Facile Preparation of Hexahydropyrrolo[3,2-*e*][1,4]diazepine-2,5-diones and Tetrahydrofuro[1*H*][3,2-*e*][1,4]diazepine-2,5-diones by Rearrangements of Cyclopropylketimines and Cyclopropylketones

Christian Funke[a], Mazen Es-Sayed[b] and Armin de Meijere*[a]

[a]Institut für Organische Chemie, Georg-August-Universität Göttingen

Tammannstr. 2, D-37077 Göttingen, Germany

Armin.deMeijere@chemie.uni-goettingen.de

[b]Bayer AG, Landwirtschaftszentrum, Alfred-Nobel-Str. 50, Geb. 6510

D-40789 Monheim, Germany

Supporting Information

General. ^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker AW 250 instrument at 250 MHz and 62.9 MHz, respectively, or Bruker AMX 300 instrument at 300 MHz and 75.5 MHz, respectively. Chemical shifts in $CDCl_3$, CD_3OD or $(CD_3)_2SO$ are reported in δ values relative to tetramethylsilane (δ = 0.00); for ^{1}H NMR chloroform (δ = 7.26), methanol (δ = 3.30) or DMSO (δ = 2.49) and for ^{13}C NMR chloroform (δ = 77.00), methanol (δ = 49.30) or DMSO (δ = 39.70) were used as internal standards unless otherwise stated. – IR spectra were registered with a Bruker IFS 66. – Low-resolution EI mass spectra were obtained with a Varian-MAT 731. – High-resolution mass spectra were obtained with a VG-70-250S instrument. – Elemental analyses were performed by the Mikroanalytisches Laboratorium, Institut für Organische Chemie, Universität Göttingen. – Melting points are uncorrected. – Preparative column chromatography was performed on Merck silica gel 60 (63–200 μm). All reactions were carried out under dry nitrogen or argon in oven- and/or flame-dried glassware. Solvents were dried according to commonly used procedures.

General Procedure for the Transformation of Chlorolactames 2 to Iminolactames 3 (GP 1). A solution of the respective chlorolactame **2** and sodium azide (10 equiv.) in DMSO was heated to 80–90 °C with a preheated oil bath (gas evolution), and stirring was continued for 5 h. After cooling down to room temperature, the mixture was poured into brine (200–500 ml), and the aqueous layer was extracted with EtOAc (4 × 50–100 ml). The combined organic layers were washed twice with brine and dried (Na_2SO_4). Evaporation of the solvent gave a yellow residue which was recrystallized from appropriate solvents.

2',3',4',5',6',7'-Hexahydro-6'-imino-4'-pentylspiro(cyclopropane-1,5'-[1*H*][1,4]diazepine)-3',7'-dione (3a). According to GP 1 chlorolactame **2a** (1.22 g, 4.71 mmol) and sodium azide (3.06 g, 47.1 mmol) gave 995 mg (89%) of imine **3a** as a colorless solid: mp 84–86 °C (CH_2Cl_2/light petroleum); IR (KBr) 3233, 3203, 3084, 2972, 2923, 2882, 2859, 1668, 1629, 1463, 1424, 1414, 1321, 1308, 1237, 1110, 1040, 997, 979, 954, 920, 812, 783 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.78 (t, *J* = 6.7 Hz, 3H), 1.08–1.26 (m, 4H), 1.28–1.47 (m, 4H), 1.81 (br s, 2H), 3.35 (br s, 2H), 4.19 (br s, 2H), 8.10 (t, *J* = 5.3 Hz, 1H), 11.09 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.74, ca. 20 (2 C×), 22.01, 27.69, 28.54, 42.87, 45.66, 46.26, 161.16, 167.37, 171.46; MS *m/z* (EI) 237 (M^+), 222 ($M^+ - CH_3$), 209 ($M^+ - C_2H_4$), 208 ($M^+ - C_2H_5$), 194 ($M^+ - C_3H_7$), 180 ($M^+ - C_5H_9$), 152 ($M^+ - C_5H_9 - C_2H_4$); Anal. Calcd. for $C_{12}H_{19}N_3O_2$: C, 60.74; H, 8.07; N, 17.71. Found: C, 60.63; H, 8.15; N, 17.64.

4'-(2-Furfuryl)-2',3',4',5',6',7'-hexahydro-6'-iminospiro(cyclopropane-1,5'-[1*H*][1,4]-diazepine)-3',7'-dione (3b). According to GP 1 chlorolactame **2b** (3.00 g, 11.2 mmol) and sodium azide (7.28 g, 112 mmol) yielded 2.07 g (75%) of imine **3b** as colorless crystals: mp 137–138 °C (EtOAc/light petroleum); IR (KBr) 3205, 3130, 3088, 2922, 1689, 1635, 1399, 1378, 1147, 1123, 1009, 964, 769, 601, 547 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.46 (br s, 2H), 1.84 (br s, 2H), 4.26 (br s, 2H), 4.58 (br s, 2H), 6.22 (d, *J* = 3.1 Hz, 1H), 6.27 (dd, *J* = 1.8, *J* = 3.1 Hz, 1H), 7.27 (dd, *J* = 0.7, *J* = 1.8 Hz, 1H), 7.40 (br s, 1H), 10.87 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ca. 20 (2 C), 42.43, 43.11, 46.32, 109.12, 110.57, 142.19, 149.42, 161.14, 166.42, 171.26; MS *m/z* (EI) 247 (M^+), 166 ($M^+ - C_5H_5O$), 81 ($C_5H_5O^+$); Anal. Calcd. for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.36; H, 5.41; N, 16.75.

2',3',4',5',6',7'-Hexahydro-6'-imino-4'-(4-methoxybenzyl)spiro(cyclopropane-1,5'-[1*H*][1,4]-diazepine)-3',7'-dione (3c). Chlorolactame **2c** (3.88 g, 12.6 mmol) and sodium azide (8.19 g, 126 mmol) according to GP 1 gave 2.79 g (77%) of imine **3c** as colorless crystals:

mp 122–123 °C (EtOAc/light petroleum); IR (KBr) 3227, 3109, 3001, 2952, 2836, 1676, 1657, 1625, 1586, 1515, 1462, 1431, 1414, 1392, 1325, 1308, 1252, 1235, 1177, 1124, 1030, 980, 820, 768, 754, 613 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.39 (br s, 2H), 1.76 (br s, 2H), 3.74 (s, 3H), 4.24 (br s, 2H), 4.53 (br s, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 7.79 (t, *J* = 5.6 Hz, 1H), 10.85 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ca. 20 (2 C), 43.49, 46.20, 49.15, 55.13, 114.00 (2 C), 128.86, 129.11 (2 C), 159.08, 161.08, 166.76, 171.55; MS *m/z* (EI) 287 (M^+), 272 ($M^+ - CH_3$), 121 ($C_8H_9O^+$); Anal. Calcd. for $C_{15}H_{17}N_3O_3$: C, 62.71; H, 5.96; N, 14.63. Found: C, 62.57; H, 6.06; N, 14.46.

4'-(4-Chlorobenzyl)-2',3',4',5',6',7'-hexahydro-6'-iminospiro(cyclopropane-1,5'-[1*H*][1,4]-diazepine)-3',7'-dione (3d). According to GP 1 chlorolactame **2d** (3.14 g, 10.0 mmol) and sodium azide (6.50 g, 100 mmol) gave 2.40 g (82%) of imine **3d** as colorless crystals: mp 155–156 °C (EtOAc/light petroleum); IR (KBr) 3223, 3109, 3024, 2972, 2907, 1673, 1654, 1492, 1466, 1432, 1409, 1320, 1237, 1123, 1085, 1036, 1018, 989, 972, 963, 840, 790, 767, 611, 554 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.33–1.39 (m, 2H), 1.80 (br s, 2H), 4.29 (br s, 2H), 4.57 (br s, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.60 (br s, 1H), 10.96 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ca. 20 (2 C), 43.81, 46.23, 49.34, 128.92 (2 C), 129.12 (2 C), 133.64, 135.41, 160.99, 166.51, 171.57; MS *m/z* (EI) 293/291 (M^+), 166 ($M^+ - C_7H_6Cl$), 137 ($M^+ + 1 - C_7H_6Cl - C_2H_4$), 129/127 ($C_7H_6Cl^+$); Anal. Calcd. for $C_{14}H_{14}ClN_3O_2$: C, 57.64; H, 4.84; Cl, 12.15; N, 14.41. Found: C, 57.59; H, 4.85; Cl, 12.43; N, 14.64.

(2'*S*)-2',3',4',5',6',7'-Hexahydro-6'-imino-4'-methyl-2'-[2-(methylthio)ethyl]spiro-(cyclopropane-1,5'-[1*H*][1,4]diazepine)-3',7'-dione (3e). According GP 1 chlorolactame **2e** (3.00 g, 10.8 mmol) and sodium azide (7.02 g, 108 mmol) yielded 2.27 g (82%) of the imine **3e** as a yellow oil which crystallized upon standing: mp 90–92 °C, $[\alpha]_D^{20} = -148.5$ (*c* 0.55, MeOH); IR (KBr) 3496, 3216, 3082, 2917, 1673, 1625, 1426, 1390, 1343, 1315, 1236, 1160, 1040, 996, 961, 808, 760, 734, 700, 602, 456 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25–1.53 (m, 3H), 1.91–2.03 (m, 1H), 2.10 (s, 3H), 2.24–2.43 (m, 2H), 2.69 (t, *J* = 6.6 Hz, 2H), 2.97 (s, 3H), 5.19 (dd, *J* = 6.9, *J* = 11.4 Hz, 1H), 7.37 (br d, *J* = 3.8 Hz, 1H), 11.07 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.55, 15.25, 24.86, 28.30, 30.23, 33.57, 43.93, 50.85, 161.29, 167.08, 171.37; MS *m/z* (EI): 255 (M^+), 227 ($M^+ - C_2H_4$), 208 ($M^+ - CH_3S$), 194

($M^+ - C_2H_5S$); Anal. Calcd. for $C_{11}H_{17}N_3O_2S$: C, 51.74; H, 6.71; N, 16.46. Found: C, 51.68; H, 6.48; N, 16.43.

(2'*S*)-2',3',4',5',6',7'-Hexahydro-6'-imino-2'-isobutyl-4'-methylspiro(cyclopropane-1,5'-[1*H*][1,4]diazepine)-3',7'-dione (3f). Chlorolactame **2f** (1.43 g, 5.53 mmol) and sodium azide (3.59 g, 55.2 mmol) according to GP 1 gave 1.11 g (85%) of imine **3f** as colorless crystals: mp 178–180 °C, $[\alpha]_D^{20} = -219.5$ (*c* 1.23, $CHCl_3$); IR (KBr) 3252, 3201, 2961, 2926, 2902, 2869, 1678, 1660, 1620, 1469, 1437, 1393, 1365, 1338, 1319, 1305, 1237, 1155, 1088, 1078, 1042, 997, 775, 759, 722, 610, 457 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.93 (d, *J* = 3.3 Hz, 3H), 0.97 (d, *J* = 3.3 Hz, 3H), 1.22–1.32 (m, 1H), 1.39–1.59 (m, 3H), 1.72–1.82 (m, 1H), 1.88–1.99 (m, 1H), 2.29–2.36 (m, 1H), 2.98 (s, 3H), 4.87–4.95 (m, 1H), 6.75 (br d, *J* = 3.3 Hz, 1H), 11.08 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.73, 22.27, 22.55, 24.51, 24.88, 33.61, 38.40, 43.92, 50.50, 161.09, 167.30, 172.72; MS *m/z* (EI) 237 (M^+), 222 ($M^+ - CH_3$), 194 ($M^+ - C_3H_7$); Anal. Calcd. for $C_{12}H_{19}N_3O_2$: C, 60.74; H, 8.07; N, 17.71. Found: C, 61.00; H, 8.11; N, 17.83.

General Procedure for Rearrangement of Cyclopropylketimines 3 and Cyclopropylketones 6 to Dihydropyrroles 4 and Dihydrofurans 7 (GP 2). A subliming apparatus charged with an imine **3** or a ketone **6** was heated with a preheated oil bath (170–220 °C) for 3–5 min. Then **4** or **7** were sublimed under high vacuum ($<5 \times 10^{-5}$ mbar) as solids within 30–60 min (180–240 °C).

General Procedure for the Dihydrogenation of Dihydropyrroles 4 and Dihydrofurans 7 with 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) to Pyrroles 5 and Furans 8 (GP 3). To a solution of the respective dihydropyrrole **4** or dihydrofuran **7** in chloroform (10–15 ml) was added DDQ (1.7–2.3 equiv.), and the mixture was stirred at 40–60 °C for 16–96 h. After cooling down to room temperature, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica (CH_2Cl_2/MeOH).

1,2,3,4,5,6-Hexahydro-1-pentylpyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (5a). According to GP 2 imine **3a** (370 mg, 1.56 mmol) was heated (200–220 °C) for 3 min. Then it was sublimed within 30 min to yield 261 mg (71%) of **4a** as a crude product. This product and DDQ (574 mg, 2.53 mmol) were stirred according to GP 3 at 40 °C for 16 h. Purification by column chromatography on silica (column 2 × 14 cm, CH_2Cl_2/MeOH = 100 : 7) gave 217 mg (84%) of pyrrole **5a** as a brown solid: mp 144–145 °C (CH_2Cl_2/Et_2O); IR (KBr) 3269, 3209, 2962, 2929,

2860, 1693, 1653, 1635, 1560, 1515, 1455, 1427, 1347, 1170, 1124, 1110, 1077, 964, 887, 791, 775, 713, 611, 539 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.86 (t, *J* = 6.9 Hz, 3H), 1.26–1.35 (m, 4H), 1.54–1.66 (m_c, 2H), 3.82 (t, *J* = 7.8 Hz, 2H), 3.93 (d, *J* = 5.2 Hz, 2H), 6.09 (t, *J* = 2.8 Hz, 1H), 6.98 (t, *J* = 2.8 Hz, 1H), 7.28 (t, *J* = 5.2 Hz, 1H), 10.98 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 13.94, 22.31, 27.37, 28.86, 46.94, 47.22, 101.47, 114.90, 123.57, 131.96, 164.53, 166.44; MS *m/z* (EI) 235 (M^+), 206 ($M^+ – C_2H_5$), 205 ($M^+ – C_2H_6$), 178 ($M^+ – C_4H_9$); Anal. Calcd. for $C_{12}H_{17}N_3O_2$: C, 61.25; H, 7.28; N, 17.86. Found: C, 61.00; H, 7.53; N, 17.76.

1-(2-Furfuryl)-1,2,3,4,5,6,7,8-octahydropyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (4b). According to GP 2 imine **3b** (440 mg, 1.78 mmol) was heated (170 °C) for 5 min. Then it was sublimed within 30 min (170 → 220 °C) to yield 302 mg (69%) of dihydropyrrole **4b** as a yellow solid which contained about 5% of the starting material (according to ^1H NMR): IR (KBr) 3257, 1669, 1465, 1419, 1378, 1196, 1147, 1075, 1020, 963, 747 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.99 (t, *J* = 9.1 Hz, 2H), 3.43 (t, *J* = 9.1 Hz, 2H), 3.88 (d, *J* = 5.6 Hz, 2H), 4.77 (s, 2H), 6.23 (dd, *J* = 0.8, *J* = 3.3 Hz, 1H), 6.28 (dd, *J* = 1.8, *J* = 3.3 Hz, 1H), 7.16 (t, *J* = 5.6 Hz, 1H), 7.30 (dd, *J* = 0.8, *J* = 1.8 Hz, 1H), one NH was not detected; ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 32.66, 41.41, 44.33, 45.91, 108.56, 110.49, 126.00, 129.88, 142.28, 149.64, 164.89, 166.16; MS *m/z* (EI) 247 (M^+), 166 ($M^+ – C_5H_5O$), 81 ($C_5H_5O^+$); Anal. Calcd. for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.49; H, 5.44; N, 16.89.

1-(2-Furfuryl)-1,2,3,4,5,6-hexahydropyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (5b). According to GP 3, dihydropyrrole **4b** (250 mg, 1.01 mmol) and DDQ (522 mg, 2.30 mmol) were stirred at 40 °C for 16 h. Purification by column chromatography on silica (column 2×14 cm, CH_2Cl_2/MeOH = 100 : 7) gave 186 mg (75%) of the pyrrole **5b** as a brown solid: mp >220 °C [(dec.), MeOH]; IR (KBr) 3205, 3010, 2908, 1674, 1653, 1623, 1561, 1514, 1462, 1424, 1324, 1142, 1107, 960, 795, 770, 743, 717 cm^{-1}; ^1H NMR (250 MHz, CD_3OD) δ 4.07 (s, 2H), 4.42 (s, 2H), 5.77 (d, *J* = 2.8 Hz, 1H), 6.30 (dd, *J* = 0.8, *J* = 3.2 Hz, 1H), 6.37 (dd, *J* = 1.8, *J* = 3.2 Hz, 1H), 6.72 (d, *J* = 2.8 Hz, 1H), 7.45 (dd, *J* = 0.8, *J* = 1.8 Hz, 1H), two NH were not detected; ^{13}C NMR [62.9 MHz, $(CD_3)_2SO$] δ 42.54, 46.27, 101.34, 108.36, 110.72, 115.85, 122.41, 129.96, 142.62, 150.81, 163.15, 167.16; MS *m/z* (EI) 245 (M^+); Anal. Calcd. for $C_{12}H_{11}N_3O_3$: 245.0800 (correct HRMS).

1-(4-Methoxybenzyl)-1,2,3,4,5,6,7,8-octahydropyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (4c). According to GP 2 imine **3c** (850 mg, 2.96 mmol) was heated (180 °C) for 5 min. Then it was sublimed (180 → 230 °C) within 60 min to yield 530 mg (62%) of dihydropyrrole **4c** as a yellow solid: mp 70–72 °C (dec.); IR (KBr) 3283, 2934, 2836, 1660, 1513, 1482, 1437, 1394, 1248, 1209, 1106, 1029, 960, 885, 819, 767 cm^{-1}; ^1H NMR (250 MHz, CD_3OD) δ 2.73 (t, *J* = 9.6 Hz, 2H), 3.16 (t, *J* = 9.6 Hz, 2H), 3.63 (s, 3H), 3.79 (s, 2H), 4.62 (s, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), two NH were not detected; ^{13}C NMR (62.9 MHz, CD_3OD) δ 33.60, 45.18, 46.98, 48.37, 55.98, 115.41 (2 C), 129.40, 129.61 (2 C), 130.44, 132.42, 160.82, 166.88, 169.11; MS *m/z* (EI): 287 (M^+), 121 ($C_8H_9O^+$), 91 ($C_7H_7^+$); Anal. Calcd. for $C_{15}H_{17}N_3O_3$: C, 62.71; H, 5.96; N, 14.63. Found: C, 63.05; H, 6.06; N, 14.39.

1,2,3,4,5,6-Hexahydro-1-(4-methoxybenzyl)pyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (5c). According to GP 3 **4c** (350 mg, 1.22 mmol) and DDQ (638 mg, 2.81 mmol) were stirred at 40 °C for 20 h. Purification by column chromatography on silica (column 2 × 14 cm, CH_2Cl_2/MeOH = 100 : 6) gave 279 mg (80%) of the pyrrole **5c** as colorless crystals: mp. >234 °C [(dec.), MeOH/Et_2O]; IR (KBr) 3312, 3186, 3127, 3055, 2957, 2930, 2840, 1640, 1561, 1514, 1444, 1422, 1348, 1295, 1251, 1185, 1111, 1029, 964, 896, 789, 735, 614 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2SO$] δ 3.68 (s, 3H), 3.76 (d, *J* = 5.0 Hz, 2H), 4.93 (s, 2H), 6.14 (br s, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.90 (br s, 1H), 7.10 (d, *J* = 8.6 Hz, 2H), 7.95 (t, *J* = 5.0 Hz, 1H), 11.57 (br s, 1H); ^{13}C NMR [62.9 MHz, $(CD_3)_2SO$] δ 46.30, 48.02, 55.18, 101.38, 114.01 (2 C), 116.00, 122.39, 128.51 (2 C), 129.64, 129.99, 158.48, 163.15, 167.40; MS *m/z* (EI): 285 (M^+), 121 ($C_8H_9O^+$), 91 (3) ($C_7H_7^+$); Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.01; H, 5.24; N, 14.58.

1-(4-Chlorobenzyl)-1,2,3,4,5,6,7,8-octahydropyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (4d). According to GP 2 imine **3d** (320 mg, 1.10 mmol) was heated (190 °C) for 5 min. Then it was sublimed (190 → 240 °C) within 45 min to yield 205 mg (64%) of **4d** as a yellow solid which contained about 5% of the starting material (according to ^1H NMR); IR (KBr) 3275, 2929, 1713, 1653, 1539, 1492, 1452, 1408, 1091, 1014, 800, 775, 729 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.78 (t, *J* = 9.6 Hz, 2H), 3.34 (t, *J* = 9.6 Hz, 2H), 3.93 (d, *J* = 4.4 Hz, 2H), 4.78 (s, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.41 (br s, 1H), one NH was not detected; ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 32.64, 44.23, 45.92, 47.38, 125.45, 128.11 (2 C), 128.92 (2 C), 130.55, 133.20, 134.93, 164.88, 166.73; MS *m/z* (EI): 293/291 (M^+), 166 (M^+ –

C_7H_6Cl), 127/125 ($C_7H_6Cl^+$); Anal. Calcd. for $C_{14}H_{14}ClN_3O_2$: C, 57.64; H, 4.83; Cl, 12.15; N, 14.41. Found: C, 57.58; H, 4.66; Cl, 12.39; N, 14.46.

1-(4-Chlorobenzyl)-1,2,3,4,5,6-hexahydropyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (5d). According to GP 3 **4d** (160 mg, 549 µmol) and DDQ (286 mg, 1.26 mmol) were stirred at 40 °C for 16 h. Purification by column chromatography on silica (column 2×14 cm, CH_2Cl_2/MeOH = 100 : 7) gave 132 mg (83%) of pyrrole **5d** as colorless crystals: mp 215 °C ($MeOH/Et_2O$); IR (KBr) 3263, 3184, 3056, 3028, 2906, 1648, 1567, 1518, 1496, 1451, 1424, 1346, 1275, 1245, 1124, 1113, 1097, 1013, 965, 898, 785, 740 cm^{-1}; ^1H NMR (250 MHz, CD_3OD) δ 3.98 (s, 2H), 5.11 (s, 2H), 6.19 (d, *J* = 2.9 Hz, 1H), 7.00 (d, *J* = 2.9 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.6 Hz, 2H), two NH were not detected; ^{13}C NMR (75.5 MHz, CD_3OD, 50 °C) δ 47.45, 50.25, 102.65, 117.02, 124.21, 129.61 (2 C), 129.74 (2 C), 132.41, 134.14, 137.28, 165.85, 169.44; MS *m/z* (EI): 291/289 (M^+), 164 ($M^+ - C_7H_6Cl$), 127/125 ($C_7H_6Cl^+$); Anal. Calcd. for $C_{14}H_{12}ClN_3O_2$: C, 58.04; H, 4.18; Cl, 12.24; N, 14.50. Found: C, 58.23; H, 4.32; Cl, 12.31; N, 14.22.

(3*S*)-1,2,3,4,5,6-Hexahydro-1-methyl-3-[2-(methylthio)ethyl]pyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (5e). According to GP 2 imine **3e** (295 mg, 1.16 mmol) was heated (200 °C) for 5 min. Then it was sublimed (200 → 220 °C) within 30 min to give 152 mg (51%) of crude dihydropyrrole **4e**. According to GP 3 this product and DDQ (311 mg, 1.37 mmol) were stirred at 40 °C for 16 h. Purification by column chromatography on silica (column 2×14 cm, CH_2Cl_2/MeOH = 100 : 5) gave 116 mg (77%) of **5e** as a yellow solid: mp >250 °C [(dec.), CH_2Cl_2/Et_2O]; $[\alpha]_D^{20}$ = +1.4 (*c* 0.36, MeOH); IR (KBr) 3201, 2867, 1670, 1609, 1555, 1503, 1421, 1368, 1350, 1275, 1191, 1075, 886, 775, 745, 623, 526 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.01–2.14 (m, 1H), 2.05 (s, 3H), 2.32–2.47 (m, 1H), 2.64 (t, *J* = 6.8 Hz, 2H), 3.38 (s, 3H), 4.04 (dd, *J* = 7.0, *J* = 11.5 Hz, 1H), 6.08 (t, *J* = 2.8 Hz, 1H) 6.92 (d, *J* = 4.3 Hz, 1H), 6.96 (t, *J* = 2.8 Hz, 1H), 11.13 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 15.31, 28.71, 30.34, 34.60, 52.78, 101.48, 114.83, 123.85, 132.91, 163.76, 167.44; MS *m/z* (EI) 255/253 (M^+); Anal. Calcd. for $C_{11}H_{15}N_3O_2S$: 253.0885 (correct HRMS).

(3*S*)-1,2,3,4,5,6-Hexahydro-3-isobutyl-1-methylpyrrolo[3,2-*e*][1,4]diazepine-2,5-dione (5f). According to GP 2 imine **3f** (427 mg, 1.80 mmol) was heated (200–220 °C) for 3 min. Then it was sublimed (200 → 240 °C) within 30 min to give 250 mg (59%) of crude dihydropyrrole **4f**. According to GP 3 this product and DDQ (549 mg, 2.42 mmol) were stirred

at 40 °C for 16 h. Purification by column chromatography on silica (column 2×14 cm, CH_2Cl_2/MeOH = 100 : 5) gave 203 mg (82%) of pyrrole **5f** as colorless crystals: mp 220–221 °C (MeOH); $[\alpha]_D^{20}$ = +54.1 (*c* 1.67, MeOH); IR (KBr) 3276, 3154, 3003, 2954, 2867, 1673, 1619, 1563, 1517, 1443, 1387, 1368, 1291, 1191, 1138, 1098, 1064, 896, 866, 827, 771, 736, 716, 687, 700, 623, 566, 470, 444 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2SO$] δ 0.77 (d, *J* = 2.8 Hz, 3H), 0.83 (d, *J* = 2.8 Hz, 3H), 1.52–1.70 (m, 3H), 3.23 (s, 3H), 3.64–3.70 (m, 1H), 6.16 (d, *J* = 6.0 Hz, 1H), 6.99 (d, *J* = 6.0 Hz, 1H), 7.76 (br d, *J* = 4.8 Hz, 1H), one NH was not detected; ^{13}C NMR [62.9 MHz, $(CD_3)_2SO$] δ 22.06, 23.05, 24.33, 34.25, 37.74, 51.92, 101.14, 115.94, 122.55, 131.13, 162.29, 168.45; MS *m/z* (EI) 235 (M^+), 220 ($M^+ - CH_3$), 192 ($M^+ - C_3H_7$); Anal. Calcd. for $C_{12}H_{17}N_3O_2$: C, 61.25; H, 7.28; N, 17.86. Found: C, 61.36; H, 7.21; N, 17.80.

2',3',4',5',6',7'-Hexahydro-4'-(4-methoxybenzyl)spiro(cyclopropane-1,5'-[1*H*][1,4]diazepine)-3',6',7'-trione (6c). A stirred solution of imine **3c** (410 mg, 1.43 mmol) in MeOH (10 ml) was treated with 2 M HCl (4 ml) at 0 °C. The mixture was allowed to warm up to room temperature within 2 h, and was poured into 150 ml of H_2O. The aqueous phase was extracted with CH_2Cl_2 (4×50 ml), and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent and recrystallization from CH_2Cl_2/light petroleum gave 275 mg (67%) of ketone **6c** as a colorless solid: mp 133–134 °C; IR (KBr) 3282, 3102, 3004, 2955, 2836, 1707, 1666, 1614, 1515, 1461, 1445, 1408, 1306, 1283, 1257, 1224, 1177, 1111, 1052, 1024, 968, 802, 607, 526 cm^{-1}; ^1H NMR (300 MHz, $C_2D_2Cl_4$, 120 °C) δ 1.56 (dd, *J* = 4.9, *J* = 8.7 Hz, 2H), 1.88 (dd, *J* = 4.9, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 4.18 (s, 2H), 4.55 (s, 2H), 6.77 (br s, 1H), 6.86 (part A of an AA'XX' spectrum, *J* = 1.8, *J* = 3.0, *J* = 8.7 Hz, 2H), 7.09 (part X of AA'XX' spectrum, *J* = 1.8, *J* = 3.0, *J* = 8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $C_2D_2Cl_4$, 120 °C) δ 22.94 (2 C), 45.38, 48.78, 48.95, 55.15, 114.81 (2 C), 128.30, 128.72 (2 C), 159.49, 162.12, 171.55, 192.80; MS *m/z* (EI): 288 (M^+), 121 ($C_8H_9O^+$), 91 ($C_7H_7^+$); Anal. Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.29; H, 5.46; N, 9.68.

4'-(4-Chlorobenzyl)-2',3',4',5',6',7'-hexahydrospiro(cyclopropane-1,5'-[1*H*][1,4]diazepine)-3',6',7'-trione (6d). A stirred solution of imine **3d** (710 mg, 2.43 mmol) in MeOH (15 ml) was treated with 2 M HCl (6 ml) at 0 °C. The mixture was allowed to warm up to room temperature within 2 h, and was poured into 200 ml of H_2O. The aqueous phase was extracted with CH_2Cl_2 (4×50 ml) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent

and recrystallization from MeOH/Et_2O gave 433 mg (61%) of ketone **6d** as a colorless solid: mp 176–177 °C; IR (KBr) 3276, 3202, 3105, 2910, 1665, 1492, 1407, 1309, 1284, 1218, 1109, 1091, 1054, 1023, 970, 795, 723, 615 cm^{-1}; ^1H NMR (300 MHz, $C_2D_2Cl_4$, 120 °C) δ 1.54 (dd, *J* = 4.9, *J* = 8.7 Hz, 2H), 1.89 (dd, *J* = 4.9, *J* = 8.7 Hz, 2H), 4.20 (s, 2H), 4.55 (s, 2H), 6.94 (br s, 1H), 7.12 (part A of an AA'XX' spectrum, *J* = 1.8, *J* = 3.0, *J* = 8.7 Hz, 2H), 7.31 (part X of an AA'XX'-spectrum, *J* = 1.8, *J* = 3.0, *J* = 8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $C_2D_2Cl_4$, 120 °C) δ 22.94 (2 C), 45.30, 48.92, 49.25, 128.72 (2 C), 128.96 (2 C), 133.88, 134.86, 162.15, 171.57, 192.75; MS *m/z* (EI): 294/292 (M^+), 167 ($M^+ - C_7H_6Cl$), 127/125 ($C_7H_6Cl^+$); Anal. Calcd. for $C_{14}H_{13}ClN_2O_3$: C, 57.44; H, 4.48; N, 9.57. Found: C, 57.58; H, 4.42; N, 9.69.

2,3,4,5,7,8-Hexahydro-1-(4-methoxybenzyl)furo[1*H*][3,2-*e*][1,4]diazepine-2,5-dione (7c). According to GP 2 ketone **6c** (394 mg, 1.37 mmol) was heated (200 °C) for 3 min. Then it was sublimed at the same temperature within 30 min to give 358 mg (91%) of dihydrofuran **7c** as a colorless solid: mp 189–190 °C; IR (KBr) 3204, 3064, 2960, 2940, 2900, 2835, 1676, 1641, 1512, 1484, 1471, 1436, 1370, 1321, 1296, 1247, 1201, 1175, 1110, 1084, 1033, 1008, 973, 945, 869, 834, 820, 788, 757 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.98 (t, *J* = 9.7 Hz, 2H), 3.75 (s, 3H), 3.96 (d, *J* = 5.5 Hz, 2H), 4.37 (t, *J* = 9.7 Hz, 2H), 4.75 (s, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 5.5 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 32.42, 45.96, 47.64, 55.19, 67.50, 114.21 (2 C), 126.15, 128.01, 128.05 (2 C), 137.04, 159.01, 163.33, 166.60; MS *m/z* (EI) 288 (M^+), 121 ($C_8H_9O^+$); Anal. Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found. C, 62.29; H, 5.37; N, 9.68.

1-(4-Methoxybenzyl)-2,3,4,5-tetrahydrofuro[1*H*][3,2-*e*][1,4]diazepine-2,5-dione (8c). According to GP 3 **7c** (230 mg, 798 µmol) and DDQ (545 mg, 2.40 mmol) were refluxed for 4 d. Purification by column chromatography on silica (column 2 × 17 cm, CH_2Cl_2/MeOH = 100 : 6) gave 207 mg (91%) of furan **8c** as colorless crystals: mp 212–213 °C (MeOH/CH_2Cl_2); IR (KBr) 3205, 3083, 2948, 2907, 2837, 1676, 1656, 1513, 1488, 1248, 1219, 1178, 1100, 1029, 892, 793, 616 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2SO$] δ 3.76 (s, 3H), 3.84 (d, *J* = 5.2 Hz, 2H), 4.95 (s, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 1.9 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 2H), 7.86 (d, *J* = 1.9 Hz, 1H), 8.26 (t, *J* = 5.2 Hz, 1H); ^{13}C NMR [62.9 MHz, $(CD_3)_2SO$] δ 45.71, 47.55, 55.30, 106.75, 114.28 (2 C), 128.76 (2 C), 128.92, 133.38, 135.43, 146.81, 158.80, 160.60, 167.55; MS *m/z* (EI) 286 (M^+), 121 ($C_8H_9O^+$), 91 ($C_7H_7^+$); Anal. Calcd. for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 63.17; H, 4.91; N, 9.71.

1-(4-Chlorobenzyl)-2,3,4,5,7,8-hexahydrofuro[1*H*][3,2-*e*][1,4]diazepine-2,5-dione (7d). According to GP 2, ketone **6d** (270 mg, 922 µmol) was heated (200 °C) for 5 min. Then it was sublimed at the same temperature within 30 min to give 229 mg (85%) of dihydrofuran **7d** as colorless crystals: mp 213–214 °C; IR (KBr) 3201, 3064, 2953, 2899, 2851, 1677, 1640, 1483, 1471, 1368, 1318, 1259, 1200, 1105, 1083, 1012, 1006, 943, 782, 551 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.99 (t, *J* = 9.6 Hz, 2H), 4.00 (d, *J* = 5.6Hz, 2 H), 4.42 (t, *J* = 9.6 Hz, 2H), 4.81 (s, 2H), 7.03 (t, *J* = 5.6 Hz, 1H), 7.09 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 32.48, 45.97, 47.65, 67.60, 125.69, 128.13 (2 C), 129.14 (2 C), 133.73, 134.52, 137.30, 162.90, 166.67; MS *m/z* (EI) 294/292 (M^+), 127/125 ($C_7H_6Cl^+$); Anal. Calcd. for $C_{14}H_{13}ClN_2O_3$: C, 57.44; H, 4.48; N, 9.57. Found: C, 57.66; H, 4.30; N, 9.56.

1-(4-Chlorobenzyl)-2,3,4,5-tetrahydrofuro[1*H*][3,2-*e*][1,4]diazepine-2,5-dione (8d). According to GP 3 **7d** (166 mg, 567 µmol) and DDQ (386 mg, 1.70 mmol) were refluxed for 4 d. Purification by column chromatography on silica (column 2 × 18 cm, CH_2Cl_2/MeOH = 100 : 5) gave 153 mg (93%) of furan **8d** as colorless crystals: mp 235 °C ($MeOH/Et_2O$); IR (KBr) 3223, 3070, 2958, 2928, 1695, 1684, 1663, 1646, 1491, 1475, 1442, 1348, 1216, 1152, 1143, 1093, 1013, 890, 782 cm^{-1}; ^1H NMR [250 MHz, $(CD_3)_2SO$] δ 3.86 (s, 2H), 5.01 (s, 2H), 6.83 (d, *J* = 2.0 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.87 (d, *J* = 2.0 Hz, 1H), one NH was not detected; ^{13}C NMR [62.9 MHz, $(CD_3)_2SO$] δ 45.65, 47.66, 106.60, 128.93 (2 C), 129.14 (2 C), 132.31, 133.32, 135.39, 136.09, 146.98, 160.59, 167.71; MS *m/z* (EI): 292/290 (M^+), 165 ($M^+ - C_7H_6Cl$), 127/125 ($C_7H_6Cl^+$); Anal. Calcd. for $C_{14}H_{11}ClN_2O_3$: C, 57.84; H, 3.81; N, 9.64. Found: C, 57.64; H, 3.79; N, 9.65.