 1H), 3.61 (dd, *J* = 11.3, 9.9 Hz, 1H), 3.50 (s, 3H), 2.61 (dd, *J* = 13.4, 8.6 Hz, 1H), 1.50 (s, 3H), 1.47 (s, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 161.8 (s), 160.2 (s), 98.2 (d), 65.7 (t), 59.3 (d), 56.4(q), 55.1 (q), 44.4 (t), 28.5 (q), 27.8 (q) ppm. ESI-MS *m*/*z* 229.4 (M^++1). **7**: (Found: C, 53.11; H, 7.10; N, 12.08. $C_{10}H_{16}N_2O_4$ requires C, 52.62; H, 7.07; N, 12.27%). $[\alpha]^{24}_D$ -43.5 (*c* = 0.4, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.92 (br, 1H), 4.72, (d, *J* = 2.2 Hz, 1H), 4.51 (d, *J* = 13.6 Hz, 1H), 4.20 (dd, *J* = 11.0, 4.0 Hz, 1H), 3.99 (d, *J* = 4.0 Hz, 1H), 3.90 (m, 1H), 3.37 (s, 3H), 2.80 (dd, *J* =

13.5, 2.5 Hz, 1H), 1.53 (s, 3H), 1,48 (s, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 162.1 (s), 160.2 (s), 88.3 (d), 77.2 (t), 60.1 (d), 56.4 (q), 44.3 (t), 29.3 (q), 29.1 (q) ppm. ESI-MS *m*/*z* 229.5 (M^++1).

(1*R*,3*R*,7*R*,9a*S*)-7-Isobutyl-3-methoxy-1-methyl-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (8) and (1*R*,3*S*,7*R*,9a*S*)-7-Isobutyl-3-methoxy-1-methyl-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (9). Compounds **8** and **9** were obtained from compound **2** (101 mg, 0.53 mmol) and Fmoc-D-Leu-Cl (239 mg, 0.64 mmol) following the general procedure A in 33% and 43% yields, respectively, after flash chromatography purification (1:1 EtOAc/petr. ether, **8**: R_f = 0. 0.22, **9**: R_f = 0.19). **8**: (Found: C, 57.84; H, 8.22; N, 10.01. $C_{13}H_{22}N_2O_4$ requires C, 57.76; H, 8.20; N, 10.36%). $[\alpha]^{24}_D$ -18.4 (*c* = 0.1, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.33 (br, 1H), 4.60 (dd, *J* = 13.0, 2.5 Hz, 1H), 4.44 (dd, *J* = 8.9, 2.4 Hz, 1H), 4.05 (m, 1H), 3.73 (m, 2H), 3.52 (s, 3H), 2.60 (dd, *J* = 12.9, 9.0 Hz, 1H), 1.67 (m, 3H), 1.51 (d, *J* = 5.3 Hz, 3H), 0.96 (dd, *J* = 5.5, 5.2 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 161.1 (s), 159.9 (s), 93.8 (d), 66.1 (t), 62.7 (d), 61.2 (d), 53.7 (q), 45.5 (t), 31.2 (d), 30.1 (q), 23.6 (d), 22.4 (q), 17.9 (q) ppm. ESI-MS *m*/*z* 271.2 (M^++1). **9**: (Found: C, 57.86; H, 8.23; N, 10.07. $C_{13}H_{22}N_2O_4$ requires C, 57.76; H, 8.20; N, 10.36%). $[\alpha]^{25}_D$ +58.4 (*c* = 0.8, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.71 (br, 1H), 4.69-4.57 (m, 2H), 4,08 (m, 2H), 3.82 (d, *J* = 9.6 Hz, 1H), 3.37 (s, 3H), 2.89 (dd, *J* = 13.5, 2.3 Hz, 1H), 1.91-1.63 (m, 3H), 1.42 (d, *J* = 6.1 Hz, 3H), 0.94 (dd, *J* = 5.8, 4.0 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 163.1 (s), 160.2 (s), 94.9 (d), 66.2 (t), 62.4 (d), 61.7 (d), 54.4 (q), 45.1 (t), 30.7 (d), 30.5 (q), 23.9 (d), 22.5 (q), 17.9 (q) ppm. ESI-MS *m*/*z* 271.2 (M^++1).

(3*R/S*,7*S*,9a*R*)-7-Isopropyl-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (10). Compound **10** was obtained from compound **1b** (100 mg, 0.57 mmol) and Fmoc-L-Val-Cl (225 mg, 0.63 mmol) following the general procedure A as a mixture of epimers in 66% overall yield after flash chromatography purification (1:1 EtOAc/petr. ether). (Found: C, 54.56; H, 7.50; N, 11.49. $C_{11}H_{18}N_2O_4$ requires C, 54.53; H, 7.49; N, 11.56%). δ_H (200 MHz, $CDCl_3$) 6.76 (br, 1H), 4.57 (dd, *J* = 13.4, 2.5 Hz, 1H), 4.40 (dd, *J* = 8.7, 3.1 Hz, 1H), 4.09 (dd, *J* = 9.8, 4.0 Hz, 1H), 3.91 (m, 2H), 3.67-3.56 (m, 1H), 3.03 (m, 1H), 2.61 (dd, *J* = 13.4, 8.8 Hz, 1H), 2.37 (m, 1H), 1.01 (d, *J* = 7.0 Hz,

3H), 0.89 (d, *J* = 6.9 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 165.2 (s), 160.1 (s), 99.1 (d), 88.2 (d), 66.0 (t), 60.7 (d), 54.8 (q), 43.9 (t), 33.5 (d), 18.6 (q), 16.1 (q) ppm. ESI-MS *m*/*z* 243.4 (M^++1).

(1*R*,7*S*,9a*S*)-7-Isobutyl-1-methyl-3-phenyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (11). Compound **11** was obtained from morpholine **4** (100 mg, 0.38 mmol) and Fmoc-L-Leu-Cl (140 mg, 0.38 mmol) according to general procedure B in 41% yield after flash chromatography purification (1:1 EtOAc/petr. ether, R_f = 0.34). (Found: C, 68.87; H, 7.35; N, 8.80. $C_{18}H_{22}N_2O_3$ requires C, 68.77; H, 7.05; N, 8.91%). $[\alpha]^{24}_D$ -33.7 (*c* = 0.1, $CHCl_3$). δ_H 7.56 (d, *J* = 6.8 Hz, 2H), 7.33 (m, 3H), 7.25 (s, 1H), 6.29 (s, 1H), 5.13 (m, 1H), 4.35 (s, 1H), 4.11 (m, 1H), 1.81 (m, 2H), 1.71 (m, 1H), 1.26 (d, *J* = 6.3 Hz, 3H), 0.99 (dd, *J* = 6.3, 5.9 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) C18 163.9 (s), 160.3 (s), 137.1 (s), 133.0 (s), 128.2 (d, 2C), 128.0 (d), 123.9 (d, 2C), 100.5 (d), 98.1 (d), 70.2 (d), 53.7 (d), 44.4 (t), 24.0 (d), 22.8 (q), 21.1 (q), 20.1 (q) ppm. ESI-MS *m*/*z* 315.3 (M^++1).

(1*R*,9a*S*)-1,7,7-Trimethyl-3-phenyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (12). Compound **12** was obtained from morpholine **4** (140 mg, 0.53 mmol) and Fmoc-α-Me-Ala-Cl (250 mg, 0.73 mmol) according to general procedure B in 62% yield after flash chromatography purification (1:1 EtOAc/petr. ether, R_f = 0.31). (Found: C, 67.14; H, 6.35; N, 7.75. $C_{16}H_{18}N_2O_3$ requires C, 67.12; H, 6.34; N, 9.78%). $[\alpha]^{25}_D$ -26.1 (*c* = 1.6, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.36-7.29 (m, 3H), 7.32 (s, 1H), 6.66 (br, 1H), 4.22 (m, 1H), 4.05 (d, *J* = 8.6 Hz, 1H), 1.84 (d, *J* = 5.9 Hz, 3H), 1.55 (s, 3H), 1.54 (s, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 164.3 (s), 161.5 (s), 141.1 (s), 133.0 (s), 128.3 (d, 2C), 126.7 (d), 123.9 (d, 2C), 100.1 (d), 72.6 (d), 58.8 (d), 56.0 (q), 28.3 (q), 27.3 (q), 19.9 (q) ppm. ESI-MS *m*/*z* 287.3 (M^++1).

(4a*S*,5*R*,9a*S*)-5-Methyl-7-phenyl-1,2,3,4a,5,9a-hexahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalene-4,9-dione (13). Compound **13** was obtained from morpholine **3** (102 mg, 0.38 mmol) and Fmoc-L-Pro-Cl (135 mg, 0.38 mmol) according to general procedure B in 92% yield. (Found: C, 68.51; H, 6.11; N, 9.32. $C_{17}H_{18}N_2O_3$ requires C, 68.44; H, 6.08; N, 9.39%). $[\alpha]^{25}_D$

-2.1 (*c* = 1.0, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.57-7.56 (d, *J* = 7.2 Hz, 1H), 7.35-7.25 (m, 5H), 4.23 (m, 2H), 4.03 (d, *J* = 9.0 Hz, 1H), 3.56 (m, 2H), 2.39 (m, 1H), 2.28 (m, 1H), 2.02 (m, 1H), 2.00 (m, 1H), 1.83 (d, *J* = 6.0 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 163.7 (s), 162.5 (s), 140.5 (s), 133.0 (s), 128.3 (d, 2C), 128.1 (d), 123.7 (d, 2C), 100.6 (d), 71.2 (d), 59.6 (d), 58.6 (d), 45.9 (t), 28.5 (t), 23.1 (t), 20.3 (q) ppm. ESI-MS *m*/*z* 299.2 (M^++1).

(1*R*,7*S*,9a*S*)-7-Isopropyl-1-methyl-3-phenyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (14). Compound **14** was obtained from morpholine **3** (100 mg, 0.38 mmol) and Fmoc-L-Val-Cl (136 mg, 0.38 mmol) according to general procedure B in 62% yield. (Found: C, 68.09; H, 6.75; N, 9.29. $C_{17}H_{20}N_2O_3$ requires C, 67.98; H, 6.71; N, 9.33%). $[\alpha]^{24}_D$ -70.8 (*c* = 0.2, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.57 (d, *J* = 7.2 Hz, 2H), 7.33 (m, 4H), 6.14 (s, 1H), 4.22 (m, 1H), 4.02 (d, *J* = 7.7 Hz, 1H), 4.01 (s, 1H), 2.61 (m, 1H), 1.80 (d, *J* = 6.0 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 165.2 (s), 161.7 (s), 141.3 (s), 132.8 (s), 128.2 (d, 3C), 123.8 (d, 2C), 99.7 (d), 73.4 (d), 59.4 (d), 58.8 (d), 30.7 (d), 19.3 (q), 18.8 (q), 15.9 (q) ppm. ESI-MS *m*/*z* 299.25 (M^- - 1).

(1*R*,7*S*,9a*S*)-7-Isobutyl-1-methyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (15). Compound **15** was obtained from morpholine **2** (102 mg, 0.53 mmol) and Fmoc-L-Leu-Cl (197 mg, 0.53 mmol) according to general procedure B in 15% yield. (Found: C, 60.59; H, 7.66; N, 11.73. $C_{12}H_{18}N_2O_3$ requires C, 60.49; H, 7.61; N, 11.76%). $[\alpha]^{25}_D$–55.8 (*c* = 0.3, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.65 (d, 4.9 Hz, 1H), 6.60 (br, 1H, NH), 6.17 (d, *J* = 4.9 Hz, 1H), 4.05 (m, 1H), 3.94 (d, *J* = 8.6 Hz, 1H), 1.98 (dd, *J* = 9.9, 3.9 Hz, 1H), 1.78 (m, 1H), 1.65 (d, *J* = 6.0 Hz, 3H), 1.60 (dd, *J* = 9.4, 4.9 Hz, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 165.1 (s), 162.7 (s), 132.3 (d), 103.8 (d), 72.1 (d), 58.9 (d), 52.2 (d), 40.5 (t), 24.3 (d), 23.4 (q), 21.2 (q), 19.6 (q) ppm. ESI-MS *m*/*z* 260.67 (M^++Na).

(4a*S*,5*R*,9a*S*)-5-Methyl-1,2,3,4a,5,9a-hexahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalene-4,9-dione (16). Compound **16** was obtained from morpholine **2** (101

mg, 0.53 mmol) and Fmoc-L-Pro-Cl (189 mg, 0.53 mmol) according to general procedure B in 76% yield. (Found: C, 59.51; H, 6.38; N, 12.57. $C_{11}H_{14}N_2O_3$ requires C, 59.45; H, 6.35; N, 12.60%). $[\alpha]^{25}_D$ -43.0 (*c* = 1.0, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.62 (d, *J* = 4.6 Hz, 1H), 6.10 (d, *J* = 4.6 Hz, 1H), 4.14 (t, J = 8 Hz, 1H), 4.05 (m, 1H), 3.93 (d, *J* = 8.8 Hz, 1H), 3.50 (m, 1H), 2.34 (m, 1H), 2.19 (m, 1H), 1.97 (m, 1H), 1.87 (m, 1H), 1.63 (d, *J* = 2.0 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 163.6 (s), 162.3 (s), 131.7 (d), 104.1 (d), 70.6 (d), 59.4 (d), 58.4 (d), 45.9 (t), 28.4 (t), 23.0 (t), 20.3 (q) ppm. ESI-MS *m/z* 223 (M^++1).

(1*R*,7*S*,9a*S*)-7-Benzyl-1-methyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (17). Compound **17** was obtained from morpholine **2** (100 mg, 0.53 mmol) and Fmoc-L-Phe-Cl (215 mg, 0.53 mmol) according to general procedure B in 34% yield. (Found: C, 66.34; H, 5.98; N, 10.88. $C_{15}H_{16}N_2O_3$ requires C, 66.16; H, 5.92; N, 10.92%). $[\alpha]^{25}_D$ –4.8 (*c* = 0.3, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.35-7.25 (m, 3H), 7.20-7.18 (m, 2H), 6.52 (t, *J* = 4.3 Hz, 1H), 6.42 (br, 1H, NH), 6.12 (t, *J* = 4.2 Hz, 1H), 4.36 (br, 1H), 3.76 (dd, *J* = 8.2, 2.8 Hz, 1H), 3.24 (dt, *J* =13.9, 3.5 Hz, 1H), 3.13 (dd, *J* = 6.5, 3.8 Hz, 1H), 1.39 (dd, *J* = 6.2, 3.8 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 165.9 (s), 163.6 (s), 134.6 (s), 133.4 (d), 129.9 (d, 2C), 128.8 (d, 2C), 127.6 (d), 103.0 (d), 73.5 (d), 59.4 (d), 55.5 (d), 39.7 (t), 18.7 (q) ppm. ESI-MS *m/z* 273.08 (M^++1).

(1*R*,7*S*,9a*S*)-7-Benzyloxymethyl-1-methyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (18). Compound **18** was obtained from morpholine **2** (101 mg, 0.53 mmol) and Fmoc-L-Ser(OBn)-Cl (231 mg, 0.53 mmol) according to general procedure B in 48% yield as a 6:1 mixture of inseparable diastereomers. (Found: C, 63.62; H, 6.04; N, 9.11. $C_{16}H_{18}N_2O_4$ requires C, 63.56; H, 6.00; N, 9.27%). Major stereoisomer: δ_H (200 MHz, $CDCl_3$) 7.31 (m, 5H), 7.21 (m, 2H), 6.96 (br, 1H), 6.61 (d, *J* = 4.9 Hz, 1H), 6.19 (d, *J* = 4.9 Hz, 1H), 4.72 (m, 1H), 4.55-4.49 (m, 3H), 4.32 (dd, *J* =10.0, 3.10 Hz, 1H), 4.10 (m, 1H), 3.91 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.84 (d, *J* = 10.4 Hz, 1H), 3.66 (dd, *J* = 9.5, 2.5 Hz, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 164.4 (s), 160.4 (s), 136.9 (s), 133.4 (d), 128.5

(d, 2C), 128.0 (d, 2C), 127.9 (d), 103.2 (d), 73.7 (d), 73.6 (d), 70.4 (d), 59.4 (t), 54.5 (t), 19.0 (q) ppm. ESI-MS *m*/*z* 303.2 (M^++1).

(1*R*,7*R*,9a*S*)-7-Isopropyl-1-methyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (19). Compound **19** was obtained from morpholine **2** (100 mg, 0.53 mmol) and Fmoc-D-Val-Cl (190 mg, 0.53 mmol) according to general procedure B in 77% yield. (Found: C, 59.00; H, 7.22; N, 12.38. $C_{11}H_{16}N_2O_3$ requires C, 58.91; H, 7.19; N, 12.49%). $[\alpha]^{19}_D$ –41.9 (*c* = 2.2, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.86 (br, 1H), 6.67 (d, *J* = 14.9 Hz, 1H), 6.20 (d, *J* = 15.0 Hz, 1H), 4.02-3.92 (m, 2H), 3.84 (t, *J* = 4.0 Hz, 1H), 2.35 (m, 1H), 1.68 (d, *J* = 5.9 Hz, 3H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 164.6 (s), 161.3 (s), 132.7 (d), 103.0 (d), 72.9 (d), 60.8 (d), 58.1 (d), 33.5 (d), 19.5 (q), 18.9 (q), 17.1 (q) ppm. ESI-MS *m/z* 225.3 (M^++1).

(1*R*,7*R*,9a*S*)-7-Isobutyl-1-methyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (20). Compound **20** was obtained from morpholine **2** (101 mg, 0.53 mmol) and Fmoc-D-Leu-Cl (239 mg, 0.64 mmol) according to general procedure B in 47% yield. (Found: C, 60.54; H, 7.67; N, 11.67. $C_{12}H_{18}N_2O_3$ requires C, 60.49; H, 7.61; N, 11.76%). $[\alpha]^{25}_D$–32.8 (*c* = 0.5, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) δ 6.87 (br, 1H), 6.65 (d, 1H, *J* = 4.9 Hz), 6.19 (d, *J* = 4.9 Hz, 1H), 4.08-3.93 (m, 2H), 3.92 (d, *J* = 8.6 Hz, 1H), 1.83-1.73 (m, 1H), 1.71-1.65 (m, 5H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) δ 164.8 (s), 162.6 (s), 132.4 (d), 103.3 (d), 71.9 (d), 57.9 (d), 53.9 (d), 43.0 (t), 24.3 (d), 23.1 (q), 21.2 (q), 19.7 (q) ppm. ESI-MS *m*/*z* 239.3 (M^++1).

(4a*S*,5*R*,9a*R*)-5-Methyl-1,2,3,4a,5,9a-hexahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalene-4,9-dione (21). Compound **21** (82 mg, 0.37 mmol) was obtained from morpholine **2** (103 mg, 0.53 mmol) and Fmoc-D-Pro-Cl (189 mg, 0.53 mmol) according to general procedure B in 69% yield. (Found: C, 59.54; H, 6.40; N, 12.53. $C_{11}H_{14}N_2O_3$ requires C, 59.45; H, 6.35; N, 12.60%). $[\alpha]^{25}_D$ +7.6 (*c* = 1.0, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.43 (d, *J* = 4.6 Hz, 1H), 6.18 (d, *J* = 4.6 Hz, 1H), 4.05 (m, 2H), 3.85 (m, 2H), 3.40 (m, 1H), 2.43 (m, 1H), 2.01 (br, 1H), 1.84 (m, 1H), 1.49 (d, *J* = 6.3 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 161.3 (s), 159.6 (s), 134.1 (d),

102.8 (d), 74.9 (d), 62.1 (d), 58.4 (d), 45.8 (t), 30.0 (t), 21.5 (t), 17.8 (q) ppm. ESI-MS *m*/*z* 223 (M^++1).

(4a*S*,9a*S*)-1,2,3,4a,5,9a-Hexahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalene-4,9-dione (22). Compound **22** was obtained from morpholine **1a** (100 mg, 0.57 mmol) and Fmoc-L-Pro-Cl (223 mg, 0.63 mmol) according to general procedure B in 59% yield. (Found: C, 57.74; H, 5.88; N, 13.39. $C_{10}H_{12}N_2O_3$ requires C, 57.68; H, 5.81; N, 13.45%). $[\alpha]^{24}_D$ +39.2 (*c* = 4.5, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.51 (d, *J* = 4.6 Hz, 1H), 6.14 (d, *J* = 4.6 Hz, 1H), 4.64 (m, 2H), 3.51 (m, 2H), 3.33 (m, 1H), 2.41 (m, 1H), 2.03 (br, 1H), 1.88 (m, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 162.0 (s), 161.1 (s), 132.4 (d), 102.2 (d), 67.2 (t), 58.7 (d), 56.3 (d), 45.3 (t), 28.8 (t), 21.2 (t) ppm. ESI-MS *m*/*z* 209.3 (M^++1).

(4a*S*,9a*S*)-1,2,3,4a,5,9a-Hexahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalene-4,9-dione (23). Compound **23** was obtained from morpholine **1a** (102 mg, 0.57 mmol) and Fmoc-D-Pro-Cl (225 mg, 0.63 mmol) according to general procedure B in 61% yield. (Found: C, 57.73; H, 5.86; N, 13.40. $C_{10}H_{12}N_2O_3$ requires C, 57.68; H, 5.81; N, 13.45%). $[\alpha]^{24}_D$ +58.7 (*c* = 0.3, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.56 (d, *J* = 4.8 Hz, 1H), 6.23 (d, *J* = 4.9 Hz, 1H), 4.77 (dd, *J* = 10.4, 2.5 Hz, 1H), 4.28 (d, *J* = 9.6 Hz, 1H), 4.10-3.95 (m, 1H), 3.90 (d, *J* = 10.0 Hz, 1H), 3.51-3,32 (m, 2H), 2,48 (m, 1H), 2,09-1,68 (m, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 159.8 (s), 159.5 (s), 133.6 (d), 102.1 (d), 65.4 (t), 58.0 (d), 54.0 (d), 45.0 (t), 29.6 (t), 22.2 (t) ppm. ESI-MS *m*/*z* 209.2 (M^++1).

(7*S*,9a*S*)-7-Benzyloxymethyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (24). Compound **24** was obtained from morpholine **1a** (101 mg, 0.57 mmol) and Fmoc-(OBn)Ser-Cl (273 mg, 0.63 mmol) according to general procedure B in 35% yield. (Found: C, 62.55; H, 5.62; N, 9.69. $C_{15}H_{16}N_2O_4$ requires C, 62.49; H, 5.59; N, 9.72%). $[\alpha]^{24}_D$ -12.2 (*c* = 2.2, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.33-7.20 (m, 5H), 6.62 (d, *J* = 5.0 Hz, 1H), 6.20 (d, *J* = 5.0 Hz, 1H), 4.72 (dd, *J* = 11.1, 3.2 Hz, 1H), 4.56-4.99 (m, 3H), 4.33 (dd, *J* = 9.9, 7.1 Hz, 1H), 4.10 (d, *J* = 3.9 Hz, 1H), 3.91 (dd, *J* = 9.7, 3.4 Hz, 1H), 3.79 (d, *J* = 10.1 Hz, 1H), 3.73-3.63 (m, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 165.5 (s),

160.0 (s), 136.9 (s), 133.1 (d), 128.4 (d, 2C), 127.8 (d, 2C), 127.3 (d), 102.7 (d), 73.5 (t), 72.2 (t), 66.1 (t), 56.2 (d), 53.2 (d) ppm. ESI-MS *m*/*z* 289.2 (M^++1).

(9a*R*)-7,7-Dimethyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (25). Compound **25** was obtained from morpholine **1b** (101 mg, 0.57 mmol) and Fmoc-α-Me-Ala-Cl (217 mg, 0.63 mmol) according to general procedure B in 14% yield. (Found: C, 55.14; H, 6.23; N, 14.21. $C_9H_{12}N_2O_3$ requires C, 55.09; H, 6.16; N, 14.28%). $[\alpha]^{26}_D$ +45.3 (*c* = 0.4, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 6.62 (d, *J* = 4.8 Hz, 1H), 6.51 (br, 1H), 6.22 (d, *J* = 5.1 Hz, 1H), 4.78 (dd, *J* = 11.0, 3.3 Hz, 1H), 4.33 (dd, *J* = 9.5, 3.3 Hz, 1H), 3.84 (dd, *J* = 21.2, 9.9 Hz, 1H), 1.54 (s, 3H), 1.52 (s, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 163.7 (s), 161.2 (s), 133.5 (d), 102.1 (d), 65.8 (t), 61.1 (d), 53.4 (s), 18.8 (q), 16.6 (q) ppm. ESI-MS *m*/*z* 197.3 (M^++1).

(7*S*,9a*R*)-7-Isopropyl-1,7,8,9a-tetrahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (26). Compound **26** was obtained from morpholine **1b** (100 mg, 0.57 mmol) and Fmoc-L-Val-Cl (225 mg, 0.63 mmol) according to general procedure B in 45% yield. (Found: C, 57.21; H, 6.75; N, 13.28. $C_{10}H_{14}N_2O_3$ requires C, 57.13; H, 6.71; N, 13.33%). $[\alpha]^{24}_D$ +89.7 (*c* = 1.9, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.48 (br, 1H), 6.61 (d, *J* = 4.9 Hz, 1H), 6.20 (d, *J* = 4.9 Hz, 1H), 4.76 (dd, *J* = 11.1, 3.2 Hz, 1H), 4.28 (dd, *J* = 9.7, 3.1 Hz, 1H), 3.88 (m, 1H), 3.80 (d, *J* = 11.0 Hz, 1H), 2.35 (m, 1H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 164.7 (s), 160.7 (s), 133.2 (d), 102.8 (d), 66.2 (t), 60.6 (d), 52.9 (d), 33.9 (q), 18.9 (q), 16.8 (q) ppm. ESI-MS *m*/*z* 211.4 (M^++1).

(3*R*,6*R*,8a*R*/*S*)-6-Isobutyl-5-oxo-hexahydro-oxazolo[3,2-a]pyrazine-3-carboxylic acid methyl ester (27 and 28). Compounds **27** and **28** was obtained from morpholine **1b** (80 mg, 0.46 mmol) and Fmoc-D-Leu-Cl (209 mg, 0.55 mmol) according to general procedure C in 24% and 20% yield, respectively, after flash chromatographic purification (EtOAc/petr. ether 3:1, R_f = 0.54 and 0.44). **27**: (Found: C, 56.35; H, 7.79; N, 10.88. $C_{12}H_{20}N_2O_4$ requires C, 56.23; H, 7.87; N, 10.93%). $[\alpha]^{26}_D$ +35.9 (*c* = 0.7, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 4.82 (dd, *J* = 10. 0, 3.9 Hz, 1H), 4.67 (d, *J* = 4.0 Hz,

1H), 4.38 (d, *J* = 9.7 Hz, 1H), 4.06 (dd, *J* = 10.9, 4.0 Hz, 1H), 3.75-3.68 (m, 1H), 3.79 (s, 3H), 3.53 (dd, *J* = 11.7, 6.2 Hz, 1H), 3.05 (dd, . = 10.8, 10.1 Hz, 1H), 1.84-1.72 (m, 3H), 0.95 (dd, *J* = 6.5, 6.3 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 171.1 (s), 170.5 (s), 86.3 (d), 76.2 (d), 63.2 (d), 54.2 (q), 43.9 (t), 43.1 (t), 39.8 (t), 24.2 (d), 21.5 (q), 18.99 (q) ppm. ESI-MS *m*/*z* 257.2 (M^++1). **28**: (Found: C, 56.31; H, 7.84; N, 10.91. $C_{12}H_{20}N_2O_4$ requires C, 56.23; H, 7.87; N, 10.93%). $[\alpha]^{24}_D$ +56.2 (*c* = 0.9, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 4.80 (dd, *J* = 9.9, 4.0 Hz, 1H), 4.66 (d, *J* = 4.0 Hz, 1H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.04 (dd, *J* = 11.0, 4.0 Hz, 1H), 3.70 (dd, *J* = 10.7, 3.2 Hz, 1H), 3.78 (s, 3H), 3.51 (dd, *J* = 11.7, 4.4 Hz, 1H), 3.00 (dd, *J* = 10.8, 10.0 Hz, 1H), 2.03 (br, 1H), 1.85 (m, 3H), 0.95 (dd, *J* = 6.2, 6.1 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 170.6 (s), 170.0 (s), 86.6 (d), 76.8 (d), 62.7 (d), 54.9 (q), 44.6 (t), 43.2 (t), 39.6 (t), 24.9 (d), 21.1 (q), 19.2 (q) ppm. ESI-MS *m*/*z* 257.3 (M^++1).

(3*R*,6*S*,8a*R*/*S*)-6-Isopropyl-5-oxo-hexahydro-oxazolo[3,2-a]pyrazine-3-carboxylic acid methyl ester (29 and 30). Compounds **29** and **30** was obtained from morpholine **1b** (100 mg, 0.57 mmol) and Fmoc-L-Val-Cl (245 mg, 0.69 mmol) according to general procedure C in 24% and 22% yield, respectively, after flash chromatographic purification (EtOAc/petr. ether 3:1, R_f = 0.41 and 0.24). **29**: (Found: C, 54.62; H, 7.54; N, 11.49. $C_{11}H_{18}N_2O_4$ requires C, 54.53; H, 7.49; N, 11.56%). $[\alpha]^{24}_D$ +22.6 (*c* = 0.5, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 4.48 (dd, *J* = 9.8, 3.7 Hz, 1H), 4.05 (m, 3H), 3.81 (s, 3H), 3.59-3.47 (m, 2H), 3.21 (dd, *J* = 10.9, 9.5 Hz, 1H), 2.13 (m, 1H), 1.80 (br, 1H), 0.96 (dd, *J* = 18.5, 6.7 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 169.6 (s), 169.3 (s), 86.5 (d), 76.4 (d), 62.7 (d), 45.8 (t), 52.4 (q), 45.8 (t), 30.0 (d), 19.0 (q), 17.6 (q) ppm. ESI-MS *m*/*z* 243.3 (M^++1). **30**: (Found: C, 54.60; H, 7.51; N, 11.51. $C_{11}H_{18}N_2O_4$ requires C, 54.53; H, 7.49; N, 11.56%). $[\alpha]^{25}_D$ +23.0 (*c* = 0.6, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 4.85 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.74 (d, *J* = 4.0 Hz, 1H), 4.36 (d, *J* = 11.8 Hz, 1H), 4.00 (dd, *J* = 11.0, 4.1 Hz, 1H), 3.78 (s, 3H), 3.56-3.47 (m, 2H), 3.04 (dd, *J* = 10.6, 10.3 Hz, 1H), 2.19 (m, 1H), 1.03 (dd, *J* = 9.0, 6.8 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 169.4 (s), 169.1 (s), 86.3 (d), 76.8 (d), 62.1 (d), 44.9 (t), 53.8 (q), 45.1 (t), 31.2 (d), 19.1 (q), 17.1 (q) ppm. ESI-MS *m*/*z* 243.2 (M^++1).

6,6-Dimethyl-5-oxo-hexahydro-oxazolo[3,2-a]pyrazine-3-carboxylic acid methyl ester (31). Compound **31** was obtained as a mixture of inseparable diastereomers from morpholine **1b** (100 mg, 0.57 mmol) and Fmoc-α-Me-Ala-Cl (217 mg, 0.63 mmol) according to general procedure C in 57% yield, after flash chromatographic purification (EtOAc/petr. ether 3:1, R_f = 0.2). 3:2 Mixture of steroisomers: (Found: C, 52.77; H, 7.11; N, 12.09. $C_{10}H_{16}N_2O_4$ requires C, 52.62; H, 7.07; N, 12.27%). δ_H (200 MHz, $CDCl_3$) 4.90 (dd, *J* = 7.9, 4.5 Hz, $1H_B$), 4.78 (dd, *J* = 9.8, 3.9 Hz, $1H_A$), 4.62 (d, *J* = 4.0 Hz, $1H_A$), 4.41 (d, *J* = 7.5 Hz, $1H_B$), 4.38 (d, *J* = 12.0 Hz, $1H_A$), 4.18 (dd, *J* = 11.4, 3.5 Hz, $1H_B$), 4.05 (dd, *J* = 10.8, 3.9 Hz, $1H_A$), 3.87-3.72 (m, $1H_B$), 3.78 (s, $3H_A$), 3.76 (s, $3H_B$), 3.54 (dd, *J* = 11.7, 4.2 Hz, $1H_A$), 3.41 (d, *J* = 8.8 Hz, $1H_B$), 3.04 (dd, *J* = 10.5, 10.3 Hz, $1H_A$), 2.77 (dd, *J* = 13.3, 8.5 Hz, $1H_B$) 1.84 (br, 1H) 1.34 (m, 12H) ppm. δ_C (50 MHz, $CDCl_3$) 169.0, 169.6, 130.4, 128.2, 86.5, 72.9, 68.2, 67.6, 64.1, 59.2, 55.8, 52.8, 43.1, 27.5, 26.3, 25.2, 24.9, 24.4 ppm. ESI-MS *m*/*z* 229.2 (M^++1).

(3*S*,6*S*,8a*R*/*S*)-6-Isobutyl-5-oxo-hexahydro-oxazolo[3,2-a]pyrazine-3-carboxylic acid methyl ester (32 and 33). Compounds **32** and **33** was obtained from morpholine **1a** (66 mg, 0.38 mmol) and Fmoc-L-Leu-Cl (134 mg, 0.38 mmol) according to general procedure C in 24% and 25% yield, respectively, after flash chromatographic purification (EtOAc/petr. ether 3:1, R_f = 0.35 and 0.31) with same characterization data as for **27** and **28**, respectively. **32**: (Found: C, 56.32; H, 7.91; N, 10.86. $C_{12}H_{20}N_2O_4$ requires C, 56.23; H, 7.87; N, 10.93%). $[\alpha]^{21}_D$ -32.6 (*c* = 0.3, $CHCl_3$). **33**: (Found: C, 56.31; H, 7.92; N, 10.88. $C_{12}H_{20}N_2O_4$ requires C, 56.23; H, 7.87; N, 10.93%). $[\alpha]^{24}_D$ -52.8 (*c* = 0.2, $CHCl_3$).

(2*R*,3*S*,6*S*,8a*S*)-6-Benzyl-2-methyl-5-oxo-hexahydro-oxazolo[3,2-a]pyrazine-3-carboxylic acid methyl ester (34). Compound **34** was obtained from morpholine **2** (103 mg, 0.53 mmol) and Fmoc-L-Phe-Cl (215 mg, 0.53 mmol) according to general procedure C in 67% yield. (Found: C, 63.27; H, 6.67; N, 9.14. $C_{16}H_{20}N_2O_4$ requires C, 63.14; H, 6.62; N, 9.20%). $[\alpha]^{23}_D$ –102.3 (*c* = 1.1, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.32-7.18 (m, 5H), 4.92 (dd, *J* = 7.2, 4.4 Hz, 1H), 4.26 (d, J = 7.5

Hz, 1H), 4.09 (m, 1H), 3.77 (s, 3H), 3.64 (dd, *J* = 10.4, 3.6 Hz, 1H), 3.28-3.20 (m, 2H), 2.89-2.79 (m, 2H), 1.48 (d, *J* = 6.0 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 169.6 (s), 169.0 (s), 138.2 (s), 129.1 (d, 2C), 128.4 (d, 2C), 126.5 (d), 86.6 (d), 76.8 (d), 62.7 (d), 58.3 (d), 52.6 (q), 43.3 (t), 36.7 (t), 19.2 (q) ppm. ESI-MS *m*/*z* 305.33 (M^++1).

(2*R*,3*S*,8a*S*)-2,6,6-Trimethyl-5-oxo-hexahydro-oxazolo[3,2-a]pyrazine-3-carboxylic acid methyl ester (35). Compound **35** was obtained from morpholine **2** (101 mg, 0.53 mmol) and Fmoc-α-Me-Ala-Cl (182 mg, 0.53 mmol) according to general procedure C in 55% yield. (Found: C, 54.61; H, 7.55; N, 11.62. $C_{11}H_{18}N_2O_4$ requires C, 54.53; H, 7.49; N, 11.56%). $[\alpha]^{23}_D$ –61.6 (*c* = 1.4, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 4.93 (dd, *J* = 9.9, 4.4 Hz, 1H), 4.16 (d, *J* = 7.7 Hz, 1H), 4.07 (m, 1H), 3.74 (s, 3H), 3.73 (m, 1H), 3.29 (dd, *J* = 13.7, 4.4 Hz, 1H), 2.74 (dd, *J* = 13.2, 8.6 Hz, 1H), 1.45 (d, *J* = 6.2 Hz, 3H), 1.34 (s, 3H), 1.32 (s, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 172.3 (s), 169.4 (s), 86.6 (d), 76.9 (d), 62.4 (d), 55.8 (s), 52.3 (q), 43.0 (t), 27.3 (q), 25.0 (q), 18.8 (q) ppm. ESI-MS *m*/*z* 243.08 (M^++1).

(1*R*,3*R*/*S*,9a*S*)-8-Biphenyl-4-ylmethyl-1-hydroxymethyl-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (36). Compound **36** was obtained from scaffold **IV** (50 mg, 0,17 mmol) and 4-phenyl-benzylamine (156 µL, 0.85 mmol) according to general procedure D in 88% yield. (Found: C, 66.74; H, 6.15; N, 6.89. $C_{22}H_{24}N_2O_5$ requires C, 66.65; H, 6.10; N, 7.07%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 7.56 (d, *J* = 7.9 Hz, 2H), 7.39 (m, 7H), 4.88 (t, *J* = 4.5 Hz, 1H), 4.74 (d, *J* = 5.6 Hz, 1H), 4.67-4.53 (m, 3H), 4.42 (dd, *J* = 14.0, 4.3 Hz, 1H), 3.99 (d, *J* = 9.7 Hz, 1H), 3.90 (d, *J* = 10.1 Hz, 1H), 3.85 (d, *J* = 3.9 Hz, 1H), 3.51 (d, *J* = 2.4 Hz, 1H), 3.39 (s, 3H), 2.89 (dd, *J* = 13.4, 4.5 Hz, 1H), 2.31 (br, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 162.7 (s), 160.5 (s), 140.9 (s), 140.2 (s), 133.5 (s), 128.7 (d, 2C), 128.6 (d, 2C), 127.6 (d), 127.4 (d, 2C), 126.8 (d, 2C), 94.8 (d), 72.7 (d), 63.3 (t), 61.5 (t), 56.1 (d), 55.7 (q), 48.9 (t), 45.1 (t) ppm. ESI-MS *m*/*z* 397.3 (M^++1).

(1*R*,3*R*/*S*,9a*S*)-8-Cyclopropyl-4-ylmethyl-1-hydroxymethyl-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (37). Compound **37** was obtained from scaffold **IV** (50 mg,

0.17 mmol) and 4-phenyl-benzylamine (59.5 µL, 0.85 mmol) according to general procedure D in 70% yield. (Found: C, 53.40; H, 6.77; N, 10.28. $C_{12}H_{18}N_2O_5$ requires C, 53.33; H, 6.71; N, 10.36%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 4.87 (t, *J* = 4.6 Hz, 1H), 4.74-4.69 (m, 1H), 4.59 (d, *J* = 5.9 Hz, 1H), 4.35 (dd, *J* = 16.5, 5.1 Hz, 1H), 3.99 (d, *J* = 10.9 Hz, 1H), 3.93 (d, *J* = 10.6 Hz, 1H), 3.78 (d, *J* = 4.2 Hz, 1H), 3.50 (d, *J* = 2.0 Hz, 1H), 3.45 (s, 3H), 2.84 (dd, *J* = 13.3, 4.4 Hz, 1H), 2.63 (m, 1H), 2.22 (br, 1H), 0.91-0.57 (m, 4H) ppm. δ_C (50 MHz, $CDCl_3$) 164.8 (s), 163.2 (q), 94.8 (d), 72.7 (d), 63.2 (t) 59.8 (d), 56.1 (q), 49.4 (t), 44.4 (d), 29.2 (t), 6.6 (t), 6.4 (t) ppm. ESI-MS *m*/*z* 271.2 (M^++1).

(1*R*,3*R*/*S*,9a*S*)-8-Isobutyl-4-ylmethyl-1-hydroxymethyl-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (38). Compound **38** was obtained from scaffold **IV** (33 mg, 0.11 mmol) and isobutylamine (56 µL, 0.56 mmol) according to general procedure D in 68% yield. (Found: C, 54.72; H, 7.79; N, 9.72. $C_{13}H_{22}N_2O_5$ requires C, 54.53; H, 7.74; N, 9.78%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 4.93 (t, *J* = 4.3 Hz, 1H), 4.76-4.67 (m, 1H), 4.69 (d, *J* = 5.6 Hz, 1H), 4.44 (dd, *J* = 13.5, 4.9 Hz, 1H), 3.99 (m, 1H), 4.01 (d, *J* = 6.7 Hz, 1H), 3.92-3.86 (m, 1H), 3.82 (d, *J* = 3.9 Hz, 1H), 3.48 (s, 3H), 3.32 (d, *J* = 8.0 Hz, 1H), 3.09 (dd, *J* = 13.5, 7.3 Hz, 1H), 2.93 (dd, *J* = 13.5, 4.3 Hz, 1H), 2.01 (m, 2H), 0.93 (d, *J* = 5.7 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 164.4 (s), 163.6 (q), 93.6 (d), 72.3 (d), 61.7 (d), 55.7 (q), 54.8 (t), 49.8 (t), 44.4 (t), 25.8 (t), 25.9 (d), 19.2 (q, 2C) ppm. ESI-MS *m*/*z* 287.2 (M^++1).

(1*R*,3*R*/*S*,9a*S*)-8-Propargyl-4-ylmethyl-1-hydroxymethyl-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (39). Compound **39** was obtained from scaffold **IV** (50 mg, 0.17 mmol) and propargylamine (54.5 µL, 0.85 mmol) according to general procedure D in 95% yield. (Found: C, 53.81; H, 6.09; N, 10.37. $C_{12}H_{16}N_2O_5$ requires C, 53.73; H, 6.01; N, 10.44%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 4.93 (t, *J* = 4.8 Hz, 1H), 4.75-4.64 (m, 1H), 4.69 (d, *J* = 5.6 Hz, 1H), 4.49 (dd, *J* = 13.4, 5.1 Hz, 1H), 4.30 (m, 1H), 4.25 (d, *J* = 2.4 Hz, 1H), 4.12 (d, *J* = 4.8 Hz, 1H), 3.83 (d, *J* = 3.8 Hz, 1H), 3.53 (m, 1H), 3.48 (s, 3H), 3.39 (m, 1H), 2.91 (dd, *J* = 13.5, 5.0 Hz, 1H), 2.52 (br, 1H), 2.31 (m, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 162.7 (s), 162.6 (s), 95.0 (d), 73.6

(d), 72.5 (d), 63.3 (t), 61.5 (t), 56.2 (s), 55.6 (q), 48.8 (t), 45.2 (t), 34.7 (d) ppm. ESI-MS *m*/*z* 269.3 (M^++1).

(1*R*,3*R*/*S*,9a*S*)-1-Hydroxymethyl-8-[1(*S*)-hydroxymethyl-3-methyl-butyl]-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (40). Compound **40** was obtained from scaffold **IV** (50 mg, 0.17 mmol) and L-leucinol (110 μL, 0.85 mmol) according to general procedure D in 72% yield. (Found: C, 54.62; H, 8.00; N, 8.40. $C_{15}H_{26}N_2O_6$ requires C, 54.53; H, 7.93; N, 8.48%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 4.89 (t, *J* = 4.5 Hz, 1H), 4.77-4.62 (m, 1H), 4.67 (d, *J* = 4.7 Hz, 1H), 4.44 (dd, *J* = 5.0, 4.2 Hz, 1H), 4.37-4.28 (m, 1H), 4.23-4.09 (m, 1H), 3.99 (d, *J* = 4.0 Hz, 1H), 3.93-3.79 (m, 1H), 3.84 (d, *J* = 3.7 Hz, 1H), 3.64 (dd, *J* = 12.3, 4.9 Hz, 1H), 3.53-3.50 (m, 1H), 3.48 (s, 3H), 2.76 (dd, *J* = 12.6, 4.1 Hz, 1H), 2.53 (br, 1H), 2.09 (m, 2H), 1.57 (m, 1H), 0.93 (d, *J* = 6.2 Hz, 6H) ppm. δ_C (50 MHz, $CDCl_3$) 163.6 (s), 163.1 (s), 94.8 (d), 72.8 (d), 62.2 (d), 61.5 (t), 56.9 (d), 55.9 (q), 47.8 (t), 45.1 (t), 36.4 (t), 35.7 (t), 24.8 (d), 23.3 (q), 22.1 (q) ppm. ESI-MS *m*/*z* 331.3 (M^++1).

(5*R*,4a*S*,7*R*/*S*,9a*S*)-5-Hydroxymethyl-7-methoxy-octahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalene-4,9-dione (41). Lactone **IV** (330 mg, 1.9 mmol) was treated with Fmoc-L-Pro-Cl (1.0 g, 1.92 mmol) and 2,6-lutidine (442 μL, 3.8 mmol) in CH_2Cl_2 (10 mL) until consumption of the reagents, then the mixture was sequentially washed with 5% HCl, 5% $NaHCO_3$ and brine. After solvent evaporation, the resulting Fmoc-L-Pro-lactone was treated with 30% diethylamine in acetonitrile (6 mL) for 1.5 h. After solvent evaporation, pure **41** was obtained by flash chromatography purification in 75% yield (EtOAc, R_f = 0.1). (Found: C, 53.65; H, 6.76; N, 10.29. $C_{12}H_{18}N_2O_5$ requires C, 53.33; H, 6.71; N, 10.36%). Major steroisomer: δ_H 4.86 (t, *J* = 2.8 Hz, 1H), 4.61 (m, 1H), 4.26-4.18 (m, 2H), 4.10-3.95 (m, 2H), 3.64-3.52 (m, 1H), 3.48 (m, 1H), 3.43 (s, 3H), 3.37 (dd, *J* = 13.7, 5.1 Hz, 1H), 2.38 (m, 2H), 2.03-1.86 (m, 4H) ppm. δ_C (50 MHz, $CDCl_3$) 166.7 (s), 162.8 (s), 96.1 (d), 95.4 (d), 72.9 (d), 72.3 (d), 63.9 (t), 61.7 (t), 59.2 (d), 58.8 (d), 58.1 (d), 56.5 (d), 55.4 (d), 45.4 (t), 43.5 (t), 43.3 (t), 29.3 (t), 29.0 (t), 22.2 (t), 21.7 (t) ppm.

(1*R*,3*R*/*S*,9a*S*)-1-Hydroxymethyl-8-(4-methoxy-benzyl)-3-methoxy-hexahydro-pyrazino[2,1-c][1,4]oxazine-6,9-dione (42). Compound **42** was obtained from scaffold **IV** (200 mg, 0.68 mmol) and 4-methoxy-benzylamine (444 µL, 3.4 mmol) according to general procedure D in 76% yield. (Found: C, 58.42; H, 6.39; N, 7.91. $C_{17}H_{22}N_2O_6$ requires C, 58.28; H, 6.33; N, 8.00%). Major steroisomer: δ_H (200 MHz, $CDCl_3$) 7.21-7.16 (m, 2H), 6.88-6.83 (m, 2H), 4.87 (t, *J* = 4.6 Hz, 1H), 4.73-4.67 (m, 2H), 4.57-4.49 (m, 3H), 4.40 (dd, *J* = 13.5, 4.5 Hz, 1H), 3.92 (d, *J* = 7.7 Hz, 1H), 3.80-3.74 (m, 2H), 3.77 (s, 3H), 3.50 (d, *J* = 2.4 Hz, 1H), 3.46 (s, 3H), 2.86 (dd, *J* = 13.5, 4.7 Hz, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 164.3 (s), 162.6 (s), 159.3 (s), 130.1 (d, 2C), 126.6 (q), 114.2 (d, 2C), 94.9 (d), 72.3 (d), 66.3 (t), 61.7 (d), 55.7 (q), 55.1 (q), 48.4 (t), 48.3 (t), 44.4 (t) ppm. ESI-MS *m*/*z* 351.3 (M^++1).

(5*R*,4a*S*,7*R*/*S*,9a*S*)-Tetradecanoic acid 7-methoxy-4,9-dioxo-octahydro-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalen-5-ylmethyl ester (43). Compound **41** (100 mg, 0.37 mmol) was dissolved in CH_2Cl_2 (20 mL), then myristic acid (101 mg, 0,44 mmol), DIPC (57 µL, 0.7 mmol) and catalytic DMAP were added, and the mixture was left reacting overnight at r.t. After solvent evaporation, pure **43** was obtained in 64% yield after chromatografic purification (EtOAc/petr. ether 1:1, R_f = 0.22). (Found: C, 65.54; H, 9.44; N, 5.74. $C_{26}H_{44}N_2O_6$ requires C, 64.97; H, 9.23; N, 5.83%). δ_H (200 MHz, $CDCl_3$) 4.87 (dd, *J* = 5.1, 4.1 Hz, 1H), 4.59 (m, 2H), 4.28-4.17 (m, 2H), 4.12-4.03 (m, 2H), 3.63-3.55 (m, 1H), 3.52-3.36 (m, 1H), 3.44 (s, 3H), 3.23 (dd, *J* = 14.1, 5.3 Hz, 1H), 2.41 (m, 1H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.98 (m, 3H), 1.60 (m, 2H), 1.25 (s, 20H), 0.87 (t, *J* = 6.4 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 173.5 (q), 166.7 (q), 162.0 (s), 96.0 (d), 70.8 (d), 62.5 (d), 58.8 (d), 56.0 (q), 55.3 (t), 45.2 (t), 43.5 (t), 42.1 (t), 34.2 (t), 31.9 (t), 29.6 (t, 3C), 29.4 (t), 29.3 (t), 29.1 (t), 24.8 (t), 23.4 (t, 2C), 22.6 (t), 22.1 (t), 14.1 (q) ppm. ESI-MS *m*/*z* 481.4 (M^++1).

(1*R*,3*R*/*S*,9a*S*)-Tetradecanoic acid 3-methoxy-8-(4-methoxy-benzyl)-6,9-dioxo-octahydro-pyrazino[2,1-c][1,4]oxazin-1-ylmethyl ester (44). Compound **42** (85 mg, 0.24 mmol) was dissolved in CH_2Cl_2 (15 mL), then myristic acid (66.2 mg, 0.29 mmol), DIPC (37 µL, 0.24 mmol) and catalytic DMAP were added, and the mixture was left reacting overnight at r.t. After solvent

evaporation, pure **44** was obtained in 66% yield after chromatografic purification (EtOAc/petr. ether 1:1, R_f = 0.47). (Found: C, 66.62; H, 8.70; N, 4.90. $C_{31}H_{48}N_2O_7$ requires C, 66.40; H, 8.63; N, 5.00%). δ_H (200 MHz, $CDCl_3$) 7.23 (d, *J* = 1.5 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 4.77 (t, *J* = 4.4Hz, 1H), 4.69-4.62 (m, 1H), 4.65 (d, *J* = 13.6 Hz, 1H), 4.55 (q, *J* = 5.1 Hz, 1H), 4.39-4.16 (m, 3H), 4.28 (d, *J* = 14.3, 1H), 3.79 (m, 1H), 3.75 (s, 3H), 3.45-3.32 (m, 1H), 3.42 (s, 3H), 2.84 (dd, *J* = 13.3, 5.7 Hz, 1H), 2.04 (m, 2H), 1.45 (m, 2H), 1.21 (s, 20H), 0.84 (t, *J* = 6.2 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 172.8 (s), 161.8 (s), 161.4 (s), 159.5 (s), 129.9 (d, 2C), 126.4 (s), 114.3 (d, 2C), 94.8 (d), 71.6 (d), 62.1 (t), 56.2 (d), 55.7 (q), 55.3 (q), 48.7 (t), 48.4 (t), 45.0 (t), 34.0 (t), 32.0 (t), 29.7 (t), 29.5 (t, 2C), 29.4 (t, 2C), 29.3 (t), 29.1 (t), 24.8 (t), 22.8 (t), 14.2 (q) ppm. ESI-MS *m*/*z* 561.4 (M^++1).

(5*R*,4a*S*,9a*S*)-Tetradecanoic acid 4,9-dioxo-2,3,4a,5,9,9a-hexahydro-1H,4H-6-oxa-3a,8a-diaza-cyclopenta[b]naphthalen-5-ylmethyl ester (45). Compound **43** (103 mg, 0.21 mmol) was dissolved in toluene (10 mL), then pTSOH was added (40 mg, 0.21 mmol) and the mixture was refluxed over 4Å molecular sieves for 2 h. After solvent evaporation, pure **45** was obtained by flash chromatography in 58% yield (EtOAc/petr. ether 3:2, R_f = 0.23). (Found: C, 67.02; H, 9.01; N, 6.15. $C_{25}H_{40}N_2O_5$ requires C, 66.94; H, 8.99; N, 6.24%). $[\alpha]^{26}_D$ +48.0 (*c* = 1.3, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 5.08 (m, 1H), 4.42-4.39 (m, 1H), 4.35-4.29 (m, 1H), 4.14 (m, 1H), 3.96 (d, *J* = 2.8 Hz, 1H), 3.66-3.58 (m, 1H), 2.54-2.42 (m, 1H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.02 (m, 3H), 1.60 (m, 2H), 1.25 (s, 20H), 0.88 (t, *J* = 6.0 Hz, 3H) ppm. δ_C (50 MHz, $CDCl_3$) 171.4 (s), 163.1 (s), 161.1 (s), 103.3 (d), 101.1 (d), 71.7 (d), 59.7 (t), 58.4 (d), 55.7 (d), 45.4 (t), 42.4 (t), 34.1 (t), 31.9 (t), 29.7 (t), 29.5 (t, 3C), 29.4 (t, 3C), 29.3 (t), 29.1 (t), 24.8 (t), 22.8 (t), 14.2 (q) ppm. ESI-MS *m*/*z* 449.4 (M^++1).

4-(4-Methoxy-benzyl)-10,12-dioxa-4,7-diaza-tricyclo[7.2.1.02,7]dodecane-3,6-dione (46). Compound **42** (50 mg, 0.14 mmol) was dissolved in a minimal amount of CH_2Cl_2, then toluene (10 mL)and acid silica gel (20 mg) were added and the mixture was refluxed over 4Å molecular sieves for 30 min. Then, the mixture was filtered over $NaHCO_3$, and the solvent was evaporated to give

pure **46** in 92% yield. (Found: C, 60.65; H, 5.78; N, 8.73. $C_{16}H_{18}N_2O_5$ requires C, 60.37; H, 5.70; N, 8.80%). $[\alpha]^{24}_D$ -6.6 (*c* = 2.8, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 7.16 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.5, 1H), 5.56 (s, 1H), 5.13 (m, 1H), 4.50 (m, 1H), 4.38 (s, 1H), 4.04 (d, *J* = 13.9 Hz, 1H), 3.86 (m, 5H), 3.78 (s, 3H), 2.92 (d, *J* = 13.2 Hz, 1H) ppm. δ_C (50 MHz, $CDCl_3$) 164.1 (s), 162.1 (s), 159.4 (s), 129.7 (d, 2C), 126.6 (q), 114.3 (d, 2C), 98.5 (d), 72.9 (d), 66.2 (t), 58.5 (d), 55.3 (q), 48.9 (t), 48.5 (t), 46.2 (t) ppm. ESI-MS *m*/*z* 319.1 (M^++1).

Compound 47. Compound **41** (61 mg, 0.23 mmol) was dissolved in a minimal amount of CH_2Cl_2, then toluene (10 mL)and acid silica gel (20 mg) were added and the mixture was refluxed over 4Å molecular sieves for 30 min. Then, the mixture was filtered over $NaHCO_3$, and the solvent was evaporated to give pure **47** in 88% yield after chromatographic purification (EtOAc/MeOH 10:1, R_f = 0.37). (Found: C, 56.01; H, 6.00; N, 11.63. $C_{11}H_{14}N_2O_4$ requires C, 55.46; H, 5.92; N, 11.76%). $[\alpha]^{24}_D$ -93.1 (*c* = 1.0, $CHCl_3$). δ_H (200 MHz, $CDCl_3$) 5.60 (s, 1H), 5.08 (m, 1H), 4.37 (s, 1H), 4.08-3.97 (m, 1H), 4.00 (d, *J* = 13.6 Hz, 1H), 3.89 (m, 2H), 3,60 (m, 2H), 3.01 (d, *J* = 13.6 Hz, 1H), 2.45 (m, 1H), 2.11-1.80 (m, 3H), ppm. δ_C (50 MHz, $CDCl_3$) 163.5 (s), 162.7 (s), 98.2 (d), 71.7 (d), 65.7 (d), 59.1 (t), 58.4 (d), 46.4 (t), 45.1 (t), 29.1 (t), 21.9 (t) ppm. ESI-MS *m*/*z* 227.0 (M^++1).

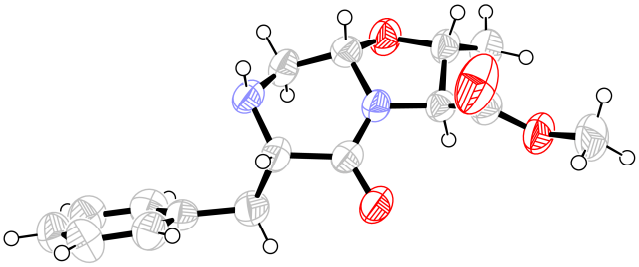

Table S2. Crystal data and structure refinement for exp_259.

Identification code	exp_259
Empirical formula	C32 H40 N4 O8
Formula weight	608.68
Temperature	293(2) K
Wavelength	1.54178 A
Crystal system, space group	Monoclinic, P 21
Unit cell dimensions	a = 7.757(1) A alpha = 90 deg. b = 18.607(1) A beta = 92.211(2) deg. c = 10.809(1) A gamma = 90 deg.
Volume	1559.0(3) A^3
Z, Calculated density	2, 1.297 Mg/m^3
Absorption coefficient	0.773 mm^-1
F(000)	648
Crystal size	0.12 x 0.10 x 0.08 mm
Theta range for data collection	4.73 to 70.56 deg.
Limiting indices	-7<=h<=9, -14<=k<=22, -12<=l<=12
Reflections collected / unique	7877 / 4396 [R(int) = 0.0239]
Completeness to theta = 70.56	95.3 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4396 / 1 / 405
Goodness-of-fit on F^2	0.994
Final R indices [I>2sigma(I)]	R1 = 0.0433, wR2 = 0.0994
R indices (all data)	R1 = 0.0696, wR2 = 0.1117
Absolute structure parameter	0.2(2)
Largest diff. peak and hole	0.367 and -0.146 e.A^-3

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for exp_259.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1A)	2448(4)	-2380(1)	-1443(2)	51(1)
N(2A)	4122(4)	-1614(2)	454(3)	56(1)
O(1A)	-131(3)	-1871(1)	-1108(2)	66(1)
O(2A)	2852(5)	-2476(2)	-4045(3)	107(1)
O(3A)	1157(3)	-3442(1)	-4051(2)	69(1)
O(4A)	4275(3)	-3307(1)	-1273(3)	71(1)
C(1A)	1663(5)	-1722(2)	-976(3)	55(1)
C(2A)	2252(5)	-1595(2)	345(3)	62(1)
C(3A)	4841(5)	-2310(2)	95(3)	54(1)
C(4A)	3836(4)	-2708(2)	-932(3)	51(1)
C(5A)	1228(4)	-2754(2)	-2262(3)	50(1)
C(6A)	-337(4)	-2247(2)	-2270(3)	56(1)
C(7A)	5077(5)	-2806(2)	1203(3)	67(1)
C(8A)	6242(5)	-2492(2)	2233(3)	58(1)
C(9A)	5637(5)	-2354(2)	3378(3)	70(1)
C(10A)	6701(7)	-2093(2)	4329(4)	79(1)
C(11A)	8403(7)	-1976(2)	4147(4)	82(1)
C(12A)	9041(5)	-2112(2)	2999(4)	78(1)
C(13A)	7974(5)	-2361(2)	2040(4)	68(1)
C(14A)	1879(5)	-2869(2)	-3541(3)	56(1)
C(15A)	1612(6)	-3615(3)	-5299(4)	89(1)
C(16A)	-2060(5)	-2605(2)	-2354(4)	71(1)
N(1B)	3475(3)	-5071(1)	-490(2)	45(1)
N(2B)	3771(4)	-4721(2)	-2940(2)	67(1)
O(1B)	775(3)	-4676(2)	-885(2)	67(1)
O(2B)	3868(4)	-5902(1)	1660(2)	74(1)
O(3B)	2849(3)	-5010(1)	2798(2)	68(1)
O(4B)	6283(3)	-4803(2)	-142(2)	63(1)
C(1B)	1957(4)	-5195(2)	-1290(3)	57(1)
C(2B)	2264(5)	-5117(2)	-2655(3)	67(1)
C(3B)	5299(4)	-5039(2)	-2262(3)	50(1)
C(4B)	5101(4)	-4959(2)	-872(3)	46(1)
C(5B)	2941(4)	-4790(2)	687(3)	45(1)
C(6B)	970(4)	-4671(2)	441(3)	56(1)
C(7B)	6875(4)	-4659(2)	-2696(3)	64(1)
C(8B)	7159(4)	-4766(2)	-4061(3)	53(1)
C(9B)	6884(5)	-4224(2)	-4912(3)	67(1)
C(10B)	7081(6)	-4330(2)	-6162(4)	76(1)
C(11B)	7580(6)	-4983(3)	-6582(4)	80(1)
C(12B)	7874(6)	-5517(3)	-5755(4)	91(1)
C(13B)	7679(5)	-5420(2)	-4499(4)	76(1)
C(14B)	3299(4)	-5308(2)	1747(3)	51(1)
C(15B)	3075(6)	-5453(3)	3903(3)	85(1)
C(16B)	271(5)	-3982(2)	910(3)	72(1)

Table S4. Bond lengths [A] and angles [deg] for exp_259.

N(1A)-C(4A)	1.339(4)
N(1A)-C(5A)	1.449(4)
N(1A)-C(1A)	1.466(4)
N(2A)-C(2A)	1.451(4)
N(2A)-C(3A)	1.468(4)
O(1A)-C(1A)	1.420(4)
O(1A)-C(6A)	1.442(4)
O(2A)-C(14A)	1.198(4)
O(3A)-C(14A)	1.316(4)
O(3A)-C(15A)	1.443(4)
O(4A)-C(4A)	1.225(4)
C(1A)-C(2A)	1.500(4)
C(3A)-C(7A)	1.517(5)
C(3A)-C(4A)	1.524(5)
C(5A)-C(14A)	1.505(4)
C(5A)-C(6A)	1.537(5)
C(6A)-C(16A)	1.493(5)
C(7A)-C(8A)	1.523(5)
C(8A)-C(9A)	1.364(5)
C(8A)-C(13A)	1.390(5)
C(9A)-C(10A)	1.382(6)
C(10A)-C(11A)	1.360(6)
C(11A)-C(12A)	1.377(6)
C(12A)-C(13A)	1.380(5)
N(1B)-C(4B)	1.359(4)
N(1B)-C(5B)	1.450(4)
N(1B)-C(1B)	1.452(4)
N(2B)-C(2B)	1.426(4)
N(2B)-C(3B)	1.492(4)
O(1B)-C(1B)	1.413(4)
O(1B)-C(6B)	1.435(4)
O(2B)-C(14B)	1.195(4)
O(3B)-C(14B)	1.322(4)
O(3B)-C(15B)	1.457(4)
O(4B)-C(4B)	1.221(4)
C(1B)-C(2B)	1.510(4)
C(3B)-C(7B)	1.504(4)
C(3B)-C(4B)	1.523(4)
C(5B)-C(14B)	1.515(5)
C(5B)-C(6B)	1.558(4)
C(6B)-C(16B)	1.489(5)
C(7B)-C(8B)	1.514(4)
C(8B)-C(13B)	1.372(5)
C(8B)-C(9B)	1.376(5)
C(9B)-C(10B)	1.380(5)
C(10B)-C(11B)	1.359(6)
C(11B)-C(12B)	1.350(6)
C(12B)-C(13B)	1.383(6)

C(4A)-N(1A)-C(5A)	121.9(3)
C(4A)-N(1A)-C(1A)	125.3(3)
C(5A)-N(1A)-C(1A)	110.0(3)
C(2A)-N(2A)-C(3A)	112.9(3)
C(1A)-O(1A)-C(6A)	104.9(2)
C(14A)-O(3A)-C(15A)	117.2(3)
O(1A)-C(1A)-N(1A)	102.7(3)
O(1A)-C(1A)-C(2A)	112.8(3)
N(1A)-C(1A)-C(2A)	110.1(3)
N(2A)-C(2A)-C(1A)	109.9(3)
N(2A)-C(3A)-C(7A)	111.3(3)

N(2A)-C(3A)-C(4A)	115.6(3)
C(7A)-C(3A)-C(4A)	108.8(3)
O(4A)-C(4A)-N(1A)	121.3(3)
O(4A)-C(4A)-C(3A)	121.4(3)
N(1A)-C(4A)-C(3A)	117.3(3)
N(1A)-C(5A)-C(14A)	113.2(3)
N(1A)-C(5A)-C(6A)	101.8(3)
C(14A)-C(5A)-C(6A)	112.0(3)
O(1A)-C(6A)-C(16A)	109.8(3)
O(1A)-C(6A)-C(5A)	103.5(3)
C(16A)-C(6A)-C(5A)	115.5(3)
C(3A)-C(7A)-C(8A)	113.2(3)
C(9A)-C(8A)-C(13A)	118.2(4)
C(9A)-C(8A)-C(7A)	121.3(4)
C(13A)-C(8A)-C(7A)	120.5(3)
C(8A)-C(9A)-C(10A)	121.6(4)
C(11A)-C(10A)-C(9A)	120.3(4)
C(10A)-C(11A)-C(12A)	119.1(4)
C(13A)-C(12A)-C(11A)	120.8(4)
C(12A)-C(13A)-C(8A)	120.1(4)
O(2A)-C(14A)-O(3A)	124.8(3)
O(2A)-C(14A)-C(5A)	124.8(3)
O(3A)-C(14A)-C(5A)	110.3(3)
C(4B)-N(1B)-C(5B)	120.7(3)
C(4B)-N(1B)-C(1B)	125.8(2)
C(5B)-N(1B)-C(1B)	109.1(2)
C(2B)-N(2B)-C(3B)	109.3(3)
C(1B)-O(1B)-C(6B)	105.6(3)
C(14B)-O(3B)-C(15B)	116.1(3)
O(1B)-C(1B)-N(1B)	103.2(2)
O(1B)-C(1B)-C(2B)	111.5(3)
N(1B)-C(1B)-C(2B)	114.3(3)
N(2B)-C(2B)-C(1B)	115.0(3)
N(2B)-C(3B)-C(7B)	107.4(3)
N(2B)-C(3B)-C(4B)	109.7(2)
C(7B)-C(3B)-C(4B)	112.1(3)
O(4B)-C(4B)-N(1B)	121.6(3)
O(4B)-C(4B)-C(3B)	124.0(3)
N(1B)-C(4B)-C(3B)	114.5(3)
N(1B)-C(5B)-C(14B)	112.6(3)
N(1B)-C(5B)-C(6B)	102.3(2)
C(14B)-C(5B)-C(6B)	111.7(3)
O(1B)-C(6B)-C(16B)	108.7(3)
O(1B)-C(6B)-C(5B)	103.6(2)
C(16B)-C(6B)-C(5B)	115.7(3)
C(3B)-C(7B)-C(8B)	113.1(3)
C(13B)-C(8B)-C(9B)	117.4(3)
C(13B)-C(8B)-C(7B)	120.6(3)
C(9B)-C(8B)-C(7B)	122.0(4)
C(8B)-C(9B)-C(10B)	122.0(4)
C(11B)-C(10B)-C(9B)	119.9(4)
C(12B)-C(11B)-C(10B)	118.7(4)
C(11B)-C(12B)-C(13B)	122.2(4)
C(8B)-C(13B)-C(12B)	119.9(4)
O(2B)-C(14B)-O(3B)	124.5(3)
O(2B)-C(14B)-C(5B)	125.8(3)
O(3B)-C(14B)-C(5B)	109.7(3)

Table S5. Anisotropic displacement parameters (A^2 x 10^3) for exp_259. The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
N(1A)	61(2)	48(2)	43(2)	-8(1)	0(1)	0(2)
N(2A)	69(2)	45(2)	54(2)	-9(1)	4(1)	-2(2)
O(1A)	69(2)	68(2)	62(2)	-18(1)	2(1)	4(1)
O(2A)	152(3)	104(2)	69(2)	-21(2)	45(2)	-51(2)
O(3A)	86(2)	69(2)	52(2)	-20(1)	3(1)	-3(2)
O(4A)	69(2)	56(2)	86(2)	-25(1)	-10(1)	5(1)
C(1A)	66(2)	48(2)	50(2)	-2(2)	1(2)	4(2)
C(2A)	70(3)	58(2)	59(2)	-18(2)	3(2)	-2(2)
C(3A)	64(2)	49(2)	49(2)	-5(2)	2(2)	-11(2)
C(4A)	59(2)	45(2)	49(2)	-3(2)	7(2)	-3(2)
C(5A)	61(2)	48(2)	42(2)	-2(2)	5(2)	-4(2)
C(6A)	67(2)	55(2)	44(2)	-8(2)	3(2)	-3(2)
C(7A)	84(3)	51(2)	66(2)	8(2)	-6(2)	-10(2)
C(8A)	76(3)	44(2)	54(2)	6(2)	-8(2)	0(2)
C(9A)	83(3)	68(3)	60(3)	11(2)	9(2)	-8(2)
C(10A)	111(4)	77(3)	50(2)	-1(2)	7(2)	-2(3)
C(11A)	109(4)	77(3)	58(3)	-7(2)	-19(2)	-1(3)
C(12A)	67(3)	98(4)	68(3)	1(2)	-7(2)	0(2)
C(13A)	75(3)	70(3)	60(2)	-7(2)	3(2)	5(2)
C(14A)	68(2)	55(2)	45(2)	-6(2)	6(2)	-1(2)
C(15A)	111(3)	104(4)	52(2)	-28(2)	-3(2)	16(3)
C(16A)	64(2)	77(3)	72(3)	-15(2)	5(2)	-5(2)
N(1B)	47(2)	53(2)	35(1)	0(1)	3(1)	-2(1)
N(2B)	58(2)	97(2)	44(2)	-2(2)	-4(1)	-2(2)
O(1B)	52(1)	100(2)	49(1)	-8(1)	1(1)	6(1)
O(2B)	115(2)	55(2)	53(2)	5(1)	15(1)	14(2)
O(3B)	100(2)	66(2)	40(1)	1(1)	12(1)	9(1)
O(4B)	52(1)	92(2)	45(1)	4(1)	-3(1)	1(1)
C(1B)	55(2)	66(2)	51(2)	-12(2)	9(2)	-12(2)
C(2B)	57(2)	96(3)	49(2)	-20(2)	5(2)	-13(2)
C(3B)	50(2)	58(2)	43(2)	-1(2)	7(1)	-1(2)
C(4B)	49(2)	46(2)	43(2)	5(2)	0(2)	4(2)
C(5B)	53(2)	41(2)	42(2)	-3(1)	5(1)	-5(2)
C(6B)	54(2)	62(2)	51(2)	-7(2)	11(2)	-6(2)
C(7B)	57(2)	87(3)	48(2)	2(2)	4(2)	-6(2)
C(8B)	47(2)	65(2)	48(2)	3(2)	9(1)	-5(2)
C(9B)	86(3)	58(2)	58(2)	-5(2)	13(2)	-15(2)
C(10B)	96(3)	76(3)	56(2)	13(2)	14(2)	-9(2)
C(11B)	101(3)	92(3)	50(2)	-3(2)	28(2)	-8(3)
C(12B)	111(4)	90(3)	74(3)	-12(3)	30(3)	33(3)
C(13B)	84(3)	79(3)	65(3)	16(2)	20(2)	24(2)
C(14B)	56(2)	54(2)	45(2)	-2(2)	10(2)	-5(2)
C(15B)	121(4)	95(3)	39(2)	10(2)	12(2)	14(3)
C(16B)	73(3)	80(3)	64(2)	-8(2)	7(2)	18(2)

	BY4742				BYDerg6						BYDsnq2						
molecule	% ΔODst	SD	% ΔGenT	SD	% ΔODst	SD	p-value	% ΔGenT	SD	p-value	%ΔODst	SD	p-value	%ΔGenT	SD	p-value	%ΔODst
1	3,28	0,25	0,42	0,00													
2	1,79	0,01	-0,72	0,02													
3	0,94	0,04	-9,90	0,01	-6,10	0,16	0,31	-23,67	0,69	0,67	3,36	0,49	0,13	-102,65	0,48	0,71	9,17
4	11,92	0,00	-1,91	0,01	-2,04	3,21	0,84	-0,05	19,28	0,40	9,08	0,33	0,05	-2,12	0,32	0,00	13,38
5	-8,93	0,31	5,40	0,01	-10,46	1,19	0,53	921,54	0,13	0,15	5,77	0,41	0,03	3,61	0,40	0,25	-8,54
6	14,18	0,11	1,80	0,01	-6,68	0,33	0,14	0,08	2,00	0,57	14,07	0,28	0,05	-0,83	0,27	0,05	22,55
7	10,15	0,05	-0,63	0,00	-4,84	0,35	0,41	0,37	2,09	0,34	-1,91	1,15	0,60	0,36	1,14	0,65	19,87
8	8,91	0,02	-4,33	0,02													
9	6,35	0,08	-2,19	0,02													
10	18,44	0,01	-0,28	0,02													
11	5,68	0,04	-7,92	0,01	8,43	0,22	0,26	7,24	3,04	0,42	8,29	0,28	0,15	1,03	0,27	0,09	9,90
12	1,11	0,06	-6,21	0,01	3,51	0,22	0,40	8,07	2,70	0,58	0,81	8,81	0,89	-0,69	8,80	0,71	11,29
13	6,13	0,01	-13,13	0,01	5,26	0,09	0,30	0,50	0,53	0,48	6,18	0,58	0,22	0,24	0,57	0,18	18,03
14	8,44	0,11	-2,73	0,01													
15	2,54	0,10	1,41	0,00													
16	4,13	0,07	-1,20	0,01													
17	11,09	0,16	-0,20	0,00	13,04	0,31	0,01	0,35	1,84	0,76	3,40	0,16	0,33	-0,15	0,15	0,09	9,98
18	7,60	0,05	-1,15	0,01													
19	4,00	0,18	0,56	0,01													
20	5,51	-0,01	-1,50	0,02													
21	1,54	0,11	-2,13	0,00													
22	-0,61	0,17	-0,46	0,00													
23	11,25	0,00	-1,80	0,01	9,50	0,42	0,28	-0,65	2,53	0,53	11,23	0,60	0,07	-0,81	0,59	0,28	18,27
24	3,92	0,17	-1,03	0,03													
25	4,28	0,28	0,06	0,01													
26	3,43	0,08	-2,73	0,01													
27	6,02	0,11	-15,51	0,02	-13,86	1,10	0,48	25,22	4,38	0,48	2,07	0,68	0,47	-0,32	0,67	0,09	15,63
28	9,30	-0,01	-19,06	0,02	-4,30	1,59	0,69	22,61	9,52	0,29	-0,59	4,35	0,80	-0,19	4,34	0,11	0,31
29	13,94	0,06	-5,41	0,01	10,56	0,80	0,43	3,90	4,78	0,42	-0,86	7,63	0,87	-0,43	7,62	0,13	20,03
30	16,89	0,05	-1,52	0,02	-2,98	0,62	0,45	6,07	3,74	0,40	6,48	0,52	0,24	-0,23	0,51	0,11	-1,66

31	3,81	0,01	-1,42	0,00													
32	-1,99	0,13	-1,96	0,02													
33	0,09	0,06	-9,57	0,00													
34	13,86	0,04	-4,85	0,00	-0,41	4,74	0,93	0,35	28,44	0,55	-13,69	0,19	0,03	-0,15	0,18	0,07	8,41
35	15,85	0,05	-0,82	0,01	-7,75	0,68	0,40	0,35	4,09	0,44	20,91	0,09	0,01	-0,15	0,08	0,51	19,21
36	4,49	0,09	-0,72	0,01													
37	9,57	0,08	-1,40	0,01	10,85	0,30	0,02	0,05	1,82	0,43	-8,31	0,11	0,09	-0,03	0,10	0,69	-18,94
38	10,13	-0,01	-2,82	0,01													
39	6,18	-0,03	0,01	0,01													
40	2,15	0,09	0,63	0,01													
41	-1,12	0,08	-0,21	0,01													
42	10,03	-0,01	-1,09	0,01	20,12	0,08	0,02	-0,85	0,51	0,44	-3,43	0,47	0,43	0,34	0,46	0,40	4,23
43	3,64	0,02	2,98	0,01	-10,20	0,55	0,34	-14,95	3,67	0,02	-4,75	0,73	0,33	-4,45	0,72	0,05	-2,54
44	-2,07	-0,02	8,31	0,02	-12,92	0,11	0,21	-2,01	1,29	0,26	-24,43	0,10	1,47	-2,17	0,82	0,18	-26,63
45	13,56	0,07	3,34	0,01	-1,50	2,63	0,82	1,88	15,79	0,94	-15,79	0,48	0,14	-0,59	0,47	0,49	2,67
46	11,37	0,09	-2,18	0,01													
47	9,13	0,04	3,25	0,01													
Ctrl	0,00	0,05	0,00	0,01	0,00	0,00		0,00	0,00		0,00	0,00		0,00	0,03		0,00

BYDpdr3						BY-YPD			BY-YPGal			
molecule	SD	p-value	% ΔGenT	SD	p-value	% mitochondrial activation	SD	T-TEST	% mitochondrial activation	SD	T-TEST	
1												
2												
3	1,34	0,21	-157,56	0,85	0,03	11,13	2,77	0,01	3,03	5,25	0,01	
4	3,75	0,01	-2,50	0,75	0,01							
5	1,48	0,25	0,47	0,30	0,33	13,43	2,89	0,09	13,60	1,90	0,02	
6	1,92	0,02	-0,83	0,38	0,49	12,63	2,69	0,08	14,79	6,37	0,13	
7	8,63	0,02	-0,44	1,73	0,12							
8												
9												
10												
11	3,00	0,26	-0,77	0,60	0,03							
12	6,87	0,11	0,45	1,37	0,41							
13	2,26	0,04	0,02	0,45	0,41							
14												
15												
16												
17	2,05	0,06	-1,33	0,41	0,14							
18												
19												
20												
21												
22												
23	6,10	0,05	-1,02	1,22	0,43							
24												
25												
26												
27	1,19	0,10	0,76	2,37	0,58							
28	2,37	0,94	0,03	0,47	0,94	19,17	6,29	0,06	14,02	2,79	0,01	
29	5,83	0,00	0,09	1,17	0,87	8,84	0,44	0,02	0,00	0,00	0,01	
30	2,08	0,73	-0,73	0,42	0,17							

31												
32												
33												
34	3,47	0,32	-1,33	0,69	0,01							
35	4,39	0,07	-1,33	0,88	0,30	15,46	2,16	0,09	11,22	5,02	0,02	
36												
37	3,35	0,01	0,61	0,67	0,43							
38												
39												
40												
41												
42	8,24	0,22	-0,80	1,65	0,06	1,67	2,89	0,01	40,09	4,76	0,12	
43	3,62	0,36	-9,00	0,72	0,03							
44	1,30	1,10	-2,01	1,52	0,79	15,90	3,59	0,08	15,71	7,42	0,18	
45	3,29	0,72	-3,54	0,66	0,01							
46												
47												
Ctrl	0,00		0,00	0,00		28,52	5,70		27,30	3,98		

	BY_YPGli			BYFOX3-YPO			BY-FOX3/GFP- YPO		
molecule	% mitochondrial activation	SD	T-TEST	% mitochondrial activation	SD	T-TEST	% peroxisomal proliferation	SD	Ttest
1									
2									
3	0,00	0,00	0,00	46,67	5,77	0,01	58,88888889	8,388705	0,047993
4									
5	9,09	3,74	0,01	44,76	12,74	0,24	12,71284271	11,00967	0,002952
6	26,11	0,96	0,01	1,83	0,24	0,06	84,09178187	2,926802	0,173946
7									
8									
9									
10									
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24									
25									
26									
27									
28	5,86	2,18	0,01	4,41	2,85	0,96	79,35171746	2,1781	0,200021
29	7,41	12,83	0,03	2,07	0,14	0,06	82,78470984	11,39036	0,659103
30									

31									
32									
33									
34									
35	25,00	0,00	0,01	2,43	2,11	0,10	71,86957961	3,420161	0,072709
36									
37									
38									
39									
40									
41									
42	31,19	7,84	0,05	3,30	2,89	0,70	83,06142144	2,213	0,149578
43									
44	34,54	7,21	0,07	4,62	2,26	0,73	80,54295792	6,074623	0,066866
45									
46									
47									
Ctrl	55,68	6,33		4,30	1,05		86,21297953	4,32037	